Epilepsia, **46** (Suppl. 6): 3 - 415, 2005
Blackwell Publishing
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26th IEC PROCEEDINGS

26th International Epilepsy Congress
Paris, France, August 28th – September 1st 2005

Sunday 28th August 2005
11:00 – 12:30
Salle 242AB
EUCARE Symposium
Influencing Policy - Achievements and Aspirations

Setting Up New Initiatives

G. Stanculescu[1]

1) National Association Of People With Epilepsy In Romania, Romania.

In Romania, just as in many other countries, epilepsy is not an important issue for the authorities or for the general public. Thus, it is our job to make epilepsy an important issue if we want to improve in any way the epilepsy services. The way in which we can make epilepsy become an important issue is by setting up new and interesting initiatives in order to get the attention of those who can make a change. In different cultures/countries, there are different problems and different solutions to those problems. This is why there is no single right way to do things. And there are no guarantees that an initiative will be successful. However, it has always been our belief that if we do nothing we will get nothing. We have to be involved and to come up with new and interesting ideas all the time. For that we can look at the experience of other organizations and in order to make the ideas to work we can use tools such as the Epilepsy Action Pack. A tool for change. Following our participation at the 9th Epilepsy and Society Conference that took place in Malta in 2004, we had the inspiration to set up a new initiative as well as the instrument that helped us to make the idea work - the Action Pack. The project that we initiated was named 'Epilepsy beyond the dark' and it aimed at bringing a change in the situation of people with epilepsy. In what follows I will present our project, its objectives and its rationale, as well as the ways in which we tried to make it work and the ways in which the Action pack was useful to us.

Obtaining Support from Third Parties

J. Mifsud[1]

1) Caritas Malta Epilepsy Association, Malta.

Collaborations and partnerships with third parties, based on trust and shared decision making are fundamental to many NGOs existence. Such successful partnerships with third parties will increase the power and capacity of NGOs without compromising their own areas of responsibility. This is particularly relevant for NGOs involved in epilepsy issues as stake holders may be extremely varied e.g. government (local and national level), authorities, professional associations, pharmaceutical and other sponsors, with a varying interest and knowledge of epilepsy and its problems. Third parties prefer to deal with umbrella groups with clear objectives. It is essential to focus and first identify the problem to be solved or
the situation to be changed with the third party. One may learn a lot by studying other successful campaigns. It is important not to just ask for support but explain how the project will be
of mutual benefit. Useful tactics and tools and media to use, pitfalls to avoid and the importance of presenting a case with concise but accurate data will be discussed. Such partnerships may also be of great indirect benefit to the chapter members as it will provide empowerment incentives.

Raising Awareness of Mortality and Other Sensitive Issues

J. Hanna[1]

1) Director Epilepsy Bereaved

This session presents the case that raising sensitive issues such as epilepsy mortality is vital in ensuring epilepsy achieves priority with governments and health policy-makers; in ensuring that the issue of avoidable deaths is addressed by policy makers and by clinicians as well as providing a vehicle for positive action following individual tragedy. The session uses the experience in the UK where the historic neglect of informing, discussing or addressing epilepsy mortality during most of the 20th century has been turned round. Clinical guidelines now include discussion of SUDEP and governments across the UK have identified reduction of epilepsy mortality as an important part of the case for developing new national initiatives on epilepsy. The session uses two case examples - the first looking at the power of a campaign based on an individual case and the second looking at the campaign for the national investigation of epilepsy deaths that took place in England, Wales, Scotland and Northern Ireland during 2000 and reported in the National Audit of Epilepsy Deaths 2002. The case examples illustrate the lessons that can be learnt concerning what makes a successful campaign. These include the power of the individual experience in raising awareness of such a sensitive issue and the importance of a unique support network for individuals involved in such a campaign. This is shown particularly in relation to the Findlay case where a family in Scotland, supported by Epilepsy Bereaved, were involved in a four year Fatal Accident Inquiry into the sudden death of a young woman at 16, following some 10 years after the death of her mother from epilepsy aged 39. The power of this individual experience led to a judicial ruling that national epilepsy guidelines should be implemented and that SUDEP should normally be discussed with patients as part of the information available. The campaign for the National Audit into Epilepsy Deaths also relied heavily on the power of individual stories from bereaved families but also showed the vital need for a strong partnership between those most affected sudden death in epilepsy and individual clinician campaigners as well as the importance of a partnership between patient and clinical organizations and the need for support from the pharmaceutical industry. The result of the Audit was that all governments across the UK placed epilepsy higher on their agenda than ever before with a large number of national initiatives that at the very least have raised the profile of epilepsy and awareness of SUDEP. Looking more closely at the development of a campaign addressing mortality the message of the campaign is analysed looking at the importance of reaching a range of audiences including governments, policy makers, clinicians, patients, the media and the general public. The sensitivity of addressing death in epilepsy raises the importance of adapting the message to different audiences. The need to avoid messages that might increase anxiety to people living with epilepsy is addressed looking at ways in which communication can individualise fatality risks in the same way as already happens with other long-term conditions.

Addressing Private Sector

Y. Noormamode[1]

1) Edycs Epilepsy Group, Mauritius.

At the onset of the new century, partnership is high on the agenda of Edycs Epilepsy Group. No single sector whether Public, Private or Ngos can solve problems associated with epilepsy alone. It is therefore an undisputable fact that ALL the three Sectors that make

our Society - The Government - The Private Sector and the NGOs despite having different needs and objectives need to recognize that strong, trusting partnerships are the foundation of successful collaborations in a diverse economic environment and social improvement. Epilepsy is one amongst the nationwide problem affecting more than 10,000 individuals, adults and children in Mauritius. Edycs Epilepsy Group established in 1997and recognized as the 'sole organization' addressing epilepsy in the country is faced with the ultimate challenge to bringing together Expertise, Resources and Cross-Sector Partnering. While pressuring constantly Government for provision of better services and adequate treatment for the individuals with epilepsy in the present health care system, Edycs Epilepsy Group at the same time looked at the Private Sector as a potential partner through mobilizing and sharing its considerable financial, professional and managerial capacities to addressing epilepsy as a serious health problem rather than merely seek profit from them. The Private Sector involvement in addressing epilepsy resulted in:
- encouraging the Private Sector as a Social Responsible Partner - raising issues such as discrimination at work and employment of individuals with epilepsy
- lobbying Government together with Ngos on pressing issues related to epilepsy
- becoming more aware of epilepsy and its associated factors
- providing funds to address various initiatives towards the improvement of quality of life of individuals with epilepsy
- participating actively in national platforms and campaigns
- providing intellectual capital and technical support Such partnership based on the understanding of each other's values, goals and constraints demonstrated mutual respect, trust, accountability and shared ownership. However, Edycs Epilepsy Group considered it extremely important when choosing partners to undertake due diligence. For example an in-depth exploration which private sector firms make into the business operations inclusive of their management and leadership styles, market-share and labor force. In 2001, Edycs Epilepsy Group initiated its first approach towards the Private Sector by establishing the Network of Companies so called 'Reseau des Entreprises' in a targeted mailing addressing a hundred of selected Companies. Only a dozen replied to the appeal by adhering to the network. Gradually the link strengthened and key 'programs' were developed in the campaign, training and fund raising sectors with more meaningful collaboration. To date, the Network of Companies has toppled to fourty adherents; thus transforming Edycs Epilepsy Group into a powerful and dynamic organization. During the nurturing of partnership with the Private Sector, Edycs Epilepsy Group chose a number of ways and methods such as: - open, two way communication - administrative transparency - frequent face to face contact and meetings - continuous electronic contact 'email' All these promote effective partnership and address the collaborative principles of participation. It is therefore vital to highlight amongst other skills required to nurturing of partnership inclusive negotiation skills, marketing skills, communication and leadership skills, decision making skills and most of all knowing the business environment and its scope.

Addressing Governments
J. Bowis, UK

Abstract not submitted

Sunday 28th August 2005
12:00 – 13:30
Salle 243
EILAT VIII Session
Improving the Effectiveness of New AEDs: Pharmacokinetic Considerations

New AEDs in the Elderly: Pharmacokinetic Optimization
R.H. Levy[1]

1) University Of Washington, USA.
The use of new AEDs in the elderly presents numerous challenges. Pharmacokinetic (PK) optimization pertains to risk of PK and pharmacodynamic drug-drug interactions associated with the presence of co-morbid disorders and age-related altered pharmacokinetic behavior. The Metabolism and Transport Drug Interaction Database (http://dept.washington.edu/didbase) was used to perform a comparative analysis between new and old AEDs in term of risk for drug interactions. Concomitant-therapy considered in this analysis included antidepressants, cardiovascular agents (anticoagulants, antiplatelets), beta-blockers, diuretics, ACE inhibitors, angiotensin receptor antagonists, calcium channel blockers, statins and fibrates. Pronounced differences in drug interaction potential between new and old AEDs pertain to the consequences of enzyme induction by PHT, PB & CBZ on the disposition of SSRIs (paroxetine, sertraline, citalopram and mirtazapine), warfarin, calcium channel blockers, (verapamil, diltiazem, felodipine, nimodipine), some statins (atorvastatin, fluvastatin, lovastatin, simvastatin) and some beta blockers (bisoprodol, carvedilol, metoprolol, timolol). Plasma levels of these drugs would be expected to increase in patients switched from PHT, PB, CBZ to a newer AED. Co-medication with SSRIs, thiazide duretics and CBZ or OXC may be associated with hyponatremia which is of significance in the elderly. Dosage reductions in elderly patients may be required for gababentin, levetiracetam, oxcarbazepine, topiramate and zonisamide because of PK alterations in older patients.

Pharmacokinetic Basis of Idiosyncratic Effects
M. Bialer[1]

1) Department Of Pharmaceutics, School Of Pharmacy, Faculty Of Medicine, The Hebrew University Of Jerusalem, Jerusalem, Israel.

Idiosyncratic effects or idiosyncratic drug reaction (IDR) are a specific type of drug toxicity characterized by their delayed onset, low incidence and reactive metabolite formation. Idiosyncratic effects are unpredictable and can result in significant morbidity and sometimes mortality. These are often discovered after a drug approval during post marketing surveillance of phase IV clinical trials. Although they are dose-dependent in susceptible individuals, they do not occur at clinical doses with most patients. To date no animal or in vitro model exist to predict these adverse drug reactions. Therefore, the understanding of idiosyncratic effects mechanism is rather limited. Antiepileptic drugs (AEDs) have been recognized as being among the most common medications associated with severe cutaneous adverse reactions. Hypersensitivity reactions to the aromatic AEDs: phenytoin (PHT), carbamazepine (CBZ) appear to have immune etiology. One of the mechanisms for drug (AEDs) idiosyncratic hypersensitivity reaction centers around the concept of drug biotransformation to reactive metabolites that irreversibly modify cellular proteins. Thus, it has been proposed that aromatic AEDs may form metabolites that contain a reactive arene oxide moiety in their chemical structure, that could bind to cellular macromolecules and cause cell necrosis or secondary immunological response. Idiosyncratic reaction associated with lamotrigine (LTG) and felbamate (FBM), appears mechanistically distinct from PHT and CBZ hypersensitivity but may involve similar processes: active metabolites that form covalent adduct with vital proteins and macromolecules and subsequently starts a cascade of cell injury that may lead to tissue and organ injury and sometimes even death . One of theories behind FBM idiosyncratic effects is the formation of a reactive electrophilic metabolite atrophaldehyde or ATPAL (that contains a terminal double bond) that is capable of forming covalent protein adduct in vivo. The liver

hepatotoxicity of valproic acid (VPA) has also been associated with a metabolite with a terminal double bond (4-ene-VPA) that inhibits VPA metabolic ß-oxidation and cause liver microvesicular steatosis that resulted in fatal cases primarily in children younger than 2 years of age that received VPA polytherapy. Unlike LTG whose idiosyncratic effects are currently thought to be related to the parent compound in the cases of FBM and VPA the putative hepatotoxic metabolite ATPAL and 4-ene-VPA, respectively have been identified. As metabolism is part of pharmacokinetics (PK) in the case of FBM and VPA there might be some PK basis in their idiosyncratic effects. Although PK cannot explain why only a minority of epileptic patients are susceptible to the above idiosyncratic effects. Nevertheless, it seems reasonable that future new AEDs should undergo screening for reactive metabolite formation in early stages of development in order to eliminate the post-marketing failure of otherwise useful therapies.

Therapeutic Monitoring of New AEDs: Which, When and Why?
S. Johannessen[1]

1) The National Center For Epilepsy, Sandvika, Norway.

The aim of this presentation is to discuss the potential value of therapeutic drug monitoring (TDM) of the newer antiepileptic drugs (AEDs) felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate, vigabatrin, zonisamide and pregabalin based on their mode of action and pharmacokinetic properties. Data on the relationships between serum concentrations and clinical efficacy are limited, and few studies have been designed primarily to study these relationships. For most drugs a wide range in serum concentration is associated with clinical efficacy, and a considerable overlap in drug concentrations related to toxicity and non-response is reported. Although the available documentation is clearly insufficient, the pharmacological properties of some of the drugs suggest that they may be suitable candidates for TDM. As yet there are no generally accepted target ranges for any of the new AEDs, but some tentative ranges have been suggested. For felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine (10-hydroxy-carbazepine metabolite), tiagabine, topiramate, vigabatrin and zonisamide these are: 125-250 µmol/L, 70-120 µmol/L, 10-60 µmol/L, 35-120 µmol/L, 50-140 µmol/L, 50-250 nmol/L, 15-60 µmol/L, 6-278 µmol/L and 45-180 µmol/L, respectively. No data is available for pregabalin. As the dose should be titrated to the optimal or target serum level for the individual patient, it would be more appropriate to focus on the concept of individualized reference concentrations rather than 'therapeutic' ranges. In, fact many laboratories do not quote a minimum therapeutic serum concentration. The primary role of TDM for both the newer and established AEDs is to identify an individual´s optimum serum concentration and thus establish a reference value in that patient. However, more clinical research is required to increase our knowledge about individualized reference concentrations. Such research should become more feasible as more patients now receive monotherapy.

Sunday 28th August 2005
17:00 – 19:00
Grand Amphitheatre
Presidential Symposium
Epilepsy Due to Transmissible Diseases

Neurobiological Aspects
A.Vezzani[1]

1) Dept Neuroscience, Mario Negri Institute for Pharmacological Res, Milano, Italy

Inflammatory reactions occur in brain in various CNS diseases, including autoimmune and neurodegenerative disorders. Proinflammatory cytokines and related molecules have been described in CNS and plasma, in experimental models of seizures and in clinical cases of epilepsy. These inflammatory reactions involve both the innate and the adaptive immune systems and share molecules and pathways also activated by systemic infection. The activation of the immune system, and the associated inflammatory reactions, appear to mediate some of the molecular and structural changes occurring in brain during and after seizure activity. Brain inflammatory reactions occur in patients with neuropathologies associated with the late development of epilepsy. Application of cytokines in rodent brain, and mice with a perturbed inflammatory system, indicate that inflammation in brain affect neuronal excitability, cell survival, neurogenesis and blood-brain barrier function. Moreover, anti-inflammatory treatments can affect seizures in experimental models, and in some instances, in clinical cases of epilepsy. However, inflammatory reactions in brain can also be beneficial depending on the tissue microenvironment, the inflammatory mediators produced, the functional status of the target cells and the length of time the tissue is exposed to inflammation.

This presentation overviews the current knowledge in this field and discuss the possibility that inflammation may be a common factor contributing, or predisposing, to the occurrence of seizures and cell death, in various forms of epilepsy of different etiologies. The elucidation of this aspect may open new perspectives for the pharmacological treatment of epilepsies.

Epidemiological and Clinical Aspects
P.M. Preux[1], P. Odermatt[2]

1) Institut D'Epidémiologie Neurologique Et De Neurologie Tropicale (EA 3174), Faculté De Médecine, Limoges, France. 2) Institut Tropical Suisse, Bâle, Suisse.

Various communicable diseases may provoke directly or indirectly epilepsy or epileptic seizures. The extensive burden of communicable diseases in resource poor, tropical and subtropical countries and the high frequency of epilepsy in the same area provide evidence for the magnitude of the contribution to this syndrome. Although evidence for an association between epilepsy and viral (measles, herpes, HIV), bacterial (meningococcal meningitis, tuberculosis), parasitic (cysticercosis, malaria, toxocariasis) and mycosal infections (aspergillosis, cryptoccocosis, histoplasmosis) are available it is a major challenge to establish causal inference between a specific infectious disease and epileptic syndrome. The multi-factorial nature of the aetiology of epilepsy poses substantial methodological challenges for these studies. In this context it is crucial to differentiate acute symptomatic seizures from remote symptomatic seizures or epilepsy. The presentation will report on recent findings in the field of infectious diseases and sequelae of epilepsy. Particularly, the role of cysticercosis, filariasis and malaria as causal agent of epilepsy will be highlighted. In view of attributing appropriate amount of resources to the control of epilepsy it is urgently required to further study the contribution of transmissible diseases to epilepsy. In particular in resource poor tropical and subtropical countries where the burden of epilepsy is very high and where potentially easily preventable infectious diseases are highly prevalent.

Social Aspects
A. Bhigjee[1]

1) Dept Of Neurology, The Nelson R Mandela School Of Medicine, Mayville, South Africa.

It is estimated that 50 million people suffer from epilepsy worldwide. Eighty percent of these individuals live in developing countries. It is in such areas that transmissible diseases play an important role in the development of epilepsy. While a variety of infections can cause epilepsy, the most important ones are neurocysticercosis, HIV and neurotuberculosis. Previously uncommon causes of seizures such as toxoplasmosis, have now become important as a result of the AIDS pandemic. The social problems are similar to that seen with non-transmissible causes of epilepsy but are of much greater magnitude and further compounded by the scourge of HIV/AIDS. The problems include the stigma attached to epilepsy, schooling difficulties and discrimination in the workplace. The specific challenges that have to be met are poverty, lack of basic health education, inadequate human resources such as doctors, nurses, social workers and health

inspectors, non-existent health facilities in some areas, lack of political will, military conflict and local beliefs and customs. A start has been made by the launching of the joint global campaign against epilepsy by the ILAE, IBE and WHO. The G8 countries should move swiftly to write off third world debt. Massive health education programmes are urgently required to prevent the transmissible diseases. Measures to retain health workers where they are needed most must be implemented.

Monday 29th August 2005
07:30 - 08:30
Salle 252AB
Morning Seminar
Attention Disorders in Children with Epilepsy

Attention Disorders in Children with Epilepsy
A.P. Aldenkamp[1], R. Reijs[1,2], S. Van Mil[1,2], M. Debeij-Van Hall[1,2]

1) Department Of Neurology University Hospital Of Maastricht, The Netherlands. 2) Epilepsy Centre Kempenhaeghe Heeze, The Netherlands.

Attention difficulties are the most common comorbid cognitive disorder in childhood epilepsy. In several syndromes attentional difficulties are a symptom of the epilepsy, e.g. in syndromes with frequent nocturnal epileptiform activity daytime arousal may be impaired (such as in ESES or the Landau Kleffner syndrome. Remarkable is also the fluctuating level of attention and arousal in the West and Lennox Gastaut syndrome. In some children attentional difficulties precede the epilepsy diagnosis and can be considered as a first sign of seizure-induced cognitive impairment. This can be illustrated in children with subtle 'difficult-to-detect' partial onset seizures. Finally also the effect of antiepileptic drug treatment (AED) must not be underestimated. Although some AEDs may have effects on higher order functions (such as anomia and dysphasia in topiramate treatment), the majority of older and newer drugs interfere with attentional functions, resulting in slowing and distractibility. Hyperactivity is a less common symptom in childhood epilepsy. Nonetheless the incidence of the Attentional Deficit Hyperactivity Disorder (ADHD) is 3-7 times higher than in the general population and even increased 2-4 times in cryptogenic and idiopathic epilepsy. We will discuss clinical implications and possible common neuronal etiologies.

Treatment of Attention Disorders in Children with Epilepsy
D.W. Dunn[1], W.G.. Kronenberger[1]

1) Departments Of Psychiatry And Neurology, Indiana University School Of Medicine, Indianapolis, USA.

Problems with attention are a major factor in academic underachievement in children with epilepsy. Initial therapy includes optimal seizure control to reduce the effect of seizures and epileptiform discharges on processing speed and alertness and modification of antiepileptic drug therapy to eliminate medications such as phenobarbital, benzodiazepines, or topiramate that might adversely affect attention. Treatment of problems with attention and attention deficit hyperactivity disorder (ADHD) includes behavioral therapies and medication. Though not tested specifically in children with epilepsy, successful behavioral interventions are parent education, instruction for parents on behavioral management techniques for ADHD, and school interventions that promote structure, immediate and frequent feedback, and appropriate disciplining of the child with ADHD. Early work on computerized training of working memory shows promise. Tutoring programs that address specific comorbid learning disabilities or that teach general organization/study skills are frequently recommended but have not been subjected to rigorous outcome research. Stimulant medications are both effective and safe for children with epilepsy and ADHD. Statistically significant increase in seizure frequency has not been reported. Both tricyclic antidepressants and bupropion have been used to treat ADHD but may lower seizure threshold. Data on the effect of atomoxetine on seizure control are not yet available.

Monday 29th August 2005
07:30 - 08:30
Salle 251
Eurepa Session - Diagnostic Issues 1
Is it epilepsy?

Is it Epilepsy?
S.R. Benbadis[1]

1) Comprehensive Epilepsy Program, Tampa, Florida, USA.

The erroneous diagnosis of epilepsy is relatively common. About a quarter of patients previously diagnosed with epilepsy and who are not responding to drugs are found to be misdiagnosed. Most patients misdiagnosed as epilepsy are eventually shown to have psychogenic non-epileptic seizures (PNES) or (more rarely) syncope. Occasionally, other paroxysmal conditions can be misdiagnosed as epilepsy, but PNES are by far the most common condition, followed by syncope. Often, EEGs interpreted as giving evidence for epilepsy contribute to this misdiagnosis. As is true of other chronic conditions (e.g., multiple sclerosis), whenever a wrong diagnosis of epilepsy has been given, it can be very difficult to 'undo.' Unfortunately, once the diagnosis of 'seizures' is made, it is easily perpetuated without being questioned, which explains the usual diagnostic delay and its significant cost. It is a disconcerting fact that despite the ability to make a diagnosis of PNES with near-certainty, the delay in diagnosis remains long at about 7-10 years, indicating that neurologists may not have a high enough index of suspicion when drugs fail. This presentation will show 'real-life' example (video clips) of episodes, some easy to categorize, some not so easy, and will point out how to recognize epileptic seizures and differentiate them from non-epilepsy mimics.

Is it Epilepsy?
A. Covanis[1]

1) Neurology Department, The Childrens' Hospital ' Agia Sophia', Athens, Greece.

Nonepileptic events refer to a variety of clinical phenomena of physiological, organic, or psychogenic aetiology, that mimic or have seizure-like symptoms in the absence of epileptogenic brain activity. A vast number of nonepileptic events are frequently misdiagnosed as epileptic leading to inadequate or potentially harmful medical treatment. In fact 20-30% of the patients who are referred to an epilepsy centre are misdiagnosed and often treated for epilepsy. The correct diagnosis of epileptic and non-epileptic phenomena is based on the careful history, the direct and indirect observation of the episodes, the clinical examination, the careful investigations including a prolonged video polygraphic EEG recording and the experience of the doctor to analyze the findings and compose the final diagnosis according to the collected material. The age of the child, the semiology, the frequency, the subjective and objective feelings before, during and after an episode, the predisposing and provoking factors, the family history, all play an important role in the differential diagnosis of epileptic and non-epileptic events. Epileptic and non-epileptic events may have in their phenotype impairment of awareness, aberrations of mental function, falls, sensory or motor phenomena and generalised convulsive movements, which are common presenting symptoms of epileptic seizures. The main reasons for misdiagnosis are inadequate history, the past history of febrile seizures, the positive family history of epilepsy, an abnormal EEG and the wrong interpretation of the clinical and EEG findings as been epileptic. Misdiagnosis of the paroxysmal clinical phenomena even in the most mild forms has a negative psychosocial profile for the individual and the family and affects the individuals psychomotor development, personality, psychological and social well-being of all members in the family.

Monday 29th August 2005
07:30 - 08:30
Salle 241
Eurepa Session - Treatment Issues 1
Evidence Based Epilepsy Treatment

Evidence Based Epilepsy Treatment
A. Sabers[1], S. Arroyo[2]

1) Dept. Of Neurology, Glostrup University Hospital, Denmark. 2) Eisai Global Clinical Development, New Jersey, USA.

In recent years several evidence-based guidelines regarding the use of antiepileptic medication for the treatment of epilepsy have been developed. The evidenced-based guidelines are based on a systematic and comprehensive literature search with the goal to answer specific clinical questions and value the strength of practical clinical recommendations. The availability of the guidelines may have significant impact to assist practitioner's decisions about specific antiepileptic treatment. A strong recommendation concerning a specific AED treatment implies that randomized controlled trials have been conducted. However, it should be stressed that lack of evidence for a given clinical practice, does not imply inefficacy of a treatment strategy but only indicate that the particular studies have not been made. Antiepileptic drugs vary in their spectrum of activity against different seizure types but efficacy differences are relatively small. Deciding which drug to use depends in addition on the epilepsy syndrome, patient characteristics, gender and age, side-effect profile, pharmacokinetic interactions and expenses.

Monday 29th August 2005
07:30 - 08:30
Salle 243
Morning Seminar
Role of Sprouting in Hippocampal Epilepsy

Is Progressive Hippocampal Damage a Consequence of Drug Resistant TLE?
G.W. Mathern[1]

1) Division Of Neurosurgery, The Mental Retardation Research Center, And The Brain Research Institute; David Geffen School Of Medicine; University Of California, Los Angeles, USA.

The goals of this lecture are to critically assess the clinical literature to address whether medically refractory TLE leads to progressive hippocampal damage and if that injury generates hippocampal sclerosis and/or independent epileptogenesis. Cross-sectional clinical studies of TLE patients support the concept that longer seizure histories or increased numbers of generalize seizures correlate with progressive loss of hippocampal neurons, increased dentate gyrus supragranular mossy fiber sprouting, greater GAD mRNA expression per GABAergic cell, increased MRI assessed hippocampal atrophy, and greater declines in measures of neurocognitive functions. Furthermore, recent longitudinal studies of TLE patients have found progressive hippocampal atrophy with repeated MRI scans spaced out over several years. However, it is important to note that in addition to seizures all TLE patients were on anti-epilepsy medications, and progressive hippocampal pathology with longer seizure histories involves all subfields without a preference for the end folium and Sommer's sector, which are the areas most severely affected in hippocampal sclerosis. Also, cross-sectional studies indicate that it takes often more than 15 to 20 years of TLE before the progressive hippocampal injury can be detected. Further, in children there is no evidence, as yet, for progressive hippocampal neuronal injury despite very frequent seizures. Hence, the clinical evidence does NOT support the hypothesis that hippocampal sclerosis is the consequence of progressive damage from years of TLE. Moreover, recent studies using more sophisticated MRI techniques find evidence for progressive loss of white matter volumes and cortical thickness in areas outside of the hippocampus and temporal lobe with longer seizure histories. TLE patients with longer seizure histories have post-surgery seizure outcomes that are the same as patients with shorter seizure histories. In other words, longer TLE seizure durations are NOT associated with inducing independent epileptogenesis outside of the hippocampus and anterior temporal lobe like that observed in animal models. Hence, clinical correlative studies support the notion that refractory TLE is associated with progressive hippocampal injury, but does not appear to induce hippocampal sclerosis or progressive epileptogenesis outside of the temporal lobe.
Supported by NIH-NINDS grants R01 NS38992 and P05 NS02808.

Is Progressive Hippocampal Damage a Cause of Drug Resistant TLE?
R.S. Sloviter[1]

1) Departments Of Pharmacology And Neurology, University Of Arizona College Of Medicine, Tucson, Arizona, USA.

This question encompasses two issues: 1) whether seizure-associated hippocampal neuron death occurs primarily as a result of an initial insult, or whether it is progressive, with neurons dying as a consequence of each spontaneous seizure, and; 2) whether hippocampal neuron loss and subsequent changes in gene expression, structure, and function are the cause of epilepsy. From my perspective, the answer is clear: we do not know. The question of progressive neuronal loss is seriously confounded by the fact that it takes a relatively long time for large numbers of dead neurons to be removed, and for tissue to shrink maximally. Therefore, hippocampal atrophy occurring over time could be the result of a slow shrinkage process that follows an initial insult, it could be the consequence of continuing cell death, or it could be the result of both processes occurring concomitantly. Experimental data clearly indicating that neurons die after each relatively brief spontaneous seizure are lacking. With regard to the issue of whether insult-induced hippocampal damage is the initiating cause of human temporal lobe epilepsy, we are almost entirely dependent on animal models to attempt to answer this question. Recent studies indicate that the kainate and pilocarpine models of status epilepticus (SE)-induced epileptogenic injury involve severe and widespread brain damage, but do not reliably produce the hippocampal neuron loss (extensive pyramidal cell and hilar cell loss) that defines human hippocampal sclerosis. Furthermore, the seizures that develop in these animals do not appear to be hippocampal-onset seizures, as indicated by recording of hippocampal activity in awake, chronically implanted, epileptic rats. Thus, although hippocampal neuron loss and synaptic reorganization may, or may not, be the cause of human hippocampal-onset epilepsy, hippocampal changes do not appear to be causally related to the development of spontaneous seizures in initially normal rats that are subjected to prolonged, generalized SE. Therefore, this presentation will focus on the need for the development of animal models that more accurately reflect the relatively focal pathology and pathophysiology of human temporal lobe epilepsy.
Supported by NIH-NINDS grant NS18201.

Monday 29th August 2005
08:45 - 09:45
Grand Amphitheatre
Main Session
Drug Resistance, Mortality and Surgical Treatment

Beyond Seizures: the Dark Universe of Medically Refractory Epilepsy
J.W.A.S. Sander[1]

1) Department Of Clinical & Experimental Epilepsy, Institute Of Neurology, University College London, Queen Square, London, UK.

For the great majority of people developing epilepsy, remission is the rule and often the history of epilepsy is just a glitch in their past. However, for up to one-third of patients, seizures will continue despite optimum treatments with all antiepileptic drugs. For this group of patients, their only hope for full seizure control lies with a new antiepileptic drug they have not been exposed to beforehand or with

epilepsy surgery. Continuing seizures are associated with increased psychosocial problems, physical injuries, progressive cognitive impairment, and premature death. Issues such as whether recurrent seizures could cause neuronal injury and facilitate further intractability are still debated, but it is possible that this happens to some patients. In this presentation, we will review risks associated with refractory epilepsy and the impact that this has on quality of life.

From Drug Resistance to Drug Dependence: Expectations from Surgery
D. Schmidt[1]

1) Epilepsy Research Group Berlin, Goethestr.5, D-14163, Berlin, Germany.

Purpose: To provide evidence-based estimates on the need for continued AED treatment, and for seizure control off AEDs following epilepsy surgery. Methods: Systematic review of studies (all without controls) exploring the association between use and withdrawal of AEDs and seizure freedom after epilepsy surgery. Results: Temporal lobe surgery is able to restore drug effect leading to 5-year seizure control on AEDs in 66% [95% CI 62,70] of all previously drug resistant patients undergoing surgery. However, only 25% [95% CI 21,30] of adults and 31% [95% CI 20,41] of children were seizure free for 5 years without AEDs, and 33% of all remain drug resistant (Schmidt et al, Epilepsy Research, 2004;60:187-201). In a review of separate studies on planned AED discontinuation where only seizure free patients following temporal lobe surgery were analysed, the mean percentage recurrence rate in adults was 34% [95% CI 32,35]. In addition, seizure recurrence was noted in two retrospective studies in 7% of seizure free patients during taper of AEDs or due to poor drug compliance (Schmidt et al, Epilepsia, 2004;45:179-186). For extratemporal surgery and palliative procedures which result in consistently lower rates of long term seizure freedom, no systematic review is available on the association of AED use and long term outcome. Conclusions: Temporal lobe surgery eliminates drug resistance in 67% of patients, and based on uncontrolled studies, 42% depend on an AED to remain seizure free and 25% can expect to be seizure free off AEDs.

Surgically Resistant Epilepsies and The Impact of Surgery on Mortality
P. Ryvlin[1]

1) Neurological Hospital Lyon, Lyon, France.

Drug resistant epilepsy has proved to be associated with an increased standardised mortality ratio (SMR), primarily due to seizure-related fatalities including sudden unexpected death (SUDEP). Recent studies have suggested that the surgical cure of temporal lobe epilepsy (TLE) was likely to normalise the SMR of patients suffering from refractory TLE. However, these studies raise a number of methodological issues, which have not always been fully addressed. Some conclusions have relied on previously reported data, indicating a SMR of approximately 5, and a SUDEP incidence of 9/1000 patient-years in drug resistant epilepsy. In fact, as shown in this review, SMR varied considerably, from 2 to 16, in the various series of patients with refractory epilepsy, whereas the average SUDEP incidence in the same populations was calculated at 3,7/1000 patient-years. Other conclusions were based on the comparison of either surgically and medically treated patients, or cured and non cured operated patients. In both situations, the two groups included a different proportion of excellent and poor surgical candidates. The biological differences that distinguish these two populations might explain part of the differences observed in the mortality rate of surgically responsive and resistant TLE. In particular, temporal plus epilepsies involving the insula, the frontal orbital, or the frontal operculum region, appear to account for a large proportion of temporal lobe surgery failures, and might favour ictal arrhythmias, central apnoea, and secondary generalisation, which in turn increase the risk of SUDEP. The preliminary results of an ongoing multicentric French study currently addressing this issue will be presented.

Monday 29th August 2005
10:00 - 11:30
Amphitheatre Bleu
Post Main Session
Understanding and Challenging Drug Resistance

Can We Predict Refractory Epilepsy at the Time of Diagnosis?
F. Semah[1]

1) SHFJ-CEA, Orsay, And Neurology Department, Ste Anne Hospital, Paris, France.

The early prediction of intractability in epilepsy is a main challenge for clinicians. Some prognostic factors have been pointed out. In adults, most of the prognostic factors underlined that partial epilepsy is more difficult to control than idiopathic generalized epilepsy. The main prognostic factors are the presence of a brain lesion (MRI or CT evidence of a lesion, neurological deficits, …) or the consequences of such a lesion (developmental delay, focal EEG abnormalities, complex partial seizures, …). Little is known about the relationships between the location of the epileptogenic area and the chance of being seizure-free. There are some evidences that temporal lobe epilepsy is often very difficult to control, but one explanation for that could be that hippocampal sclerosis is the main prognostic factor in partial epilepsy and that hippocampal sclerosis occurred mainly in temporal lobe epilepsy. Some studies have investigated if the epileptic syndrome itself or if the nature of the brain lesion are reliable prognostic factors. They are some clear evidences that the nature of the lesion is one of the main prognostic factors for partial epilepsy. Several studies have shown that patients with partial epilepsy associated with hippocampal sclerosis or with cortical malformation often suffered from medically refractory epilepsy. At the time of diagnosis several prognostic factors are available to predict refractory epilepsy but further studies are needed focusing on different types of brain abnormalities to evaluate the real impact of the etiology of the epileptic syndrome on the prediction of refractory epilepsy.

Mechanisms of Drug Resistance
W. Löscher[1]

1) Department Of Pharmacology, Toxicology And Pharmacy, University Of Veterinary Medicine Hannover, Hannover, Germany.

Despite the use of new antiepileptic drugs, approximately one third of patients with epilepsy have seizures that cannot be controlled satisfactorily by medical treatment. Drug resistance may exist at time of first seizure or may develop later as result of the disease process. The mechanisms of these different scenarios of drug resistance in epilepsy are likely to be multifactorial, and may include alterations in brain uptake or brain targets of antiepileptic drugs. Such alterations may be constitutive (intrinsic), thus underlying de novo drug resistance in epilepsy, or induced, e.g., as a consequence of recurrent seizures or disease progression. Alterations in drug efflux ('multidrug') transporters and drug targets, such as voltage-gated sodium channels, have been found in epileptogenic brain tissue from both patients with epilepsy and rodent models of epilepsy. However, although the multidrug transporter and target hypotheses are biologically plausible, proof-of-principle is lacking for these hypotheses. An advantage of the multidrug transporter hypothesis is that it can be validated both experimentally and clinically by combining antiepileptic drugs with inhibitors of such transporters. Selective inhibitors of the major efflux transporter P-glycoprotein are currently in clinical trials for reversing chemotherapy resistance in oncology and may soon be used to determine whether such inhibitors can prevent or reverse drug resistance in epilepsy.

Will the Future Deliver the Magic Bullets? Novel Strategies Emerging from Basic Research
R. Fisher[1]

1) Department Of Neurology, Stanford Medical Center, USA.

The 16th century philosopher, Paracelsus, pointed out that the only difference between a drug and a poison is dose. Antiepileptic medications have considerable systemic and CNS toxicity. The therapeutic ratio might be improved by more specific delivery of the medication to the region of brain involved in generating seizures. Therefore, new dosage forms of medications have received considerable attention. At the present time, alternate dosage routes include medications delivered via rectal, nasal or buccal mucosa, skin and inhalation. Only the rectal route currently has a marketed product. Benzodiazepines have been tested via nasal and buccal application, and may soon be available. Direct delivery to the CNS might in the future include: CSF (intraventricular or intrathecal), drug-eluting polymer wafers, local perfusion via implanted catheters, seizure-activated drugs, liposomes or microsomes, cell transplants and gene therapy. Intrathecal medication presently is used for pain and spasticity. A trial of the peptide conotoxin CGX-1007, a selective NMDA antagonist, delivered via CSF, was deferred because of toxicology issues, but other CSF trials are under consideration. Polymerized plastic-containing medications are commercially available for treatment of brain tumors. One study demonstrated that controlled release phenytoin was useful for ameliorating cobalt-seizures in rats; another showed utility of TRH-containing wafers against amygdala kindling. Medications can be applied by local perfusion to a seizure focus. Diazepam is effective, but may not be the safest drug; adenosine and other candidates are under investigation. Seizures produce local chemical changes that can be employed to activate inactive prodrugs, such as DP-VPA. At a seizure focus, phospholipase cleaves a phospholipid group from DP-VPA and activates the drug to valproic acid. Phase II trials of this drug are underway. Liposomes package drugs for delivery over days-to-weeks, and attach a targeting agent to the package. The targeting may utilize immune recognition or receptor binding to confer specificity. Transport of liposomes across the blood brain barrier is difficult, but one possible strategy may be linkage to transport systems, such as transferrin for iron. Cell transplants can produce local drug delivery systems, independent of any connections made by the cells. Encapsulation usually is important to protect against attack on the transplanted cells by the host immune system. Encapsulated myoblasts implanted into rat lateral ventricle have conferred protection against kindled seizures. Gene therapy could in theory repair defective genes, replace defective gene products, provide neuroprotection during seizures, or produce modulators of excitation and inhibition. Many strategies are employed in animal laboratories, but definitive human trials remain to be done. Future drug delivery strategies should employ 'Sutton's law,' coined by the Baltimore bank robber who said he robbed banks because 'that's where the money is.' Increasingly, antiepileptic drug therapy will attempt to target the seizure focus 'where the money is.' Acknowledgment: The author is supported by the Maslah Saul M.D. Chair, the James and Carrie Anderson Epilepsy Research Fund, and the Susan Horngren Fund.

Monday 29th August 2005
10:00 - 11:30
Salle Maillot
Parallel Session
Psychiatric Issues in Epilepsy Surgery

Survey on Neuropsychiatric Care in Epilepsy Surgery Centers
S. Koch-Stoecker[1]

1) Center Of Psychiatry And Psychological Medicine And Epilepsy Center, Bethel,, Bielefeld, Germany.

Psychiatric care in epilepsy surgery units has been markedly improved during the last decade. An increasing number of studies have been published, and postoperative outcome evaluation starts to focus at psychosocial well-being of the patients, not merely at seizure outcome. But still it is not clear if or in how far the individual surgery centers have sufficient psychiatric supplies, which assessment strategies they use, and how they value their psychiatric findings. Some years ago the subcommission on epilepsy surgery of the ILAE-Commission on Psychobiology (Prof. Trimble, Prof. Schmitz) decided to pursue these questions in a two step approach. First the heads of epilepsy surgery centers were asked about their estimations concerning psychiatric topics in their surgery units, and to communicate name and address of their psychiatrists for further contact. In a second step those psychiatrists received a complex questionnaire that had been developed by the subcommission as a result of numerous expert discussion-groups. Eleven psychiatrists from 7 nations answered. As a main focus of their activities they highlight preoperative psychiatric assessment and treatment as a contribution to ameliorate postoperative quality of life. Another important aim is to improve the prediction of postoperative psychiatric complications. An exclusion of patients from surgery by psychiatric contraindications on the other hand is of very little importance. Their own role in the perioperative process is rated as being of equal importance as the neuropsychologists' role. There is a variety of assessment tools being used; congruence only exists in the use of the Beck Depression Inventory in all centers. Many psychiatrists highlight the value of clinical interviews as superior to standardised paper pencil tools. The best time for postoperative follow-up evaluation is 3 to 6 months after surgery, when the psychiatric complication rate is highest. After more than one year psychiatric complications are seen rarely. The findings encourage promoting the communication and networking between psychiatrists in epilepsy surgery units, with the aim to reach a basic uniformity in assessment strategies, to improve outcome quality, to obtain comparability of results, and to provide counselling for smaller centers.

Psychiatric Issues in Pre-surgical Evaluation
A.M. Kanner[1]

1) Rush Medical College And Rush University Medical Center, Chicago, Illinois, USA.

Post-surgical psychiatric complications (PSPC) following a temporal lobectomy for the treatment of pharmaco-resistant temporal lobe epilepsy (TLE) have been recognized for a long time. In recent studies, however, a higher incidence of PSPC has been reported, with depressive/anxiety disorders being the most frequent ones. PSPC can present as a de-novo psychiatric occurrence or an exacerbation of a previous psychiatric disorder that requires re-introduction, change or dose increments of psychotropic drugs. A prior history of psychiatric disease, and specifically of depression was found to be the strongest predictor of PSPC in a study of 90 consecutive patients who underwent a temporal lobectomy at the Rush Epilepsy Center. Prior history of depression and not working before surgery were also two variables that predicted failure to work after surgery. Recent data has suggested that a past psychiatric history is not only predictive of PSPC, but may also be associated with a worse post-surgical seizure outcome, as reported by Koch-Stocher in 100 consecutive patients who underwent a temporal lobectomy in Germany. In a recent study completed at the Rush Epilepsy Center, a history of depression was found to be a predictor of failure to reach post-surgical Engel class I-A (= no seizures, no auras) or Class I-B (no disabling seizures since surgery) outcomes, independently of the cause of TLE. These data clearly indicate the need to carry out a careful psychiatric and vocational evaluations as part of the overall presurgical evaluation to identify patients at risk for PSPC, and patients who may require psychiatric treatment in addition to vocational rehabilitation to help them return to the work force after surgery. In addition, patients with a history of depression must be advised of their increased risk of PSPC, the need for post-surgical investigations of depressive/anxiety disorders and the recommendation that they be kept on antiepileptic drugs for a longer period of time or indefinitely, even if they remain seizure-free, given their greater risk of recurrent seizures.

Affective Disorders after Epilepsy Surgery
C.G. Kohler[1], M.A. Carran[2]

1) Neuropsychiatry Section, Dept. Of Psychiatry, University Of Pennsylvania, Philadelphia, USA. 2) Neurology Division, University Of Medicine And Dentistry New Jersey, Cooper Hospital, NJ, Camden, USA.

Affective disorders represent frequent comorbidities in persons with epilepsy. Epilepsy surgery, in particular temporal lobectomy, and resultant changes in seizure frequency have been associated with at times unpredictable effects on mood and anxiety. The presentation reviews the recent literature on presence and course of mood and anxiety disorders following epilepsy surgery and possible treatment, including pharmacotherapy and behavioral interventions.

Psychosocial Adjustment after Epilepsy Surgery
S.J. Wilson[1]

1) School Of Behavioural Science, University Of Melbourne, And Comprehensive Epilepsy Program, Austin Hospital,, Melbourne, Australia.

The purpose of this presentation is to provide a framework for understanding psychosocial outcome after epilepsy surgery. This framework has arisen from many years of research with chronic epilepsy patients undergoing neurosurgery for the treatment of intractable complex partial seizures in the Comprehensive Epilepsy Program of the Austin hospital, Melbourne. The framework spans the pre- to post-operative period and incorporates both psychosocial and neurobiological predictors of patient post-operative functioning. The process of post-operative adjustment will be described, using patient trajectories to examine the transition from chronically ill to well after surgery. This will include identification of symptoms of the previously uncharacterised psychosocial syndrome, the 'burden of normality'. The talk will emphasise the clinical relevance of the framework for providing a comprehensive epilepsy surgery follow-up and rehabilitation program. If time permits, issues relating to the measurement of psychosocial outcome will also be addressed, as well as the general applicability of the framework to the treatment of other chronic conditions and the way these shed light on the unique characteristics of adjustment following epilepsy surgery.

Monday 29th August 2005
10:00 - 11:30
Salle 252AB
Parallel Session
Artistic Perception of the Epilepsies

Epilepsy in the Visual Arts
J.R. Cuanang[1]

1) St. Luke's Medical Center, Quezon City, The Philippines.

Epilepsy in the Visual Arts: Aura and Shadows A survey of representations of epilepsy in artistic traditions and artworks This paper surveys the relationship of epilepsy and the visual arts, and the cultural matrices that inform both. The original objective of this presentation was to construct counter-consciousness against the collective stigma against epilepsy and epileptics. It is hoped to dispel the popular notion that epilepsy is debilitating by citing noted artists living with epilepsy and by presenting their works. However, in lieu of extensive or comprehensive neurological studies that explore the link of epilepsy to creativity or artistry, this paper investigated the relationship tangentially by studying 1) representations of epilepsy as subject matter in artworks 2) collating and considering testimonials of artists living with epilepsy and 3) by examining artistic and cultural practices that take off from epilepsy or the phenomenon of seizures. In the process of research, we discovered two important things:
1.The stigma of epilepsy, is a carryover of a persistent Western medieval belief of its supposed demonic causes. Underlying many ideas of 'curing' epilepsy is derived from practices of exorcism. In this perspective, epilepsy is a disease that is a deterrent to achieving a 'normal' life.
2. That there are non-Western cultures that uphold epilepsy (and the phenomenon of seizures) as a mark of blessedness and intense spirituality, and recognized by the community as one of the signs for an individual's inward journey or initiation. In this view, consciousness that is transformed by epilepsy gives one access to intuitional or extra sensory information, and is seen as a mark of deep wisdom. In its present expanded form, this paper takes on epilepsy and the phenomenon of seizures, as life experience and considers the critical role of cultural attitudes as determinants of its place and regard in the community and by the individual who lives with it. Thus, this paper proposes that by examining the matrix of culture, through its artistic traditions and forms, we can descry different notions of health and well-being, and two different attitudes towards epilepsy. This paper uses the metaphors of aura and shadow, of light and darkness, to describe cultural apparatuses of affirmation and rejection - two main attitudes that define epilepsy as an experience. As Shadow, it shall present epilepsy in the perspective of stigma, through a survey of artworks that illustrate this attitude. We shall also present testimonials by artists living with epilepsy who work with this notion. As Aura, it shall explore epilepsy as what Mircea Eliade calls 'shamanic disease' and we shall consider works, practices and forms of mystical/spiritual experiences in cultures in Asia that derive their inspiration from the phenomenon of seizures. Further more, this paper shall also explore contemporary images and works from art and popular media to gauge which attitude dominates in certain communities and groups. This paper also proposes outlines of a culture-conscious art-based therapy in rehabilitating patients with epilepsy.

Epilepsy at the Movies
S. Baxendale[1]

1) Department Of Clinical & Experimental Epilepsy, Institute Of Neurology, Queen Square, Londond, UK.

This presentation examines the portrayal of epilepsy, seizures, and non-epileptic attack disorder in movies produced over three-quarters of a century, across four continents, covering nine cinematic genres. While similar reviews of epilepsy in literature have suggested a progression in the understanding of epilepsy over time, this survey of the cinematic medium found examples of all of the ancient beliefs about epilepsy including demonic or divine possession, genius, lunacy, delinquency, and general deviance from the norm. Nevertheless there has been a progressive trend towards more overt depictions of epilepsy. Male characters with idiopathic epilepsy tend to be mad, bad, and are frequently dangerous, whereas characters with post-traumatic epilepsy are usually cast as heroes triumphing against the odds. Epilepsy in female characters tends to signify exotic vulnerability. The dramatic potential of seizures remains highly tempting to film writers and directors alike. Although it is not for the medical profession to dictate or censor cinematic content, a keen eye on these depictions will help us to understand and perhaps combat some of the stereotypes and myths that continue to surround epilepsy in the 21st century.

Epilepsy in Literature
P. Wolf[1]

1) Danish Epilepsy Centre Dianalund & National Hospital Copenhagen, Neurocentre, Copenhagen, Denmark.

Medical and non-medical traditions together form the cultural history of epilepsy, and works of fiction may convey important information on public images, views and attitudes about epilepsy which is not found in medical textbooks. Epilepsy is a frequent feature in fiction all over the world, which can be analyzed from a multitude of viewpoints such as the correctness of information and descriptions, possible prejudices, views on causes of seizures, images of patients and doctors, ideas about treatment, epilepsy as an affliction and burden, but also epilepsy as an element of literary structure. Remarkable metaphors have been created around epilepsy. The literary fiction may

be built upon personal knowledge when the writer has observed seizures, experienced epilepsy in a close relative or friend, or has epilepsy himself. But it may also be based on stereotyped, often prejudiced ideas about seizures and epilepsy, and for the epileptologist it is often possible to tell the difference. When analyzing fictional uses of epilepsy, one has to be aware, however, that most authors do not intend to write case histories but have a literary purpose. Many writers also see themselves as belonging to certain literary traditions, and sometimes refer to other authors and their work, e.g. as an homage to a revered master. Such references are not always immediately apparent. It is fascinating to follow how also epilepsy can be integrated into and become part of a literary genealogy.

Monday 29th August 2005
10:00 - 11:30
Salle 242AB
Parallel Session
Epilepsy Surgery as a Window to the Human Brain

Rhinal-Hippocampal Coupling during Human Memory Formation
C. Elger, Germany

Abstract not submitted

Image and Memory: Single Unit Recordings in the Human Temporal Lobe
I. Fried, USA

Abstract not submitted

Neuronal Activity in Human Temporal Cortex during Language, Verbal Memory and Learning
G.A. Ojemann[1]

1) Neurological Surgery, University Of Washington, Seattle, WA, USA.

Single neuronal activity was recorded from human temporal cortex during various language, verbal memory and learning measures in the context of awake neurosurgery for epilepsy. For all tasks, neurons with significant changes in the frequency of activity are widely distributed in both hemispheres. The instruction to retain the identified item in recent explicit memory changes activity in a substantial proportion of neurons; even more are recruited with learning. Within temporal cortex, regional differences are present in the likelihood of finding neurons related to different tasks, patterns and timing of activity as well as task accuracy. Early, sustained inhibition is prominent in dominant hemisphere recordings, especially for language. Individual neurons are often related to only one task, except for sustained polymodal activity in dominant hemisphere during memory. These studies emphasize the importance of lateral temporal cortical activity in memory and learning, establish the nature and regional differences in that activity and emphasize the role of sustained changes perhaps related to attentional mechanisms. Supported by NIH grants NS 36527 and EB 2663 and a McDonnell-Pew Cognitive Neuroscience grant

Monday 29th August 2005
10:00 - 11:30
Salle 251
Parallel Session
Neurosteroids - Effects and Clinical Consequences

Neurosteroids and Brain Excitability
M.A. Rogawski[1]

1) Epilepsy Research Section, National Institutes Of Health, Bethesda, USA.

Neurosteroids are endogenous steroids that rapidly alter the excitability of neurons by binding to membrane receptors. The best recognized action of neurosteroids is as positive allosteric modulators of GABAA receptors, which confers protective activity in a broad range of animal seizure models. Our work in recent years has focused on understand the roles of neurosteroids as endogenous regulators of seizure susceptibility and we have developed evidence from animal models of their involvement in catamenial epilepsy, stress-induced alterations in seizure susceptibility, and the hypoandrogenism that occurs in some men with intractable temporal lobe epilepsy. We developed a rat model of perimenstrual catamenial epilepsy in which withdrawal of the neurosteroid allopregnanolone was associated with marked enhancement of seizure susceptibility, supporting the view that catamenial epilepsy is due to neurosteroid withdrawal. We found that conventional antiepileptic drugs had reduced efficacy during the period of enhanced seizure susceptibility in the catamenial epilepsy model; this drug resistance could, in part, account for the difficulty of controlling seizures during the perimenstrual period in women with catamenial seizure exacerbations. We have also developed evidence for a role a neurosteroids in stress-related fluctuations in seizure susceptibility. Although the underlying mechanisms are poorly understood, it is well recognized that emotional stress can be a factor affecting seizure control in temporal lobe epilepsy and other seizure syndromes. Our studies have focused on the neurosteroid tetrahydrodeoxycorticosterone (THDOC), which is derived from the adrenal steroid deoxycorticosterone. THDOC levels are increased during stress and could be one of several hormonal factors involved in stress-induced changes in seizure susceptibility. We have recently begun to address the possibility that male sex steroids and their metabolites could also play a role in the regulation of seizure susceptibility. In men, temporal lobe epilepsy is recognized to adversely affect testicular function and to be associated with reduced testosterone levels, diminished libido and sexual dysfunction. Reductions in the levels of the neurosteroid testosterone metabolites androsterone and etiocholanolone could represent a factor leading to poor seizure control in these men.

Neurosteroid Derivatives as Potential New AEDs
S. Czuczwar[1]

1) Department Of Pathophysiology, Medical University, Lublin, Poland.

Neurosteroids are endogenous compounds (or synthesized derivatives), which can positively or negatively modulate the steroid site on the GABAA receptor complex. Their antagonistic or agonistic activity at N-methyl-D-aspartate (NMDA) receptors has been also postulated. Consequently, some neurosteroids apparently inhibit seizure activity whilst some of them act as proconvulsants. Allopregnanolone, a positive allosteric modulator of GABAA receptors, has been shown to protect against seizures induced by GABA antagonists, pilocarpine and amygdala-kindled convulsions. On the other hand, pregnenolone sulfate and dehydroepiandrosterone sulfate may precipitate seizure activity upon systemic or intracerebral administration. Both endogenous neurosteroids inhibit GABAA receptor-mediated events and behave as moderate NMDA receptor agonists. Their seizure precipitating potential is, however, unlikely at concentrations encountered in vivo. Alphaxalone (a synthetic neurosteroid) raised the threshold for electroconvulsions in mice but, surprisingly, the neurosteroid impaired the protective activity of

valproate against maximal electroshock-induced seizures in mice, despite significantly elevated free plasma concentration of this antiepileptic. A similar situation was observed in the pentylenetetrazol model in mice. The anticonvulsant action of other conventional antiepileptic drugs was not affected by alphaxalone. Ganaxolone (a synthetic analogue of allopregnanolone) has been documented to exert anticonvulsant activity in a variety of convulsive procedures, including pentylenetetrazol-, NMDA-, cocaine-induced convulsions as well as in electrical or chemical kindling models. In contrast to alphaxalone, ganaxolone potentiated the protective activity of diazepam against pentylenetetrazol-induced convulsions in mice. However, chronic ganaxolone has been shown to induce anticonvulsant tolerance to diazepam although not to itself. Ganaxolone has been also evaluated in volunteers and epileptic patients with infantile spasms or complex partial seizures. Encouraging data in case of efficacy, tolerability and safety have been obtained, however, accompanied by sedation. Preliminary data indicate that ganaxolone have been found effective against catamenial seizures. It may be concluded that the search for newer antiepileptic drugs among neurosteroids is warranted. Considering a negative interaction of alphaxalone with valproate, detailed preclinical studies are required to select beneficial drug combinations for an effective add-on therapy. The potential use of neurosteroids for the modulation of cocaine effects has to be considered.

Catamenial Epilepsy: Criteria, Occurrence and Management

A.G. Herzog[1]

1) Harvard Neuroendocrine Unit, Beth Israel Deaconess Medical Center, Wellesley, USA.

Catamenial epilepsy refers to cyclic seizure exacerbation in relation to the menstrual cycle. In one of our investigations, analysis of 292 cycles recorded in 100 consecutive women with localization-related epilepsy showed that the distribution of seizures was not uniform across the days of the menstrual cycle (ANOVA $p < .0001$). Pair-wise statistical comparisons of seizure occurrence on the various days of the cycle showed that seizures occurred significantly more frequently on perimenstrual days and less frequently on mid-luteal and mid-follicular days than on any of the other days of the cycle. From a knowledge of the neuroactive properties of reproductive steroids and the variation of their serum levels during the menstrual cycle, we have proposed the existence of three patterns of catamenial seizure exacerbation. Their existence was supported by an investigation of 184 women with localization related epilepsy. Among 98 women with ovulatory cycles, average daily seizure frequency was significantly greater during the perimenstrual and preovulatory phases. Among 86 women with anovulatory cycles, average daily seizure frequency was significantly less during the mid-follicular phase than during the remainder of the cycle. A plot of the proportion of women who showed each of these patterns of exacerbation versus the level of seizure exacerbation expressed as multiples of the frequencies obtained during the mid luteal and mid follicular phases that were used as baseline, showed reverse S-shaped curves. The points of inflection of these curves represent the mathematically based point that optimally distinguishes women with seizures that show high versus low hormonal sensitivity. Over 1/3 of the women were thus determined to have catamenial epilepsy. If seizures show hormonal sensitivity in their occurrence, they may also be more sensitive to hormonal treatment. Open-label investigations support a role for cyclic natural progesterone therapy in the treatment of catamenial epilepsy.

Menopause and Hormone Replacement Therapy - Effects on Seizure Control and AEDs?

C.L. Harden[1], A.G. Herzog[1], B.G. Nikolov[1], B.S. Koppel[1], K. Fowler[1], D.R. Labar[1], W.A. Hauser[1]

1) Comprehensive Epilepsy Center, Department Of Neurology And Neuroscience, Weill Medical College Of Cornell University, New York, USA.

BACKGROUND: Previous reports have suggested that hormone replacement therapy (HRT) could increase seizure activity in women with epilepsy. We sought to determine whether adding HRT to the medication regimen of postmenopausal women with epilepsy was associated with an increase in seizure frequency. METHODS: This is a randomized, double-blind, placebo-controlled trial of the effect of HRT on seizure frequency in postmenopausal women with epilepsy, taking stable doses of antiepileptic drugs (AEDs) and within 10 years of their last menses. After a three month prospective baseline, subjects were randomized to placebo, Prempro (0.625 mg of conjugated equine estrogens plus 2.5 mg of medroxyprogesterone acetate or CEE/MPA) daily, or double-dose CEE/MPA daily for a three month treatment period. RESULTS: Twenty-one subjects were randomized after completing baseline. The subjects ages ranged from 45-62 years (mean=53 years, SD= +/-5), number of AEDs used ranged from 1-3 (mean=1.6, SD=+/-0.8). No differences between treatment arms were present at baseline. Five out of seven subjects on double-dose CEE/MPA had a worsening seizure frequency of at least one seizure type, compared to 4/8 on single dose CEE/MPA and 1/6 on placebo. Chi-square analyses revealed that an increase in frequency of the subject s most severe seizure type was associated with increasing CEE/MPA dose ($p=0.03$). Increased complex partial seizure frequency on study drug correlated with increasing CEE/MPA dose ($p=0.048$, $r=0.436$), as did increased frequency of the subject's most severe seizure type ($p=0.006$, $r=0.577$). Subjects taking lamotrigine had a decrease in lamotrigine levels of 25-30% while taking CEE/MPA. CONCLUSIONS: CEE/MPA is associated with a dose-related increase in seizure frequency in postmenopausal women with epilepsy. CEE/MPA may decrease lamotrigine levels.

Monday 29th August 2005
10:00 - 11:30
Salle 241
Parallel Session
Epilepsy Genetics Clinical Research: Methods, Ethics and Outcomes

Do Large Families Grow on Trees (Vines)?

C. Marini[1]

1) Neurogenetics Laboratory, Department Of Child Neurology And Psychiatry, IRCCS Stella Maris Foundation, Pisa, Italy.

In the past decade the understanding of the role played by genetic factors in epilepsy has improved greatly. Several genes causing idiopathic epilepsies with simple Mendelian inheritance have been identified through single large families linkage analysis. The insights gained have reframed our concepts of the idiopathic epilepsies as disorders of ion channels. Mutations in such genes have only been found in a minority of patients/families with similar phenotypes. Thus, the genetic and phenotypic heterogeneity and the uncertain mode of inheritance in some common epilepsies have produced unconfirmed and controversial results. The approach of using large families that have sufficient power to independently establish linkage is particularly helpful in epilepsies where there is variation in the phenotype since it can provide special insights into the phenotype-genotype relationship. The accurate delineation of the phenotype is the essential first step in the investigation to minimize the problem caused by phenotypic heterogeneity. How do we find large families, do they grow on trees (vines)? Definitely not. Many individuals presenting with their first seizure have a distant relative with a history of seizures, but the pedigree during the routine evaluation is usually done quickly and at the end of the consultation. However from this initial pedigree in order to enlarge it, a detailed family history is mandatory. The investigator should never take 'no' for an answer but try to directly interview as many family members as possible particularly the elderly matriarchs who may know of early childhood attacks in other family members, long since forgotten. Attention to details is important in constructing a pedigree, it is worth recording surname changes, the country of origin of a person's ancestor and it is important to ask about miscarriages or stillbirths. The pedigree should denote both sides of the family and, the investigator should enquire whether family members have had any

type of paroxysmal attack including febrile seizures or isolated seizures. The use of a validated questionnaire with a structured interview might be useful to systematically collect all these relevant clinical information. The review of all previous medical records and EEG recordings could also be helpful for the correct phenotyping of subjects. Thus, the family history plays a central role in genetic studies of diseases with simple inheritance and more so in cases of complex inheritance. Properly obtained and interpreted, family history is one of the most useful and accessible tools available to clinicians and their role in genetic studies should be emphasized.

Genetic Epidemiology Studies: the How and Why
A.T. Berg[1]

1) BIOS, NIU, DeKalb, Illinois, USA.

Epidemiology has traditionally been the research branch of public health. Genetic - increasingly we would say 'genomic' - epidemiology involves the identification of genomic elements that influence the occurrence and course of diseases and other health states in populations. Such knowledge may contribute to improved prevention and treatment of disorders in the population. In other areas of medicine (e.g. cardiovascular), genomic elements are incorporated as risk factors in standard epidemiological investigations and studied side by side with other more traditional epidemiological risk factors (age, sex, environmental exposures). Most work to date in the field of epilepsy has consisted of traditional genetic analyses largely focused on identifying markers or genes in selected multiplex families. Such studies often tell us a great deal about these families and provide glimpses into potential mechanisms underlying epilepsy. To date, they have been of limited value in explaining the majority of epilepsy occurring in populations. Association (essentially case-control) studies have so far been disappointing with tantalizing initial results rarely being replicated. Prospective studies to predict disease states have yet to be done for epilepsy. Important challenges to exploiting the power of genomic techniques and making major breakthroughs in our understanding of epilepsy include the complex genetic basis of most forms of epilepsy, the relatively low frequency of epilepsy in the population and even lower frequency of specific types of epilepsy. Identification of biologically relevant phenotypes is, arguably, an even greater hurdle for epilepsy which must be overcome for significant progress to be made.

Ethical Genetics Research: Prioritizing the Interest of the Patient through Advocate Directed BioBanking
E.W. Johnson[1], N. Senanayake[3], S.F. Terry[4,5]

1) PreventionGenetics, Marshfield, WI, USA. 2) Barrow Neurological Institute, Neurogenetics, Phoenix, Arizona, USA. 3) Department Of Medicine, University Of Peradeniya, Sri Lanka. 4) PXE International, Inc, Washington DC, USA. 5) Genetic Alliance, Washington DC, USA.

Genetic disease cannot discern national borders. Lay advocacy groups for both common and rare diseases accelerate and focus research efforts and ideally have as their primary goal the advancement of progress on the research into their diseases, again without regard to institutional or international borders. A diverse set of advocacy organizations, such as The Genetic Alliance BioBank in the United States, have created small, niche repositories of biological materials or 'BioBanks'. These BioBanks provide an invaluable asset to the research community by streamlining what is perhaps the most logistically difficult aspects of searching for a gene: local 'red tape', including accessing and collecting appropriate DNA samples, protecting patient confidentiality, recontacting/redrawing patients as needed, and making sure the patient community is regularly informed about progress in the field, often needing to be done in an international, multi lingual, multiracial but always culturally appropriate context. It is the exceptional opportunity to aid and foster the global effort to find the causes and cures for these diseases that empowers these groups and the communities that support them. Lessons learned from BioBanking efforts, all born of advocacy, for different diseases, using different models, will be discussed. Familial Eating Epilepsy (FEE) was initially described in over one hundred and fifty Sri Lankan patients who experienced seizures in association with a meal. A strong indication of a family history was noted at that time. The search for this FEE gene led to a unique international collaboration between the two centers, one in the University of Peradeniya, Sri Lanka focusing on the collection and clinical characterization of the 'eating seizure' families and the Neurogenetic gene discovery laboratory at the Barrow Neurological Institute, Phoenix Arizona, USA. The model of this Sri Lankan controlled, American assisted, collaboration will be presented.

Monday 29th August 2005
10:00 - 11:30
Salle 253
Parallel Session
Country Assessment Of Epilepsy-Related Healthcare: A Survey Approach Based On The WHO Model

A Framework for Country Assessments of Epilepsy Care
C. Begley

The Commission on Health Care Policy has been working in consultation with the WHO on mapping the WHO's Health Systems Performance Assessment framework onto epilepsy. Our goal is to provide planners and policymakers with a standardized epilepsy-specific assessment template that complements and extends the treatment gap/resource availability framework reflected in the recently drafted ILAE/IBE/WHO, Atlas of Epilepsy Care in the World. In my presentation, I provide the rationalization for going beyond measuring treatment gaps and resource availability in country assessments of epilepsy burden and health care performance. I describe the path of the Commission in adopting the WHO Health Performance Framework as a basis for more comprehensive assessment. I also describe the domains of the WHO framework and what they mean in terms of a specific condition like epilepsy.

Epilepsy Related Country Assessments: Perspective of Developed Country
S. Wiebe[1]

1) University Of Calgary, Alberta, Canada.

The organization of health care systems varies among developed countries. It is conceivable that such variability also translates into differences in health care delivery in the population with epilepsy, and in the way health care adequacy is evaluated among developed countries. Further, variations in health care also exist within developed countries by region, sociodemographically or by other variables. Epilepsy-specific, within-country variations in health care are also expected to occur but have not been well documented. Evaluation of Epilepsy-Related Healthcare within and between countries requires a standardized approach. We explore the applicability of the WHO Model on Assessment of epilepsy related Healthcare in Canada, which has a publicly funded health care system with universal access. Our analysis highlights the challenges in applying the WHO model, identifies important knowledge gaps and research areas, and points out particular difficulties encountered in health care delivery for epilepsy in the Canadian context.

Epilepsy-Related Country Assessments: Perspective of Developing Country
J. Butler[1]

1) Department Of Neurology, University Of Stellenbosch, Cape Town, South Africa.

Health care systems in developing countries are very heterogenous. In the African context, South Africa ranks as a relatively affluent, yet developing country. Its dual health care system permits the minority to use the majority of the resources with privately funded health insurance, while the majority of the population has access to a

minority of the resources in a state-funded health system. The provision of services to people with epilepsy likely parallels this inequity. The evaluation of care to people with epilepsy between countries using standardized methodology may usefully highlight differences between developed and developing countries, and within health care systems in a developing country like South Africa. The challenges of applying the WHO Model on Assessment of Epilepsy-related Healthcare to a developing country like South Africa are discussed.

Assessing Financial Burden: Epilepsy-Related Financial Fairness
P.L. Levy[1]

1) LEGOS, University Of Paris-Dauphine, Paris, France.

Fairness in Financial Contribution (FFC) was developed by the WHO in its 2000 Report as a key dimension of a health system's performance. A definition, a measure and an index of FFC were designed and developed to be applicable across and within countries with varying types of health systems. Application of such an equity index to epilepsy as a specific condition would be useful to better assess the burden of epilepsy but this raises two issues. Conceptually, it is not clear whether such an index makes any sense to compare equity among patients with epilepsy as it is debatable whether more severe patients should benefit from a reduced share of out of pocket payments. Empirically, equity could be assessed comparing FFC for specific populations with epilepsy and for the general population but needed data are not available. An alternative rough index of financial coverage is proposed in order to better assess financial situation of people with epilepsy in each country and facilitate international comparison. Such an index is calculated for several developed countries.

Assessing Health Care Performance: Epilepsy-Related Responsiveness
G. Baker, UK

Abstract not submitted.

Assessing Disease Burden: Epilepsy-Related DALYs
J. Langfitt[1]

1) Depts. Of Neurology & Psychiatry, University Of Rochester, Rochester, New York, USA.

WHO Disability-Adjusted Life Years (DALYs): Application to Epilepsy Disability-adjusted-life years (DALYs) were developed by the WHO as a measure of disease burden. DALYs extend mortality-based estimates of burden by incorporating information about morbidity. The intents is to more accurately assess the impact of diseases and the policies and treatments aimed to ameliorate them. The goal of this presentation is to describe the methods for deriving DALYs and their strengths and weaknesses in assessing the burden of epilepsy, relative to other conditions. DALYs attributable to epilepsy in the US, Canada, UK, France and Italy are calculated based on WHO methods and compared to original WHO estimates and DALYs for other diseases in other regions. The effects of uncertainty around key components of the DALY model (prevalence rates, age-weighting, disability weight) on relative rankings of disease burden and on estimates of treatment effectives are examined.

Monday 29th August 2005
10:00 - 11:30
Salle 243
Parallel Session
Excitatory Action of GABA in Epilepsy

Excitatory Actions of GABA in Human Epileptogenic Tissue
G. Huberfeld[1], L. Wittner[1], I. Cohen[1], M. Baulac[1], S. Clemenceau[1], R. Miles[1]

1) INSERM U739, Dépt Epilepsie, CHU Pitié-Salpêtrière, Paris, France.

Tissue obtained from operations on patients with temporal lobe epilepsies associated with a hippocampal sclerosis retains the ability to generate an interictal-like activity in vitro. This activity is generated in the subiculum and is suppressed by antagonists at GABAA or at Glutamate receptors. About 20% of subicular pyramidal cells and most interneurons fire simultaneously with rhythmic field potentials (1-3 Hz), while the majority of pyramidal cells recieve inhihibitory or excitatory - inhibitory field potentials. Synaptic events recorded in excited pyramidal cells in the presence of glutamate receptor antagonists are depolarising at resting potential and are suppressed by antagonists at GABAA receptors. These data suggest that depolarising GABA-mediated responses contribute to interictal-like synchrony in the human epileptic subiculum. Consistent with a perturbed Cl homeostasis, bumetanide, an antagonist of the Na-K-Cl transporter, suppresses interictal-like population activity. Reduction of external Cl, together with a modest increase in cellular excitability can initiate longer duration ictal-like synchronous events in the subiculum. We are pursuing the identity of the molecules involved in the perturbation of Cl-homeostasis.

Excitatory Actions of GABA in Experimental Mirror Foci
I. Khalilov[1], M. Le Van Quyen[1], G. Holmes[1], Y. Ben-Ari[1]

1) Inmed-Inserm U-29, Marseille, France.

Patients with active epileptogenic foci may develop secondary epileptic focus at a site distant from the original focus. The mechanisms underlying generation of a secondary epileptic focus are poorly understood. Using an in vitro preparation in which two intact hippocampi and the interconnecting fibres each placed in separate compartments, we have shown that seizures generated in one hippocampus propagate to the contralateral hippocampus and transform it to an epileptic mirror focus. We have found that the expression of the secondary epileptic focus is associated with long term alterations of GABA-ergic synapses that become excitatory because of a shift in chloride reversal potential. The formation of the mirror focus was prevented by continuous perfusion of the contralateral hippocampus with antagonists of NMDA or GABA(A) receptors. We further found that propagating seizures only produce a mirror focus when they include synchronous activities in the gamma frequency band. In addition, blocking GABAergic synapses or NMDA receptors in the contralateral hippocampus reduces the frequencies of the propogated seizures to the sub-gamma band, and these seizures do not transform a naïve network to an epileptic one. Thus, we suggest that propagating seizures are only pathogenic when they are associated with activation of GABA(A) and NMDA receptors and when seizures include gamma frequency oscillations.

Clinical Relevance
M. Baulac[1], G. Huberfeld

1) Hôpital Pitié-Salpêtrière, Paris, France.

Some clinical implications of these findings concerning GABAergic processes may be considered both during development and in epilepsy situations. The phenomenon of sequential maturation of GABA and glutamate synapses is likely to occur in humans also, although the precise timings are unknown. The shift between excitatory and inhibitory GABA synapses occurs probably in utero, and it may

depend on the brain structure involved. This raises the question of the innocuity of GABAergic drugs, benzodiazepines in particular, when taken by the pregnant mother. The finding of the role of chloride homeostasis in human tissues obtained after mesial temporal lobe epilepsy surgery raises several questions and may sugest therapeutical avenues. Approximately 20% of the pyramidal cells may be depolarised by a GABA input, inducing a bursting activity in the subiculum which is very similar, in vitro, to the interictal activity as recorded in vivo. This paradoxical response of pyramidal cells, reminiscent of what happens during development, may be regarded as a potential cause of pharmacoresistance, especially when gabamimetic dugs are used. Another consequence is that drugs that modulate chloride homeostasis may interfere with this abnormal behaviour. Diuretic agents are known to have such type of action. Bumetanide was selected due to its selective antagonistic effect on the KCC1 transporter which triggers chloride influx into the cell. This agent was shown, in vitro, to block the interictal-like bursting activity on human sclerotic hippocampal formation. This property, which recalls the well known anticonvulsant effects of diuretics in general, deserves being tested in animal models and in patients with temporal lobe epilepsy.

Monday 29th August 2005
14:15 – 15:15
Grand Amphitheatre
Main Session
Epilepsy And Neurological Co-morbidities Across the Lifespan

Impact of Co-morbidities on Health Outcomes
F. Gilliam[1]

1) The Neurological Institute, New York, USA.

Epilepsy is a chronic disorder due to abnormal interactions of excitatory and inhibitory neuronal systems. It is not surprising, therefore, that a variety of comorbid neurological and psychiatric disorders have been associated with epilepsy. More than a century ago William Gowers described progressive memory and cognitive problems in a subgroup of patients with recurrent seizures. In recent decades migraine headaches, sleep disorders, depression, and anxiety have been shown to have increased prevalence in epilepsy compared to the general population. Toxic effects of pharmacotherapy, especially central nervous system symptoms, occur in a significant proportion of patients taking most antiepileptic drugs. During the past 10 years advances in health outcome research have allowed reliable and valid assessment of the interaction of epilepsy with specific aspects of subjective health status and quality of life. The presence of depression or antiepileptic drug toxicity appear to have the strongest adverse effects on health in epilepsy from the patients' perspective, but anxiety, headaches, and cognitive dysfunction have not been thoroughly investigated. Also, the problem of comorbid substance abuse and dependence have not been adequately studied in this at risk population. Few clinical trials have evaluated the best methods of diagnosis or treatment of comorbid disorders, and many questions remain unanswered. Do patients with brain injury or dysfunction respond to antidepressant or migraine therapy similarly to otherwise neurologically normal patients? Does the additional risk of adverse central nervous system side effects mitigate the benefits of pharmacological therapy of mood disorders or migraine in epilepsy? Can memory dysfunction in temporal lobe epilepsy be treated with agents shown to improve early Alzheimer's disease? The evidence supporting the benefits of systematic screening for comorbid problems will be reviewed in this lecture, as well as the preliminary data suggesting the importance of aggressive intervention.

Epidemiology of Co-morbidities as a Function of Age
P. Jallon[1]

1) Epilepsy Unit. University Hospital, Geneva, Switzerland.

Co-morbid conditions frequently occur in epilepsy which may affect its presentation and evolution and consequently its treatment. Conversely, epilepsy and anti-epileptic drugs may change these associated conditions. The epidemiology of comorbidity is not well known and it is limited to some data on the cumulative incidence and prevalence of various conditions in children and adults with epilepsy. Two recent studies, one in children (Neurology 2004; 62: S17-S23) and the other in adults (Epilepsia 2004; 45: 1613-1622) have brought some original data. Nevertheless, neurological co-morbidities are limited to some disorders and will differ between children and adults. The overall prevalence ratio of co-morbid diseases of the nervous system in a cross sectional study, irrespective of age and gender, has been found around 1.40 and decreased slightly with age. There is, however, a difference between saying that epilepsy is caused by these neurological disorders and that, in some instances, epilepsy is only associated with them. The temporal association between epileptic seizures and a co-morbid disease is often impossible to ascertain except in CVA, CNS neoplasia, cranial trauma or CNS infectious diseases. Likewise, some neurological disabilities increase the risk of childhood epilepsy, specifically severe developmental disabilities and cerebral palsy. The incidence of epileptic disorders associated with mental retardation and cerebral palsy is 15 to 40 %. Conversely, the association of multiple sclerosis and epilepsy has been often debated. In a recent review of twenty nine studies reporting the association of clinically diagnosed multiple sclerosis and epilepsy, the prevalence of so called epileptic disorders, ranges from 0.5% to 10.8 %. The mean prevalence is 2.3% but the relation cause-effect seems unusual. We will emphasize on some more or less frequent neurological conditions, in children and in adults, which could be associated with epileptic disorders. Migraine has long been considered as a frequent association with epilepsy, affecting nearly 20 % of adult patients with epilepsy. Although often associated with some benign epileptic syndromes its exact prevalence in children is not well known. The overall rate ratio for dementia and /or cerebral degeneration in adults aged under 64 years is 25 and nearly 40 for Alzheimer disease. It decreases logically with advanced ages. The association between parkinsonism and epilepsy is still debated, some population-based studies reporting a rate ratio of co-morbidity from 2.51 to 3.29 and other hospital studies suggesting that neurodegenerative changes occurring in the basal ganglia would protect against the occurrence of epileptic seizures. The risk of some specific neurological diseases seem clearly increased in people with epilepsy as well as epileptic seizures occur more frequently in some neurological conditions. In these patients, treating not only epilepsy but also any other present neurological disease requires more caution in prescribing medications.

Monday 29th August 2005
15:30 - 17:00
Amphitheatre Bleu
Post Main Session
Seizures Associated with Neurological Disorders

Provoked Seizures or Seizures in Symptomatic Epilepsies
L. Forsgren[1]

1) Department Of Neurology, Umeå University Hospital, Sweden.

Are provoked seizures synonymous to seizures in symptomatic epilepsies? Epidemiological studies show that the risk of an unprovoked seizure following a first acute symptomatic (provoked) seizure is around 18% at 10 years follow-up (Hesdorffer et al, 1998). This is much lower than 34% risk of further unprovoked seizures at 5 years follow-up following a first unprovoked seizure (Hauser et al, 1990). A population-based study from the UK also show significantly lower recurrence in acute symptomatic seizures compared to unprovoked seizures (Hart et al, 1990). Mortality also differs between the groups. The 30-day mortality in cases with acute symptomatic seizures is 15-50% when the seizure is due to stroke, and 10-35% when due to a traumatic brain injury. This is much higher than in cases with a first unprovoked seizure where the 30-mortality only is a few percent. Furthermore, prophylactic treatment with antiepileptic drugs in cases with traumatic brain injury lower the risk for acute symptomatic seizures, but do not lower the risk for later unprovoked seizures. Thus, clear differences in seizure prognosis, in mortality, and in the effect of prophylactic treatment show that acute symptomatic

(provoked) seizures should be distinguished from unprovoked seizures in symptomatic epilepsies.

Stroke

A. Guekht[1], A. Lebedeva[1], O. Kurash[1], A. Feyguina[1], E. Gusev[1]

1) Russian State Medical University, Russia.

Stroke (S) is the most common life-threatening neurological disease, with incidence 200-400/100,000. S. prevalence is estimated as 5/1000 in general population, but becomes 50/1000 in man and 25/1000 in women aged 65-74. (1). Especially in the elderly population, S. is the most common cause of seizures and epilepsy. On the other hand, the onset of seizures in late life is associated with a striking increase in the risk of S. (2). About 10% of all S. patients experience seizures, from onset until several years later. Five percent are early-onset seizures (ES, within 7 days of stroke, peak onset within the first day after the stroke) and another 5% are late-onset seizures (LS, peak onset within 6 to 12 months after the stroke). Epilepsy develops in 3% to 4% of the S. patients (in about one third of patients with ES and about one half of patients with LS). (3,4). Acute or remote S is the most common etiology of status epilepticus in the elderly, with acute S being reported to cause 22% of all cases of status epilepticus in adults (5). ES represent provoked seizures and occur in 2% to 6% of strokes; they are considered to be predictors of recurrent seizures. Very early seizures constitute an important risk factor for in-hospital mortality after atherothrombotic S. (6). In our study early seizures occurred in 6.1% of ischemic S. Only atrial fibrillation was a significant risk factor for ES, while ES themselves were a strong predictive factor for recurrent S. and LS. Thirty percent of patients with ES subsequently had LS. Cumulative risk of LS was 5.7% after 2 years of S. As for ES, only atrial fibrillation was a significant risk factor for LS in multivariate analysis. LS and epilepsy after ischaemic S. are accompanied by increase of lesion size on CT and worsening of the disability of patients (7). In many studies severe S is considered to increase the incidence of post-stroke epilepsy (PSE), up to five-fold compared to minor strokes (4,8). Seizures are more common in hemorrhagic S. and S. with cortical involvement. LS/PSE usually are reported with 6 months - several years after S., though almost a doubling of incidence of PSE one year to five years after S. was demonstrated (8), that might be explained by a long epileptogenesis or by high morbidity in this age group. Mechanisms underlying S-induced epileptogenesis require further investigation. A number of studies indicated that brain plasticity is involved in the formation of PSE. In the last several years, evidence has accumulated indicating that the prolonged alteration in neuronal calcium dynamics plays an important role in the induction and maintenance of the prolonged neuroplasticity changes underlying the epileptic phenotype (9) and the glutamate injury-induced epileptogenesis model of stroke-induced epilepsy is calcium dependent and requires NMDA-receptor activation. The influence of seizures on epilepsy outcome is still a matter of controversy. Although epileptic seizures after stroke are considered easy to control, this is not supported by evidence from randomized controlled trials (4). Advantages and disadvantages of treatment of single seizure should be considered. Treatment strategies should be carefully selected with understanding of co-morbidity, co-medication, alterations in pharmacokinetics and pharmacodynamics. References: 1.Bots M.L. et al. (1996). Stroke,27: 1499-501 2.Cleary P. et al., (2004). The Lancet, 363:1184 - 1186 3.Hauser W.A. et al.(1993) Epilepsia, 34(3):453-68. 4.Olsen T.S. (2001). Curr Atheroscler Rep., 3(4): 340-4. 5.Labovitz DL et al. (2001). Neurology, 57(2): 200-6 6.Arboix A. et al. (2003). Eur Neurol. 2003; 50(2): 78-84 7.De Reuck J.et al., (2005). Cerebrovasc.Diseases, 19 (Suppl.2): 7 8.Lossius M.I. et al (2004). Tidsskr Nor Laegeforen. 124(5): 620-6229. 9.Delorenzo R.J. et al (2005) Pharmacol Ther. 105(3): 229-66.

Alcohol and Illicit Drugs

J.C.M. Brust[1]

1) University Of Columbia, USA.

Recreational drugs, including ethanol, cause seizures both indirectly (CNS infection, stroke, trauma, metabolic derangement) and directly, (either a toxic effect or a withdrawal phenomenon). Although opioids lower seizure threshold, seizures are rarely caused by heroin overdose, and except in newborns they are not a feature of opioid withdrawal. Seizures are frequently encountered in psychostimulant abusers, and with cocaine, they can be the only sign of toxicity. With sedative drugs and ethanol seizures are a prominent feature of withdrawal; in addition, however, heavy drinkers are at increased risk for seizures independent of withdrawal or concomitant medical/surgical disorders. Epidemiological evidence suggests that marijuana use decreases seizure susceptibility. With other recreational drugs, including hallucinogens, inhalants, phencyclidine, and anticholinergics, seizures can follow overdose.

CNS Infections

C.T. Tan[1]

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Four CNS infections with seizures are discussed, neurocysticercosis for its impact on prevalence of epilepsy, malaria and Japanese encephalitis for the potential in improving the outcome, and Nipah encephalitis for helping to understand the pathogenesis of the encephalitis. Neurocysticercosis is an important cause of seizure and epilepsy in many developing countries. For a particular country or region, the precise contribution of neurocysticercosis to the prevalence rate of epilepsy in the community is important. For example, in India, the syndrome of seizures associated with single enhancing CT lesions (SSELs) usually attributed to neurocysticercosis has been said to account for 10% of epilepsy patients seen in the neurological centres. On the other hand, a recent community-based prevalence study in Andra Pradesh showed only 3% of 379 patients with CT scan features consistent with neurocysticercosis. Data from clinical setting may exaggerate the contribution of neurocysticercosis to epilepsy prevalence. Malaria causes 0.5 to 2.5 million, and Japanese encephalitis 15,000 deaths yearly world wide. In both infections, convulsive seizures and status epilepticus are common; and are associated with raised intracranial pressure and increased mortality. Seizure and raised intracranial pressure may thus be potentially reversible factors in improving the outcome of both diseases. However, a double blind control trial of Phenobarbital in malaria showed reduced seizure frequency but increased mortality. Nipah encephalitis is an emerging infection first seen among pig farmers and related workers in Malaysia and Singapore in 1998/99. Subsequently, it has been occurring as recurrent outbreaks in Bangladesh and neighbouring India. The pathogenesis of Nipah encephalitis was initially thought to be widespread vasculitis causing diffuse microinfarction of the brain. Distinctive clinical features including segmental myoclonus suggest predilection for certain group of neurons. This is confirmed by immunohistochemical staining showing direct viral infection of the neuron. About 10% of patients with Nipah encephalitis develop relapsed encephalitis after an interval of up to 4 ½ years. Significantly more patients with relapse have seizures as compared to acute encephalitis. Pathological study confirmed focal encephalitis during relapse.

Tuesday 30th August 2005
07:30 - 08:30
Salle 252AB
Morning Seminar
Chromosomal Disorders and Epilepsy Syndromes

Chromosomal Disorders Associated with Epilepsy
A. Battaglia[1]

1) Stella Maris Clinical Research Institute For Child And Adolescent Neuropsychiatry, Calambrone, Pisa, Italy. 2) Italy & Division Of Medical Genetics, Dept. Of Pediatrics, University Of Utah Health Sciences Center, Salt Lake City, UT, USA.

Epilepsy is among the most common findings in chromosome aberrations, particularly those involving autosomal chromosome imbalance. Most chromosome aberrations can be associated with different seizure types, but there are a few aberrations featuring specific seizure and electroencephalographic (EEG) patterns. The analysis of electro-clinical patterns associated with chromosomal aberrations is a major tool in the identification of epilepsy susceptibility genes. Advances in molecular cytogenetic techniques (FISH; Subtelomeric analysis; CGH microarray) have great diagnostic potential, allowing for the detection of cryptic chromosome rearrangemets. As a result, an increasing number of individuals previously diagnosed as having 'cryptogenic' epilepsy will turn out to have an underlying chromosomal aberration. We present a review on the types of seizures, EEG findings, and their natural history in the chromosomal disorders that are consistently associated with epilepsy.

Ring Chromosome 20
S.M. Zuberi[1], A.J. Biraben[2]

1) Fraser Of Allander Neurosciences Unit, Royal Hospital For Sick Children, Glasgow, Scotland. 2) Unité D'épileptologie, CHU De Rennes, Rennes, France.

Introduction: The ring chromosome 20 syndrome (r(20)) has been considered rare with less than 50 cases reported since 1972. However informal discussions with epileptologists from large institutions suggest that they frequently have one or two patients who present great challenges in epilepsy care . Clinical descriptions have been in small series of 6 or fewer cases. Single case reports have suggested specific efficacy of certain therapies. Our series of >50 new patients aims to provide a comprehensive clinical overview of the syndrome. Methods: Patients were reported from international paediatric and adult neurology/epileptology centres. Data was collated by AB and SZ using a database and written questionnaire. Patients had clinical, imaging and neurophysiological evaluation. Neuropathology was performed in one patient. Results: r(20) mosaicism varied between 0.5% and 100% of lymphocytes, and fibroblasts in 1 child post mortem. Dysmorphic features were exceptional. Epilepsy presented day 1 to 17 years, with a peak 4-8y. Most children were in normal education prior to presentation. 70% described seizures with fear, often with visual illusions. Brief nocturnal seizures were common. All had refractory epilepsy, non-convulsive status and characteristic EEGs. SUDEP occured in two patients. Several had surgical evaluations. Diagnosis was delayed 2 months to 36 years. There was no correlation between % mosaicism and age of onset or cognitive outcome. Cognition varied from severely impaired to normal. A behavioral phenotype with impulsivity, inattention and aggression was seen. No single therapy appears to have a specific benefit however clinicians reported certain therapies worsening seizure control. Discussion: Ring 20 syndrome is commoner than previously thought. Mosaicism means at least 100 cells need to be studied. Cognitive outcome is heterogenous. It should be considered in children and adults with refractory epilepsy, non-convulsive status and neuropsychiatric symptoms even in the absence of dysmorphic features or learning disability.

Tuesday 30th August 2005
07:30 - 08:30
Salle 251
Eurepa Session - Diagnostic Issues 2
Is it a Partial or a Generalised Seizure?

Is it a Partial or a Generalized Seizure?
E. Trinka[1]

1) Universitätsklinik Für Neurologie Innsbruck, Innsbruck, Austria.

Though the concept of generalized and partial, or better called focal seizures, dates to the mid-nineteenth century, it did not became widely accepted until the early 70ies and found finally broad consent in the current classification from 1981. A valid seizure classification is not only vital to the interest of the patient under treatment, but also to scientific communication and advancement of knowledge using a common language (glossary of terms). Critizism on the strict dichotomy between generalized seizurs 'in which the first clinical changes indicate initial involvement of both hemispheres', and focal seizures 'in which, in general, the first clinical and electroencephalographical changes indicate initial activation of a system of neurons limited to part of one hemisphere' arose with increasing knowledge on seizure semiology due to widespread use of video-EEG for presurgical evaluation of medically refractory epilepsies: Firstly, it became clear, that some unequivocal focal seizures may clinically involve both sides of the body, or all 4 extremities simulating bilateral seizure onset (e.g. SSMA-seizures), secondly, many generalized seizures are erroneously classified as focal, due to some more or less pronounced asymmetric motor activity or focal elements in their seizure semiology. Furthermore seizures charcterized by paroxysmal loss of consciousness may occur as focal (complex-focal) or as generalized (absences) seizures, which can only be correctly identified with ictal EEG recordings and therefor leading to methodological and conceptual problems in a purely clinical seizure classification. Some attempts to overcome these problems have been made (e.g. semiological seizure classification by the Cleveland Group) but there is still no consensus to what extend the strict distinction between focal and generalized remains arbitrary. For clinical purposes and as illustrative exampels video demonstration of seizures which can not be classified unconstraintly into focal or generalized will be given. At the end of the session the attendees should be able to understand the conceptual frameworks of the dicotomy (focal vs. generalized) but also to recognize the weakness of the current classification.

Is it a Partial or a Generalized Seizure?
F. Vigevano[1]

1) Children's Hopsital Bambino Gesu, Scientific Institute, Rome, Italy.

It is not always easy to distinguish between partial and generalized seizures in the first months of life. There are some age-dependent kinds of seizure, having features which are strictly related to the maturation of the Central Nervous System. The massive myoclonic jerks and brief absence with myoclonia, which can be observed in the Benign Myoclonic Epilepsy with onset around the age of 10-12 months, are considered as the first occurrence of a generalized seizure within a generalized idiopathic epilepsy. Tonic-clonic generalized seizures may occur during the first months of life, but they actually are, in most cases, partial seizures with a secondary generalization, in the framewok of symptomatic epilepsies. The syndrome of Benign Infantile Familial Seizures, with onset at the age of 3-7 months, is characterized by clusters of focal seizures with secondary generalization. The seizure may originate sometimes on one emisphere, and sometimes on the other. These seizures are likely to be the equivalent of tonic-clonic generalized seizures, which the brain is unable to express at this age, due to immaturity. Even the prolonged febrile seizures, which can be observed at the onset of the Severe Myoclonic Epilepsy, may acquire clinical aspects of partial seizures, but they actually are generalized seizures. Finally, we have to consider that Epileptic Spasms, a typical seizure of the first months of life,

present with features that make it difficult to classify them as partial or generalized. In the genesis of spasms, in fact, subcortical structures are likely to be involved.

Tuesday 30th August 2005
07:30 - 08:30
Salle 241
Eurepa Session - Treatment Issues 2
How to Avoid Misinterpreting Results of Clinical Trials

How to Avoid Misinterpreting Results of Clinical Trials
B. Schmidt[1]

1) Neurology & Psychiatry Clinic,, Wittnau, Germany.

Literature related to 'evidence-based medicine' is growing at exponential speed. In principle evidence as a result of methodologically clean studies and systematic reviews of a multitude of those studies is highly wellcome. However, what at first glance seems to be unequivocal evidence favoring treatment strategy A over B or demonstrating no difference between A and B may be easily flawed by trial designs, the processes involved in the analyses, or the generalizability of the results to a practice population. In trials with modern AEDs methodological issues evolving to misleading conclusions include inadequate distribution of epilepsy syndromes and inadequate titration schedules as well as target doses. Retention rates are strongly influenced by the posology and formulation of study drug versus comparator. Studies resulting in 'non-inferiority' are sometimes underpowered. Metaanalyses suffer from heterogeneity of studies included, from selection bias and from criticism for some of the statististical procedures used e.g. to calculate NNT ('number needed to treat'). In the first part of this session examples from adult trials, mainly in partial epilepsy, will be presented, evaluated and discussed.

How to avoid Misinterpreting Results of Clinical Trials
J.W. Wheless[1]

1) University Of Tennessee Health Science Center, Le Bonheur Children's Medical Center, Memphis, TN, USA.

The proper interpretation of published clinical trials is critical when considering antiepileptic drug therapy in children. The clinician must be able to ascertain, when reading the manuscript, if the unique pediatric epilepsy syndrome was properly ascertained, and then have an understanding of how the results fit into clinical practice. The results may apply to only a small subgroup of those studied or may be more universal in their application. In the second part of this session we will evaluate representative clinical trials conducted in children with various epilepsy syndromes. Trials will be discussed for various pediatric epilepsy syndromes, including febrile seizures, Dravet Syndrome (Severe Myoclonic Epilepsy in Infancy), BECT (Benign Childhood Epilepsy with Centro-Temporal spikes), and Juvenile Myoclonic Epilepsy. These trials will be used as examples to discuss the difficulties in designing pediatric treatment trials, measuring outcomes, and applying these to patients in clinical practice. This will be an interactive session.

Tuesday 30th August 2005
07:30 - 08:30
Salle 243
Morning Seminar
Critical Decisions in Status Epilepticus?

Can Refractory Status be Prevented, and How Crucial is the Time Window? - Clinical Evidence and Management Implications
M.C. Walker[1]

1) Department Of Clinical And Experimental Epilepsy, Institute Of Neurology UCL, London, UK.

Refractory status epilepticus has a high mortality and a significant morbidity, and it is critical to identify factors that may prevent this condition. There is considerable animal evidence that status epilepticus is an evolving state with progressive difficulty in treating and progressive neuronal damage; animals have a better prognosis the sooner the status epilepticus is stopped. In addition there is evidence for a role of new antiepileptic drugs and putative neuroprotective agents in its treatment. How do these data translate to the human condition, and are there factors that prevent the evolution to refractory status epilepticus? Controlled studies in humans of response to delayed treatment and the time window before neuronal damage occurs are not possible. There are however a few retrospective studies that have investigated, the factors that contribute to the development of refractory status epilepticus, and its outcome. Some factors are beyond the control of the treating physician, such as aetiology, but there is evidence to support the animal data that the longer status epilepticus continues the harder it is to treat and the greater are the consequences. Urgent treatment of prolonged seizures with adequate doses of appropriate drugs is necessary to prevent this potentially devastating condition; yet audits of treatment continue to demonstrate a failure to instigate these simple measures.

When should General Anaesthesia Not be Considered in Status Epilepticus?
P. Thomas[1]

1) UF EEG-Epileptologie, Université De Nice-Sophia-Antipolis, Nice, France.

General anaesthesia is not indicated in the vast majority of true nonconvulsive status epilepticus, and also in myoclonic status epilepticus occurring in the background of idiopathic generalized epilepsy. In a number of patients with primary or secondary generalized convulsive status epilepticus, monotherapy with lorazepam or combination therapy with benzodiazepine and phenytoin is often effective to control the situation, especially when status epilepticus presents at its early phase. When general anesthesia is considered, many studies have found evidence that emergency management is often inappropriate, because of poor standardisation of therapy and use of inadequate dosages. In a study by Celesia (1983), seven of the 27 deaths seemed ascribable either to inadequate monitoring or to errors in the dosage or route of administration of medications. Walker et al. (1995) reported that only 12% of physicians followed a predefined management protocol. In 1996, the same group conducted an audit of 26 patients admitted to a neurological intensive care unit. Failure to diagnose factitious SE was noted in six patients, four of whom underwent tracheal intubation, and phenytoin therapy was inadequate in nearly half the patients (Walker et al., 1996). Among the Rochester cohort patients given appropriate first-line drugs, three in every four received inadequate dosages, and when a second antiepileptic drug was given the dosage was inadequate in 80 % of cases (Cascino et al., 2001). Scholtes et al. (1994) found that treatment was suboptimal in 44.7% of patients who died, 22.7% of those with sequelae, and 10.3% of those with a favourable outcome. These data favor the optimal cooperation between neurologists and anaesthetists, which appears to be critical in this field.

Tuesday 30th August 2005
08:45 - 09:45
Grand Amphitheatre
Main Session
Brain Maturation & Epileptogenesis: Basic Rules

Why is the Developing Brain so Prone to Seizures?
Y. Ben-Ari[1]

1) Inserm, Marseilles, France.

The construction of cortical networks follows a number of principles that have been kept throughout evolution including initially excitatory actions of the inhibitory transmitter GABA and the presence in all animal species including humans of a single pattern of activity in developing networks -'developing networks play a similar melody'. Studies performed for the first time on hippocampal neurons in primates that were recorded in utero have provided an unprecedented snap shot picture fo the developmental sequences. I shall describe some of the steps that lead to the formation of networks in rodents and primates and illustrate how these rules are responsible for the higher incidence of seizures in developing brains. I shall also demonstrate that in the developing brain 'seizures beget seizures' and the epileptogenic actions of seizures have now been determined providing a mean to determine which type of seizures is potentially endowed with possible deleterious consequences. Finally, we can now also directly evaluate the effects on brain maturation, network construction and seizure generation of widely used agents notably GABA acting agents such as benzodiazepines or anti epileptic agents. Indeed, the opposite actions of GABA on the brain of the pregnant mother and the fetus at certain developmental stages raise a series of problems that must be taken in consideration. Similarly, the deleterious actions of agents on neuronal migration and can now be quantitatively determined opening the paving the way for more rational determination of actions of a large number of agents on the immature brain. The developing brain is not a small adult brain and it has its own rules and molecules that often are only expressed at some stages - or not expressed at all- indicating that studies on the properties of immature networks are not only essential because they will enable us to understand how genes and activity interact in the nature and nurture procedure that leads to brain formation. They also are crucial to determine how much the disorders observed later are not in fact due to early insults that follow the developmental sequences to have their signature when the network is sufficiently mature to express the disorder. References Ben-Ari Y. : Developing networks play a similar melody. Trends Neurosci., 2001; 24: 353-360. Ben Ari Y : Excitatory actions of GABA during development: the nature of the nurture. Nat.Rev. Neurosci., 2002; 3: 728-739. Demarque M, Represa A, Becq H, Khalilov I, Ben Ari Y., Aniksztejn L. :Paracrine Intercellular Communication by a Ca(2+)- and SNARE-Independent Release of GABA and Glutamate Prior to Synapse Formation. Neuron, 2002; 36: 1051-1061. Leinekugel X, Khazipov R, Cannon RC, Hirase H, Ben-Ari Y., Buszaki G. : Correlated bursts of activity in the neonatal hippocampus. Science, 2002; 14;296(5575):2049-52. Khalilov I, Holmes GL, Ben Ari Y. :In vitro formation of a secondary epileptogenic mirror focus by interhippocampal propagation of seizures. Nat. Neurosci., 2003; 6: 1079-1085. Khazipov R, Sirota A, Leinekugel X, Holmes GL, Ben-Ari Y., Buzsaki G. Early motor activity drives spindle bursts in the developing somatosensory cortex. Nature. 2004 Dec 9;432(7018):758-61.

Clinical Relevance?
R. Guerrini[1]

1) Department Of Child Neurology And Psychiatry, Pisa, Italy.

Age relatedness of (anatomo) electroclinical patterns provides an important basis for understanding how epileptogenesis may be related to brain maturation but also on how some conditions may disrupt, modify or be independent of the habitual age related expression of some disorders. For example epileptic spasms, are typically expressed in infancy. However, some severe, usually diffuse, malformations can cause epileptic spasms that may be expressed well beyond that age range. In such circumstances one may speculate that the normal maturation of networks is prevented by the severe disruption of cortical architecture and that, consequently, epileptogenesis continues to be expressed in an archaic fashion. Other examples are represented by epilepsies with spike and wave discharges such as absence seizures, and epilepsy with continuous spike and waves during slow sleep. These conditions are typically manifested within the same age range, although they may have different etiologic backgrounds. It is as if the brain were predisposed to express hypersynchronous epileptogenesis within a definite age range, beyond which epileptogenesis is attenuated and remission is almost the rule, irrespective from the etiology. Rolandic epilepsy is expressed within the same age range of childhood absence epilepsy but if accompanied by atypical EEG abnormalities, predisposes to a complicated evolution that may include the appearance of spike and wave related generalized seizures and can be paradoxically aggravated by the same drugs that may aggravate absence epilepsies. Therefore drug sensitivity may also be age related in some individuals. On the other hand, some etiologies, are manifested by a type of epileptogeneiss that is never influenced by age and is invariably regional. It is as if the epileptogenic area were so badly connected to the rest of the brain as to act as a cerveau isolé, only producing epileptic activity and never undergoing any influence from the surrounding networks. The best example for this is focal cortical dysplasia. The development of experimental models of neural networks where specific molecular or morphologic abnormalities are expressed will help better understanding the processes of age related epileptogenesis.

Clinical Relevance?
S.L. Moshé[1]

1) Albert Einstein College Of Medicine/Montefiore Medical Center, New York, USA.

The immature brain is not a small version of the adult brain and this is evident in issues relating to Pediatric Epilepsies. The incidence of epileptic seizures as well as their phenomenology are highly age dependent. Recent advantages in basic science research have begun elucidating some of the reasons related to the age-specific features of epileptogenesis and epilepsies in the developing brain. The initial studies have provided evidence for the increased seizure susceptibility of the immature brain as indicated by lower thresholds to various exogenous epileptogenic stimuli, rapid development of kindling, a great ease of emergence of multifocal forci and the propensity to develop status epilepticus. All these are features frequently seen in human infants and children with epileptic seizures. In addition, several studies have indicated that there age-specific mechanisms involved in seizure suppression depending on the differential maturation of excitatory and inhibitory systems within particular sites of the brain. Furthermore, there is ample evidence that the consequences of seizures are highly age-specific. Additional research is attempting to create models of catastrophic epilepsies which is an area that is lagging behind. The advances in understanding the development, expression, and consequences of seizures in the immature brain has pushed forward the notion that age-specific treatments are needed to control epileptic events in the developing brain. Supported by grants NS-20253 and K12 NS 48856 from NINDS and the Heffer Family Medical Foundation.

Tuesday 30th August 2005
10:00 - 11:30
Amphitheatre Bleu
Post Main Session
Migration and Epilepsies: Basic Rules

Genetics and Environment in Neuronal Migration
P. Rakic[1]

1) Department Of Neurobiology And Kavli Neuroscince Institute, Yale University School Of Medicine, New Haven, CT, USA

The identity, synaptic relationship and, ultimately, function of neurons is defined by their position. Neurons in the cerebral cortex acquire their position by active migration from multiple sites of origin to their final, increasingly distant, destinations by orchestration of multiple molecular events regulated by sequential gene expressions and complex cell-cell interactions that can be modulated by environmetal factors. We have identified several families of signaling molecules that control migration of neurons in the cerebral cortex. These include selection of a proper pathway by membrane-bound cell recognition receptors, formation of adhesive interactions with cellular and extracellular substrates and activation of specific ion channels and receptor complexes that control the rate of motility via second messenger-mediated signals. As a result, neuronal migration and precise inside-to-outside sequence of their deployment can be disrupted by specific gene mutations as well as by various physical (e.g., ionizing radiation, ultrasonic waves, heat), chemical (e.g., drugs, alcohol), and biological (e.g., neurotrophic viruses) agents. Disruption or even slowing down of neuronal migration results in either gross or subtle abnormalities in neuronal positioning that eventually affect the pattern of synaptic circuits. In addition to severe malformations are easily detectable, migratory abnormalities can be manifested in the mature brain by the presence of small groups or solitary ectopic neurons that have failed to reach their proper targets. Since the improper position of isochronously generated neurons requires DNA labeling and/or use of transgenes, not applicable to human, the subtle migratory abnormalities could be entirely missed by routine examination in the either alive or autopsied brain. Such misplaced neurons may be involved in a variety of idiopathic neurological disorders including the childhood epilepsy.

Basic Mechanisms of Neuronal Migration
A. Kriegstein[1], S.C. Noctor[1], V. Martinez-Cerdeno[1]

1) Dept. Of Neurology, UCSF, San Francisco, USA

The precise radial and laminar organization of the cerebral cortex arises in embryonic stages through coordinated processes of neurogenesis and migration that are still not completely understood. However, it is now known that inhibitory interneurons and excitatory pyramidal cells arise in different proliferative areas and migrate along different paths to reach the developing cortex. We examined the patterns of cell division and migration during late stages of neurogenesis by injecting a retrovirus that expresses green fluorescent protein (GFP) into the lateral ventricles of the developing rat cerebral cortex on embryonic day 16. These injections resulted in GFP labeling of progenitor cells and their clonal progeny. We prepared organotypic slice cultures 24 hours after retroviral infections, and observed neural precursor cell divisions and migratory behavior in real time through confocal time-lapse microscopy. We found that many cortically derived neurons do not migrate directly to the cortical plate, but instead undergo four distinct phases of migration. Phase one consists of rapid movement to the subventricular zone (SVZ); phase two of migratory arrest in the SVZ; phase three of retrograde migration toward the ventricle; and phase four of migration to the cortex. By following the lineage of cortical neurons, our data directly confirm that neurons born in the cortical ventricular zone pause in the SVZ as multipolar neurons before resuming migration. The four distinct phases of neuronal migration may have clinical significance in relation to neuronal migration disorders, as some disorders, associated with epilepsy, may reflect a failure of neurons to make the transition from one phase of migration to another.

Molecular Biology of Neuronal Migration Disorders
B. Chang[1], C.A. Walsh[1],

1) Beth Israel Deaconess Medical Center And Harvard Medical School, USA

Malformations of cortical development (MCD) are increasingly being recognized as a common cause of refractory epilepsy and other neurological disorders. Technical advances in two areas, genetics and neuroimaging, have led to an increased understanding of the molecular biology and anatomy of MCDs, which are often now classified using genetic or radiological criteria. The cognitive and behavioral consequences of disruptions in cortical development, however, remain relatively less well understood although they have taken on increasing importance as MCDs become more widely diagnosed.
Two sets of MCDs serve as instructive examples of the relationship between genotype and both radiological and behavioral phenotype. First, a number of bilateral symmetric region-specific polymicrogyria (PMG) syndromes have now been described, each of which appears genetically and clinically distinct. The relationship between the regional nature of the malformation and the clinical signs, including epilepsy, is discussed. The identification of genetic mutations responsible for these bilateral PMG syndromes may reveal much about the regional specificity of genetic influences during cortical development. Second, the disorder of periventricular nodular heterotopia (PNH) is an example of a striking alteration in gray matter development that is nevertheless associated with grossly normal intellectual function. More detailed testing demonstrates that most PNH subjects have normal intelligence but exhibit a specific reading impairment comparable to developmental dyslexia. The underlying cognitive deficits in PNH, as well as their potential neural basis, are discussed.

Clinical Relevance
R Spreafico[1], L Tassi[1], R Mai[1], I Sartori[1], M Cossu[1], C Galli[1], F Villani[1], A Pincherle[1], R Gabelli[1], G Lo Russo[1]

1) "C. Besta" Neurological Institute And "C. Munari" Epilepsy Suregry Center - Niguarda Hospital

Malformations of cortical development and particularly focal cortical dysplasia (FCD) are among the most frequent lesions recognized in patients operated on for drug resistant epilepsy. Although in approximately 20 % of the patients MRI is unable to identify FCD, recent neuroradiological data have defined some of the neuroradiological characteristics of different subtypes of FCD. According with the recent classification by Palmini et al (2004) two main subtypes of FCD are recognized in addition to the so called "mild "form. While Type II, characterized by early age of seizure onset and by high seizure frequency, are mainly found in extratemporal brain regions, Type I group are found most frequently in temporal areas. Although hippocampal sclerosis is considered the most frequent cause of temporal lobe epilepsy, recent studies suggest a frequent association of HS with temporal lobe malformation questioning about the existence of the so called "dual pathology" and suggesting a common pathogenetic malformative mechanism.

Tuesday 30th August 2005
10:00 - 11:30
Salle Maillot
Parallel Session
Do we need WADA test?

Indications, Usefulness and Clinical Implications of WADA Test - PROs
D. Loring, USA

No abtract submitted

Indications, Usefulness and Clinical Implications of WADA Test - CONs
C. Helmstaedter[1]

1) Universitätsklinik Für Epileptologie Bonn, Bonn, Germany.

WADA tests are traditionally performed before brain surgery in order to prevent postoperative aphasia or amnesia. The WADA test is still the gold standard for the detailed description of graded or dissociated language dominance patterns and for reversible simulation of lateralized hemispheric damage. Its clinical indication, however, has dramatically changed. In the Bonn epilepsy center with currently about 150 presurgical evaluations per year, indication of the WADA has steadily decreased from 50-70% of the patients between 1988 and 1995, to about 10-20% until 1998, and <5% in 2004. This decrease reflects better patient selection due to expanding knowledge about the clinical features indicative for atypical dominance (left sided epilepsy, cortical site of lesion or focus, developmental lesions, onset of epilepsy before puberty, left handedness, female gender, non-corresponding neuro-psychological profiles, non-corresponding ictal/postictal impairments. Now, the language WADA has become largely replaced by fMRI Knowledge of language dominance is required in candidates for callosotomy, hemispherectomy, or for resections close to or within presumed eloquent cortex. In these cases the WADA test is still indicated if fMRI is not possible or if it fails to show complete left dominance. Preoperative or intraoperative cortical electrical stimulation is necessary for intrahemispheric delineation of areas involved in language processing. Neither IAT nor fMRI can replace stimulation mapping in this respect. As for memory, no amnesic syndrome has ever been predicted from WADA test alone. Graded predictions of memory outcome for the individual patient are debatable. In selected cases, a selective posterior WADA would be appreciated for memory prediction. However, the value this procedure is questionable facing the increased risk of brain stem infarcts and the lack of reference data for its interpretation. Memory outcome can grossly be predicted by other methods as well, and it appears that in this domain fMRI will also set standards. In summary, the WADA test still represents a comparably safe and valuable tool for determination of language dominance, but clinically this method has currently very limited indications.

Can MRI Studies Make the WADA Test Redundant
J.S. Duncan[1], P.J. Thompson[1], S.A. Baxendale[1]

1) Institute Of Neurology UCL And National Society For Epilepsy, London, UK.

The principal roles of the Wada test in presurgical evaluation have been to lateralize language function, and to assess the memory capacity of the contralateral hemisphere prior to an anterior temporal lobe resection. Subsidiary roles are to help predict the decline in memory that may occur following resection and to assist in confirmation of the lateralization of the epileptic focus. Advances in non-invasive investigations have resulted in a much-reduced role for the Wada test. With some caveats, language lateralization is achievable with functional MRI. The capacity of the contra-lateral hemisphere to subserve basic memory and to assure that an amnesic syndrome will not occur after unilateral anterior temporal lobe resection is determinable from the neuropsychological profile and MRI evidence of normal temporal lobe structures. The extent of decline in memory following temporal lobe resection is predictable from the baseline neuropsychological profile, clinical features and structural MRI, and with functional MRI studies of memory for words, pictures and faces now beginning to provide additional useful data.The lateralization and localization of the epileptic focus is achieved primarily by establishing a consensus of scalp ictal and interictal video-EEG recordings with MRI and neuropsychological profile. In some cases functional imaging and invasive EEG may be required and a Wada test would not obviate these.

Can Magnetocephalography replace WADA Test?
A.C. Papanicolaou, E.M. Castillo, J.I. Breier, R.L. Billingsley-Marshall, P.G. Simos

In order for Magnetoencephalography (MEG) to replace the Wada test, MEG mapping should, at the very least, match closely the results of that test regarding hemispheric dominance for language and memory. In this presentation we will summarize the progress made in our laboratory towards attainment of that objective: Such a close match has already been obtained for receptive language, in an on-going series of surgical candidates, now numbering over 100. Currently, using neurologically intact volunteers as well as additional patients, we are evaluating the efficacy with which MEG mapping matches the Wada test results using expressive language tasks and a memory task involving simultaneous verbal and non-verbal encoding identical, in its essential features, with the memory task used in our center during the Wada procedure, with encouraging results. Although at present we are not substituting the Wada test with MEG mapping (and we would not encourage such a substitution in other centers) we are fairly optimistic that we will do so in the near future.

Tuesday 30th August 2005
10:00 - 11:30
Salle 252AB
Parallel Session
Co-morbidities in Infants and Children

Epilepsy in Inherited Metabolic and Mitochondrial Disorders
D.R. Nordli[1]

1) Children's Memorial Hospital, Northwestern University, Chicago, USA.

Inherited metabolic and mitochondrial disorders are important, albeit rare causes of epilepsy in infants and children. Recognition is important for relevant treatment, accurate prognostic information and genetic counseling. Some disorders are associated with specific presentations, and a few have rather unique EEG features which can be attributed to the underlying pathophysiology (e.g. neuronal ceroid lipofuscinosis). In the majority, however, the clinical and electrographic expression of these disorders is strongly influenced by the age of presentation. In these circumstances one can derive a differential diagnosis from a consideration of the epilepsy syndrome. In particular neonatal seizures, early myoclonic epilepsy, West syndrome, 'pleomorphic' epilepsies (term to be explained further) and progressive myoclonus epilepsies are all important red flags for metabolic diseases. Appropriate screening tests can be done based upon the diagnosis of the epilepsy syndrome.

Epilepsy and Cerebral Palsy
J. Aicardi[1]

1) Univesrity Hospital Robert Debré, Epilepsy Unit, Child Neurology And Metabolic Diseases Dpt., Paris, France.

Cerebral palsy (CP) is associated with epilepsy in 15-60% of cases. It is present in 50% of cases of quadriplegia,47% of hemiplegia and 25-27% of diplegia and dystonic CP. In preterm infants with diplegia, epilepsy seems less common (11%) probably because the location of damage in the deep white matter rather than the cortex.. All types of seizure can occur in all forms o CP including infantile spasms in 15% of cases. Partial motor seizures are predominant in hemiplegia, generalized seizures in other forms.Onset of epilepsy is before 2 years of age in 50% of bilateral CP but later in hemiplegic types. The incidence of epilepsy is highest (80%) in children with acquired postconvulsive hemiplegia., Epilepsy in CP tends to be severe and remission is obtained in less than 2 years in less than 15% of patients. Benign cases are however encountered especially with hemiplegia. The presence of epilepsy is associated with a considerable aggravation of the disability resulting from CP both sociopathological and neurocognitive consequences. Mental retardation was found in 71% of children with hemiplegia and seizures vs 27% of those

without. Decrease in achievement and neurological deficits seem more frequent and severe for the same form of CP and for a similar extent and nature of the causal lesion when epilepsy is present, suggesting that epilepsy itself and not only its causal damage plays a significant role and that control of epilepsy may decrease the overall disability. Although control of seizures is usually difficult to obtain in CP as in most cases of lesional epilepsy and surgical treatment may be necessary, drug therapy may be efficacious and should be tried.

Infections and Meningitis
S. Rosemberg[1]

1) Santa Casa Of Sao Paulo School Of Medicine, São Paulo, Brazil.

Clinicians are frequently confronted with provoked seizures during acute infections of the nervous system including bacterial, viral, fungic or parasitic. Early diagnosis and treatment is fundamental in order to prevent structural lesions leading to a poor outcome and chronic epilepsy. Irrespective to the etiology, the presence of seizures may be a negative predictive factor. Other negative predictive factors include age and familial history of epilepsy. HSV-1 is world-wide the most important infectious agent related to severe chronic temporal lobe epilepsy. In developing countries, cysticercosis is a frequent cause of acute symptomatic seizures. However, chronic epilepsy due to cysticercosis is seldom severe. It is important to emphasize that in countries where cysticercosis is endemic, the occurrence of epilepsy may not be related to this agent even when it is found on MRI. Status epilepticus is frequently found in acute malaria but the true incidence of chronic epilepsy remains to be determined, seeming to be quite low. In cases of severe acute encephalitis with intractable seizures Bartonella henselae might be looked for when HSV-1 and other viruses are ruled out.

Coeliac Disease and Epilepsy
G. Gobbi[1]

1) Child Neurology Unit. Maggiore C.A. Pizzardi Hospital, Bologna, Italy.

In symptomatic (Classic) Celiac Disease (CD) neurological complaints have been reported in 8-10% of the patients, but the true prevalence of neurological manifestations is unknown and it must been take in account patients with Silent and Latent CD. In fact, Silent or Latent CD has been frequently reported in patients with neurological disorders of unknown origin, such as spinocerebellar ataxia, occipital epilepsy with/without cerebral calcifications, peripheral neuropathies, and headache with CNS white matter abnormalities. The prevalence of epilepsy in patients with CD has been estimated to be between 1,5-5%. Patients with CD, Epilepsy and Cerebral Calcifications (CEC) usually have partial occipital epilepsy, frequently intractable. Severe evolution of occipital epilepsy with secondary generalization has also been reported. The likelihood of seizures stopping after starting a gluten free diet was inversely related to the duration and age of onset of epilepsy. CD and Epilepsy without Cerebral Calcifications, CD and Cerebral Calcifications without epilepsy, and Epilepsy and Cerebral Calcifications without CD have also been described. In all these conditions the most frequent typed of epilepsy is occipital in type. Occipital epilepsy with cerebral calcifications may be considered extraintestinal markers of silent and latent CD. Considering that most of CEC patients are from Mediterranean area (Italy and Spain) and Argentina, it may be hypothesized that CEC is a genetic, non-inherited, ethnically and geographically restricted syndrome associated with environmental factors. A genetic linkage between cryptogenic occipital epilepsy and CD may be, also, hypothesized in some cases of early onset occipital epilepsy. Preferential involvement of the occipital lobe still remains an unresolved issue. Although attractive, the attempt to correlate an hypothetical vascular vulnerability with the posterior localization of the vascular changes found both in Sturge Weber Syndrome and in CD with epilepsy and occipital calcifications is not sufficiently supported by the available data. All these data strongly suggest the opportunity of a neurological assessment in all patients with CD and the opportunity of CD assessment in all patients with neurological disorders of uncertain origin because of the really important above reported clinical implications.

Tuesday 30th August 2005
10:00 - 11:30
Salle 242AB
Parallel Session
Meeting the Challenges of Drug Resistance

Differentiating between Refractory and Pseudorefractory Epilepsy
P. Genton[1]

1) Centre Saint Paul - HHG, 13258, Marseilles, France.

Epidemiological studies have shown that refractory epilepsies represent ca 25% of all epilepsies. Refractoriness is a compound result with many factors and markers, which will be discussed elsewhere. While the syndromic approach to epilepsy diagnosis has highlighted the electro-clinical characteristics of refractoriness, studies now focus on individual, genetic factors of drug activity. However, clinical practice is often confronted with the puzzling question of the reality of refractoriness : in which circumstances can epilepsies be considered ' pseudo-refractory ' ? Refractoriness is when drug treatment does not significantly decrease the severity of epilepsy. Pseudo-refractoriness might be defined as a state where factors unrelated to the epilepsy intervene that cause seizures to occur in a patient who should respond to drug treatment. The most frequent causes of pseudo-resistance are the occurrence of non-epileptic seizures (NES), organic or psychogenic, and low compliance. Logically, NES do not respond to anticonvulsants. The diagnosis of NES may be difficult when EEG is abnormal and when there is a prior history of epilepsy, and should be systematically called to mind whether the patient has proven epilepsy or not. Low compliance has many causes, and is a major problem in patients with psychiatric conditions or in certain cultures (and we should keep in mind that economic factors may also play a part when anticonvulsants are unaffordable). External factors of refractoriness are multiple. Copathologies may render epilepsies difficult to control. In diabetes mellitus, hyper- or hypoglycemia may provoke seizures ; thyroid dysfunction (hyper- or hypothyroidism), hyper- or hypocalcemia, or a marked premenstrual syndrome in premenopausal women, may have the same consequences. Abuse ol alcohol, illicit drugs or psychotropic medication may also provoke seizures, and patients with psychiatric disorders who receive antidepressants or antipsochotics are exposed to lowered seizure threshold. Other drugs may provoke pharmacokinetic interferences. Sleep deprivation, which represents a major factor of drug resitance in some cases, may be a consequence of deviant lifestyle, but also of medical conditions, e. g. the sleep apnea syndrome. We must also keep in mind that (difficult-to-quantify and often hidden) psychological factors, leading to unhappiness and stress, may be sufficient to provoke refractoriness. Last but not least, an inadequate choice of anticonvulsants may be the major factor of refractoriness. A ' paradoxical ' refractoriness occurs because the treatment chosen is inefficient or, worse, aggravating. This may occur in some syndromes, but also, unexpectedly, on a more individual basis. A detailed clinical evaluation of the personal case of a patient should be made before epilepsy can be considered refractory. This is part experience, part common sense, and part knowledge - as most of clinical epileptology

The Medical Management of Drug Resistant Epilepsy: Challenging Commonly Held Dogmas
E. Perucca[1]

1) Clinical Pharmacology Unit, University of Pavia, Pavia, Italy

While more efficacious antiepileptic drugs (AEDs) are awaited to tackle the challenge of drug refractory epilepsy, the best way to minimize inadequate seizure control is to exploit at best available treatments. There are at times discrepancies between commonly held

opinions, and the scientific evidence which exists to support them. This presentation will deal with a number of topics where misperceptions are widely prevalent, by addressing the following questions: (i) what proportion of patients with newly diagnosed epilepsy respond to concentrations of AEDs below the 'therapeutic range' quoted in the literature? (ii) what proportion of patients unresponsive to low to moderate AED dosages achieve seizure control after increasing dosage further up to the limit of tolerability? (iii) does knowledge of mechanisms of AED action aid in the rational use of AEDs in the clinic? (iv) can monitoring of the serum levels of new generation AEDs be usefully exploited to improve clinical management? and (v) can epilepsy surgery be regarded as curative? It is hoped that increased awareness of these issues could eventually contribute not only to an improved clinical outcome, but also to the design of high quality studies in the many areas where gaps in knowledge prevent application of a truly evidence-based management.

Improving Quality of Life Beyond Seizure Control
S.C. Schachter[1]

1) Departments Of Neurology, Beth Israel Deaconess Medical Center And Harvard Medical School, Boston, Massachusetts, USA.

More than 50 years ago, Lennox and Markham urged physicians who treat patients with epilepsy to 'match modern drug and surgical therapy with practical sociopsychological therapy' and to be 'concerned not only with turbulent brain waves but with disturbed emotions'. Indeed, while seizure frequency and severity correlate with quality of life and psychosocial outcomes for patients with drug resistant epilepsy, numerous other epilepsy-related factors may also be significant determinants. These factors include medication related side effects (physical, cognitive and affective), sleep disorders, fear of seizure recurrence/seizure worry, fear of dying, mood disorders (especially depression and anxiety), behavior problems, academic difficulties, neuropsychological functioning, perceived and enacted stigma, self esteem and social adjustment, enjoyment of life, family dynamics/parental anxiety, vocational/employment status, autonomy/independence concerns, knowledge about epilepsy, self-mastery/self-management, and reproductive functioning and decision-making. Importantly, these epilepsy-related factors may be amenable to educational or therapeutic interventions, which if successful may benefit patients even without a concomitant reduction in seizure frequency or severity. Therefore, to improve quality of life beyond seizure control in patients with drug resistant epilepsy, physicians and other health care providers should comprehensively attend to these factors and refer patients, when appropriate, for further evaluation and treatment.

Tuesday 30th August 2005
10:00 - 11:30
Salle 251
Parallel Session
Epilepsy and Psychosis

Postictal psychosis
F. Leutmezer, Austria

Abtract not submitted

Psychosis and the Role of Amygdala
M. Trimble[1]

1) Institute Of Neurology, UK.

In recent times much interest has been expressed in the role of the amygdala in themodulation of memory and emotional behaviour. In this presentation the results of studies in patients with epilepsy and various forms of psychopathology will be discussed in which amygdala structure and function have been assessed using various imaging techniques. These data will be set alongside studies in non-epileptic patients with various psychiatric disorders in which the amygdala has been examined. It seems that in several forms of psychopathology particularly chronic affective disorders the amygdala is increased in size in comparison with controlled subjects, and this needs some explanation, particularly in epilepsy where other limbic structures such as the hippocampus are more likely to show no change of size or be smaller than comparison groups. This will lead into a discussion of neural plasticity in the central nervous system, and arguments as to the trait or state nature of these findings. There will also be discussion of the relevance of the findings in epilepsy with regards to what it tells us about psychopathology in epilepsy when compared with psychopathology in non-epileptic populations.

Transition between Episodic and Chronic Psychosis in Epilepsy
N. Adachi[1]

1) Adachi Mental Clinic, Japan.

The course and prognosis of a disease are essential matters for a full understanding of its nature. In the last few decades, these issues have seldom been taken into account in studies on epilepsy psychosis. As often pointed out, the lack of standard diagnostic criteria still prevents us from drawing a clear picture of the conditions. When diagnosing an epilepsy-related psychosis, 'postictal' and 'interictal' are terms often used to describe its chronological relation to epileptic seizures. In parallel, 'chronic' may be used in contrast to 'episodic' to describe its duration. These terms appear to be confused at times. As for postictal psychosis, most researchers have used duration of 1 month or less as an operational criterion. Accordingly, the term 'chronic postictal psychosis' is hardly used in practice. In contrast, as for interictal psychosis, there are a variety of cut-offs for 'episodic' and 'chronic' psychoses which have been set arbitrarily without supporting evidence. This situation has caused a vicious circle: the mixed usage of terms and inconsistent definitions keep us out from obtaining distributional data for their course, and this lack of evidence in turn does not allow us to set a reliable cut-off criterion. There is a high risk of recurrence in patients with epilepsy psychosis, particularly postictal psychosis. Among those with repeated psychoses, clinical features may vary from episode to episode. Fourteen (7.7%) of 180 epilepsy patients with psychosis showed postictal and chronic psychoses independently (Adachi et al. 2003). Furthermore, a transition from episodic (if < 1 month) to chronic (if > 1 month), or vice versa, occurred in approximately 20% of patients with epilepsy psychosis. The bilateral transition suggests that there may be common vulnerabilities for psychoses in epilepsy patients regardless of their modes or forms.

Anticonvulsants and Antipsychotics: Risks and Benefits
B. Schmitz[1]

1) Charité, Department Of Neurology, Berlin, Germany.

The aetiology of psychotic episodes in epilepsy is heterogenous, antiepileptic drug (AED) treatment representing a risk factor which is often not recognised. Studies suggest that up to 40% of consecutive cases with psychoses in epilepsy are iatrogenic, triggered by a change of AED treatment. The two main pathomechanisms for the development of AED induced psychoses are 'forced normalisation' in patients who become seizure free, and idiosyncratic effects related to the drug´s mode of action. The risk for psychotic drug reactions further depends on the patient´s predisposition (positive family history for psychiatric disorders and previous psychotic episodes increase the risk). Psychotic reactions may occur with all AEDs, however there are drugs which are associated with an increased risk such as phenytoin, topiramate, vigabatrin, tiagabine and zonisamide. The identification of drug induced psychosis in epilepsy is clinically relevant since these psychotic reactions are usually reversible with appropriate interventions; often lowering the dosage of the responsible anticonvulsant is sufficient. In most cases additional antipsychotic treatment is not necessary. The etiological relationship to AED treatment may be difficult to recognize when the psychosis develops gradually after longterm treatment (e.g. with phenytoin). Antipsychotics may and should be used in psychotic epilepsy patients if clinically indicated. The new generation of antipsychotics is not

associated with a clinically relevant proconvulsive risk. The only antipsychotic drug which should be avoided is clozapine because of the high proconvulsive property. Usually, in epilepsy patients antipsychotics are effective at relatively low dosages. Therefore titration should be performed carefully (start low, go slow), longterm treatment is often not necessary. Pharmacokinetic interactions are usually not a problem, however additive side effect profiles should be considered when combining AEDs with antipsychotics (e.g. weight gain).

Tuesday 30th August 2005
10:00 - 11:30
Salle 241
Parallel Session
Sodium Channel Epilepsies

Structure and Function of the Sodium Channel
A.L. Goldin[1]

1) Departments Of Microbiology & Molecular Genetics And Anatomy & Neurobiology, University Of California, Irvine, USA.

The voltage-gated sodium channel plays a critical role in regulating electrical excitability of the nervous system, being primarily responsible for the depolarization phase of the action potential. It is comprised of a large subunit that forms a functional channel whose properties can be modulated by association with one or more accessory subunits termed 1, 2, 3 and 4. The * subunit consists of four homologous domains termed I-IV, with six transmembrane segments called S1-S6 within each domain. Specific regions of the subunit are responsible for different functional properties of the channel. The fourth transmembrane segments (S4) in the four domains serve as the voltage sensors to initiate channel gating. The cytoplasmic linker connecting domains III and IV functions to inactivate the channel. The regions between the S5 and S6 segments in the four domains comprise the actual pore of the channel. Mutations in the genes encoding the sodium channel cause at least three different epilepsy syndromes including Generalized Epilepsy with Febrile Seizures Plus, Severe Myoclonic Epilepsy in Infancy, and Intractable Childhood Epilepsy with Generalized Tonic-Clonic Seizures. The mutations include single amino acid changes throughout the subunit, single amino acid changes in the 1 subunit, and truncations of the subunit. Consistent with the variety of alterations, the mutations have different effects on the properties of the channel, demonstrating that a similar epilepsy phenotype can result from many different changes in sodium channel function.

Epilepsy Syndromes with Sodium Channel Defects
I.E. Scheffer[1], Y.H. Zhang[1], J.M. McMahon[1], J.P. Malone[1], J. Pelekanos[1], S.F. Berkovic[1], J.C. Mulley[1], L.A. Harkin[1]

1) Epilepsy Research Centre, Heidelberg West, Australia.

Mutations in sodium channel subunit genes have afforded the first major clinical impact in the field of epilepsy genetics. The finding that mutations in SCN1A, the gene encoding the alpha-1 subunit of the sodium channel, underlie the epileptic encephalopathy of Severe Myoclonic Epilepsy of Infancy (Dravet Syndrome) and related phenotypes, allows the clinician to find a definitive etiology for patients with these devastating disorders. SCN1A mutations are found in around 80% of patients with SMEI and more than 90% of these mutations occur de novo. Thus the finding of SCN1A mutations in this cohort may obviate the need for invasive investigations looking for alternative etiologies. One of the most intriguing issues is the spectrum of phenotypes associated with sodium channel mutations. At the very severe end of the spectrum is SMEI but there are a number of intermediate phenotypes such as Severe Myoclonic Epilepsy of Infancy - Borderland, Intractable Childhood Epilepsy with Generalised Tonic-Clonic seizures, and Myoclonic-Astatic Epilepsy of Doose. At the very benign end of the spectrum, individuals with sodium channel defects may simply have febrile seizures. Many of these phenotypes come under the broad umbrella of the familial epilepsy syndrome, Generalised Epilepsy with Febrile Seizures Plus (GEFS+). GEFS+ is associated most commonly with febrile seizures and febrile seizures plus, which may be associated with other seizure types such as absence, myoclonic, atonic or partial seizures of temporal or frontal origin. More recent data shows that afebrile generalised tonic-clonic seizures alone may be part of the GEFS+ spectrum and there is some overlap with the classical Idiopathic Generalised Epilepsies. GEFS+ has been associated with mutations of sodium channel subunits SCN1A, SCN1B and SCN2A. It has also been associated with mutations of the gamma-2 subunit gene of the GABAA receptor. Sodium channel mutations are also important in the autosomal dominant seizure syndromes of infancy. In particular, Benign Familial Neonatal-Infantile Seizures (BFNIS) is associated with mutations of SCN2A, the alpha-2 subunit of the sodium channel. BFNIS occurs with a mean onset of three months and falls between the better known syndromes of Benign Familial Neonatal Seizures and Benign Familial Infantile Seizures. Many BFNIS families have an individual with neonatal seizures within the family but this is not always the case. These patients do not have GEFS+ phenotypes within families and BFNIS is a distinct entity. Ongoing work in genotype/phenotype correlation suggests that SCN1A mutations may have a broader range of phenotypes than currently understood. Further understanding of these correlations will certainly impact on our diagnosis and management of children and adults with severe epileptic encephalopathies.

Sodium Channel Mutations in Epilepsy Syndromes
E. LeGuern[1]

1) U679 INSERM And Neurogenetics Laboratory, Department Of Genetics, Cytogenetics And Embryology, Pitié-Salpêtrière Hospital, paris, France.

Epilepsies are frequent and heterogeneous neurological disorders determined by numerous factors of various origins2. The inheritance of epilepsies is usually thought to be complex or polyfactorial, resulting from an interaction between many genes and environmental factors. However, the identification of large families in which an epileptic trait segregated, demonstrated the existence of monogenic forms of epilepsy. In these cases, the phenotype is determined by a mutation in a major gene, although others genes with minor effects and environmental factors may modulate its expression, explaining incomplete penetrance or variable expression (in terms of age at onset, type and frequency of seizures, resistance to treatment….). Major advances in the genetics of epilepsy have been made in the past ten years. Nearly all concern epilepsies with a monogenic mode of inheritance, the least frequent of the inherited epilepsies. Progress has been spectacular in the idiopathic epilepsies, with the discovery that some of them may involve mutations in ion channels, leading to the concept of ' channelopathies '. Febrile seizures (FS) are frequent events, the genetic component of which is important. In some families, FS are associated with non-febrile seizures, constituting a new syndrome described in 1997 as ' Generalized Epilepsy with Febrile Seizures Plus ' (GEFS +). In this heterogeneous familial phenotype, some affected members often have multiple FS that persist beyond the age of 6, whereas other family members have classical FS that disappear before the age of 6. Variable non-febrile seizures are also observed. Initially, generalized seizures (tonic-clonic, myoclonic, atonic, absences seizures) were described, but hemiconvulsives, temporal or frontal seizures were later observed in other families. These afebrile seizures may begin in childhood in association with the FS, after a seizure-free period or later in life. Furthermore, not all affected members have FS. Several types of seizures can coexist in a given patient with more or less typical electroclinical features of generalized idiopathic epilepsies or myoclono-astatic epilepsy (Doose syndrome), but electroclinical patterns that don't correspond to the international classification of epilepsies are also observed. Some patients are intellectually disabled34. Outcome and pharmacosentivity are very variable in the same family. When available, neuroimaging is normal. This syndrome is transmitted as an autosomal dominant trait with incomplete penetrance, and is genetically heterogeneous. The first locus was localized on chromosome 19q13.1, and a mutation

in the SCN1B gene encoding the 1 subunit of the neuronal voltage-gated sodium channel was found in a single family. A second locus on chromosome 2q21-q33 seems to be more frequently implicated since several families have already been published. In two French families, two different mutations were identified in the SCN1A gene, which encodes for the 1 subunit of the same voltage-gated sodium channel. Functional studies in Xenopus oocytes have demonstrated that mutations in the 1 and 1 subunits interfere with the functional properties of the sodium channel. Although many mutations have been now reported in SCN1A and SCN1B, their responsibility was excluded in some families. The coding sequence of SCN2A, encoding the 2 sub unit of the same voltage-gated sodium channel was analyzed in some patients with GEFS+ and a mutation was found. Severe myoclonic epilepsy in infancy (SMEI) is characterized by generalized or unilateral clonic seizures, mainly febrile, that occur during the first year of life in a child with no previous psychomotor delay, followed later by myoclonic jerks and often partial seizures and absences. Psychomotor development is delayed from the second year of life and ataxia appears49. Although there is no evidence of brain damage in this disorder and MRI at onset is normal, the prognosis of this epileptic syndrome is very severe in terms of pharmaco-resistance and mental delay. Singh et al., (2001) have considered SMEI as a severe phenotype of GEFS+, particularly because of the presence of patients with SMEI in families with GEFS+. Molecular biological studies have provided new insight into the etiology of SMEI and confirmed this hypothesis. Indeed, Claes and coworkers (2001) identified seven de novo mutations in SCN1A in 7 sporadic cases of SMEI. The vast majority (5/7) of these mutations led to truncated proteins. More recent studies confirmed the high frequency of the mutations of SCN1A in SMEI, but to a lesser extent. Other genes are thus involved in this syndrome.

Neurobiology of Sodium Channel Epilepsies

E. Thomas[1], R. Xu[1], S. Petrou[1]

1) Howard Florey Institute, Parkville, Australia.

R85C and R85H mutations in SCN1B cause familial epilepsies including GEFS+. Standard electrophysiological analysis of mutant subunits co-expressed with SCN2A in HEK cells reveal hyperpolarised shifts in voltage dependence of both fast activation and fast inactivation and slow inactivation in the case of R85C. A hyperpolarizing shift in inactivation predicts hypo-excitability and a shift in activation predicts hyper-excitability. To predict the effect of combined changes in voltage sensitivity, we constructed Hodgkin-Huxley models of mutant and wild type subunits, which in turn, were incorporated into model neurons. Constructing models required data on the rate of slow inactivation over a range of voltages for which it has not previously been measured. This revealed that the 1 subunit does not effect the slow inactivation rate. Model construction also showed that the R85H mutation has more rapid fast inactivation than wild type and R85C. Simple neuron models made of a Na channel type, a fast delayed rectifier and a leak conductance were simulated. Rather than construct an average model for each Na channel type, neurons were simulated with Na models constructed from individual HEK cells and responses pooled. In response to current injection mutant subunits or SCN2A alone had lower thresholds and fired more action potentials than when wild type SCN1B was co-expressed. The R85H mutation was the most excitable because it lacked the partially compensatory hyperpolarizing shift in voltage dependence of slow inactivation. This approach enables the reconciliation of combined changes in biophysical properties to a single physiologically relevant descriptor.

Tuesday 30th August 2005
10:00 - 11:30
Salle 253
Parallel Session
Vocational Rehabilitation and Resective Surgery

Gaps in Psychosocial Intervention Around Epilepsy Surgery: The U.S. Case

R.T. Fraser[1]

1) University Of Washington Epilepsy Center, Seattle, USA.

The presentation will first overview epilepsy and employment issues as based upon a survey sent to 47 epilepsy centers in the summer of 2001 in the United States. A second survey was recently done specific to vocational intervention and how it is handled around the epilepsy surgery event. Reasons for the presence or absence of vocational services will be reviewed and the mechanics/structure of service delivery will be described when available at these sites. Finally, the development of a vocational services program within an Epilepsy Treatment/Surgical Center will be described both as to rationale (as perceived by surgical staff) and initial funding/staffing pattern. Concerns as to future directions in this needed area of service will be reviewed.

Vocational Rehabilitation in Relation to Epilepsy Surgery in Colombia

J. Fandiño-Franky[1], L. Salas[1]

1) Colombian League Against Epilepsy, Neurological Hospital - Institute For The Rehabilitation Of People With Epilepsy (FIRE), Cartagena, Colombia.

Purpose: The Colombian League against Epilepsy was founded in 1964. In September 1989 we started the epilepsy surgery program as an answer to our long experience in treating epilepsy. With this aim a neurological hospital as a non profit institution was built by the League, being able to present a minimum of international requirements necessary for epilepsy surgery. A peculiar situation of our country leaded the Colombian League to acquire properties, being probably the only in the world with this special modality. A rehabilitation department for people with epilepsy and a special program for patients operated on epilepsy surgery are part of our center. Nowadays about 50'000 patients with epilepsy are controlled and 640 epilepsy surgeries for the different forms of medically intractable epilepsy have been done. The great majority of these patients belong to the rehabilitation program. Methods: We took a total of 65 patients operated on since January 2000, when we begun with a new method for the rehabilitation of these patients. The vocational program is now based on the following criteria: The ablation of cerebral zones or the disconnection of areas leads to a lost of functions. In order to restitute as far as possible these functions it is necessary to use neuropsychological and pedagogical methods. We have rescued the theories of ENGRAM by Karl Spencer Lashley (1890-1958), defined by him as the fixation of knowledge in the brain. As the ablation or disconnection abolishes knowledge it is - previous to neuropsychological research - possible to transfer the lost knowledge to other regions of the brain. Three months after surgery, patients and their families are initiated to the first program by the group of vocational rehabilitation and receive training for these tasks. Every three month the patient is evaluated until a total of ten times. Every step is evaluated by a mathematic calculation in order to allow a percentage of his progress He also receives vocational rehabilitation, preparing him for domestic labors or adjutancy in small agricultural or family companies. Results: With this method we have been able to rehabilitate partial or totally the following patients: right temporal lobe 28; left temporal lobe 9; frontal lobe 6; frontal lobe and 2/3 callosotomy 3; callosotomy 13; hemispherectomy 6. Conclusion: If we compare the progress of the patients operated on before 2000 with those operated on after this date, we find that our present method is more efficient and fast, due to the exigency made to the rehabilitation staff in fixing progress goals previously.

Vocational Rehabilitation in Relation to Epilepsy Surgery at Bethel Epilepsy Centre, Germany
R. Thorbecke[1], S. Koch-Stoecker[1], B. Loer[1], T. May[1], U. Specht[1], A. Ebner[1], H.. Pannek

1) Bethel Epilepsy Centre: Dept. For Epilepsy Surgery & Dept. For Rehabilitation, Germany.

Purpose: The Bethel epilepsy surgery program exists since 1990. Patients get pre- and postoperatively psychosocial counseling. In 1997 rehabilitation was intensified: About 75% of the patients are transferred postoperatively to a rehabilitation department, where they also are prepared for vocational integration. If the patients at the 6 month control still have employment difficulties they are again transferred to the rehabilitation department to get support. Methods: Vocational outcome was assessed in Phase I 1991 - 1996 respectively Phase II 1998 - 2002 (N = 103/118; 56%/54% men; age 32,8/35,1 ; duration of epilepsy 21,3/22,2 y; Engel class I 61%/69%) two years after surgery. Results: Phase I: Unemployed pre 19% post 15% p = n.s.; disability pension pre 15% post 23% p=n.s.; unsatisfactory employment situation (rating social worker) pre 64% post 43% p <.001; quality of life improvement p=.01. Phase II: Unemployed pre 20% post 10% p= .02; disability pension pre 16% post 18% p=n.s.; unsatisfactory employment situation (rating social worker) pre 36% post 25% p <.001; no difficulties employment situation (rating patients) pre 40% post 75% p= .002; quality of life (work related) improvement p <. 001. Conclusion: It seems that the results after introduction of the specific rehabilitation program are better. However there might be a patient selection effect.

Factors Influencing Vocational Outcome of Epilepsy Surgery
H. Kubota, Japan

Abstract not submitted

Tuesday 30th August 2005
10:00 - 11:30
Salle 243
Parallel Session
Imaging Epilepsy in the Developing Brain

Epilepsy and the Developing Brain: the Clinical Problem
J.H. Cross[1]

1) Neurosciences Unit, Institute Of Child Health And Great Ormond Street Hospital For Children NHS Trust, London, UK.

Developmental changes in the brain provide challenges to epilepsy management in the very young. In many children presenting with early onset epilepsy, ongoing seizures are associated with developmental plateau or slowing. The exact pathophysiological mechanisms involved remain unknown. There is evidence that seizure control, whether from medication or surgery in many of the more severe epilepsy syndromes, is associated with better developmental outcome. The challenges within the epileptic encephalopathies however remain not only seizure control but also to what degree reversibility of any developmental compromise may exist, as well as distinguishing between the effect of seizures, medication and underlying pathology. Any suggestion of a focal onset to a seizure disorder requires further evaluation as to whether surgical resection of such a focus would lead to seizure control and therefore improved developmental outcome. This may prove a challenge in itself as localisation by seizure semiology and electrophysiology may be unclear. Further questions that remain unanswered however are the mechanisms involved in the more global effect of apparent focal disease on developmental progress, and at what stage intervention is optimal. There is also the question of the effect of early seizures on relocalisation of function in the developing brain. The exact degree of plasticity of brain function that is possible at what age remains unclear. We cannot presume eloquent cortex to reside away from abnormal brain in the context of seizures; issues of language dominance are often critical to surgical evaluation, and the relative contribution to age of onset of seizures, aetiology and possibly other factors also remain unknown. Many of these questions remain unanswered in the clinical setting. The modalities of imaging now available to us may help however to provide answers.

SPECT in Children with Epilepsy
A. Kaminska[1], C. Chiron[3], V. Bouilleret[4], M. Fohlen[5], O. Delalande[5], C. Soufflet[2], O. Dulac[3]

1) Groupe Hospitalier Cochin-Saint Vincent De Paul, Necker Enfants Malades, Paris, France. 2) Necker Enfants Malades, Hôpital Saint Anne, Paris, France. 3) Université Paris Descartes, INSERM U663 Et Hôpital Necker Enfants Malades, Paris, France. 4)Hôpital Kremlin Bicêtre, Paris, France. 5) Service De Neurochirurgie Fondation Ophtalmologique De Rothschild, Paris, France.

Surgical treatment of epilepsy in childhood is increasing due to major advances in structural and functional imaging as well as in EEG monitoring and surgical techniques. However it may be difficult to delineate the epileptogenic zone (EZ) especially under the age of 3 in children with apparently normal MRI and where ictal semiology is difficult to assess in terms of topography. Peri-ictal SPECT provides additional information to guide intracranial implantation in these patients. Its value for localizing the EZ correlates to other non-invasive methods (video-EEG, MRI) especially when using subtraction ictal-interictal SPECT co-registered with MRI (SISCOM) (90 % in temporal and 70-85 % in extra-temporal epilepsy). Studies comparing the SISCOM localisation (maximal increase of perfusion) with the site of cortical resection in children who recovered after surgery, showed good agreement in about 70-80 % of cases. In the remaining patients, SISCOM probably misses the EZ and shows the area of propagation, even with early ictal injection. Since it shows the whole brain, ictal SPECT may contribute to a better understanding of the pathophysiology of seizure propagation in pediatric patients. In contrast, interictal SPECT is a better method to study the impact of epilepsy on the developing brain. Focal hypoperfused areas are detected in the regions including the EZ and the propagation, corresponding well to the predominant cognitive deficit of children. SPECT imaging contributed to a better understanding of some specific neuropsychological disorders associated with childhood epilepsy such as aphasia, dyspraxia or frontal syndrome. Cerebral blood flow defect may decrease or even disappear when the corresponding cognitive performances improve or even recover. Using dynamic SPECT, it is also possible to study the functional value of each cerebral hemisphere in hemimegalencephaly (HME), a unique model of unilateral and highly epileptogenic lesion. Function of the non-malformed hemisphere is rapidly impaired often within the first months (due to the contralateral propagation of the epileptic discharges), but can be restored after surgery. These data support the recommendations to operate on the children suffering from such a lesional epilepsy as early as possible.

PET Imaging of the Effect of Epilepsy on the Child's Brain
C. Juhasz[1], H.T. Chugani[1]

1) PET Center, Children's Hospital Of Michigan; Pediatric Neurology, Wayne State University School Of Medicine`, Detroit, USA.

Positron emission tomography (PET) studies have improved pre-surgical localization of epileptic foci in children with intractable epilepsy and are also useful to assess the detrimental effects of epilepsy on the developing brain. Glucose PET often demonstrates cortical (and subcortical) hypometabolism extending beyond the EEG-defined seizure onset zones and is useful to evaluate the functional integrity of the entire brain, including non-epileptic areas. This information is helpful to predict post-surgical cognitive outcome: children with bilateral hypometabolism involving homologous areas may have a poor chance for cognitive improvement even if structural abnormalities on MRI are unilateral and the seizures improve following resection of the primary epileptogenic region. The cognitive effects of epilepsy surgery also depend on the underlying pathology:

children with unilateral involvement (e.g., Rasmussen's encephalitis or most cases of Sturge-Weber syndrome) may respond better than those with more widespread pathology (e.g., multifocal cortical dysplasia or hemimegalencephaly; the latter often has some involvement of the opposite hemisphere). Patients with frequent seizures tend to have larger areas of cortical hypometabolism and are more likely to have decreased binding of GABAA receptors (as measured by 11C-flumazenil PET) remote from the primary epileptic foci. These changes are likely attributed to the effects of seizures involving the affected areas as either sites of seizure onset or via seizure propagation, as detected by intracranial EEG. Some of the metabolic abnormalities progress over time if the seizures persist; early resective epilepsy surgery may prevent such a progression and facilitate brain development. On the other hand, longitudinal PET studies also demonstrated that at least some of the cortical hypometabolism may be reversible and may recover, indicating functional normalization, if the seizures come under control. Whether these metabolic improvements are reliable predictors of concomitant restitution of cognitive or behavioral functions, requires further, prospective studies. PET studies combined with neuropsychological data remain an important clinical approach to assess and quantify the effects of seizures on the developing brain and to guide clinical management aimed at minimizing cognitive and behavioral consequences of chronic epilepsy.

Imaging Pediatric Functional and Structural Anatomy with MRI
W.D. Gaillard[1,2]

1) Neuroscience Department, Children's National Medical Center, George Washington University, Washington DC, USA. 2) Clinical Epilepsy Section, NINDS, NIH, Bethesda, MD, USA.

MRI provides the ability to image the effect of childhood epilepsy on brain structure and function. Structural MRI demonstrates signal changes following prolonged localization related seizures, and has been used to follow the evolution of mesial temporal sclerosis. These studies show that MTS is present early in the course of epilepsy, typically before age five and can be identified during the first year of life. In limited series, MRI also shows evidence of progressive atrophy in association with continued complex partial, generalized seizures, or status epilepticus. Larger cross sectional studies show evidence of grey and white matter volume loss beyond temporal lobe, including projections from the ipsilateral hippocampal formation. These studies provide some evidence that, in some circumstances, epilepsy may be a progressive degenerative disease. Functional MRI (fMRI) demonstrates the effect of epilepsy on functional reorganization of higher cognitive functions. fMRI language tasks identify the areas that mediate expressive speech processing in the left inferior frontal and mid frontal regions, and the areas that mediate receptive language processing in the temporal cortex along superior temporal sulcus. Studies in patients with childhood onset epilepsy demonstrate atypical language representation in one quarter of patients. Reorganization of language functions occurs within a broad distributed network for language processing that includes homologous regions in the right hemisphere. It is uncommon to find activation outside these areas. There is fMRI imaging evidence that temporal lobe epilepsy also has local, remote, and non-specific effects on language activation maps. Atypical language is associated with better language measures. Factors associated with atypical language include early brain insult (before age 6), including early seizure onset, atypical handedness (in this setting interpreted as evidence for early brain insult), and congenital/acquired structural lesions such as stroke, mesial temporal sclerosis, tumors, and dysplasia. There is evidence for functional re-organization, in diminishing capacity, in later childhood. Both epilepsy and other pathological factors that serve as the remote cause for epilepsy appear to play important roles in language reorganization during the critical period of language network development and consolidation in early childhood.

Can we Image Epileptogenesis?
W.H. Theodore[1]

1) Clinical Epilepsy Section, National Institutes Of Health, Bethesda, MD, USA.

The possibility of epilepsy prevention, as well as treatment, must be based on better knowledge of the process of epileptogenesis. What are the underlying structural and functional conditions that predispose to the onset of seizures, and to the differential vulnerability among brain regions? Are these factors, perhaps genetic, present, but dormant, in patients who never develop overt epilepsy? Epileptogenesis may occur silently over a prolonged period, at several levels of structural or functional integration: cellular, microsystem, macrosystem. The challenge for imaging is to relate a functional disorder based on altered cellular structure to identifiable abnormalities, at millisecond and micron resolution, combining imaging and electrophysiologic data. Approaches using small animal models have already produced valuable data. These Animal models could be used to compare groups of animals that develop frequent seizures, rare seizures, or no seizures after stimulus-evoked status epilepticus, or a putative subclinical epileptogenic stimulus. Imaging gene expression may be a fruitful potential approach. For human applications, multicenter studies will be essential. These should be driven by specific clinical hypotheses, rather than application of new technology for its own sake. There are additional crucial issues: is epilepsy a progressive disease, and do persistent seizures cause neuronal injury? The results of clinical studies are inconclusive. Cross-sectional, and limited longitudinal human studies have shown volume reductions ipsilateral to the epileptic focus in hippocampal and extrahippocampal regions; the former, in cross sectional studies, increase with increasing epilepsy duration. Other factors associated with increasing hippocampal atrophy include a history of complex or prolonged febrile seizures, and generalized tonic-clonic seizure number. Positron emission tomography has shown supporting results. Imaging offers as excellent opportunity to link clinical investigation to epilepsy models. Appropriate manipulation of experimental conditions in animal imaging studies may be able to answer some of the important questions raised by human data.

Tuesday 30th August 2005
13:30 – 15:00
Salle 242AB
The Global Campaign Against Epilepsy
The Global Campaign Against Epilepsy: Looking Backward and Looking Forward

The ILAE/IBE/WHO Global Campaign Against Epilepsy
H.M. De Boer[1], J. Engel Jr.[1], L.L. Prilipko[1]

1) SEIN, WHO Collaborating Centre For Research, Training And Treatment In Epilepsy, Heemstede, The Netherlands.

Since 1997 ILAE, IBE and WHO have been working in partnership in the ILAE/IBE/WHO Global Campaign 'Out of the Shadows' with as its mission statement: to improve the acceptability, tratment, services and prevention of epilepsy worldwide The strategy of the Campaign is: I. To provide platform for general awareness and II. To assist Departments of Health in the development of a national epilepsy strategy After an initial awareness raising phase the Campaign, in its second phase, is engaged in the initiation and implementation of Demonstration Projects in all WHO Regions. A number of these projects have already been completed and the results thereof will be discussed during this symposium. Furthermore the Campaign has been engaged in the WHO Atlas Project on country resources for epilepsy and a survey questionnaire was developed covering the profile of epilepsy resources available on the country level. Regional Reports on Epilepsy have been prepared or are being prepared in all WHO Regions containing basic knowledge on epilepsy and the basic facts on the epidemiological burden. The reports are advocacy tools and function as instruments for dialogue.. Finally the Campaign is involved in: the Collaborative Research On Epilepsy Stigma Project -

CREST - which is founded through a grant from the NIH - Fogarty grant. A progress report on all of the above activities will be given. Now the Campaign is entering its 3rd phase and a strategic planning meeting took place, involving the Joint Executive Committee of IBE and ILAE and other stakeholders in order to plan and initiate the Campaign's future activities. The results thereof will be reported.

Regional Reports
S. Li[1], H.M. De Boer[1]

1) China Association Against Epilepsy, Global Campaign Secretariat, China.

Introduction During this presentation the background and the development of Regional Reports on Epilepsy will be discussed. Regional Reports are a series of similar publications that have been developed jointly by the Regional Offices of WHO, WHO Headquarters, ILAE and IBE chapters and the Global Campaign Secretariat. The reports provide a panoramic view of the epilepsy situation in the Regions, outline the initiatives taken to address the problems, define the current challenges and offer appropriate recommendations. Furthermore the reports include data collected through a questionnaire on country resources for epilepsy which was developed by a group of experts with the aim to map the resources for epilepsy world-wide. The data was collected with the help of IBE and/or ILAE members and WHO member states. Purpose The reports are meant to be political tools and aim at assisting with dialogues with governments, health care providers and others, and will serve as potent advocacy tools for dialogue with governments, health care providers and other interested parties this bringing epilepsy 'out of the shadows' in all WHO Regions. The reports introduce both the lay reader and the professional to epilepsy, which affects more than 50 million people world wide, thus making this medical condition an important public health problem. Conclusion The reports provide panoramic views of the epilepsy situation in the Regions, outline the initiatives taken by WHO and its partners ILAE and IBE to address the problems, define the current challenges and offer appropriate recommendations.

Atlas: Epilepsy Care in the World
T. Dua[1], H.M. De Boer[1], L.L. Prilipko[1]

1) World Health Organization, Geneva, Switzerland.

The information about resources available within the countries to tackle the huge medical, social and economic burden caused by epilepsy is lacking. To fill this information gap, a survey of country resources available for epilepsy care was conducted within the framework of GCAE 'Out of the Shadows' under WHO's Project Atlas. The study represents a major collaborative effort involving WHO Headquarters, Regional and Country Offices, ILAE and IBE Headquarters and their members. Data collection Data was collected in the form of a questionnaire from key persons identified by official delegates of member chapters of ILAE/IBE or WHO regional and country offices. Countries were grouped into the six WHO regions and four World Bank income categories. Data organization and presentation The Atlas presents information from 159 WHO Member States, areas and territories representing 97% of the world population. The information is presented in 4 broad sections; Epilepsy: the disorder; the services; the care-providers; and the public health aspects. The data included is organized in 17 themes and is presented as graphics, world maps and written text. The results are presented as global, WHO regions and income categories within each theme. Limitations specific to each theme are to be kept in mind when interpreting the data and their analyses. Selected implications of the findings are highlighted with each theme. It also includes brief reviews of selected topics summarizing the medical, lifestyle, social and economic issues surrounding people with epilepsy. Conclusions The results confirm that epilepsy care is grossly inadequate compared to the needs in most countries. The value of the Atlas is in replacing impressions and opinions with facts and figures. We hope that the realities uncovered by the Atlas will motivate governments and health care providers to improve epilepsy care.

Partners in Health
G. Birbeck[1], R. Baskind[2]

1) Michigan State University, Departments Of Neurology, Epidemiology & African Studies, Chikankata Health Services Epilepsy Care Team, Mazabuka, Zambia. 2) McGill University, Department Of Neurology & Neurosurgery, Montreal, Canada.

The relationship between physicians and traditional healers (TH) has long been one of misunderstanding and distrust. These attitudes were initiated to some extent by colonial authorities who employed expatriate physicians and enacted legislation making the practice of traditional medicine illegal. The animosity has been reinforced by iatrogenic complications witnessed by each group as well as market forces placing healers and physicians in direct competition. The importance of THs in healthcare provision in Africa should not be underestimated. Almost all people with epilepsy (PWE) who seek care from physicians are simultaneously receiving traditional therapies, too. TH care has the advantage of being more accessible geographically for most PWE and the etiologic explanations provided to PWE and their families by the traditional healer is consonant with their native beliefs. Among important social entities in Zambia (teachers, clerics, police), more than 30% would recommend that someone with epilepsy go to a TH for care. Furthermore, the AIDS epidemic is fueling activists and health policy makers into mainstreaming TH care or at least recognizing it as one component of the formal healthcare system. Within rural Zambia, the Chikankata Epilepsy Care Team (ECT) has been working with THs to develop a professional dialogue to allow us to improve the care of PWE in the region. Through community-based meetings, focus group discussions, and ethnographic studies, we have begun to develop a better understanding of TH epilepsy care. Important findings from this work include: (1) Traditional healers' care tends to focus upon acute rather than chronic management. Healers are very willing to refer people with uncontrolled, frequent seizures to the Epilepsy Care Team for management. (2) For people who experience a first seizure or rare seizures, the healers' 'curative' approach to care allows the patient to avoid epilepsy-associated stigma and return to the social fold as 'normal.' (3) Where contagion beliefs are common, healers offer treatment to family members to protect them from contracting the disease. This may increase the protective assistance provided to PWE when they experience a seizure. (4) Among people with non-epileptic, psychogenic seizures, THs provide interventions aimed at the entire community, which are often effective. (5) Herbal remedies for seizures prescribed by THs warrant investigation for their potential anticonvulsant properties. As a consequence of this TH-physician dialogue, collaborative relationships that benefit PWE have evolved. THs will be important in future interventions aimed at decreasing epilepsy-associated stigma and narrowing the treatment gap in Zambia.

Surgery in Countries with Limited Resources
J. Engel Jr.[1]

1) UCLA, Los Angeles, CA, USA.

Surgery has been an accepted alternative treatment for epilepsy for over 100 years, and is now widely applied in industrialized countries. For patients with surgically remediable epilepsy syndromes in these countries, 70- to 90% can expect to become seizure free postoperatively; however, 90% of patients with medically refractory epilepsy live within the developing world, where surgical treatment is rarely performed. Surgery has not been considered a feasible approach to addressing this overwhelming health burden because of the belief that it is an expensive high technology-bound therapy beyond the means of countries with limited resources for health care delivery. This is an erroneous assumption because advances in presurgical evaluation that have led to new, more cost-effective approaches in the industrialized world are being successfully applied,

at a greatly reduced cost, in a number of so-called developing countries, including China, India, Turkey, and Brazil, with results similar to those in the industrialized world. The most important investment for epilepsy surgery centers in developing countries, as for industrialized countries, is in properly trained personnel. Establishing a critical mass of multidisciplinary experts requires commitment but is relatively inexpensive. Most developing countries can afford at least one medical center with the required MRI and video-EEG monitoring unit. Those that cannot may be able to work with neighboring countries to develop regional centers serving several countries. These centers could then limit their practice to patients with surgically remediable syndromes, such as mesial temporal lobe epilepsy, who can be easily diagnosed noninvasively and have the greatest potential for becoming seizure free postoperatively. When these patients fail to respond to one or two appropriate antiepileptic drugs, surgical treatment in countries with limited resources may be more cost-effective than continued pharmacotherapy.

Phenobarbital in Newly Diagnosed Epilepsy
M.J. Brodie[1]

1) Epilepsy Unit, Western Infirmary, Glasgow, Scotland, UK.

Phenobarbital (PB) is the most widely used antiepileptic drug (AED) in the developing world and remains a popular choice in many industrialized countries. Its advantages include ease of use with once daily dosing, reliable supply and affordable cost. For these and other reasons, it is recommended by WHO as first-line for partial and tonic-clonic seizures in developing countries, where up to 85% of patients do not currently receive any treatment. Meta-analyses of randomized controlled trials suggest that few differences in efficacy exist between PB and other established AEDs1. However, PB's purported adverse effects on behaviour and cognition, quantified in randomized controlled trials in industrialized countries, have raised genuine ethical concerns. Yet the drug was well tolerated in open-label studies performed in developing countries, although some of these had serious methodological deficiencies. A possible explanation for this discrepancy in the tolerability of PB could be the dose, which tended to be higher in trials undertaken in developed than in developing countries. Recent longterm outcome in newly diagnosed epilepsy suggest that the majority (>90%) of patients who enter remission on their first ever monotherapy require no more than a modest or moderate drug dose2. This could account for a comparable degree of efficacy with lower doses of PB used in open label studies in developing countries, while avoiding the excessive toxicity associated with the higher doses employed in randomized trials in developed countries. It is not known either whether pharmacogenetic differences exist in PB's tolerability among people from different ethnic backgrounds, or whether patients in the developing world are more likely to tolerate adverse effects because they have little choice in AED treatment. A pragmatic, comprehensive outcomes study is needed to optimize the efficacy and tolerability of low-dose PB, so that many more people around the world can benefit from this cost-effective medication and live more fulfilling lives.

References

1. Kwan P, Brodie MJ. Phenobarbital for the treatment of epilepsy in the 21st century: a critical review. Epilepsia 2004;45:1141-49
2. Mohanraj R, Brodie MJ. Pharmacological outcomes in newly diagnosed epilepsy. Epilepsy Behav 2005;6:382-7

Tuesday 30th August 2005
14:15 – 15:15
Grand Amphitheatre
Main Session
Epilepsy Genes: Exploring Function and Clinical Significance

Epileptogenesis in Monogenic Epilepsies
S. Berkovic, Australia

Abstract not submitted

Does the Gene Predict Prognosis?
O. Dulac, France

Abstract not submitted

Tuesday 30th August 2005
15:30 - 17:00
Amphitheatre Bleu
Post Main Session
Epilepsy Genes: Complex Inheritance

Genetic Epidemiology: Insights into Inheritance of Epilepsy
R. Ottman[1]

1) G.H. Sergievsky Center And Department Of Epidemiology, Mailman School Of Public Health, Columbia University, New York, USA.

Great progress has been made in the discovery of genes that influence risk for some forms of epilepsy. However, most gene discoveries to date have been in epilepsies with Mendelian modes of inheritance, which comprise only a tiny fraction of all epilepsies. The great majority of all epilepsies are genetically complex--multiple genes contribute to their etiology, none of which has a major effect on disease risk. Gene discovery in the genetically complex epilepsies is a formidable task. Defining the phenotypes most advantageous to study, and localizing genes and mutations are much more difficult than in Mendelian epilepsies. Allelic association studies are promising for the identification of complex epilepsy genes, but we are still in the earliest stages of their application. In the genetically complex epilepsies, well-designed genetic epidemiologic studies can provide information about phenotype definition, mode of inheritance, and familial risk that is crucial for both molecular genetic research and genetic counseling.

Why is it Difficult to Find Genes in Common Idiopathic Epilepsies?
M. Gardiner[1]

1) Department Of Paediatrics, University College London, London, UK.

Common familial idiopathic epilepsies are 'complex' traits. This term implies that their genetic aetiology arises from the combined effects of susceptibility alleles in multiple genes which act to alter seizure threshold. This mode of inheritance is quite distinct from that of mendelian (monogenic) traits in which any one of a number of highly penetrant (major effect) alleles at any one of a number of single genes is necessary and sufficient to generate the phenotype. Positional cloning strategies which have been so successful in identifying genes for such monogenic disorders are not easily applicable to 'complex' traits. Strategies such as linkage and association depend for their success on the underlying 'genetic architecture' of these traits which remains uncertain. Critical parameters include the number, effect size and mode of interaction of susceptibility genes and the frequency and diversity of susceptibility alleles at these genes. The spectrum of possible architectures ranges from favourable - few genes of moderate effect, with susceptibility alleles of high frequency (5-10%) and low diversity, to the unfavourable scenario of multiple genes of small effect harbouring a very diverse collection of low frequency (<1%) susceptibility alleles. Potential lack of correlation between phenotype and genotype is an additional difficulty. It can however be assumed that the causative alleles are amongst the millions of single nucleotide polymorphisms (SNPs) which account for most variation in the human genome. Many published association studies in the epilepsies have lacked power to identify their genetic aetiology even under the most favourable assumptions. Recent advances in documenting the pattern and distribution of SNPs in the human genome, together with the technology required for high throughput genotyping, should allow successful analysis if sufficiently large collections (>500) of well characterized patients can be phenotyped, sampled and typed for thousands of SNPs.

Advances in Polygenic Idiopathic Generalized Epilepsies
J.M. Serratosa[1]

1) Epilepsy Unit, Fundacion Jimenez Diaz, Madrid, Spain.

Although several major genes for the idiopathic generalized epilepsies (IGEs) have been identified and biologic functional effects suggested based on these findings, these genes account for only a very small proportion of IGE cases. Multifactorial or complex inheritance appears to be responsible for most forms of IGE. Several gene polymorphisms have been associated with the IGEs in case-control studies but none have been convincingly confirmed and the final biologic functional effect or significance of these variations has not been established. Moreover, positive genetic associations are reported and, frequently, conflicting negative results communicated soon afterwards. New methodologies and working strategies in the field of genetic studies of complex diseases are needed before the genes and mechanisms involved in the pathogenesis of the common IGEs are unraveled. The question remains on how many genes are involved, how important the effect of each is and how to detect them. In the future association studies that are genome-wide and complete genome sequencing in large populations of cases and controls offer the greatest promise to advance in our understanding of the genetic basis of common idiopathic generalized epilepsies.

Wednesday 31st August 2005
07:30 - 08:30
Salle 252AB
Morning Seminar
Temporal Lobe Epilepsy in Children

Temporal Lobe Seizures in Children: are they the Same as in Adult Patients?
E. Wyllie[1]

1) The Cleveland Clinic Foundation, Cleveland, Ohio, USA.

In adults, temporal lobe epilepsy is a rather homogenous entity, almost axiomatic with hippocampal sclerosis. Hallmarks include seizures with altered awareness and automatisms, in the setting of anterior temporal ictal and interictal epileptiform discharges. Hippocampal sclerosis, when present in children, is usually associated with dual pathology such as cortical dysplasia in the temporal pole; but this etiology is overshadowed by other developmental lesions including tumors and malformations of cortical development. These lesions tend to involve extensive extramesial temporal areas, and result in diverse presentations due to complex age-related interactions between the epileptogenic lesion and normal brain maturational processes. For example, infants with temporal lobe lesions may present with bland hypomotor seizures, infantile spasms, or seizures with other complex semiology. Automatisms are simple at a young age and grow increasingly complex and elaborate with age. Lateralizing clinical signs are infrequent in infants, and ictal and interictal EEG features may be poorly localized. Very young children with focal epilepsy, including temporal lobe epilepsy, may present with clinical and EEG features that are non-partial or generalized in character. Recognition of these diagnostic challenges is important for identification of pediatric patients who may be rendered seizure free after epilepsy surgery.

Early Surgery in the Mesio-temporal Lobe Epilepsy Syndrome : is it Realistic?
M. Duchowny, USA.

Mesial temporal lobe epilepsy (MTLE) is widely recognized to be a pharmaco-resistant disorder that begins in early life. Although pediatric MTLE constitutes a smaller proportion of chronic epilepsy compared to adults, it nonetheless mandates definitive treatment. It is preferable to operate as early as possible- infants with MTLE may have catastrophic seizure presentations. Several features differentiate young surgical candidates from adults with mesial temporal lobe seizures. Seizure onset in the first decade of life, especially infancy, may be associated with arrested development or frank regression. The pathological substrate of mesial TLE in young children differs significantly from adults in that developmental rather than acquired or neoplastic lesions predominate. Hippocampal sclerosis, the most common pathology in adult temporal lobe specimens, is routinely detected in pediatric patients but is often associated with developmental anomalies of the temporal neocortex. Lastly, the clinical semiology and electrographic features of MTLE exhibit age-specific patterns that may be difficult to identify on preoperative evaluation. For these reasons, the surgical evaluation relies heavily on video/EEG monitoring of ictal and interictal electrographic patterns and careful study of ictal semiology. Older children with MTLE usually show a buildup of rhythmic theta or delta activity over one temporal lobe ('adult pattern') whereas younger patients are more likely to demonstrate low voltage fast frequencies or poorly localized sharp waves. MR imaging utilizing high field strength magnets assists in the detection of subtle cortical malformations, while functional imaging with ictal SPECT has been used to localize or confirm seizure origin. More recently, functional MRI has been employed successfully in school-age or older children to define language cortex in the dominant temporal lobe. Invasive monitoring with subdural electrodes may be required to further localize seizure origin in non-lesional cases, or to confirm receptive language sites. Surgery usually involves tailored temporal lobe resection rather than en bloc amputation of the anterior temporal tip. Seizure-freedom is possible in 60-70% of infants and children undergoing tailored temporal resections. The occurrence of postoperative compromise of verbal memory performance in children undergoing temporal resection for MTLE is controversial.

Wednesday 31st August 2005
07:30 - 08:30
Salle 251
Eurepa Session - Diagnostic Issues 3
Is It Non-Convulsive Status?

Is it Non-convulsive Status?
S. Shorvon[1], H. Hogenhaven[2]

1) Department Of Clinical Neurology, Institute Of Neurology, University College London, London, UK. 2) Dept. Of Clinical Neurophysiology 3063, Neuroscience Center, Copenhagen University Hospital, Rigshospitalet, Denmark.

In the light of the more widely use of continuous EEG recording (cEEG) to monitor the critically ill neurological patients it is likely that clinicians will be faced with the question 'is it non-convulsive status epilepticus ' more often than now. A clinical overview of the classification systems(s) of status epilepticus will be given with emphasis on non-convulsive types and their management. Examples of common non-convulsive EEG-seizure patterns will be presented. The electro-clinical classification of the different EEG-patterns of periodic discharges (PEDs) will be given with emphasis on periodic lateralized epileptiform discharges (PLEDS) and generalized periodic epileptiform discharges (GPEDs), and diagnostic and treatment strategies will be discussed.

Wednesday 31st August 2005
07:30 - 08:30
Salle 241
Eurepa Session - Treatment Issues 3
Treating Epilepsy In The Absence Of Randomized Trials

Treating Epilepsy in the Absence of Randomized Trials
M.J. Brodie, UK

Abstract not submitted.

Treating Epilepsy in the Absence of Randomized Trials
R. Kuba, Czech Republic

Abstract not submitted.

Wednesday 31st August 2005
07:30 - 08:30
Salle 243
Morning Seminar
Novel Neurons and Novel Synapses in the Epileptic Tissue

Novel Neurons and Novel Synapses in the Epileptic Tissue
T. Sutula[1], N. Schloemer[1], J. Shanton[1], S. Dustin[1], R. Qazi[1]

1) Institution Details: Dept Of Neurology, University Of Wisconsin, Madison, WI, USA.

The dentate gyrus is prominently reorganized in the epileptic human hippocampus and in experimental models of epilepsy. The reorganization includes alterations in membrane receptors, cell death, gliosis, neurogenesis, axon sprouting, and synapse formation including novel synapses that modify connectivity. These cellular alterations can be induced by initial injury or various etiologies, and are also acquired in a predictable sequence as a result of repeated seizures, which induce gradually evolving changes in the proportions of inhibitory and excitatory synapses converging on dentate granule cells. In experimental models, spontaneous seizures are observed when there is a critical shift in the proportion of inhibitory to excitatory synapses. As the dentate gyrus functions as a 'gate' that 'filters' converging activity into the hippocampus, reorganization of the proportion of inhibitory and excitatory synapses on granule cells is likely to be an important determinant of hippocampal epileptogenesis and an influence on intractability in established epilepsy.

Aberrant Kainate Receptor-Mediated Synaptic Transmission in Hippocampal Granule Cells in a Model of Temporal Lobe of Epilepsy
V. Crépel[1], J. Epsztein[1], A. Represa[1], I. Jorquera[1], Y. Ben-Ari[1]

1) INMED, INSERM U.29 & Université De La Méditerranée, Marseille, France.

In both human patients and animal models of temporal lobe epilepsy (TLE), glutamatergic fibers sprout and establish novel synapses leading to an enhanced glutamatergic excitatory drive that may contribute to seizure generation. In epilepsies, hippocampal glutamatergic mossy fibers sprout and establish aberrant synapses on Granule Cells (GCs) from which they originate. Despite the important role of kainate receptors (KARs) in synaptic transmission at control mossy fiber synapses, it is at present not known whether recurrent mossy fibers trigger the expression of functional KAR-operated synapses following sprouting to aberrant targets. We report that the sprouting of mossy fibers onto granule cells in the pilocarpine model of TLE leads to the formation of KAR-operated synapses that are not present in control granule cells. These EPSCKA have slow kinetics and play a key role in the ongoing synaptic activity since they represent half of the non-NMDARs-mediated glutamatergic transmission in these cells. Together with AMPARs, KARs also contribute to the generation of epileptiform bursts since their blockade reduce the severity of these bursts evoked in the dentate granule cell layer. Our observations show that in addition to axonal rewiring -that leads to a recurrent excitatory circuit- mossy fiber sprouting provides the granule cells of epileptic animals with a modified kinetics repertoire for glutamatergic currents that may contribute to the physiopathology of the epileptic dentate gyrus.

Wednesday 31st August 2005
08:45 - 09:45
Grand Amphitheatre
Main Session
Health And Disease: a Cross-Cultural Approach

Health and Disease: a Cross-Cultural Approach
A. Kleinman[1]

1) Harvard University, Boston, USA.

Epilepsy, like other chronic disorders, needs to be understood in a global perspective that frames health and disease in comparative cross-cultural terms. The lecture will introduce key concepts from medical anthropology such as the distinction between illness (the patient and family's experience of symptoms and impairment) and disease (the physician and researcher's understanding of the pathophysiology); the arena's model of health care systems; the cultural differences in the meaning of suffering; the local world context of moral experiences of illness; the impact of globalization on these experiences and practices; new theories of stigma and its consequences. Epilepsy will be examined in these contexts, and, drawing from my own research experience in China, with special attention to Chinese. Finally, I will put epilepsy in the perspective of global brain disorders, including both neurological and neuropsychiatric conditions, in order to demonstrate the burden of disease, disability, and constraints on treatment and rehabilitation in low and middle income countries. Emphasis will be put on the policy relevant issues for global epilepsy health care policy.

Wednesday 31st August 2005
10:00 - 11:30
Amphitheatre Bleu
Post Main Session
Epilepsy Management with Limited Resources

Cost of Epilepsy and Selecting Cost-effective Treatment
E.M.T. Yacubian[1], C. Nasser[1], C. Nobre[1], R. Muzskat[1], G. Chermont[1], M. Bossi Ferraz[1]

1) Escola Paulista De Medicina / UNIFESP, Brazil.

Knowledge of medical and surgical costs of the treatment of epilepsy in developing countries, where 90% of the costs generated by epilepsy are produced, will allow adequate distribution of scarce health care resources. Chisholm, on behalf of WHO-CHOISE, recently addressed medical costs in the developing world (Epilepsia 2005; 46(5): 751-59). Across nine developing WHO sub regions, extending antiepileptic drug treatment coverage to 50% of primary epilepsy cases would avert between 150 and 650 DALYs per one million population (13-40% of the burden of epilepsy), at an annual cost per capita of I$ 0.20-1.33. Phenobarbital and phenytoin were more effective than carbamazepine and valproate on account of their similar efficacy yet at a lower acquisition cost. On the other hand, surgical therapy may represent an alternative for refractory epilepsy but is considered very expensive. However, epilepsy surgery is a reality in about 28 developing countries (Wieser and Silfvenius, 2000). Cost of anterior temporal lobectomy (ATL), including initial outpatient evaluation and average total pre and surgical protocol cost was estimated at US$ 38,500 per patient in the US (King et al., 1997) and 24.169 E in France (Picot et al., 2004). In these series, 53% (plus 16% with auras) and 83% of the patients, respectively, were seizure free at the first year of follow-up. We report costs and results of ATL of 50 patients with refractory epilepsy related to mesial temporal sclerosis (MTS) consecutively operated on at UNIFESP, a University Epilepsy Center in São Paulo, Brazil. Direct medical and nonmedical costs as well as indirect costs measured in physical units and intangible costs assessed with quality-of-life measures (SF-36) were evaluated. All patients had non-invasive presurgical protocol including video-EEG monitoring, a 1.5T MRI, neuropsychological and psychiatric evaluation; 3 also had Wada test for speech and memory lateralization. Mean age was 37.4 y. (range 20-57); age at seizure

onset 13.6 (2-47) and epilepsy duration 23.7 (6-51). At 1 year of follow-up, 27 (54%) patients were completely seizure free and 7 (14%) were presenting only auras. The Brazilian national public security health system pays US$ 4701 for each epilepsy surgery, including presurgical work-up, an amount considered very attractive by most university hospitals in the country. ATL for MTS could also be performed in other developing countries at a low cost and with results comparable to those of the developed countries.

Drug Therapy with Limited Resources
R. Teckle Haimanot, Ethiopia

Abstract not submitted

Epilepsy Surgery with Limited Resources
A. Palmini[1]

1) Porto Alegre, Brazil.

The better delineation of surgically-remediable epilepsy syndromes and the need for a surgical alternative to a significant percentage of patients with medically refractory seizures whose lives are seriously compromised by recurrent attacks, have prompted specialists in developing countries to find ways to implement epilepsy surgery programs with limited resources. It is now clear that the major assets for a safe, ethical, and productive implementation of epilepsy surgery programs in developing countries are professional commitment and technical skills, in an environment of strong support from public health systems. High-cost technology lags behind, because the most common surgically-remediable epilepsy syndromes do not demand cutting edge technology for their evaluation and surgical treatment. Thus, epileptologists and social workers must collaborate to (i) raise the level of awareness of the problems faced by persons with epilepsy and the possible solutions, at both public and governmental levels; (ii) be prepared to organize referral centers where patients with refractory seizures can be evaluated, selected for surgery, and operated with the resources available; and (iii) guarantee universal access (meaning the access of poor people) to these programs. In Brazil, it is now 10 years since the implementation of an official program of accreditation of epilepsy surgery centers offering presurgical evaluation and surgical treatment of epilepsy to the Brazilian population. The program is fully sponsored by the Ministry of Health, guaranteeing universal access to the system. The presentation will include: (i) a discussion of objective ways to approach patients with refractory epilepsies, to identify surgically-remediable syndromes that can be treated with limited resources; (ii) the role of education in epilepsy surgery programs in developing countries; and (iii) the results obtained with the Brazilian experience, including the ways the implementation of referral Cenbters have raised the level of Brazilian epileptology as a whole.

Optimising Psychosocial Outcome with Limited Resources
A. De Marinis[1]

1) Chilean League Against Epilepsy And Clinica Alemana, Santiago, Chile.

There is increasing awareness of the importance of an effective management of psychosocial issues in patients with epilepsy. They not only are determinant for quality of life but also have a strong impact in the outcome of epilepsy itself. Dealing with psychosocial issues in an environment with limited resources is an extra challenge. To face it, at least two different aspects of resource limitations must be considered. On the one hand, the health system resource limitations and in the other hand the patients socioeconomic restrictions which have a psychosocial impact of their own , interacting with the one of epilepsy. The scientific evidence to handle both aspects of the problem is scarce and the experiences of more wealthy countries are not always applicable in a more restricted socioeconomic scenario. The handling of psychosocial issues has to be visualized within the broader concept of an integrated management of the epilepsies. This includes diagnostic and therapeutic issues leading to the development of specific management strategies for specific populations such as children with abnormal psychomotor development, patients with learning and cognitive limitations, adolescents , women in childbearing age and elderly patients. Medical, psychiatric and behavioral co morbidity issues also need to be considered. It is a common experience that efforts to improve the psychosocial condition of patients with epilepsy are fragmentary or poorly coordinated with medical care. All too frequently, psychosocial problems tend to be dismissed as a secondary goal in a context of limited resources. The inclusion of this issues as one of the main priorities in the care of patients with epilepsy is the first and most important goal to achieve. In our experience, there are some priorities that can be identified when addressing psychosocial issues with limited resources. These priorities may be adjusted in each particular setting . a)Continuous and reliable access to classic antiepileptic drugs (AED). b)Systematic clinical screening of AEDs adverse effects.c)Early and systematic screening of learning disorders, cognitive impairment and psychiatric co morbidity with emphasis on mood disorders. d)Establishing a permanent feedback channel between the patients and the healthcare system. e)Patient education. f)Facilitation of access to psychosocial and socioeconomic support resources available through government agencies and non profit organizations. g)Development of simple, reliable and accessible archiving systems . These are essential for realistic planning, execution and evaluation of interventions.h)Development of simple, reliable and locally validated psychosocial and socio economic evaluation instruments.i)Evaluation and analysis of patients psychosocial and socio economic profile.j)Performance of precise psychosocial interventions with patients and in the community . These interventions should be initially focused in the pediatric and adolescent group of patients. The organization of a dedicated health team specially motivated in the integral treatment of patients with epilepsy is essential for success. Even if the team has not a formal training in epilepsy, in some settings, an organized and motivated group with access to continuous education may be a major step in improving the medical and psychosocial condition of patients with epilepsy. Nurses with special interest and / or training in epilepsy play a key role in organizing and giving continuity to medical care, in getting psychosocial feedback from patients, in educational activities and in psychosocial interventions. This is specially true in an environment of scant and overexploited medical resources with a high physician turnover at the primary care level. Volunteer work is also an important resource for the detection of psychosocial needs, collaboration in psychosocial interventions and evaluation and improvement of quality of care. The contribution of psychiatrists, psychologists, neuropsychologists, social workers and teachers with expertise in psychopedagogic support can make a definite contribution by addressing specific issues that have a clear impact in quality of life and psychosocial well being of patients with epilepsy. To be really effective, they must interact closely with the rest of the team and develop a specific expertise in epilepsy issues. In practice this kind of services are rarely available in a context of limited resources . One way to overcome this is that centers with expertise in this areas can develop simple and reliable diagnostic and interventional instruments to be used.

Wednesday 31st August 2005
10:00 - 11:30
Salle Maillot
Parallel Session
Debates on the Place of Alternative Treatments in Drug Resistant Epilepsy

PRO: Is the Ketogenic Diet Under-utilised?
E.P.G. Vining[1], E. Kossoff[1], J. Rubenstein[1], J.M. Freeman[1]

1) Johns Hopkins Medical Insitutions, USA.

The ketogenic diet has been available since 1921. As anticonvulsants have been developed, it has been relegated to a therapy of last resort. Prospective studies of its efficacy typically report its use in children who have failed an average of 6-7 medications, but 40-50% of those started on the diet have >50% improvement in seizure control at 1 year. We believe there are many reasons for reluctance to prescribe

the diet: lack of familiarity with it, the need for extensive well-trained nutritional support, perceived inability of the child or family to tolerate it, concern for side effects, cost and perhaps uncertainty related to not understanding how it works. Recognizing that less than 100 centers offer the diet in the US and that the average number of patients on the diet in other countries is 72, it is clear that the diet is underutilized.

CON: Is the Ketogenic Diet Under-Utilised?
E.P.G. Vining, USA

Abstract not submitted.

PRO: VNS Stimulation Versus the Latest AED
E. Ben-Menachem[1]

1) Department Of Clinical Neuroscience, Sahlgrenska Academy, University Of Göteborg, Göteborg, Sweden.

Vagal nerve stimulation (VNS) is a new treatment available for patients with refractory epilepsy. The first implant was performed in l988, and since then more than 20000 patients have received this therapy. Still VNS is used almost exclusively for refractory epilepsy patients and has not been generally accepted for use as a first line or even second line therapy for epilepsy. Why not? Of course it is an invasive procedure but once implanted and functioning has very few bothersome side effects. Indeed there is really no rational reason why it should not be considered for early treatment of epilepsy. What are the advantages of VNS that could be envisioned for use in refractory and even in early on in treatment. The safety profile of VNS is very favorable and the side effects are totally different from those seen with AEDs. Cognitive and sedative side effects are not generally reported. Compared to the new AEDs, VNS has similar efficacy results in clinical trials, but the long-term efficacy results are even more positive. Retention after 3 to 5 years is better then for AEDs . Unlike drugs, where efficacy declines with time, efficacy with VNS continues to improve over a period of 3 to 18 months and there have been no new emergent side effects or tolerance development over observation times of up to 8 years. Compliance is guaranteed automatically and the physician has total control over dosing and delivery. The additional use of the magnet or 'therapy on demand' feature of the VNS can give patients a method to exert some control over their seizure situation. The cost of the implantation of the VNS, when spread out over 8 years (battery length), is actually less than the cost of using one new AEDs over an eight year period and real savings on hospital costs due to seizures can be expected. Therefore, VNS is a viable and effective method for the treatment of epilepsy.

CON: VNS Stimulation Versus the Latest AED
J. French[1]

1) Department Of Neurology, University Of Pennsylvania, USA.

AEDs have established themselves as an effective therapy for the majority of patients with epilepsy. Yet, 30-40% of patients will fail to gain seizure control. For these individuals, the chance of becoming seizure free on an alternative antiepileptic drug may be as low as 11%. Adding AEDs carries the potential for increased side effect burden. For these reasons, it might certainly be an attractive alternative to consider a device such as a VNS. Although both strategies carry certain advantages, for the purpose of this debate, I will discuss only the potential advantages of AEDs over VNS. The central issue in medical decision-making is risk-benefit assessment. Surgery of any type is still considered to be a major undertaking. In order to warrant these risks, the patient has a right to expect that they have a greater chance of a good outcome with an invasive therapy than with a non-invasive one. The main question is when, if ever, this becomes the case when comparing implantation of vagus nerve stimulator vs adding an AED? After the first drug? The second? After all AEDs have failed? To date, no randomized trial of adding AED vs VNS has been attempted, although several are currently being contemplated. Absent this information, it is more difficult to make a case for early adoption of vagus nerve stimulation. Unfortunately, little data is available regarding the potential for patients to become seizure free after implantation of the vagus nerve stimulator. Another issue is side effects. It is important to remember that VNS does, indeed produce adverse events, albeit very different in character than AED side effects to which physicians have become accustomed. These include cough, dyspnea, pharyngitis, voice alteration and sleep apnea. A less frequently discussed potential negative consequence of implantation of vagus nerve stimulation relates to ability to obtain imaging of the patients when necessary. Patients with vagus nerve stimulator implantation are not candidates for imaging of the chest, breast, or abdomen. A second issue is that imaging of the brain can only be performed on MRI scanners that meet certain requirements, and as MRI technology develops, scanners meeting these requirements may become harder to find. In summary, Vagus Nerve Stimulation is an excellent and useful therapy. Fortunately, the choice between AEDs and VNS is no an 'either or' decision. Each has a role in the treatment of patients with epilepsy, and the advantages and disadvantages of each should be kept in perspective.

PRO: To Cut or Not to Cut in MTLE: Gamma Knife versus Resective Epilepsy Surgery?
J. Régis[1], F. Bartolomei[1], M. Rey[1], P. Chauvel[1]

1) Stereotactic And Functional Neurosurgery Department, Timone Hospital Marseille (APM)., Marseille, France.

Purpose : Short middle term safety efficacy of radiosurgery in mesial temporal lobe epilepsies (MTLE) have been documented in several prospective trials. Long term results are now available. Methods : Between March 1993 and May 2005, 53 patients with MTLE illegible for a temporal cortectomy and deciding for radiosurgery have been operated in Marseille by Gamma Knife Surgery (GKS). A minimum, 3 years follow up is now available for 38 patients. The prospective evaluation was including clinical, visual field, neuropsychological and radiological evaluation. The preoperative investigations included; video EEG, magnetic resonance imaging, neuropsychological testing and when requested deep electrode recording was performed. The dose at the margin was 24-25 Gy in 18 patients, 20 Gy in 14 and 18 Gy in 6 patients. The target included the anterior parahippocampal cortex, the basal and lateral part of the amygdala and anterior hippocampus (head and body). Results : Marginal dose is turning out to have a major impact on efficacy. In patients treated with 24-25 Gy at the margin the percentage of Engel I at two years after treatment was 67 % (12/18) and only 33 % (6/18) and 15 % (1/6) for those treated respectively with 20 and 18 grays. Five patients, due to insufficient results have been subsequently operated microsurgically. Three of these five are seizure free. Five patients had transient side effects (headache, nausea, vomiting, imbalance). Three patients have presented with transient depression episode (including 2 with a past history of depression). There was no permanent neurological deficit reported out of ten asymptomatic visual field deficits (26%). No neuropsychological deterioration and special no verbal memory decline was observed. Conclusion : The long term safety efficacy of GKS in MTLE appears good in this group of patient. The delay of the seizure cessation turned out to be the major disadvantage of this treatment. A potential cognitive (and mood) advantage of radiosurgery need to be better documented.

CON: To Cut or Not to Cut in MTLE: Gamma Knife Versus Resective Epilepsy Surgery?
J. Engel Jr.[1]

1) UCLA, Los Angeles, CA, USA.

Mesial temporal lobe epilepsy (MTLE) is the prototype of a surgically remediable syndrome. Surgical treatment has been successfully performed to treat medically refractory MTLE since the clinical application of EEG. In 2001, the only randomized controlled trial (RCT) ever carried out on surgical treatment for epilepsy demonstrated it to be safe and effective for MTLE, and significantly better than continued pharmacotherapy with respect to both seizure

control and quality of life. In 2003, the American Academy of Neurology, in collaboration with the American Epilepsy Society and the American Association of Neurological Surgeons, issued a practice parameter recommending temporal resection as the treatment of choice for medically refractory MTLE. With modern diagnostic technology and microsurgical technique, recent studies indicate that 70- to 90% of patients with MTLE can expect to become free of disabling seizures following temporal resection, with mortality from this procedure less than 1%, and morbidity approximately 6%, half of which is transient. Recent experience with the gamma knife has suggested that this is also a promising alternative treatment for medically refractory epilepsy, including MTLE. At least one center has reported outcome with respect to seizures to be as good as with resective surgery; however, other centers have reported less beneficial results. Although gamma knife surgery is considered less invasive than resective surgery, the resultant edema and necrosis can cause neurological deficits. Furthermore, it takes many months to abolish all seizures, during which time patients may suffer injury or death from their epilepsy, whereas successful surgical resection usually (although not always) has an immediate effect on seizure control. Gamma knife surgery has considerable promise, particularly when comorbidity may be a contraindication to resective surgery, and further research is definitely indicated. However, there has not, as yet, been a RCT to compare gamma knife surgery to resective surgery or pharmacotherapy for any form of epilepsy. Until a RCT finds gamma knife superior to resective surgery with respect to seizure outcome, quality of life, morbidity, and mortality, resective surgery must be considered the treatment of choice for pharmacoresistant MTLE.

Wednesday 31st August 2005
10:00 - 11:30
Salle 252AB
Parallel Session
Epilepsy and Autism Spectrum Disorders

Autism Spectrum Disorders in Children with Active Epilepsy and Learning Disabilities
C. Gillberg[1]

1) Göteborg University, Gothenburg, Sweden.

The association of autism and epilepsy has received relatively scant attention in systematic research study, and the nature of the link is poorly understood. We have performed population-based studies of epilepsy in autism and of autism in epilepsy. Whichever perspective is taken, the links between the two conditions are strong. Almost forty percent of people with autism will develop epilepsy before age forty years. Only a minority of these cases of epilepsy in autism appear during adolescence, and some develop in adult age. About 25% of all individuals with epilepsy and learning disability meet full diagnostic criteria for autism, and many more show several autistic features. All types of epilepsy can be combined with autism, but the strongest links are with partial complex epilepsy. It is still not clear to what extent the link is direct or indirect, i.e. is due to common underlying brain dysfunction. Affected individuals and their families have a very high degree of clinical impairments.

Epilepsy in Autism
R. Tuchman[1]

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Numerous studies have shown an increased but variable risk of epilepsy in individuals with autism. Three main factors may account for the variability in epilepsy rates: (1) the age of the groups studied, with epilepsy rates being higher in studies that included adolescent and young adults; (2) the level of cognitive function, with higher rates of epilepsy in those with severe cognitive deficits; and (3) the type and severity of the language dysfunction, with epilepsy being more likely in individuals with severe receptive language deficits. Landau-Kleffner Syndrome (LKS or acquired epileptic aphasia) is the epileptic encephalopathy model that has been most frequently compared to children with autism whom have an abnormal EEG, especially the 30% of children with autism that in addition have loss of language or communicative intent. Children with autism, regression, severe receptive language disorders and an abnormal epileptiform EEG without clinical seizures have been termed autistic regression with an epileptiform EEG (AREE). Autism is not an epileptic encephalopathy but the behavioral syndrome of autism is commonly found among the epileptic encephalopathies. When autism is part of an epileptic encephalopathy the prognosis in this group of individuals is usually worse than in those with an epileptic encephalopathy and no autism. In general when epilepsy is present in autism, treatment with antiepileptic medications results in good control of the epilepsy. The impact on the quality of life that epilepsy has on those with autism is different than the impact that autism has on individuals with epilepsy. The use of antiepileptic medications in the treatment of interictal epileptiform abnormalities in autism without clinical convulsions is controversial.

Medical or Surgical Treatment in Children with Focal Epilepsy and Autistic Regression: Is it Enough?
A. Arzimanoglou[1]

1) Epilepsy Unit, Child Neurology And Metabolic Diseases Dpt., Paris, France.

The term of 'autistic regression' is used to designate the disturbances that affect, specifically but not exclusively, the socio-cognitive processing. Behavior and cognitive disorders are frequently reported in several studies on the evolution of childhood onset epilepsies. However, the majority of these studies lump together all types of epilepsies or pay particular attention to the group of epilepsies and syndromes recently grouped under the heading 'epileptic encephalopathies'. Focal epilepsies, idiopathic and non-idiopathic, represent more than 50% of the epilepsies in children. For the great majority, seizures can be controlled either by antiepileptic drugs or by surgery. Unfortunately, and despite of this fact, up to now only few studies dealt with the behavioral and neuropsychological outcome of children with focal, particularly non-idiopathic, epilepsies. Most of the available data derives from studies in adults, usually surgical candidates. Even in these studies, differences in neuropsychological outcome between those with childhood onset focal epilepsy as compared to onset in adolescence or adulthood are rarely looked in detail. We will focus our presentation on issues related to progressive alteration of socio-cognitive perceptions in children with focal epilepsies. Autistic symptoms are often additional source of significant impairment and distress. On the basis of available data, from the literature and from our studies on influence of seizures on auditory and visual perceptual processing (Laurent el al - poster this meeting), we will highlight the limits of drug treatment, the successes and risks of epilepsy surgery and above all the need for early implementation of educational interventions. We will insist on limits and methodological issues for prospective research projects assessing the neuropsychological profile of these children. A step further would be a better understanding of the ways to evaluate the installation process and the underlying mechanisms of such dysfunctions, a prerequisite for a preventive attitude in future patients.

New Therapeutic Approaches in Autism and Developmental Disorders
R. Jouvent, France

Abstract no submitted

Wednesday 31st August 2005
10:00 - 11:30
Salle 242AB
Parallel Session
Drug Resistant Epilepsy and Mortality

Mortality and Causes of Death in Epilepsy: a Global Perspective
W. Allen Hauser[0], D.C. Hesdorffer[3]

1) Department Of Neurology, College Of Physicians And Surgeons, USA. 2) Sergievsky Center, College Of Physicians And Surgeons, USA. 3) Department Of Epidemiology, Mailman School Of Public Health, Columbia University, USA.

The high risk for Sudden Unexpected Death among people with intractable epilepsy has alerted the epilepsy community to risks for premature death. It is not only this group that is at risk for premature mortality. Better understanding of causes of mortality within epilepsy subgroups may allow specific interventions. It appears that people with epilepsy identified in incidence cohorts have a 2 to 3 fold increase risk for mortality when compared to that of the general population. Mortality risk is greater in males. The risk is minimal for those with epilepsy of unknown cause and is greatest for those with symptomatic epilepsy, particularly those with progressive neurologic illness. There is a 2 year decrease in life expectancy for those with epilepsy of unknown cause, and 10 years for those with symptomatic epilepsy. The mortality RATE is lowest in the young, highest in the elderly. The mortality RISK is highest in the young and lowest in the elderly. The risk of death is highest shortly after diagnosis and decreases with increasing duration of illness. This belies the high mortality in people with intractable epilepsy. Mortality is higher in people with epilepsy in developing countries but is not proportionately high when higher general mortality is taken into account. Increased mortality due to accidents, suicide, status epilepticus and SUDEP are well recognized but mortality due to neoplasm, (particularly brain tumors), vascular disease, and pulmonary disease is also increased. Is the increase in risk due to epilepsy per se or the underlying condition? Mortality is greater in children with mental retardation and epilepsy than those with mental retardation alone but this analysis does not take into account severity of MR.

Risk Factors and Mechanisms for Sudden Unexpected Death in Epilepsy
Y. Langan, UK

Abstract not submitted

Life Threatening Reactions to AEDs
P. Kwan[1]

1) Division Of Neurology, The Chinese University Of Hong Kong, Hong Kong, China.

Life threatening adverse drug reactions (ADRs) have been associated with a range of antiepileptic drugs (AEDs). These ADRs are mostly rare idiosyncratic reactions, manifesting as severe cutaneous reactions, serous haematological disorders, hepatic failure, or multi-system hypersensitivity syndrome. In the case of felbamate, its association with hepatoxicity and aplastic anaemia has relegated it to the drug of last choice for the treatment of epilepsy. The pathogenesis underlying life-threatening ADRs associated with AEDs is largely unknown and such reactions are often regarded as unpredictable and unavoidable. There is, however, high percentage of cross-reactivity among the aromatic AEDs (carbamazepine, phenytoin, phenobarbital) in their association with skin rash. Emerging evidence suggests a genetic predisposition to the occurrence of severe cutaneous reaction or hypersensitivity syndrome. Other forms of AED-associated ADRs that are potentially life threatening include exacerbation of seizures, or even the occurrence of status epilepticus. In particular, tiagabine has been implicated to induce nonconvulsive status epilepticus. In addition, pharmacokinetic interactions between AEDs and other medications can sometimes have life threatening consequences. To reduce the risk of life threatening ADRs, clinicians must be familiar with the pharmacological properties of AEDs. On initiating a new AED, the patient must be explicitly warned of the relevant symptoms so that they may seek medical help without unnecessary delay should they develop such reactions.

Communication and Prevention: Informing Patient and Relatives
L. Nashef[1]

1) King's College Hospital, London, UK.

Unfortunately, epilepsy is associated with an increased risk of sudden death. Risk factors associated with increased risk in case-controlled studies include a history of convulsive seizures, more frequent seizures, frequent medication changes, polytherapy and IQ less than 70; sharing a room with someone capable of giving assistance has been found to be protective. Although the majority of SUDEP cases are unwitnessed, witnessed deaths also occur, showing that at least some of these deaths are not avoidable by simple measures. Some argue that patients and carers have a right to know risks associated with their condition, while others believe that there is little point in informing patients of a potential outcome they may not be able to influence, particularly if such information may be harmful. Guidelines on best practice may recommend the provision of information but there is little evidence to guide the clinician on when and how this is best done. Furthermore, there may well be a disparity between guidelines and practice. This presentation will address these issues and focus on the potential for prevention of SUDEP cases.

Wednesday 31st August 2005
10:00 - 11:30
Salle 251
Parallel Session
Epilepsy and Reproductive Function in Males

Male Reproductive Dysfunction - The Role of Seizures and Epilepsy
M. Morrell, USA

Abstract not submitted

Male Reproductive Dysfunction - The Role of AEDs
G. Luef[1]

1) Institution Details: Department Of Neurology, Medical University Innsbruck, Innsbruck, Austria.

Alterations in sexual and reproductive functions have been reported to occur more frequently in both men and women with epilepsy than in subjects with other chronic neurological disorders or in healthy subjects. Sexual dysfunction occurring in epilepsy may be due to the disease itself, psychosocial factors or AEDs. Men with epilepsy commonly have diminished sexual interest and potency. In men, libido largely depends on androgens; therefore, low testosterone levels may cause impotence. In some studies, decreased urinary 17-ketosteroid was detected and confirmed by diminished total testosteron or free testosterone (FT). Some authors demonstrated estrogen (E2) levels to be significantly increased in epileptic patients, probably as a result of peripheral aromatization of T into E2 stimulated by AEDs. These results are in agreement with other studies reporting increased E2 levels in men taking AEDs compared to untreated patients and controls. Jürgen Bauer et al. compared testicular function between 200 men with epilepsy - 178 localization-related epilepsy (LRE) and 22 primary generalized epilepsy - who were treated with various AEDs or no drugs and 105 healthy controls. Free testosterone was less than control values in all patient groups, and the free testosterone/luteinizing hormone ratio was less in all groups except patients with primary generalized epilepsy and patients receiving valproate. Valproate was associated with higher free testosterone and lower luteinizing hormone values as well as higher free testosterone/luteinizing hormone ratios than carbamazepine. These data support the hypothesis that therapy itself may indeed have

a direct effect. Lower circulating FT levels are related to circulating SHBG - higher levels of these substances have been reported in epilepsy, but these changes are associated with most AEDs. Isojarvi et al. evaluated reproductive function in 60 men with epilepsy (15 on carbamazepine and 18 on oxcarbazepine for partial epilepsy, as well as 27 men on valproate for generalized epilepsy) and 41 controls. Serum reproductive hormones were assayed. Semen was analyzed. Testicular volume was determined by ultrasound. The frequency of morphologically abnormal sperm was higher among men treated with carbamazepine, oxcarbazepine or valproate than among controls. Both carbamazepine and valproate were associated with poor sperm motility. The frequency of abnormally low sperm concentration was abnormally high in men on carbamazepine and the frequency of any sperm abnormality was high in men on valproate. The valproate-treated men with abnormal sperm had smaller testicular volumes than controls. In conclusion, carbamazepine, oxcarbazepine, and valproate are associated with sperm abnormalities in men with epilepsy. Valproate-treated men with generalized epilepsy who have abnormal sperm may also have reduced testicular volume. Andrew Herzog et al. compared sexual function and reproductive hormone levels among men with LRE taking various AEDs and normal controls. The participants were 63 men with LRE - enzyme-inducing antiepileptic drugs (EIAEDs), 36; lamotrigine, 18; no AEDs, nine - and 18 normal controls. Sexual interest and function (S-score), hormone levels of bioactive testosterone (BAT) and bioactive estradiol (BAE), hormone ratios (BAT/BAE), and gonadal efficiency (BAT/luteinizing hormone) were compared among the groups. In conclusion, sexual function, BAT levels, BAT/BAE, and gonadal efficiency are greater with lamotrigine than with EIAEDs. Abnormally low BAT levels are reached at an earlier age with EIAEDs than with lamotrigine. Mikkonen et al. carried out a population-based, controlled study to evaluate reproductive endocrine function in boys and young men with epilepsy. Seventy patients and 70 controls matched for age and pubertal stage participated in this study. Twenty-eight patients were taking carbamazepine; five, lamotrigine; 12, oxcarbazepine; and 25, valproate. Serum testosterone levels were within the normal range for all groups. Valproate use was associated with elevated androstenedione levels at all pubertal stages. Even prepubertally, androstenedione values were fivefold elevated. Serum sex hormone-binding globulin levels were increased, and serum DHEAS concentrations were decreased in the pubertal patients taking carbamazepine. The mean testicular volumes did not differ between the patients and the controls. In summary, sexual dysfunction, low bioavailable testosterone and abnormalities in sperm number and motility are unusually common among men with epilepsy. Both epilepsy and AED use have been causally implicated. Antiepileptic drugs stimulating the mixed oxidative enzyme therapy may contribute to sexual dysfunction by direct cortical effects or through alterations in the hormones supporting sexual behavior. AEDs are associated with changes in serum concentrations of sex hormones. These drugs induce liver enzymes and increase the serum concentration of SHBG, resulting in decreases in serum free androgen concentrations and serum dehydroepiandrosterone (DHEA) Different drugs may have different effects on endocrine function.Among AEDs, sexual function scores and bioavailable testosterone levels are lower among men who take EIAEDs (carbamazepine, phenytoin) than among those on non-inducers (lamotrigine, valproate)

Impact of Epilepsy Surgery on Libido and Sexual Function
D. Reutens, Australia

Abstract not submitted

Wednesday 31st August 2005
10:00 - 11:30
Salle 241
Parallel Session
Sleep and Epilepsy

Paroxysmal Behaviors During Sleep: Differential Diagnosis
P. Tinuper[1]

1) Department Of Neurological Sciences. University Of Bologna, Bologna, Italy.

The widespread adoption of polysomnographic recordings performed under audio-visual control has better characterized some known motor sleep-related disorders and described many previously unrecognized new entities. The differential diagnosis between nocturnal epileptic seizures and other sleep pathological motor phenomena focuses on some known movement disorders and on new sleep-related motor disorders, many of them still undergoing full description and clinical characterization. Movement disorders include motor phenomena arising at the sleep-wake transition (rhythmic movement disorder and sleep starts), related to NREM sleep (arousal disorders) and related to REM sleep (REM sleep behaviour disorders). Rhythmic movement disorder is characterized by stereotyped, repetitive movements involving large muscles, usually of the head and neck, often associated with injury. Sleep starts (hypnic jerks) are non periodic muscle contractions simultaneously involving the trunk and the extremities, arising when the subject is falling asleep or during light sleep, frequently associated with a perception of falling. Arousal disorders (confusional arousals, sleep terrors and sleepwalking), more common in children, are characterized by a sudden arousals from slow-wave sleep with different behavioural and autonomic manifestations. REM sleep behaviour disorder consists of episodes of motor agitation arising during REM sleep without atonia. The episodes usually arise in the middle of the night or early hours of the morning. The new described sleep-related motor entities include propriospinal myoclonus (PSM) and nocturnal facio-mandibular myoclonus (NFMM). PSM is a type of spinal myoclonus characterized by massive jerks arising in an axial muscle and extending via slowly conducting pathways both caudally and rostrally for several segments. Jerks arise mainly during relaxed wakefulness when patients try to fall asleep and disappear abruptly at sleep onset. NFMM is a sudden forceful myoclonus of the masticatory muscles, evident only during sleep, often associated with biting of the tongue and lips. NFMM may represent a variety of sleep bruxism but also presents as an independent sleep-related movement disorder.

Sleep Disorders and Epilepsy
S. Noachter[1]

1) Dept. Of Neurology, Epilepsy Center Munich, University Of Munich, Munich, Germany.

Epilepsy and sleep are related in several respects. Epileptic seizures may occur in relation to the sleep wake cycle and sleep deprivation precipitates epileptic seizures in some epilepsy patients. EEG studies show that there is a tendency towards higher discharge rates of epileptiform discharges during NREM sleep than in REM sleep and waking. Arousal and transitions between sleep stages seem to facilitate generalized epileptiform discharges. Very little data is available on the sleep of unmedicated epilepsy patients. No significant difference was found between generalized and focal epilepsy as long as photosensitive patients with generalized epilepsy were excluded. Patients with epilepsy may have sleep disturbances and excessive daytime sleepiness due to seizures, particularly nocturnal seizures, and side effects of antiepileptic drugs (AED). AEDs have different effects on the sleep of patients with epilepsy. There were only minor differences, particularly in the first REM cycle, between patients with generalized epilepsy as compared with patients with focal epilepsy. Newer antiepileptic drugs have less impact on sleep than older drugs such as phenobarbital. Sleep disorders such as sleep apnea can lead to an increase of seizure frequency and, thus, need appropriate

treatment. The analysis of sleep microstructure using the cyclic alternating pattern (CAP) may provide a more sophisticated approach to analyze the relation of sleep and epilepsy.

Effects of AEDs on Sleep
C.W. Bazil[1]

1) Columbia Comprehensive Epilepsy Center, New York, USA.

Quality sleep is an important and frequently overlooked component of general health, but is particularly essential to patients with epilepsy. Their sleep can be affected by seizures themselves (especially when nocturnal), by concurrent sleep disorders, and by comorbid conditions (especially depression). One factor that has attained increased attention recently is the effect anticonvulsant drugs have on sleep. These can obviously improve sleep by reducing or eliminating seizures, but also may have independent neuromodulatory properties that can influence sleep in both positive or negative ways. Finally, most AEDs have the potential to improve or worsen certain sleep disorders. Studies of anticonvulsant drug effects on sleep stucture have had many designs. Studies in patients with epilepsy on chronic treatment most closely represent the population to be studied, but these can be confounded by improvement in seizures and often by comedications and comorbid conditions. There have also been studies of anticonvulsants in normal volunteers. These avoid many confounding factors, but are typically of relatively short duration and may therefore show acute effects that would typically decrease with time. Overall, older anticonvulsant drugs such as phenytoin, phenobarbital, and benzodiazepines have the advantage of causing some drowsiness, thus can shorten sleep latency if taken at bedtime. These agents also disrupt normal sleep structure, however, by reduction in REM sleep and, in some studies, increases in nonrestorative (stage 1) sleep. Studies of newer agents do not in general show these problems. Gabapentin and tiagabine have actually been shown to increase slow wave sleep, which in turn may reduce awakenings and arousals thereby improving sleep continuity. Many agents can have beneficial or detrimental effects on sleep disorders.or comorbid conditions that in turn affect sleep. Particular drugs to keep in mind include sedative drugs (barbiturates and benzodiazepines) which can worsen obstructive sleep apnea. Valproate can also worsen sleep apnea if significant weight gain occurs. Carbamazepine and gabapentin have both been shown to improve periodic limb movements, although paradoxically carbamazepine sometimes causes this condition. Agents that treat bipolar disease (lamotrigine and valproate) or anxiety (gabapentin and benzodiazepines) can improve sleep by treating these conditions. Overally, sleep and sleep disorders are an important comorbid condition in patients with epilepsy that are frequently overlooked. When recognized, careful choice of anticonvulsant drug can enhance rather than disrupt particular patient's sleep, resulting in improvement in overall quality of life.

Wednesday 31st August 2005
10:00 - 11:30
Salle 253
Parallel Session
The Role and Historical Evolution of Comprehensive Epilepsy Programmes

Comprehensive Epilepsy Care in North America
F. Andermann, Canada

Abstract not submitted

Comprehensive Epilepsy Centers in Brazil
F. Cendes[1]

1) Department Of Neurology, University Of Campinas - UNICAMP, Campinas, Sao Paolo, Brazil.

Surgical treatment of epilepsies has been performed in Brazil since early 50's. One of the pioneers of epilepsy surgery in Brazil was Paulo Niemeyer who described the 'transventricular amygda-hippocampectomy' in 1957. Unfortunately, the few centers that were capable of performing epilepsy surgery in Brazil during the 50's and 60's could not perform this procedure in a systematic way for a number of reasons. In the 70's, starting at University of São Paulo, there was an increasing interest of some institutions and professionals for developing epilepsy surgery programs. In 1994 the Brazilian Ministry of Health launched a national program for epilepsy surgery after a few years of demand by professionals from the Brazilian League of Epilepsy. Today there are 8 Comprehensive Epilepsy Centers in Brazil accredited and sponsored by our Ministry of Health, and a few other centers that are waiting for accreditation or that are located in private hospitals. These 8 Comprehensive Epilepsy Centers are monitored by a commission formed by representatives of the Ministry of Health and medical associations, including the Brazilian League of Epilepsy. There are minimum standards required for these centers that include a multidisciplinary team with appropriate training and experience in clinical epileptology, neurophysiology, neuropsychology and neurosurgery, as well as local infrastructure such as equipment for video-EEG monitoring, magnetic resonance imaging, adequate operating room and intensive care unit. Since all but one of these Epilepsy Centers are located in public Universities (where the professionals receive a flat salary and patients receive free medical care) the overall cost of the procedure is difficult to estimate. From 1994 to 2003 these 8 centers performed 3,802 presurgical investigations and 2,400 surgical procedures for epilepsy, with excellent results. However, given the large population of the country (169.8 million habitants), these numbers are still very low and there is a need for more Comprehensive Epilepsy Centers in Brazil. Each of these Comprehensive Epilepsy Centers have a tremendous impact on the management and care of patients with epilepsy; in addition, they foster specialized professional training in different areas of expertise, and promote local development of neuroscience research.

Bethel Epilepsy Center - a Concept dedicated to Comprehensive Care
B. Pohlmann-Eden[1]

1) Epilepsy Center Bethel, Bielefeld, Germany

Comprehensive care (CC) in its strict sense means to treat an affected individual as an integral human being with all his needs, impairments, wishes and potential within his social and professional environment. The subjective assessment is the core of this idea and concept. Single seizures and epilepsy are very frequent neurological conditions. SS already lead to a significant irritation of the autonomy of the human being and create a complex situation for counselling. Epilepsy, defined as recurrent seizures, has a major impact in the individual on the self-estimation, life-quality and the possibilities to grow in psychological, social and professional dimensions often as a consequence of unjustified stigmatization. This holds true even for those patients who experience long-term remission or achieve complete seizure freedom. To the historically evolved understanding of the Bethel comprehensive epilepsy program it is not only necessary to provide the best and high-standard technical diagnostic and medical treatment, it also continuously needs a complementary systematic approach and specific instruments to address the following issues: 1) psychological impairment, 2) life-quality, 3) social and occupational situation, 4) co-morbidity, and 5) self-management, compliance and education. Validated life-quality questionnaires, assessment scales and rehabilitation programmes support this approach. The current and future challenge is to further realize this concept despite budget restrictions and major health care changes. It will be necessary i) to improve the interactive network with referring physicians, ii) to develop new platforms and structures, and iii) to learn from each other by an on-going trans-cultural discussion.

Comprehensive Epilepsy Care in Japan
Y. Inoue[1]

1) National Epilepsy Center, Shizuoka Institute Of Epilepsy And Neurological Disorders, Shizuoka, Japan.

Patients with epilepsy (PWE) are suffering not only from seizures, but also from comorbidities of various kinds and their social consequences. With the purpose of eliminating or minimizing the burden of having epilepsy and its consequences in daily lives, a specialized center for comprehensive care for PWE was first established in Japan in 1975, around when the new AEDs such as VPA were introduced and the Association for PWE was established, and two smaller centers in 1983. They provide outpatient and inpatient treatment and care for PWE from infancy to late adulthood by a multidisciplinary team. The treatment includes medical, surgical as well as rehabilitative procedures. The training of professionals and research activities were also involved. A close networking with the job and educational professionals, epilepsy help-line and voluntary organizations have been established in each region. The number of epilepsy outpatients visiting these centers was more than 8,000 during 3 months period last year, and there are ca.300 beds for PWE with average hospital stay of 40 days. However, the number of multidisciplinary teams and networking with other resources in the community are still limited, and there is no residential care system for most intractable PWE or PWE with psychiatric disorders. There is also financial problem that restricts the activities for comprehensive care. The result of a questionnaire survey concerning the role and present status of comprehensive care for PWE in Japan will be presented.

Wednesday 31st August 2005
10:00 - 11:30
Salle 243
Parallel Session
Epileptogenesis Recapitulates Ontogenesis

Bursting Neurons during Development and in the Epileptic Mature Brain
Y. Yaari[1]

1) Department Of Physiology, Institute Of Medical Sciences, Faculty Of Medicine, The Hebrew University, Jerusalem, Israel.

Neonatal rat CA1 pyramidal cells display spontaneous network bursting that is driven by depolarizing GABAergic postsynaptic potentials. This activity disappears during the second week of life with the maturation of GABAergic inhibition. During network-driven bursts, individual neurons generate a synaptically driven burst of high-frequency (up to 100 Hz) spikes associated with a large increase in intracellular calcium concentration. Here, using intracellular recordings in hippocampal slices from P8 to P25 rats, we show that as the network-driven burst activity fades out, most CA1 pyramidal cells become intrinsically bursting neurons. The incidence of intrinsic bursters begins to rise at P11 and attains a peak of 74% by P18/19, after which it decreases over the course of a week, disappearing almost entirely at ~ P25. Pharmacological analysis of intrinsic bursting in developing CA1 pyramidal cells reveals a somato-dendritic 'ping-pong' mechanism. It involves recruitment of nickel-sensitive, voltage-gated calcium channels in distal apical dendrites by the back-propagating somatic spike, which in turn facilitates the somatic spike after-depolarization. Interestingly, this sequence of developmental events can be recapitulated in the adult brain by inducing intense network bursting, i.e. status epilepticus (SE), with the convulsant pilocarpine. A few days after such treatment, intrinsic bursting appears in over 50% of regular firing CA1 pyramidal cells. Like natural intrinsic bursting in developing neurons, SE-induced intrinsic bursting in adult neurons also requires nickel-sensitive calcium electrogenesis in the apical dendrites. These similarities instigate the hypotheses that (i) early network bursting triggers the molecular changes underlying the subsequent appearance of intrinsic bursting in developing neurons, and (ii) that SE may activate the same cellular program responsible for the transitional appearance of intrinsic bursting during development. Thus, epileptogenesis may recapitulate some aspects of ontogenesis. Supported by the DFG (SFB TR3), the Neidersachsen Foundation, and the Henri J. and Erna D. Leir Chair for Research in Neurodegenerative Diseases.

Initially Glutamatergic, Mossy Fibres are also GABAergic after Seizures
R. Gutiérrez[1], M. Treviño[1], C. Vivar[1]

1) Centro De Investigacion Y Estudios Avanzados, Mexico DF, Mexico.

In the adult rat, the granule cells and their mossy fibers (MF) are glutamatergic but, after seizures, they transiently express the GABAergic markers. In these conditions, responses of CA3 cells to MF stimulation (in the presence of Glu-R blockers) have revealed monosynaptic GABAergic transmission with the physiological and pharmacological characteristics of MF signaling. Because interneurons in CA3 are the main targets of the MF, and they control feed-forward inhibition and tune the synchronization of this hippocampal area, we have explored whether the dual glutamatergic-GABAergic transmission from MF disinhibits area CA3. High frequency stimulation of the MF produces, in control pyramidal cells, frequency-dependent summation of EPSPs that leads to repetitive spiking, whereas interneurons display an activity-dependent summation of IPSPs. By contrast, in pyramidal cells from epileptic rats, IPSP summate and inhibition is build up in a frequency dependent manner. Interestingly, in the latter group, interneurons present an opposite behaviour, i.e., high frequency stimulation produces building up of excitation. This suggests that MF glutamatergic transmission onto interneurons surpasses MF GABAergic effects, allowing a more efficient inhibition of pyramidal cells. With field recordings we corroborated that paired pulse stimulation does not produce disinhibition of population responses in CA3. Moreover, by blocking GluR, we could isolate an underlying GABA-R-dependent field potential in slices from rats having seizures, which, by current source density analysis, was shown to have the same dendritic origin as the glutamatergic component. Thus, for GABA-R-dependent monosynaptic field potentials to be detected, a considerable amount of boutons of a well defined GABAergic pathway should simultaneously release GABA to act on a large number of receptors. Therefore, MF GABAergic transmission is likely to affect hippocampal activity at the network level after seizures. This hypothesis led us to explore the effect of the dual glutamatergic-GABAergic transmission on the spontaneous activity of the CA3 network. As expected, depressing MF-GABAergic transmission with the mGluR agonist L-AP4, or cutting the MF tract revealed a strong modulation of MF GABAergic input on activity of CA3. All this evidence suggests that the MF projection is more plastic than hitherto suspected and that it can transiently change the network activity in epileptic conditions. Its function after seizures resembles the fine tuning capability that displays during development, when the MF normally express this dual phenotype.

Relevance to Human Epilepsies
I. Najm, USA

Abstract not submitted

Wednesday 31st August 2005
14:15 – 15:15
Amphitheatre Bleu
Main Session
Issues for Mothers with Epilepsy

Giving Birth to a Child - Opportunities and Risks for the Woman with Epilepsy
M.S. Yerby[1]

1) North Pacific Epilepsy Research, Providence St. Vincent's Epilepsy Program, Portland, Oregon, USA.

The care of women with epilepsy (WWE), is an area in which marked improvements in both medical care and social attitudes have resulted in an i\mproved quality of life. In terms of seizure control, fertility and pregnancy, bone health and the effect of hormones on seizure control our knowledge base and ability to intervene effectively has grown exponentially. Not very long ago the social stigmas directed against persons with epilepsy were substantial. Legislation discriminating against persons with epilepsy, making it illegal for persons with epilepsy to marry, and forcing, involuntarily sterilization were common. As these obstacles have been overcome, these patients face significant risks when considering pregnancy. They have lower birth rates and a higher risk for adverse pregnancy outcomes. Our knowledge base has increased from clinical experience and the information from Pregnancy Registries, so that we recognize not only the risk of congenital malformations, but of developmental delay, premature labor and fetal loss. Antiepileptic drugs (AED) appear to increase the risk of congenital malformations and in certain settings developmental delay. Maternal seizures however also contribute to risks for developmental delay, premature labor and fetal loss. This paper reviews these issues and suggests principles for effective management of the pregnant woman with epilepsy.

Mechanisms of Developmental Toxicity - Key to Prediction and Prevention?
D. Lindhout[1]

1) DBG-Department Of Medical Genetics University Medical Center Utrecht, Utrecht, The Netherlands.

The teratogenic risks of antiepileptic drugs pose women with epilepsy, physicians as well as drug manufacturers for difficult dilemmas with regard to pregnancy. Most if not all antiepileptic drugs have a teratogenic profile or its profile with regard to fetal risks is unknown. At all levels in the chain - from drug design to actual administration to a pregnant woman - there is uncertainty as to how to predict the safety of a compound given to pregnant women and thereby inadvertently to the human fetus. A rational approach towards prediction and prevention of teratogenic effects starts with knowledge about the mechanisms of action and the factors that co-determine the adverse effects. Therefore it seems logical to critically review what is currently known about the teratogenic mechanisms of antiepileptic drugs as well as the methods to detect, predict and prevent teratogenic effects. Knowledge of the pathogenic pathways conferring teratogenic effects may help drug manufacturers to develop compounds that are void of such effects while maintaining the therapeutic effects. The major pathways proposed for this purpose are folate metabolism, epoxide formation with covalent binding of metabolites to macromolecules, ion channel-mediated fetal cardiovascular dysfunction and inhibition of histone deacetylase with altered patterns of gene expression. A second approach may be the identification of individuals (women, foetusses) that are particularly susceptible to the teratogenic side effects of antiepileptic drugs. Indeed, a number of selected case reports and family studies suggested that familial and possibly genetic predisposition may play a role in the teratogenic effects of a drug. Genetic variation in drug metabolism and in pharmacodynamics, seems to be an easy target in view of the current availability of the human genome sequence, the HAPMAP project, high-throughput SNP typing facilities, and sophisticated biomedical statistical techniques. However, this approach requires extensive international collaboration in order to obtain the necessary number for adequate statistical power. In addition, it also requires a complete change of approach from drug manufacturers as to how to deal with the potentiality of side effects. Only if one welcomes all evidence for side effects, tailor-made medication and tailored prescription will remain a realistic prospect. Knowledge of the kind, frequency and determinants of side effects is a prerequisite for the development of new tools for identification, prediction and prevention of teratogenic side effects.

After Delivery: Challenges for the Mother with Epilepsy
P. Crawford[1]

1) Dept Of Neurosciences, York Hospital, York, UK.

Although there has been a lot of research about pregnancy and epilepsy, little has been written about the challenges for mothers with epilepsy. Puerperium: If the dose of an AED has been increased during pregnancy, it is usually advisable to gradually reduce to the preconception dose over the few weeks following delivery. Breast feeding: All women with epilepsy should be encouraged to breast feed their babies. The AED concentration profiled in breast milk follows the plasma concentration curve, but a delay is often observed. The total amount of drug transferred to infants via breast milk is usually much smaller than the amount transferred via placenta during pregnancy. Drug elimination mechanisms are not fully developed in early infancy, drugs such as lamotrigine may accumulate in the infant. Maternal benzodiazepines and barbiturates therapy can cause drowsiness. The care of children: Although there is much anxiety about the possible risks to a child from the mother's epilepsy there is little published evidence. Advice about safety precautions should be given to mothers, even those who have not had a seizure for some time, because it is possible that seizures may return or their frequency increase due to stress, sleep deprivation and exhaustion in the puerperium. This risk is probably small if time is taken to train mothers and carers in safety precautions.

Wednesday 31st August 2005
15:30 - 17:00
Amphitheatre Bleu
Post Main Session
Latest on Human Developmental Toxicity

Update from the UK Pregnancy Registry
J.I. Morrow[1], A. Russell[1], P. Morrison[1], I. Robertson[1], E. Guthrie[1], L. Parsons[1], B. Irwin[1], R. Waddell[1], J. Craig[1]

1) Dept. Of Neurology, Royal Victoria Hospital, Belfast, UK.

The UK Epilepsy and Pregnancy Register is a prospective, observational, registration and follow up study. Women with epilepsy who become pregnant, whether or not they are taking an AED, in any combination, and whose details are forwarded before the outcome of the pregnancy is known are included for study. The presence of a major congenital malformation (MCM) recorded within the first three months of life in exposed pregnancies is the main outcome measure. Full outcome data has been collected on >3000 cases. Almost 96% of live-births born to women with epilepsy did not have a MCM. The MCM rate for polytherapy exposed pregnancies was significantly greater than for monotherapy exposures. Polytherapy regimes containing valproate had significantly more MCMs than those not containing valproate. For monotherapy exposures differences in rates of MCM were noted between drugs, with carbamazepine being associated with the lowest risk. There is also a trend towards lamotrigine being associated with fewer MCMs than valproate. Total daily dosage may be important for both valproate and lamotrigine.

Update from the North American Pregnancy Registry
L.B. Holmes[1], D.F.. Wyszynski[1], E. Baldwin[1], C.R. Reilly Smith[1]

1) AED Pregnancy Registry, MassGeneral Hospital For Children, Boston, USA.

The North American AED (antiepileptic drug) Pregnancy Registry was established at the Massachusetts Hospital in Boston in 1996. Between February, 1997 and April 30, 2005, the 4,274 women enrolled while taking anticonvulsant drugs to prevent seizures (95%) or to treat the symptoms of mood disorders (5%). The woman signs and returns an Informed Consent document. She is interviewed about dose of AED, her medical condition, demographic characteristics and potential confounders (smoking, alcohol, etc.) in the initial 12-minute computer assisted telephone interview (CATI). She is called again at 7 months gestation and 2 to 3 months postpartum. She signs a written release for copies of the medical findings in her infant. Enrollees must be pregnant; they are 'pure' prospective (63%), if enrolled before any prenatal screening and 'traditional', if after screening. Women taking 22 monotherapies (77% of enrollees) and 182 polytherapies. An independent Scientific Advisory Committee meets separately and decides when findings are to be released, first as abstracts at national meetings and then as published articles. The first two publications concerned significant risks of teratogenicity: 1) Holmes LB et al: Arch Neurol 2004; 61:673-8) (phenobarbital); 2) Wyszynski DF et al: Neurology 2005; 64:961-5 (valproate). Experience has shown: 1) a low lost to follow-up rate (5%); 2) the need for inclusion/exclusion criteria in both drug-exposed and unexposed comparison population; 3) controls can be enrolled; 4) many women are reluctant to have their medical records released. The initial products focus on all malformations. In several studies (Ex: N Engl J Med 1989; 320:19-23), the baseline rate of major malformations identified at birth has been about 2%, with the rate lower, e.g. 1.6%, after excluding genetic disorders and chromosome abnormalities. Several studies (Freid S et al: Drug Safety 2004; 27:197-202) have shown that the woman with a history of epilepsy, but not taking an anticonvulsant drug, does NOT have an increased rate of major malformations. Excluded as not major malformations are: minor anomalies, birth marks, deformations, prematurity-related features and abnormalities detected by prenatal ultrasound but not by the examining physician at birth. With larger sample sizes, the rates of specific malformations, e.g. heart defects, spina bifida, etc., can be determined. It is hoped that when the woman is taking a supplement of multiple vitamins with folic acid, her risks from the fetal effect of the anticonvulsant drug she takes will be reduced. However, all of the mothers taking VPA who had a major malformation (in Wyszynski et al, cited above) had been taking a folic acid supplement. Trials at the higher dose of 4 to 5 mg per day are recommended. The Registry is supported by Abbott, Eisai, GlaxoSmithKline, Novartis, Ortho-McNeil and Pfizer.

Update from EURAP
D. Battino[1], E. Bonizzoni[1], J. Craig[1], D. Lindhout[1], E. Perucca[1], A. Sabers[1], T. Tomson[1], F. Vajda[1]

1) EURAP Study Group

EURAP (The International Registry of Antiepileptic Drugs and Pregnancy) is a multinational observational prospective study with the purpose of determining the comparative risk of major foetal malformations following intake of antiepileptic drugs (AEDs) during pregnancy. Originally set up in Europe in 1999, it is now an international project receiving data from 40 countries worldwide. The Registry is based on an electronic database enabling real time checks of case record forms and periodical audits, both favouring prospectiveness and data reliability. To date more than 6500 pregnancies have been enrolled of which 77% are prospective. Data presented here are based on the 5704 pregnancies registered by November 2004 with the exclusion of 581 records (due to changes in AED treatment during 1st trimester; unmet inclusion criteria; unavailable outcome classification, drop-out status) and of other 2601 cases that were ongoing or pending at the time of the analysis. Of the 2522 completed pregnancies with one year follow-up after birth, 1744 were prospective with 40 stillbirths, 20 perinatal deaths, 78 abortions, 163 miscarriages, and 1443 livebirths. With regards to treatment, 1390 (80%) were on a single AED, 302 (17%) on two AEDs and 53 (3%) on three or more. The most frequently used AEDs in monotherapy were carbamazepine (n=521), valproic acid (n=361), lamotrigine (n=236) and phenobarbital (n=109). Lamotrigine and valproic acid (n=43) and lamotrigine and carbamazepine (n=35) were the most common combinations. It should be emphasized that these are preliminary results. Malformation rate and comparison between different AEDs will be made when sufficient statistical power has been obtained to enable multivariate analysis taking account of all possible confounding factors (e.g. maternal age, type of epilepsy, seizure occurrence, family history of malformations, exposure to other teratogens etc). Scientific Advisory Board: Bernd Schmidt and Martin J Brodie Supported by educational grants from GlaxoSmithKline, Johnson-Johnson PRD, Novartis, Pfizer, Sanofi-Synthelabo, and UCB SA.

Prenatal Exposure to Antiepileptic Drugs and Post Natal Cognitive Function, an Update from The NEADS Study
K. Meador, USA

Abstract not submitted

Is it Time to Revise Treatment Guidelines?
T. Tomson[1]

1) Department Of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden.

Optimal medical management during pregnancy is a major health issue for women with epilepsy and their physicians. Potential adverse effects of antiepileptic drugs (AEDs) on the foetus need to be weighed against the foetal and maternal risks associated with uncontrolled seizures. Several guidelines have been published to assist physicians in their effort to optimise the treatment of women with epilepsy considering pregnancy. The physician is advised to optimise treatment before conception, to select the drug that is most effective for the seizure type or syndrome and to prescribe it as monotherapy at the lowest effective dosage. However, in general, these guidelines have been vague leaving the physician with unanswered questions as to which AED is safest to use, how to dose it and what additional measures that could be taken to reduce the foetal and maternal risks. The major problem has been the lack conclusive data comparing different AEDs with respective human developmental toxicity. Emerging data from large prospective epilepsy and pregnancy registries is beginning to provide a better basis for a rational management of epilepsy during pregnancy. This presentation will discuss the implications that the most recent findings from pregnancy registries and other studies presented during this session may have for treatment recommendations including data suggesting higher malformation rates with valproate exposure.

Thursday 1st September 2005
07:30 - 08:30
Salle 251
Morning Seminar
Women and Local Attitudes Towards Epilepsy

Prevalence of Epilepsy in Eastern Mediterranean Regions
B. Yaqub[1]

1) Riyadh Armed Forces Hospital, Saudi Arabia.

East Mediterranean countries (EMR) are diverse in language, socioeconomics, national resources and welfare. We analyzed publications from EMR for the last 3 decades regarding epidemiology, seizure types, health related quality of life (HR-QOL) and local attitudes towards epilepsy of EMR countries. Community-based studies on the prevalence of epilepsy were reported from Tunisia (4 per 1000 population), Libya (2.3 per 1000 population), Iran (12 per 1000 population), Pakistan (10 per 1000 population) and Saudi Arabia

(6.5 - 8 per 1000 population). No reports on epidemiology are available from other countries in the region. However, prevalence of epilepsy in special population such as school children and children with mental sub normality were reported from Sudan, Egypt and Saudi Arabia, with higher prevalence of epilepsy than community studies. In all studies generalized epilepsies were more common in all age groups. Symptomatic epilepsies were reported 15-30%, higher in older age. In Saudi Arabia the frequency of Juvenile Myoclonic Epilepsy was reported, 8% compared to 3% in Pakistan. Although epilepsy was not reported to stigmatize patients in most of EMRO countries, the HR-QOL were worse than those in Europe. The quality of care were diverse in EMR. In some countries new AED are scarcely available, anti-epileptic drug (AED) were taken by not more than 2% in rural areas in Pakistan compared to 80% in some gulf countries. Discrimination against epilepsy in the region was evident in marriage, schooling and employment but this was not universal in all countries. In conclusion the study shows inadequate community based prevalence studies for epilepsy and diversity of clinical care not only between EMR and developed countries but within the region itself.

Maternal Epilepsies and AEDs
A. Beydoun, Lebanon

Abtract not submitted

Pregnancy Registry in EMR: How to Proceed?
H. Hosny[1], F. Talaat[1]

1) Cairo University, Alexandria University, Cairo, Egypt.

The East Mediterranean region comprises 23 countries with a fast growing birth rate. Epilepsy is still considered a social stigma and constitutes a major concern for the patient and family especially in marriage and conception issues. The lack of awareness and ignorance about the facts on this issue compounds the problem. There are efforts carried out by different association in different countries in the region linked to the international bureau of epilepsy to educate and raise awareness about this sensitive issue. The East Mediterranean region with it's fast growing population constitutes an ideal setting to study the teratogenic effects of the old and new AEDs due to a large sample size. To demonstrate a model for such a study a registry is currently conducted in Egypt by the Egyptian bureau of epilepsy. The study is a telephone based interview where the patient, family members and even the doctor can call and register and give the necessary information about the pregnant Woman. To encourage more participants, an additional counseling service is offered providing counseling and guidance for women planning for pregnancy. A bi monthly advertisement is published in the national newspaper with a toll free telephone number to spread the message. Flyers and brochures are distributed at major obstetric hospitals and clinics in the country. Didactic lectures are given whenever possible in obstetric and neurology meetings explaining the need for the information and the current information from the previous literature. We aim this model would be suitable to be adopted in most countries in the region.

Thursday 1st September 2005
07:30 - 08:30
Salle 253
Morning Seminar
The New Antiepileptic Drugs: Focus on the First Two Years of Life

What Do we Know from Clinical Trials?
J.M. Pellock[1]

1) Virginia Commonwealth University/Medical College Of Virginia, Richmond, VA, USA.

The use of the newer AEDs in the treatment of neonates and young infants is poorly studied for a number of reasons. Ethical considerations frequently do not permit truly placebo controlled studies to be performed. The second factor is that seizure semiology similar to that seen in adults are frequently not present in this age group, but trials are designed to extend the same indication. The classic partial seizure studies utilized in older children and adults either cannot be performed or lead to mixed results. The main emphasis of new AED infant trials performed to date were frequently safety and clinical pharmacokinetics with limited efficacy results. These studies have been or are being performed for the majority of the newer AEDs. A newly released study concerning the efficacy of oxcarbazepine in infants demonstrates success in the treatment of partial seizures. An ongoing trial using a placebo versus various doses of topiramate for the study of partial seizures includes those with other types of epilepsy, more typically encephalopathic, to enter a study where the primary endpoint is partial seizure reduction, but information regarding efficacy for other seizure types is also collected. Studies in neonates must be designed to be similar to those performed for status epilepticus. Studies evaluating the efficacy of newer AEDs for infantile spasms are promising. Smaller studies or clinical observations suggest that some medications may worsen certain seizure types in infants. In conclusion, more studies in neonates and infants must be performed. Fifty to seventy-five percent of drugs used in pediatric medicine have not been studied adequately and AEDs, like other medications, frequently lack well designed studies in epilepsy of various types in infants.

What Do We Know from Anecdotal Data and Clinical Practice?
M. Mikati[1]

1) American University Of Beirut, Beirut, Lebanon.

Of the new antiepileptic drugs gabapentin is approved for partial seizures above the age of three years, oxcarbazepine for children above the age of four years, topiramate for partial and primary generalized seizures for children above the age of two years and lamotrigine for partial seizures for children above the age of 2 years. Vigabatrin is considered in some countries as the drug of first choice for infantile spasms. There is uncontrolled data that suggests efficacy of felbamate, topiramate, lamotrigine, and zonisamide in infantile spasms. Uncontrolled studies and experience have also provided encouraging evidence of efficacy of against partial seizures for all new antiepileptic drugs except for pregabalin in which the data so far is lacking. Uncontrolled studies have also demonstrated the pharmacokinetics of most of these medications in the neonatal period and in childhood. Vigabatrin and topiramate half lives in neonates is comparable to that of adults, of zonisamide about 1.5 times, of gabapentin, about twice, and that of lamotrigine even longer as compared to adults. The clearance of those medications in infancy is generally higher by 20-17% as compared to adult clearance (leading to shorter half lives than adults) with the higher clearance rates usually seen in infancy and early childhood.

Thursday 1st September 2005
08:45 - 09:45
Amphitheatre Bleu
Main Session
Affective Disorders in People with Epilepsy

Spectrum of Affective Disorders in People with Epilepsy
E.S. Krishnamoorthy[1]

1) TS Srinivasan Centre For Clinical Neurosciences (University Of Madras), Chennai, India.

What is so unique about affective disorders in epilepsy? Several aspects would be the answer as aetiological and pathophysiological explanations; phenomenology and clinical features; diagnosis, prognosis and management all vary from the conventional norm. What characterises the spectrum of ictally related affective disorders however are a few core features: intensity of the mood change (a profound dysphoria described as a black mood); significant anxiety accompanying this mood change, resulting sometimes in agitation and irritability; physical (somatic) symptoms causing weakness, fatigue and disability; quasipsychotic phenomena (paranoia for example); and

the general brevity of this symptom complex leading to a quick (sometimes unexpected) termination of illness. Affective disorders in epilepsy are influenced by the temporality to seizures and may be preceded, followed, set-off or be terminated by a seizure episode. They may mimic major depression, dysthymia or recurrent brief depressive disorder as described in established psychiatric classifications or differ from these in significant ways. These commonalities and differences as well as the making of a clinical diagnosis will be discussed in some detail during the course of this lecture. Selected Reading: Krishnamoorthy ES. An approach to classifying neuropsychiatric disorders in epilepsy (editorial). Epilepsy & Behaviour 2000; 1: 373-377. Blumer D. Dysphoric disorders and paroxysmal effects: recognition and treatment of epilepsy-related psychiatric disorders. Harvard Rev Psychiatr 2000; 8(1): 8-17.

Interictal Dysphoric Disorders of Epilepsy
D. Blumer[1]

1) University Of Tennessee, USA.

Apart from more subtle personality changes and the serious late complications of interictal psychoses and suicidal episodes, the key psychiatric syndrome associated with epilepsy consists of the interictal dysphoric disorder, with its characteristic intermittent and pleomorphic symptomatology. This disorder was clearly identified about a century ago, by Kraeplin, when he established a comprehensive basis for the modern classification of the psychiatric disorders, at a time when epilepsy represented an area of major interest to psychiatrists. A practical method of recognizing the dysphoric disorder is reported. The disorder tends to be very treatable by combining psychotropic (chiefly antidepressant) with antiepileptic medication. The variations in treatment approach required are discussed.

The Management of Affective Disorders in People with Epilepsy
E. Brodtkorb[1]

1) Department Of Neurology And Clinical Neurophysiology, St. Olav's Hospital, Trondheim University Hospital, Norway.

Biological and psychosocial factors may interact in a complex way in affective and seizure disorders. This fact is important when considering management of mood dysfunction in patients with epilepsy. Psychological difficulties and social/vocational disability may be a greater problem than the seizures and may be related to the perceived social stigma associated with the diagnosis. Insufficient information about the disorder and inadequate professional support is common. Supportive cognitive therapy, specialist epilepsy nursing, and structured educational programmes are essential parts of an operative comprehensive epilepsy service. Intervention of this kind has demonstrated a beneficial effect on the quality of life in patients with active epilepsy. During recent years, it has been increasingly recognized that AEDs have different pharmacodynamic properties and multiple applications. Some may have CNS side effects which may negatively influence affective disorders, whereas others have mood stabilizing or even thymoleptic or anxiolytic effects. It is important to be familiar with the various potential effects of the different treatment modalities, including vagal nerve stimulation. The therapy should be carefully tailored to the clinical profile of each patient. Both benefits and risks should be weighed when treating epileptic patients with antidepressants. Mutual pharmacokinetic and pharmacodynamic interactions should be considered. Compounds without known association with seizures should be preferred. SSRIs are usually safe and effective, but further research is needed to define optimal strategies. In mood disorders, attempts to analyze intrinsic neurobiological factors and the pharmacological profiles of prescribed AEDs, as well as individual psychosocial aspects should be performed. All these considerations have to be taken into account for the individual patient.

Thursday 1st September 2005
10:00 - 11:30
Amphitheatre Bleu
Post Main Session
Anxiety Disorders in People with Epilepsy

Biological Basis of Anxiety with Special Reference to Epilepsy
A.B. Ettinger[1]

1) North Shore-LIJ Comprehensive Epilepsy Center, New Hyde Park, New York, USA.

While a preponderance of studies of psychiatric issues in epilepsy have focused on depression, anxiety is also a common comorbid condition. Anxiety may be ictal, a reaction to early seizure symptoms, post-ictal, or interictal. Interictal anxiety may be due to effects of the underlying CNS condition giving rise to seizures, a side effect of antiepileptic therapy, or relate to anticipation of seizure-related danger, conditioned fear responses and models of learned helplessness. Although limitations in our understanding of mechanisms underlying generalized anxiety disorder also challenge our concept of biological mechanisms of anxiety in epilepsy, there is intriguing commonality in neurochemical and structural aspects between these two disorders. For example, seizures involving anteromedial temporal region or the cingulate gyrus may produce anxiety and fear symptoms. The amygdala, (a structure commonly involved in temporal lobe epilepsy), is an integral part of a neural network with connections to diverse cortical and limbic structures and is involved in the generation of fear responses and associated behavioral and autonomic changes. Compounds that inhibit neuronal activity through the inhibitory neurotransmitter GABA, (also the mechanism of several antiepileptic therapies), reduce fear symptoms when these substances are applied to the amygdala. Similarly, NMDA antagonists may block conditioned fear. Stimulation of 5-HT1A receptors may be anxiolytic while reduced 5-HT1A binding may be seen in mesial temporal structures in epilepsy patients. Learned helplessness is associated with norepinephrine depletion, a phenomenon seen in the genetic epilepsy-prone rat. Studying comorbid anxiety and epilepsy offers an opportunity to examine the pathophysiology of each disorder.

Spectrum of Anxiety Disorders in People with Epilepsy
J.E. Jones[1]

1) Department Of Neurology, University Of Wisconsin-Madison, USA.

Psychiatric comorbidity in epilepsy is a significant clinical problem. A considerable amount of research has focused on major depression and its impact on individuals with epilepsy; however, only recently has the field begun to focus on anxiety disorders in epilepsy. In the general population, anxiety disorders are the most common DSM-IV disorder. In the United States the National Comorbidity Survey (NCS) reported that 24.9% of adults experienced a lifetime anxiety disorder. In the European Study of Epidemiology of Mental Disorders (ESEMeD) 13.6% reported a lifetime history of any anxiety disorder. In both children and adults with epilepsy it appears that anxiety disorders are quite common and occur more frequently when compared to the general population. In a multicenter study in the US involving adults with chronic epilepsy, anxiety disorders were reported in 52.1% of the sample (Jones et al., 2005). The most frequent anxiety disorders were agoraphobia (15.5%), generalized anxiety disorder (13.2%), and social phobia (10.9%). In pediatric epilepsy it appears that anxiety disorders are quite common and are often under-recognized and under-treated. In children aged 5-16 years with complex partial seizures or absence seizures, Caplan et al. (2005) reported 63% of the sample had a current anxiety disorder. Similarly, in a sample of adolescents and young adults aged 14-24 years with generalized seizures, Alwash et al. (2000) reported 48.5% with an anxiety disorder. In summary, this post main session will discuss issues related to the prevalence, spectrum, and potential impact of anxiety disorders on adults and children with epilepsy.

Ictal Fear Versus Panic Attacks
G. Heinen[1]

1) Psychotherapist At The Epilepsy-Center Berlin-Brandenburg, Berlin, Germany.

Ictal fear is very often misinterpreted as panic attack. Therefore it is treated insufficiently. The cause of this false diagnosis is on one hand due to similarities between panic and ictal fear. On the other hand doctors are hesitant to diagnose epilepsy. But even if they are aware that epilepsy might be a possible diagnoses The EEG often does not help in clarifying. First this is because panic and epilepsy could exist parallel in the same patient and second because you may find a dynamic relationship between panic and epilepsy. During my presentation I will discuss diagnostic options that could help distinguish panic attacks from ictal fear. Special attention will be paid to the links between the two. This will be presented through case studies. Finally it will be shown that during treatment it is decisive to clarify the differences and also to recognize this possible relationship between the two.

Influence of Antiepiletic Drugs on Anxiety Disorders
M. Mula[1]

1) Department Of Neurology, Amedeo Avogadro University, Novara & Department Of Psychiatry, Neurobiology, Pharmacology And Biotechnology, Section Of Psychiatry, University Of Pisa, Pisa, Italy.

A variety of drug groups have been shown to be effective in the treatment of anxiety disorders, with selective serotonin reuptake inhibitors being considered first-line agents. The successful use of antiepileptic drugs (AEDs) in mood disorders has led clinicians and researchers to investigate their potential efficacy in other psychiatric disorders, particularly in anxiety disorders. There have been a number of investigations conducted in the form of case reports, case series and open-label trials, suggesting the potential usefulness of AED treatment in a variety of anxiety disorders. More reliable evidence of their use can be gleaned from recent placebo-controlled trials. So far, the strongest evidence has demonstrated the efficacy of pregabalin in treating social phobia and generalized anxiety disorder, while smaller or less robust controlled trials have suggested potential efficacy of gabapentin in social phobia, lamotrigine in post-traumatic stress disorder and valproic acid in panic disorder.AEDs may have a place in the treatment of anxiety disorders. Further investigation is warranted to determine in what circumstances they should be used as monotherapy or as augmenting agents in individuals who are partially or non-responsive to conventional therapy.

Thursday 1st September 2005
10:00 - 11:30
Salle 252AB
Parallel Session
Epilepsy and Language in Children

Overview of Epilepsy-Aphasia Syndromes
A.S. Harvey[1]

1) Children's Epilepsy Program And Departments Of Neurology, Royal Children's Hospital And Austin Hospital, Melbourne, Australia.

The epilepsy-aphasia syndromes are a heterogeneous group of paediatric neurological disorders in which children have acquired or developmental language impairment, epileptic seizures and prominent EEG abnormalities. The disorders are conceptualised as age-limited epileptic encephalopathies affecting language areas. The prototypic epilepsy-aphasia syndrome is the Landau-Kleffner syndrome of acquired epileptic aphasia in which young children with normal or near-normal early language development undergo language regression with prominent verbal/auditory agnosia, continuous bitemporal epileptiform activity on EEG, and a complex partial seizure disorder of usually mild severity. Related syndromes include the epileptic opercular syndrome with prominent oromotor and verbal dyspraxia and orofacial seizures, the syndrome of atypical benign rolandic epilepsy or pseudo-Lennox syndrome with milder language impairment but more prominent ataxia and negative myoclonic seizures, and the syndrome of continuous spike-waves in slow wave sleep with more severe global deficits and mixed seizures. Developmental dysphasias and autistic spectrum disorders with EEG abnormalities have an uncertain place in the spectrum of epilepsy-aphasia syndromes. Frequent, usually continuous and bisynchronous, focal epileptiform activity is common to all these syndromes, with marked sleep activation and tangential dipoles being prominent EEG features. While the epilepsy-aphasia syndromes may be associated with some cortical malformations and white matter abnormalities on MRI, most patients have normal brain imaging and no identifiable underlying aetiology. The syndromes however share many clinical and EEG features with the idiopathic partial epilepsies of childhood and would appear to severe manifestations of such disorders, with the heterogeneity of interictal language/motor/cognitive deficits, seizure manifestations and EEG patterns in part related to the location and extent of the focal epileptic disturbance. The natural history of the epilepsy-aphasia syndromes is for remission of the seizures and EEG disturbance in the second decade, like with the benign partial epilepsies of childhood, but with significant residual language and cognitive disability if the epileptic encephalopathy persists for long periods through the important developmental years in the first decade. As a result, aggressive and prolonged treatment and monitoring are indicated to maximise the child's development through the usually protracted course of these conditions.

Non-language Deficits in Epilepsy-aphasia Syndromes
B. Neville[1]

1) Institute Of Child Health, London, UK.

The range of impairments seen in children who present with acquired aphasia and a centro-temporal epileptiform EEG abnormality is wide and it may be arbitrary as to where lines are drawn to separate Landau-Kleffner syndrome (LKS) from CSWS. Gestural communication problems are common as evidence by poor facial expression and use of gaze: of the published patients with LKS on whom there are data less than a quarter could use signing. Approximately 40% suffer a reduction in non-verbal cognition. About 2/3 have behaviour problems comprising of hyperkinesis, oppositional and aggressive behaviour with some it amounts to mania. Some loss of social function is common and at least 10% satisfy the criteria for autistic spectrum disorder. The behavioural impairments are often of the most difficult aspect for families and require structured diagnosis and management. In the 30-40% who have an outcome of severe impairment the above elements usually contribute to the disability complex although behaviour tends to improve in the second decade.

Genetic Aspects of Epilepsy-Aphasia Syndromes
P. Roll[1], G. Rudolf[1], S. Pereira[1], B. Royer[1], I.E. Scheffer[1], M.P. Valenti[1], M.N. Metz-Lutz[1], M. Delepine[1], N. Lévy[1], S.F. Berkovic[1], E. Hirsch[1], G.M. Lathrop[1], P. Cau[1], P. Szepetowski[1]

1) Inserm Umr491, Marseille, France.

In the recent years, genetic studies have led to the identification of several genes responsible for rare idiopathic epileptic syndromes inherited as simple Mendelian traits. Most epilepsy genes encode ligand- or voltage-gated ion channels. More recently, genes coding for other types of proteins that may participate in protein-protein interactions (LGI1 in temporal lobe epilepsy) or in apoptosis (EFHC1 in families with juvenile myoclonic epilepsies), have been identified. In a subset of families with epilepsy, another non-epileptic, cerebral phenotype may be co-inherited. This includes migraine, paroxysmal dyskinesia, autism, and language impairment. In particular, the association of epileptic disorders with language dysfunction is well known but remains poorly understood. The Landau-Kleffner syndrome (LKS), the continuous spikes-waves during slow sleep syndrome (CSWSS) and rolandic epilepsy (RE) are childhood epilepsies with unknown pathophysiology. They all may represent a

continuous spectrum of disorders where language impairment is associated with epilepsy. In all these related syndromes, genetic etiology remains a matter of debate. Concordant as well as non-concordant twins have been reported in LKS. Although various modes of genetic inheritance have been proposed in RE families, twin studies recently pointed against clear genetic influence in most RE. The language centres in the human brain are associated with the two major cerebral fissures - the rolandic and sylvian sulci. Seizure disorders localized to this region may be associated with language difficulties. In 1995, Scheffer et al.1 described an Australian family with Mendelian inheritance of rolandic epilepsy associated with oral and speech dyspraxia and mental retardation (ADRESD syndrome). Genetic studies on such families, where rolandic epilepsy and language impairment concur, provide a unique opportunity to understand the molecular bases of both the disorders, and of their relationship. We recently studied a French family with Mendelian inheritance of a phenotype similar to ADRESD. Genetic analyses led to the mapping and subsequent identification of the disease gene (provisionally named RESDX) in this French family. The involvement of RESDX in a rolandic/sylvian pathology suggests an important role for this gene in the perisylvian region. Whether the RESDX gene is mutated in patients with related syndromes such as LKS or CSWSS remains to be established. Nevertheless, these data open new and exciting insights in the pathophysiology and inter-relationship of rolandic epilepsy and speech impairment. (1) Scheffer IE.et al. Ann. Neurol 38, 633-642 (1995).

Treatment Approaches in the Epilepsy-Aphasia Syndromes
E. Hirsch[1], A. De Saint-Martin[1], M.P. Valenti[1], M.N. Metz-Lutz[1], C. Seegmuller[1]

1) Department Of Neurology And Department Pediatry, Strasbourg, France.

Various childhood epileptic syndromes associated with a great amount of 'interictal EEG abnormalities' manifest with psychomotor decline (epileptic encephalopathies). The main representatives are the continuous spike and waves during slow wave sleep syndrome (CSWS) and the Landau-Kleffner syndrome (LKS). In 1992, Landau W. published a letter with the statement that: Landau-Kleffner syndrome is an eponymic badge of ignorance.(Arch Neurol. 1992; 49:353). Findings lead to the view that 'Atypical partial benign epilepsy', LKS and CSWS are could be characterized by acquired aphasia of different types and other neuropsychological deficits secondary to an 'epileptogenic' disturbance affecting an associative cortical area involved in cognitive functions. In 1992, W.Landau raised the need of international study on: delineation of the LKS syndrome, etiology, pathophysiology. About treatment, W Landau pointed on the necessity of randomized double blind studies to demonstrate the effectiveness of rationale or empirical therapies. Unfortunately, Landau's hopes in 2005 are not achieved. Treatment of classical focal seizures, symptomatic spike and waves, cognitive deficit and behavior problems are still based on empirical opinion experts. Early treatment with benzodiazepines, ethosuximide, sulthiam and steroids might improved long term outcome but standardized protocol is not established. The place of surgical treatment with subpial transection in LKS is a subject of discussion. Specific language rehabilitation and treatment of behavior problems are still cornerstone.

Thursday 1st September 2005
10:00 - 11:30
Salle 242A
Parallel Session
Towards a Consensus on Defining the Epileptogenic Zone

Different Conceptual Hypotheses Framing Human Focal Epilepsy
H.O. Lüders[1]

1) Cleveland Clinic Foundation, USA.

The epileptogenic zone has been defined as the area of cortex that is necessary and sufficient to generate epileptic seizures and whose complete resection or complete isolation leads to seizure freedom. There is no method to measure this zone directly. Presurgical evaluation uses a variety of tests that measure 5 other zones that have variable spatial relationships with the epileptogenic zone. This includes the following:
1. The irritative zone which is the area of cortex that generates intetrictal spikes and can be measured by interictal EEG, interictal MEG, and fMRI of interictal spikes.
2. The seizure onset zone which is the area of cortex that generates ictal events. It is measured by EEG, ictal Spect but also infrequently by EEG fMRI, MEG or ictal PET scanning.
3. The epileptogenic lesion which is assessed best by MRI (high resolution).
4. The symptomatogenic zone which is defined by a careful analysis of ictal semiology (clinical history, video recordings of seizures)
5. The functional deficit zone which can be assessed by a variety of methods including neurological exam, neuropsychological exam, PET and SPECT scanning. There are general principles that govern the relationship of these different zones with the epileptogenic zone. Situations in which all these five zones clearly overlap permit exact and reliable localization of the epileptogenic zone. Unfortunately in most cases there is only partial overlap of the different zones. In general, the accuracy with which we can localize the epileptogenic zone is a function of the degree of spatial overlapping of these 5 different zones. The introduction of new techniques usually has increased the precision with which we can localize and define the extent of the 5 zones mentioned above. However, since we are unable to localize or define the extent of the epileptogenic zone directly, the introduction of new presurgical evaluation techniques has usually been added to our presurgical assessment techniques without dropping older methodologies. This has resulted in a progressively more complicated presurgical evaluation methodology not infrequently with only marginal increase in the precision with which we define the epileptogenic zone. On the other hand, new assessment methodologies have actually led to non-invasive techniques of sufficient precision making invasive evaluations progressively less frequent. The typical examples are patient with very clear unilateral mesial temporal sclerosis visible on MRI in which all the other tests are consistent with this diagnosis. In the future, we hope that we eventually will be able to measure directly the epileptogenic zone making assessment of the other 5 zones redundant. This could greatly simplify the presurgical evaluation making the surgical treatment option available to a much larger percentage of patients with pharmacoresistent epilepsy.

The concepts of Jean Bancaud and Jean Talairach
P. Kahane, France

Abstract not submitted

The Large Network Hypothesis
S.S. Spencer[1]

1) Yale University School Of Medicine, USA.

Epilepsy as a Disorder of Large Neural Networks Observations from multiple diagnostic and clinical investigations in humans and experimental models of epilepsy suggest seizures are the result of interactive, cumulative alterations in connected cortical and

subcortical regions of large epileptic networks. Several kinds of observations lead to this conclusion: variable intracranial EEG recording localization of initial changes at the onset of stereotyped clinical seizures; widespread distribution of abnormalities on imaging epileptic brain with magnetic resonance spectroscopy, PET, and interictal SPECT; evidence of atrophy in the medial temporal structures and also contralateral hippocampus, thalamus, amygdala, lateral temporal neocortex, and inferior frontal lobe in patients with refractory medial temporal lobe epilepsy associated with mesial temporal sclerosis; modification (even cure) of seizures by operations without true anatomical overlap, or by subcortical or vagal nerve stimulation in selected patients. Measurable changes in multiple different network regions are likely to considerably precede the expression of the clinical seizure itself, as well as its first appearance on visual analysis of the EEG. The earliest manifestations of these alterations in the connected network of cortical/subcortical structures, represent the process of seizure generation. Identification, illustration, and definition of the accompanying physiological changes that express this process by examination of potential network components in different ways before visually identified seizures are detected would support the large network hypothesis, and allow better understanding of its distribution, and opportunity for improved diagnosis and treatment. Examples of such observations, of the accumulated, altered cortical excitability in the distributed epileptic network preceding traditionally recognizable seizure expression, are available. These changes are reproducible, provoked by medication withdrawal in the epileptic brain, and recognizable as patterns associated with specific epileptic networks. Surprisingly, it is a reduction in tonic cortical excitatory activity (as expressed by reduction in glutamate, spiking, NAA, and Teager energy, and often an increase in blood flow) that culminates in eventual traditionally understood seizure activity.

Propagation and Seizure Spread
H.G. Wieser[1]

1) Neurology, Dept. Epileptology And EEG, University Hospital Zurich, Zurich, Switzerland.

Electroclinical spatiotemporal analysis of seizures with focal origin teached us that seizure spread is usually not random and isotropic, but anisotropic along hodologically preformed pathways. These pathways - leading to anisotropic discharge propagation have been well studied with stereo-electroencephalography (SEEG) analyzing the stepwise appearance of spontaneous epileptic discharges in differently located depth electrodes, and confirmed by intracerebral electrical stimulation and recording the evoked responses and/or afterdischarges. In seizures with focal mesial temporal lobe (TL) onset at one side propagation to the ipsilateral retrosplenial cingulate cortex and to the anterior cingulate cortex (Brodmann area 24), as well as to the ipsilateral basal frontal lobe (presumably over the uncinate fascicle) and frequently to the contralateral TL has been well documented. Occipital seizures frequently spread to TL (inferior path) or to parieto-frontal cortex (superior path). Callosal section tries to prevent seizure spread to the opposite hemisphere. Seizure spread may be limited or widespread depending on seizure threshold (measured by the strength of intracerebral electrical stimuli) which is influenced by antiepileptic drugs, vigilance/sleep, etc. In mesial TL epilepsy rapid contralateral propagation is associated with a less good seizure outcome after mesial TL resections. If the seizure onset zone is located in a relatively 'silent' brain area first detectable clinical signs and symptoms may be due to seizure spread to 'eloquent' brain areas (the symptomatogenic zone). To study the sequential involvement of different brain areas, spatiotemporal source mapping using LORETA (low resolution electromagnetic tomography) is very useful and examples of such analyses will be given.

Thursday 1st September 2005
10:00 - 11:30
Salle 242B
Parallel Session
Advanced MRI Techniques

Post Processing of MRI for Detection of Cortical Dysplasia
H-J. Huppertz[1]

1) Epilepsy Center, University Hospital Of Freiburg, Freiburg, Germany.

Focal cortical dysplasia (FCD), a frequent cause of pharmaco-resistant epilepsy, can be difficult to detect in MRI. We present three novel techniques for post-processing of MRI which may improve lesion detection by enhancing image properties not readily accessible by visual analysis. Following the principles of voxel-based morphometry a T1 - weighted MRI volume data set is normalized and segmented using standard SPM algorithms. The distribution of gray and white matter is analyzed on a voxelwise basis and compared with a normal database. Based on this analysis, 3-dimensional maps are created which characterize different features of FCD, i.e. abnormal thickness of the cortical ribbon, abnormal extension of gray matter into white matter, and blurring of the gray - white matter junction. These methods were applied to the MRI data of 25 epilepsy patients with histologically confirmed FCD. In each feature map the locations of the maximum deviations from the normal database were automatically determined and compared with the sites of the lesions or - in cryptogenic epilepsy - with the subsequent resections in the conventional MRI. With all feature maps combined, this approach was able to identify 23 out of 25 dysplastic lesions, including four cases with lesions not or incompletely recognized on conventional MRI despite acquisition and assessment in a tertiary epilepsy center. The novel techniques for post-processing of MRI presented here facilitate the detection and delineation of FCD and increase the diagnostic yield of MRI. Thereby, they provide a valuable additional diagnostic tool in the presurgical evaluation of epilepsy patients and may improve the therapeutic options especially in case of cryptogenic epilepsy.

Novel MRI Sequences
F. Rugg Gunn[1]

1) Department Of Clinical And Experimental Epilepsy, Institute Of Neurology, London, UK.

20% of patients with refractory focal epilepsy have an undetermined aetiological basis for their epilepsy despite extensive investigation. Surgical treatment of this group is associated with a less favourable post-operative outcome. This may be due to incomplete resection of a discrete, isolated lesion or the presence of unrecognized, widespread pathological change or multifocal abnormalities. Even with improvements in imaging techniques, a proportion of these patients will remain 'MRI-negative'. It is likely, however, that some of the discrete macroscopic focal lesions that are currently occult, will be identified by imaging techniques interrogating different microstructural characteristics. These methods may also provide pathological specificity when used in combination. The description and application of these techniques in epilepsy are the focus of this talk.

Potential and Pitfalls of MRI at High Field Strength
G. Jackson, Australia

Abtract not submitted

EEG-fMRI Studies
J. Gotman[1]

1) Montreal Neurological Institute, McGill University, Montreal, Canada.

Patients with epilepsy often present in their EEG short events (spikes or spike-wave bursts) which are not accompanied by clinical manifestations but are of important diagnostic significance. It is not easy to determine the location of the cerebral generators of this activity and the other brain regions that may be involved as a result. The possibility to combine EEG recording with functional MRI (fMRI) scanning opens the opportunity to uncover the regions of the brain showing changes in metabolic activity in response to epileptic spikes seen in the EEG. These regions are presumably involved in the abnormal neuronal activity at the origin of epileptic discharges. We will review the methodology involved in performing such studies, particularly the challenge of recording a good quality EEG inside the MR scanner while scanning, and the methods required for analyzing the combined EEG and fMRI signals. We will present the results obtained in patients with different types of focal epileptic disorders and with generalized discharges, and discuss the difficult theoretical problems raised by the interpretation of activation and deactivation, both frequently seen in response to epileptic activity.

Thursday 1st September 2005
10:00 - 11:30
Salle 251
Parallel Session
Gender-Related Aspects of AED Treatment

Gender Issues in Pharmacokinetics
I. Leppik[1]

1) University of Minnesota and MINCEP Epilepsy Care, USA

Pharmacokinetics (PK) is the study of the time course of drugs in the body, and it is essential to understand alterations in the processes of absorption, distribution and elimination which occur in women in order to provide optimal care. Antiepileptic drug (AED) concentrations must be maintained at effective concentrations during chronic therapy, but there are a number of factors, which may disturb the equilibrium between the dose and level. In addition AEDs may affect other treatments. Women undergo major life changes, which may affect the metabolism of AEDs. In the pediatric age group, the onset of puberty probably has an effect on the metabolism of AEDs, which are metabolized by the liver and compete with hormone metabolism. However, the PK of AEDs during this time of life has not been studied sufficiently to make recommendations other than to adjust doses as needed to compensate for growth and hepatic enzymatic activity. Menopause is the other stage with major changes in hormone levels, but again, few studies have been done. The stage of life most studied is the childbearing years. During childbearing years, issues regarding pregnancy are paramount. Efforts center around preventing pregnancy or managing the pregnancy. Hormonal contraceptives use the same pathways used by many AEDs, and AEDs may alter these routes of elimination. This is of greatest concern for AEDs, which induce the enzyme systems, which metabolize hormones used for contraception. The AEDs most likely to alter the effectiveness of oral contraceptives by decreasing their concentrations are phenobarbital, phenytoin, carbamazepine and oxcarbazepine. Using contraceptives with higher hormone concentrations or using AEDs which do not induce metabolism of contraceptives can circumvent this issue. On the other hand, contraceptives may affect the concentrations of AEDs, This appears to be most pronounced for lamotrigine, whose clearance is greatly increased by certain hormonal contraceptives. This effect is most troublesome for contraceptives which are used for 21 days followed by 7 days of no hormone and lamotrigine levels will fluctuate considerably during the monthly cycle under these circumstances. AED concentrations often change during pregnancy. Changes in AED levels may occur due to alterations in compliance, absorption, distribution (protein binding) or elimination. All of the AEDs are subject to non-compliance. Indeed, fear of teratogenicity may be the major factor in this. Absorption, especially of phenytoin, may be altered by antacids containing calcium. The highly protein bound AEDs, such as phenytoin and valproate, may have their total concentrations decreased in greater proportion than can be accounted for by increased clearance. Alterations in hepatic metabolism, however, play the major role in lowering of AED concentrations. Possibly because of non-linear kinetics, phenytoin appears to be most affected by pregnancy, with levels falling throughout pregnancy by as much as 50% in some women. Decreases in carbamazepine, valproate and Phenobarbital levels are less dramatic. Of the newer AEDs, lamotrigine levels can drop dramatically, by as much as 150%. This decrease often happens during the first trimester, and clearances return to pre-pregnancy values shortly after delivery. Other new AEDs have not been well studied. Optimal management of AEDs in women requires vigilance, especially during periods of transition, such as puberty, menopause, addition or discontinuation of hormonal contraceptives and pregnancy.

Gender Aspects on Efficacy and Tolerability of AEDs
R. Kälviäinen, Finland

Steroid hormones influence neuronal excitability. Neuronal excitability is enhanced by estrogen, whereas progesterone exerts anticonvulsant effects. Testosterone and corticosteroids have less consistent effects. Levels of estrogen and progesterone fluctuate throughout the menstrual cycle, and, in up to 70% of women with epilepsy, these fluctuations may be related to a significant increase in seizures in relation to the menstrual cycle, also known as catamenial epilepsy. Variations in concentrations of antiepileptic drugs across the menstrual cycle may also contribute to increased seizure susceptibility. Animal studies have shown that antiestrogen and antiandrogen can enhance the protective action of some AEDs against maximal electroshock-induced seizures. Co-administration of these antihormones with subprotective dose of AEDs, results in significant shortening of both seizure and afterdischarge durations in amygdala-kindling. Reproductive dysfunction is reported both in women and men with epilepsy treated with AEDs. In women, the most common symptoms are hyperandrogenism, menstrual disorders with ovulatory failure, polycystic ovary-appearing ovaries and hyperinsulinemia. In men, effects on sperm quality and motility, delayed sexual development, and small testicular size have been. Women also face the fear of AED-related birth defects. The gender differences are always important to evaluate when efficacy and tolerability of an AED are reported.

Women in Clinical Trials for Drug Licensing
C. Sampaio[1]

1) Lab. Clinical Pharmacology And Therapeutics, Institute Of Molecular Medicine, Lisbon School Of Medicine, University Of Lisbon, Lisbon, Portugal.

An underlying principle of drug development is that 'patients entering clinical trials should be reasonably representative of the population that will be later treated by the drug' [ICH guideline E7: Studies in Support of Special Populations: Geriatrics.] as subpopulations may respond differently to a given drug treatment. Given the evidence available children (different subgroups) and elderly are recognized as target subpopulations. The issue is to understand if gender should also be considered as a particular subpopulation. There are several levels where drug effects might potentially be distinct according with gender: (1) The disease may have a different natural history; (2) Drug PK/PD is distinctive; (3) Beneficial effect size differs; (4) safety profile (in particular drug interactions) differs. There are not many examples where these distinctions are apparent and certainly there are not systematic differences according with gender, as they are for children and elderly. Yet, it is important to recognize that while PK/PD differences are formally sought during clinical development and the safety profile is characterized according with sex even if by crude descriptive methods, differences in effect size are not commonly

looked after. Another potentially source of concern is the adequacy of gender representation in pivotal trials given the gender prevalence in the community. Three systematic reviews of the trials submitted to American, European and Japanese authorities show that genders are fairly represented.

Thursday 1st September 2005
10:00 - 11:30
Salle 241
Parallel Session
Pathophysiology of Headache and Pain in Epilepsy

Peri-ictal Headache
A. Bernasconi[1]

1) Montreal Neurological Institute, Montreal, Quebec, Canada.

The association between headaches and epileptic seizures is a well-known phenomenon. The headache in some epileptic patients may be severe and represent a considerable disability. In a study of 100 consecutive patients with partial epilepsy, we found that peri-ictal headache occurred in about 50% of patients. Post-ictal headache was the most common form of peri-ictal headache. Peri-ictal headache was more likely to be ipsilateral to the seizure focus in patients with temporal lobe epilepsy than those with extra-temporal epilepsy (90% vs. 12%). For both groups, peri-ictal headaches usually conformed to the diagnostic criteria for common migraine. Possible pathophysiological mechanisms of peri-ictal headache will be discussed.

Ictal Epileptic Pain
F. Mauguière[1]

1) Functional Neurology And Epilepsy Department. Neurological Hospital Lyon, Lyon, France.

Stereo-Electro-Encephalographic (SEEG) recording of spontaneous seizures aims at localizing the epileptogenic area before surgical treatment in patients with drug-resistant partial epileptic seizures. During SEEG investigation direct electric stimulation of the parietal operculum and insula as well as intra-cerebral recordings of evoked responses to painful stimulations brought consistent information on the role of this part of the cortex in pain processing. Insular lobe seizures The insular cortex is one of the targets of stereo-electroencephalographic (SEEG) electrodes implantation in patients with temporal lobe epilepsy (TLE) whose seizures are suspected to originate from, or to rapidly propagate to, the peri-sylvian cortex. A stereotyped sequence of ictal symptoms associated with intra insular discharges can thus be identified. Insular epileptic seizures occur in full consciousness; they begin with a sensation of laryngeal constriction and paresthesiae that are often unpleasant or painful and affect large cutaneous territories. This sensation is eventually followed by dysarthric speech and/or elementary auditory hallucinations, and seizures often finish with focal motor convulsive symptoms. The insular origin of these symptoms is confirmed by data from functional cortical mapping of the insula using direct cortical stimulations. Pain responses can be evoked by stimulating the parietal operculum and the posterior part of the insula, they are localized mostly, but not exclusively, in the body half contralateral to stimulation. Moreover, by recording simultaneously SII and insula pain EPs in response to skin CO2 Laser stimulation (LEPs) distinct LEPs can be obtained in both areas. Insular LEPs culminate at about 50 ms later than SII LEPs. Pain responses in SII and insula are bilateral, responses ipsilateral to stimulus peaking 15 ms later than contralateral ones. The amplitude of LEPs in both areas correlates with stimulus intensity and subjective rating from perception to pain threshold. No pain LEPs with shorter latencies can be recorded anywhere else in the human cortex including SI, cingulate gyrus and amygdala. The insula and the SII area, which both receive direct afferent fibers from posterior thalamus nuclei, can thus be considered as a primary cortical areas for pain sensation. When lateralized pain occurs at the onset of seizures an origin in the parietal operculum or the insular cortex must be suspected and direct recordings of these two areas must be performed before making any decision regarding epilepsy surgery.

Pathophysiological Links between Migraine and Epilepsy
P.J. Goadsby[1]

1) Institute Of Neurology, Queen Square, London, UK.

Migraine is a disorder of the brain (1) manifest as episodic attacks of pain with associated sensitivity to afferents, such as light, sound and head movement. Approximately 30% of migraine sufferers have a neurological disturbance known as aura. The most severe form of aura involves hemiplegia: familial hemiplegic migraine (FHM). FHM is now recognized to be due to mutations in either CACNA1A or ATP1A2 genes. Both of these mutations lead to ionopathic dysfunction that shares important biology with epilepsy (2). The relatively recent widespread use of neuromodulators developed for epilepsy, such as valproate and Topiramate, in migraine prophylaxis, and the convincing clinical trials showing their efficacy, suggest a further important link between these conditions.

1. Goadsby PJ, Lipton RB, Ferrari MD. Migraine- current understanding and treatment. New England Journal of Medicine 2002;346:257-270.
2. Kullmann DM. The neuronal channelopathies. Brain 2002;125:1177-1195.

Thursday 1st September 2005
10:00 - 11:30
Salle 253
Parallel Session
Impact of ILAE Guidelines: Initital Monotherapy Treatment of Epileptic Seizures and Syndromes with Antiepileptic Drugs

The Purpose and Development of the Guidelines
T. A. Glauser [1]

1) Children's Hospital Medical Center, Cincinnati, USA.

In 1998, the Commission on Therapeutic Strategies of The International League Against Epilepsy (ILAE) began to develop an evidence based guideline to assist clinicians worldwide on the initial antiepileptic drug (AED) therapy for patients with newly diagnosed epilepsy. The main goal of the guideline was to provide an evidence based answer to the following question: For patients with newly diagnosed or untreated epilepsy, which AEDs have the best evidence for long term efficacy or effectiveness as initial monotherapy? The guideline was intended for use by individual clinicians, hospitals, health authorities and providers, and individual Chapters of the ILAE. The guideline was developed with the understanding that it would need local scrutiny and adjustment in order to make it relevant to the social and economic environments in which it would be used. This local process would lead to a sense of ownership of any adjusted guideline that would be essential for effective implementation and lead to improvement in health care outcomes for people with epilepsy. This guideline should not be construed as including every proper method of care or as excluding other acceptable methods. The ultimate judgment for therapy must be made in the light of all the clinical data presented by the patient and by the treatment options that are locally available for the patient and his/her clinician.
The methodology used to construct the this guideline combined elements of guideline development used by, among others, The Scottish Intercollegiate Guideline Network, the Cochrane Database of Systematic Reviews, and the American Academy of Neurology. A series of literature searches using MEDLINE and Current Contents included the words epilepsy, monotherapy and at least one of the 36 antiepileptic medications available around the world. Identified studies were divided into groups based on the study population's seizure type or epilepsy syndrome (using the ILAE classification) and then further subdivided (if possible) by age. Each potentially relevant study found through this search methodology was abstracted for specific data which was placed in evidence tables. All identified

randomized controlled clinical trials were evaluated for their class of evidence by predetermined criteria that focused on variables related to minimizing potential bias. These studies were used to determine the level of evidence for each AED in each category. Details of the guideline's methodology and its findings will be presented.

Practical Applications and Pitfalls in USA and Europe
R. Mattson[1]

1) Yale University, USA.

The ILAE Guidelines for Monotherapy have yet to be finalized and approved by ILAE and published. Consequently, the extent of use of these instruments must remain conjectural. For the well trained and experienced clinicians the Guidelines will contribute little that the expert does not know. For the general caregiver less familiar with the literature, the availability of summarized recommendations developed from evidence based analyses should increase the possibility of providing optimal care. The Guidelines also point to areas of insufficient knowledge The Guidelines provide a document based on critical and expert review of evidence to allow an opinion to justify use of agents not approved for medical use by licensing agencies. Insurance providers, government agencies funding health care, hospital formulary committees among others are increasingly driven by evidence-based medicine. It can be expected such groups will avail themselves of the ILAE Guidelines in decision making. The Guidelines have pitfalls that result from multiple factors. These include insufficient Class 1 or 11 evidence to make useful recommendations. Many trials of AEDs are conducted to show efficacy but were not designed to correspond to clinical practice. Guidelines give recommendations that apply to a population, but can't individualize for a specific patient. Concern may arise that Guidelines constitute a required avenue of care although this is not meant to be the use of these or other Guidelines. Despite these and other pitfalls, the availability of evidence-based guidelines provides a means of optimizing patient care.

Practical Applications and Pitfalls in Countries with Limited Resources
C. Guerreiro[1]

1) Department Of Neurology, State University Of Campinas (UNICAMP), Brazil.

Most people with epilepsy (85%) live in developing countries according to the International League Against Epilepsy (ILAE). Developing countries are extremely heterogeneous in their social, economic and health care status. The diagnosis and treatment gap ranges widely within these regions. In some countries there are very poor areas while other countries have basic health care attributes. In the first areas the primary goal is to have phenobarbital distributed by the health system while in more organized areas the four basic AEDs (carbamazepine, phenobarbital, phenytoin and valproate) are available. In some areas government agencies provide even the new AEDs. The Demonstration Project of Global Campaign Against Epilepsy in Brazil revealed that cumulative prevalence and estimated prevalence of active epilepsy were respectively 9.1/1,000 and 5.3/1,000 people. The prevalence of active epilepsy was higher in the more deprived social classes (range from A=richest to E=poorest) in Campinas, São Paulo state (Class D+E = 8.1/1,000 [95%CI = 4.4-11.9] vs. Class A = 1.6/1,000 [0.4-2.9]) and in São José do Rio Preto, São Paulo state (Class D+E = 7.3/1,000 [5.7-8.9] vs. Class B = 3.1/1,000 [1.5-4.7]). Thirty-seven percent of patients with active epilepsy had inadequate treatment, including 19% who were on no medication; the figures were similar in the different socio-economic groups. The main purpose of guideline such as the current one is education: to teach physicians on method, result and limitation based on scientific evidence and practical application to assist practioners about the choices of initial therapy. Pitfalls in countries with limited resources are lack of correct information to health professionals, cost, and cost-benefit choices of AED. Cost is one parameter used for selection of AED in the treatment of epilepsy, particularly important in non-affluent societies. The current guideline takes into account these factors considering that traditional AEDs are among the many options for treatment of seizures and subtypes of epileptic syndromes. ILAE Commission on Therapeutic Strategies strongly supports the proposal for international organizations and governments to provide medical treatment based on evidence with available first-line drugs.

Thursday 1st September 2005
10:00 - 11:30
Salle 243
Parallel Session
Gamma Oscillations and Seizures

Gamma Oscillations and Seizures
S. Kalitzin[1], D. Velis[1], P. Suffczynski[3], J. Parra[1], F.H. Lopes Da Silva[2]

1) Medical Physics Department, Dutch Epilepsy Clinics Foundation, Heemstede, The Netherlands. 2) Centre Of Neurosciences, University Of Amsterdam, The Netherlands. 3) Department Of Medical Physics, University Of Warsaw, Poland.

A novel stimulation and analysis paradigm to monitor spatial distribution and temporal changes of the excitability state in patients with temporal lobe epilepsy (TLE). Information about the dynamical state of neuronal networks involved in the process of generating epileptic activity was obtained through the analysis of neuronal signals evoked by local electrical stimulation of specific brain areas with pulse trains in patients with Temporal Lobe Epilepsy (TLE) who were investigated using indwelling electrodes. We searched for the information contained in the phase domain of these evoked activities, inspired by our finding in photosensitive patients where the enhancement of phase clustering (rPCI) of frequency components in the gamma range was shown to anticipate the transition to an epileptic seizure during intermittent light stimulation. First, the site of onset of seizures in TLE patients could be identified by measuring the rPCI interictally during intermittent electrical stimulation. The second objective was to explore the possibility and to present a 'proof-of-principle' for this methodology with respect to seizure prediction. We found that values of rPCI >0.6 indicate in general impending seizure (<2 h, more than 80% accuracy), while values between 0.1 and 0.3 indicate probable seizure expectancy within 10-30 h (>80% accuracy). We note that understanding the mechanisms relating interictally measured EEG features, such as rPCI of frequency components in the gamma range, to the probability of an ictal transition occurring within a certain time, can give important clues about possible dynamical processes that lead to epileptic seizure onsets. The rPCI of gamma frequency components, can be a reliable measure of the 'closeness' to an ictal transition in a probabilistic context, while the dynamics of this feature may indicate the mechanisms by which neuronal dynamics can drift close to, or further away from, an ictal transition threshold.

Gamma Oscillations Mediate the Long-Term Effects of Seizures
M. Le Van Quyen[2], I. Khalilov[1], H. Gozlan[1], Y. Ben-Ari[1]

1) INMED U29 INSERM, 163, Route De Luminy,, Marseille, France. 2) LENA-CNRS UPR640, Hôpital De La Salpêtrière, paris, France.

We do not know why some seizures permanently transform a naive network to an epileptic one and others do not. To study the mechanisms that underlie epileptogenesis, we used a novel preparation composed of a triple chamber that accommodates the two intact hippocampi and their commissural connections in three independent compartment, thus allowing the applications of two different agents on the two interconnected hippocampi. With this preparation, it is possible to generate seizures in one hippocampus by the local application of a convulsive agent and determine whether the seizures transform the contra-lateral naïve hippocampus to an epileptogenic mirror focus. We report that, in the developing hippocampus, at a time when GABA excites many neurons, seizures are epileptogenic only when they include high-frequency oscillations

from 60Hz to 120Hz. Seizures generated when GABAergic synapses are blocked included only low frequency events <20Hz and did not produce permanent epileptic alterations of the network. Therefore, in the developing brain, high-frequency oscillations and operative GABA synapses are needed for seizures to genet seizures. These observations may be particularly useful both to evaluate correctly the deleterio

Clinical Relevance
P. Chauvel[1], F. Bartolomei[1], F. Wendling[1]

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Low-voltage rapid discharges (or fast EEG ictal activity) constitute a characteristic electrophysiological pattern in focal seizures of human epilepsy. They are characterized by a decrease of signal voltage with a marked increase of signal frequency (typically beyond 25 Hz). They have long been observed in stereoelectroencephalographic (SEEG) signals recorded with intra-cerebral electrodes, generally occurring at seizure onset and simultaneously involving distinct brain regions. Spectral properties of rapid ictal discharges as well as spatial correlations measured between SEEG signals generated from distant sites before, during and after these discharges were studied. Cross-correlation estimates within typical EEG sub-bands and statistical tests performed in ten patients suffering from partial epilepsy (frontal, temporal or fronto-temporal) reveal that SEEG signals are significantly de-correlated during the discharge period compared to periods that precede and follow this discharge. These results can be interpreted as a functional decoupling of distant brain sites at seizure onset followed by an abnormally high re-coupling when the seizure develops. They lead to the concept of 'disruption' that is complementary of that of 'activation' (revealed by significantly high correlations between signals recorded during seizures), both giving insights into our understanding of pathophysiological processes involved in human partial epilepsies as well as in the interpretation of clinical semiology.

Monday 29th August 2005
15:30 - 17:00
Salle Maillot
Platform Session
Adult Epileptology - Mortality

001
SUDEP in a Dutch Tertiary Epilepsy Setting: Frequently Feared but Rarely Seen
M.C.G. Vlooswijk[1], H.J.M. Majoie[2], M.C.T. De Krom[1], I.Y. Tan[2], A.P. Aldenkamp[2]

1) University Hospital Maastricht, Maastricht, The Netherlands 2) Epilepsy Centre Kempenhaeghe, Heeze, The Netherlands

Purpose: To evaluate risk factors for sudden and unexpected death in epilepsy (SUDEP) in a high-risk population, i.e. patients treated in a Dutch tertiary referral centre for epilepsy.
Methods: All patients who died between January 1999 and April 2004 while under treatment of the epilepsy centre were identified. Based on clinical data, deaths were classified as definite, probable, possible or non-SUDEP. Potential risk factors were compared in SUDEP cases and non-SUDEP cases.
Results: SUDEP incidence was 1.24 per 1,000 patient years. SUDEP patients died at a younger age than patients from the control group of non-SUDEP deaths with epilepsy and had an earlier onset of epilepsy. However, the frequently mentioned factors in previous studies, i.e. male sex, generalised tonic-clonic seizures, high seizure frequency, specific antiepileptic drugs (AEDs), polytherapy with several AEDs, mental retardation, psychiatric illness and psychotropic comedication, were not found to be correlated with SUDEP.
Conclusion: Even in this high-risk population of patients with refractory epilepsy, treated in a tertiary referral centre, SUDEP is not a frequently occurring phenomenon. Specific risk factors could not be identified within an already high-risk population.

002
Sudden Unexplained Death in Epilepsy: Related to Compliance with Medication Judged by Hair Analysis
C. Lawthom[1], J. Williams[2], F.D. Dunstan[3], T.P. Dawson[5], M.P. Kerr[4], J.F. Wilson[2], P.E.M. Smith[1]

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Purpose: Variable compliance with antiepileptic drugs (AED) is a potentially preventable cause of epilepsy-related death, but the association remains unproven. Hair AED concentrations provide a retrospective insight into AED intake variability.
Methods: In this retrospective study, we compared hair AED concentration variability in patients with epilepsy identified at autopsy (either sudden unexplained death in epilepsy [SUDEP] or non-SUDEP death) with epilepsy outpatients and epilepsy inpatients. Hair samples were collected at 25 autopsies (16 SUDEP, 9 non-SUDEP) between 1998 and 2002. Hair from 31 hospital-based epilepsy outpatients and from 38 highly supervised inpatients was already available. AED concentrations were measured in 1 cm hair segments using high performance liquid chromatography. Individual patient hair AED concentration profiles were corrected for 'washout' effects using linear regression analysis; the corrected mean, standard deviation (SD) and coefficient of variation (CV) were calculated for each subject. The CV gave an index of variability of an individual's AED-taking behaviour. Sample numbers varied between subjects, and so weighted regression estimates of the CV were derived for each group.
Results: The CV regression estimates for each group were: SUDEP 20.5% (SE 1.9), non-SUDEP 15.0% (3.9), outpatients 9.6% (1.4), and inpatients 6.2% (2.7). The SUDEP group therefore showed greater hair AED concentration variability than either the outpatients or the inpatient groups ($p<0.0001$).
Conclusion: These results demonstrate patients dying from SUDEP demonstrate greater variability of AED ingestion (as evidenced by hair AED concentrations) over time than epilepsy outpatients or epilepsy in-patients. SUDEP, therefore, may be preventable by improved compliance with AED medication.

003
Value of Simultaneous Holter-Electrocardiography (ECG) and Holter-Electroencephalography in Patients with Epilepsy
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Purpose: Electrocardiographic (ECG) changes are well known accompanying manifestations of numerous neurological diseases (ischemic brain disease, intracranial haemorrhage, expansive processes and epilepsy). In patients with epilepsy ECG changes can be responsible for sudden death. The aim of the study was to exclude or prove influence of epileptogenic discharge on ECG abnormalities by simultaneous continuous Holter ECG (HECG) and Holter EEG (HEEG).
Methods: We included 24 patients in our study with clinically observed epileptic seizures and previous epileptic anamnesis. All patients underwent simultaneous 24h Holter ECG/Holter EEG
Results: 9 patients showed specific graphic elements in HEEG without changes in HECG. In 4 patients HEEG and HECG findings were normal. In 8 patients in HECG we observed episodes of heart rhythm

disorders which were time related with specific epileptogenic discharges in HEEG. In 3 patients we observed simultaneous specific graphic elements in HEEG and VT (ventricular tachyarrhythmias) episodes in HECG.
Conclusion: Observed findings indicate possible origins of sudden death in patients with epilepsy which are the consequence of cardiac complications of epileptogenic discharge. The results of our study support the idea of neural structural involvement in the pathogenesis of cardiac complications and their electrophysiological correlates.

004
Five Cases of Ictal Asystole
M. Cenusa[1], I.W. Mothersill[1], T. Grunwald[1], G. Krämer[1]

1) Swiss Epilepsy Centre

Purpose: 5 male patients (age range of 36-67 years) with symptomatic or cryptogenic epilepsy and focal seizures were diagnostically re-evaluated due to a change in seizure semiology. In addition to the known complex focal seizures they had all developed additional 'atonic' falls with or without convulsive symptomatology.
Methods: Continuous ambulatory EEG/ECG recordings were performed, when possible with video recording, until the 'new' seizure semiology was registered. The average duration of recording was 72.5 hours (1-270 hours). All recordings were carried out under normal conditions, no provocation methods including drug reduction were used.
Results: Focal seizures were recorded in all patients. The seizure onset in the surface EEG could be localised to the fronto-temporal leads, in 4 cases left sided and in 1 right. In the co-registered ECG, asystoles with a duration between 10 and 14 seconds were seen, accompanied in the EEG with typical hypoxic-anoxic signs which were clinically associated with syncopal events.
Conclusion: Documented cases of ictal bradycardia or asystole are rare; to date only about 30 cases have been published. In all our patients the cardial syncopal events had been misinterpreted as a 'new' seizure semiology. Our findings show the importance of diagnostic re-evaluation in patients whose seizure semiology changes over time, especially if they present 'atonic' like falls.

005
Sensitivity of Epilepsy Bed Alarms and Pulse Oxymeters in the Danish Epilepsy Centre, Dianalund
R.M. Mathiasen[1], C.P. Hansen[1]

1) Danish Epilepsy Centre, Dianalund, Kolonivej 1, DK-4293 Dianalund, Denmark

Purpose: We present a pilot study evaluating the sensitivity of epilepsy bed alarms and pulse oxymeters in patients of the Danish Epilepsy Centre, Dianalund.
Methods: Patients from short term departments were prospectively subjected to close supervision using video camera when they were undergoing significantly increased risk of potentially dangerous epileptic seizures. The inclusion period was from April 2004 to January 2005. When the patients were in bed, they were constantly supervised by video recording. The patients were carrying a pulse oxymeter, and the beds were equipped with epilepsy alarms. The video supervision allowed identification of epileptic seizures, and the nursing staff registered alarms by the bed alarms and pulse oxymeters (desaturation and/or change of pulse). Trained physicians classified seizures observed during video recording as generalised tonic clonic, tonic, myoclonic, focal motor seizures or other seizures.
Results: 71 patients (39 females and 32 males), aged 1-54 years (mean 21.8 years) were included. 16 had no seizures in the time observed. 9 patients had unclassified seizures. The sensitivity of epilepsy bed alarms was 31.0% in tonic-clonic seizures, 9.4% in tonic seizures, 5.2% in focal seizures, and the sensitivity of pulse-oxymeters was 34.0% in tonic-clonic seizures, and 15.5% in tonic seizures.
Conclusion: The sensitivity of epilepsy bed alarms and pulse oxymeters was 30 to 35% in the case of generalised tonic-clonic seizures and lower for other seizure types. Further studies will aim at optimising the use of these technical devices and assess their specificity in our specialised epilepsy centre.

006
Mortality Risk from Drowning for People with Epilepsy
A. Gaitatzis[1], G. Bell[1], A.L. Johnson[2], J.W. Sander[1]

1) Institute of Neurology, University College London, London, UK 2) MRC Biostatistics Unit, Institute of Public Health, Cambridge, UK

Purpose: To calculate the risk of death from drowning for people with epilepsy in the community.
Methods: As part of a national audit into epilepsy-related deaths we reviewed the death certificates (DCs) of people who died in England and Wales between September 1999 and August 2000 and for whom epilepsy was recorded on the DC. During that time 2,042 such deaths were reported. Standardised mortality ratios (SMRs) were calculated as the ratio of the observed to the expected number of deaths in this epilepsy population. We identified 22 people (age range 18-93 years, mean 38 years) who died as a result of drowning, immersion, or submersion in water (ICD 9, E910). All deaths were investigated and certified by a Coroner. The expected number of deaths was calculated by applying the year 2000 ICD9 E910 death rates of the population of England and Wales per age group and sex to the epilepsy population. The total number of people with epilepsy was estimated from prevalence rates of treated epilepsy in England and Wales per age group and sex extrapolated to the general population. An assumption was made that all deaths occurred amongst people with treated epilepsy.
Results: The overall SMR was 15.3 (95% confidence interval, 10-23). The SMR in women was 23.9 (11.4-50) and in men 13 (7.9-21.7). Only 5 deaths occurred during the summer months.
Conclusion: Our findings strongly suggest that people with epilepsy are at a 15- fold increased risk of dying from drowning compared with the general population; the risk seems higher in women. Adequate seizure control and taking of precautions should be established for all patients in order to avoid more deaths.

Monday 29th August 2005
15:30 - 17:00
Salle 252A
Platform Session
Genetics 1

007
Genetic Predisposition to Severe Myoclonic Epilepsy of Infancy (Dravet Syndrome): Analysis of Cases with and without SCN1A Mutations
R. Gaggero[1], M. Mancardi[1], P. Striano[2], F. Fazzini[1], L. Siri[1], C. Dravet[3], E. Gennaro[4], F. Zara[5]

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Purpose: Severe myoclonic epilepsy of infancy (SMEI) or Dravet syndrome is an intractable epileptic encephalopathy considered as "undetermined whether focal or generalized" in the ILAE classification. A strong genetic predisposition was recognised in families of SMEI patients (Benlounis et al, 2001). Mutations, usually de novo, of alpha subunit of voltage dependent sodium channel (SCN1A) are found in about 30-80% of the patients. However, other unknown genetic factors are probably involved in its pathogenesis. To better clarify the role of the genetic background of SMEI, we searched for familial antecedents of epilepsy (E) and febrile seizures (FS) in our large series of SMEI patients and performed preliminary correlations with status of the SCN1A gene.
Methods: 100 SMEI patients coming from the Italian League Against Epilepsy database were investigated. Diagnosis of SMEI were done according to ILAE description (Epilepsia, 1989). All patients were

screened for SCN1A mutations. Furthermore, familial antecedents for E and FS were investigated in the first, second and third-degree relatives.
Results: Familial history for E or FS were found in 62 SMEI patients. 32 cases showed mutations of the SCN1A gene. In the latter, the first-degree relatives were affected in 13 (40%) cases whereas the second and third-degree relatives were affected in 21 (65%) cases. FS were found in 14/32 (43%), idiopathic generalised epilepsy (IGE) in 11/32 (34%), partial E in 4/32 (12.5%), SMEI in 2/32 (6.25%) and not specified E in 4/32 (12.5%) individuals. In the group of patients without SCN1A mutations, the first-degree relatives were affected in 19 (63%) cases whereas the second and third-degree relatives were affected in 22 (73%) cases. FS were present in 10/30 (26%), IGE in 10/30 (26%), SMEI in 3/30 (10%) and not-specified E in 7/30 (23%) individuals.
Conclusion: These preliminary data support the strong genetic background of SMEI. In particular, we confirmed the higher incidence of FS and IGE in relatives of SMEI patients. No difference was found between patients carrying or not carrying SCN1A mutations except from a higher frequency of FS in the first group. Further studies are needed in order to clarify the genetic factors underlying the predisposition to SMEI as well as to better understand its relationship with generalised epilepsy febrile seizures plus (GEFS+) syndrome.

008
Novel Susceptibility Locus at 2p24 for Generalised Epilepsy with Febrile Seizures Plus
D. Audenaert[1], L. Claes[1], K. Claeys[1], L. Deprez[1], T. Van Dyck[1], D. Goossens[1], J. Del-Favero[1], W. Van Paesschen[2], C. Van Broeckhoven[1], P. De Jonghe[1]

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Purpose: Generalised epilepsy with febrile seizures plus (GEFS+) is a familial epilepsy syndrome that links febrile seizures with epilepsy. It encompasses a continuum of phenotypes with mild and severe forms of epilepsy. Clinical and genetic heterogeneity for GEFS+ and febrile seizures has been demonstrated. This study aimed at the identification of a novel locus involved in GEFS+ and febrile seizures.
Methods: We ascertained a four-generation family with GEFS+ and performed a 10 cM density genome-wide scan. Parametric linkage analysis was used to identify a novel GEFS+ locus in this family. To confirm our findings, non-parametric linkage analysis, TDT testing, and association studies were performed in an additional collection of 50 nuclear and multiplex families with febrile seizures and GEFS+.
Results: In a four-generation family, we obtained conclusive evidence for a novel GEFS+ locus on chromosome 2p24. Fine mapping and haplotype analysis delineated a candidate region of 3.24 cM, corresponding to a physical distance of 4.2 Mb. Linkage to 2p24 was confirmed ($p = 0.007$) in a collection of families with febrile seizures and GEFS+. TDT testing and association studies provided further evidence for a GEFS+ locus at 2p24. Based upon an ancestral haplotype, we could reduce the candidate region to a 2.14 cM interval.
Conclusion: The locus at 2p24 represents a novel genetic entity for GEFS+. Our findings indicate that a susceptibility allele at 2p24 contributes to febrile seizures and GEFS+ in the population.

009
Outcome in Absence Epilepsy
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1) Serviço Neuropediatria, Hospital Maria Pia, Porto, Portugal

Purpose: Our purpose was to correlate the outcome of absence epilepsy, according to the type of syndrome, particularly in patients with childhood absence epilepsy (CAE).
Methods: We selected patients followed from 1993 until 2004, with absences as the first type of seizure and with an ictal video-EEG. We excluded those with reflex epilepsy, myoclonic absence epilepsy and symptomatic epilepsy. Patients were classified as CAE, if they had diary absences as the only type of seizure, before age of 10, with generalised 3-3, 5Hz SW, without photosensitivity.
Results: We found 73 patients. 50 were classified with CAE, 6 with juvenile absence epilepsy (JAE) and 3 with juvenile myoclonic epilepsy (JME). 14 patients could not be classified in any of these syndromes (absence syndrome group (AS)). In the CAE group, 27 patients are seizure free after discontinuing treatment. 23 are medicated. 4 patients, from this last group, still have seizures, 3 of them older than 13 years. All patients with JME, JAE are under medication, as are all but one of the AS group.
Conclusion: Outcome is more difficult to predict when absences start by the age of 9, since there may be an overlap between CAE and JAE. For patients with absences and PSW, it is also difficult to say which one will have an evolution to JME or to photosensitivity epilepsy. Even for patients that we considered as 'pure' CAE, the outcome is not always good, as 6% of our patients need to be treated even after puberty.

010
Anatomoclinical Spectrum of Periventricular Heterotopia and Correlations with FLNA Mutations: A Study of 167 Patients
E. Parrini[1], A. Ramazzotti[1], D. Mei[1], F. Moro[1], C. Marini[1], P. Veggiotti[2], E. Said[3], P. Striano[4], E.H. Brilstra[5], B. Dalla Bernardina[6], M.C. Jones[7], M. Nangeroni[8], S. Palmeri[1], Y. Takahashi[1], M. Viri[1], M. Wright[1], L. Sander[1], W.B. Dobyns[1], C.A. Walsh[1], R. Guerrini[1]

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Purpose: Periventricular nodular heterotopia (PNH) is a cortical malformation in which a subset of neurons remains as nodules of heterotopic grey matter along the lateral ventricles. Mutations of FLNA have been associated with classical X-linked bilateral PNH, often accompanied by focal epilepsy of variable severity. The purpose of this study was to define genotype-phenotype correlations in a population of patients with PNH.
Methods: We studied the clinical and MRI characteristics of 167 patients with different types of PNH, 110 of whom underwent mutation analysis of FLNA.
Results: We defined 15 PNH subtypes including classical bilateral PNH (BPNH) (88 patients: 52%) and 14 additional phenotypes (79 patients: 47%. We identified 22 FLNA mutations in 87% of females and in 3% of males. Mutations were present in all families with classical X-linked BPNH. The probability of identifying a FLNA mutation in individuals with classical BPNH was 61%; but it decreased to 8% in patients with other PNH phenotypes. 17 nonsense/frameshift and 5 missense mutations were identified. The high prevalence of nonsense and frameshift mutations suggests that complete loss of function of the mutated FLNA allele was the major disease causing mechanism in most patients.
Conclusion: Genetic counselling in individuals with PNH must take into account that FLNA mutations are associated with 100% of classical familial and 25% classical sporadic BPNH cases, but rarely with either Ehlers-Danlos syndrome or unilateral PNH. FLNA is not expected to be involved in any other class of PNH.

011
Tuberous Sclerosis: Comparative Study of Epilepsy in Children with or without Subependimal Giant Cell Astrocytoma
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Purpose: We compared the clinical characteristics of seizures in patients with tuberous sclerosis complex (TSC) without or having subependymal giant cell astrocytoma (SEGA).
Methods: In a group of 62 children and adolescents (29 male, 33 female; mean age 8.5 years), with definite diagnosis of TSC, 9 patients (4 male, 5 female; mean age 14.7 years) had SEGA with postoperative histological confirmation. Mean age of SEGA diagnosis was 11.2 years. Family history of TSC was found in 29.8% including 2 children with SEGA. Mean clinical follow-up was 6.7 years for children with TSC without tumour, and 9.4 years for patients with SEGA.
Results: Seizures occurred in 56 (90.3%) TSC patients, including all children with SEGA. History of febrile seizures was noted in 3 children without SEGA, but not in any SEGA patients. The age of seizure onset in patients with SEGA was 4.1 (range 1.5-16.4). Convulsive epileptic status was the initial epileptic event in a 13.5 year old girl. When compared with the SEGA group, the first seizure in patients without tumour occurred earlier (2.3 years, range 0.3-15.2). Focal seizures mainly secondarily generalised occurred in all but one patient with SEGA. Infantile spasms were diagnosed in 1 case. TSC patients without SEGA had partial epilepsy in 37.7%, until infantile spasms were noted in 21 of 47 (44.7%) patients. Favourable, long-term seizure control was achieved in 3 SEGA patients only, when compared with 57.4% of TSC patients without tumour. Epileptic status occurred in 11 (23.4%) TSC children without SEGA and in 6/9 patients with SEGA (before tumour removal in 4 and after the surgical treatment in 2 cases). Mental insufficiency and/or behavioural disorders were observed in all SEGA patients and in 37/53 (69.8%) children with TSC without tumour.
Conclusion: When compared with TSC patients without tumour, the SEGA group had mainly focal and pharmacoresistant seizures occurring with later onset. All had mental insufficiency and/or behavioural disorders. Surgical removal of SEGA did not appear to significantly improve epilepsy course.

012
Mild Epilepsy Phenotype in TSC2 Patients with Codon 905 Mutations
A.C. Jansen[1], O. Sancak[2], M.D. D'Agostino[1], A. Badhwar[1], P. Roberts[3], G. Gobbi[1], R. Wilkinson[4], D. Melanson[5], R. Koenekoop[6], M. Gans[6], A.M.W. Van den Ouweland[2], M. Nellist[2], M. Pandolfo[7], K. Sims[8], E. Thiele[8], F. Andermann[1], F. Dubeau[1], D. Kwiatkowski[3], D.J.J. Halley[2], E. Andermann[1]

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Purpose: To report the epilepsy phenotype, the clinical manifestations, and functional aspects of codon 905 mutations in tuberous sclerosis type 2 (TSC2).
Methods: We carried out a detailed study of the TSC phenotype in a large French-Canadian family (Family A). Linkage analysis of the TSC loci and mutation analysis of the TSC2 gene were performed. In addition, clinical and molecular data on three families and six sporadic patients with a mutation at the same codon were collected. The functions of the codon 905 mutations were studied and related to the phenotype.
Results: A 2714G>A (R905Q) missense mutation in exon 23 of TSC2 was identified in 25 individuals in Family A. The mild TSC phenotype in this family was characterised by the absence of cortical tubers, intractable epilepsy, disfiguring skin lesions, severe mental retardation or other major organ involvement. Diagnostic criteria were met in only a minority of family members, delaying diagnosis. Three other families with the same mutation were found to have a similar mild phenotype. Six patients with a different mutation at the same codon (2713G>T or R905W) had a more severe phenotype. Functional studies of the R905Q/R905W mutated tuberin demonstrated only a mild impact on tuberin function.
Conclusion: We have described ten new families with mild TSC2 phenotypes, all of which had codon 905 mutations. The epilepsy phenotype was unusually mild, characterised mainly by seizures that remitted spontaneously or were easily controlled with anti-epileptic drugs. Functional studies showed a minimal effect of the R905Q/W mutation on tuberin function. Genotype-phenotype correlations among families with R905Q and R905W were carried out.

Monday 29th August 2005
15:30 - 17:00
Salle 252B
Platform Session
Paediatric Epilepsy 1

013
Benign Myoclonic Epilepsy in Infants: Initial Features and Long-term Follow-up
S. Auvin[1], F. Pandit[1], J. De Bellecize[2], N. Badinand[2], H. Isnard[2], J. Motte[3], N. Villeneuve[4], M.D. Lamblin[5], L. Vallée[1]

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Purpose: Benign myoclonic epilepsy in infants (BMEI) is a rare epileptic syndrome characterised by only generalised myoclonic seizures in normal children during the first two years. Limited data describe the long-term follow-up.
Methods: We included the patients with BMEI confirmed by EEG between 1981 and 2002 in four neuropaediatric units in France. Clinical and electroencephalographic findings at diagnosis and during the follow-up were collected. Vineland scale and/or Wechsler scale were used to perform neuropsychological evaluations.
Results: We report 34 patients with BMEI. A family history of febrile seizures (FS) or epilepsy was noted in 6 patients. A personal history of FS was noted in 11 patients. 11 patients presented reflex myoclonic seizures. Monotherapy with valproate acid was effective in 23 of the 30 treated patients. Epileptic evolution was known in all patients. 4 patients presented seizures after the initial symptoms. 2 patients developed a juvenile myoclonic epilepsy and 1 a cryptogenic partial epilepsy. Neuropsychological outcome was evaluated in 20 patients (10 with Wechsler scales and 17 with Vineland scale). Cognitive functions were normal in 17 patients. Mental retardation was observed in 3 patients.
Conclusion: The positive family history of FS or epilepsy suggests that the genetic factor is important in the pathogenesis of BMEI. Reflex myoclonic seizures were frequently observed suggesting that the distinction of two distinctive syndromes is not necessary. Valproate monotherapy was effective. BMEI may be followed by juvenile myoclonic epilepsy. Despite a generally favourable neuropsychological outcome, mental retardation can be observed

014
Benign Focal Epilepsy in Infancy with Vertex Spikes and Waves During Sleep: Delineation of the Syndrome and Renaming as "Benign Infantile Focal Epilepsy with Midline Spikes and Waves During Sleep" (BIMSE)
G. Capovilla[1], A. Montagnini[1], F. Beccaria[1]

1) Epilepsy Centre, Department of Child Neuropsychiatry, 'C. Poma' Hospital, Mantova, Italy

Purpose: To describe the electroclinical features of infants who presented with focal seizures and typical midline sleep EEG abnormalities with a benign outcome. We previously described this new entity in 2000 and called it "Benign focal epilepsy in infancy with vertex spikes and waves during sleep" (BVSE). We discuss the

significance of the typical EEG marker in non-epileptic patients.
Methods: Patients were selected from a group of subjects with epilepsy with seizure onset in infancy. Inclusion criteria were the presence of a typical sleep EEG marker and focal seizures with a benign outcome. Cases with less than 18 month follow up period were excluded.
Results: There were 19 patients (12 males, 7 females). Pre-, peri- and post-natal personal history was uneventful. Psychomotor development was normal, both before and after seizure onset. Neuroradiological investigations gave normal results. Seizure manifestations were typical, characterised by cyanosis, staring and rare lateralising signs, of short duration. Onset age was between 4 and 30 months. The typical EEG marker, a spike followed by a bell-shaped slow-wave, localised in the midline regions, was present only during sleep. All had a favourable outcome and the overwhelming majority of patients were not treated. We found the same EEG marker in 4 patients presenting with a febrile convulsion and in 3 other patients without any convulsive illness.
Conclusion: Our patients have an homogeneous electroclinical picture to constitute a new epileptic syndrome not included in the ILAE classification. We propose to call it "benign focal epilepsy in infancy with midline spikes and waves during sleep" (BIMSE).

015
Epilepsy with EEG Paroxysmal Discharges During Slow Sleep and Arousal: A Sub-type of Nocturnal Frontal Lobe Epilepsy or a New Epileptic Syndrome?
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Purpose: To study the significance of very frequent EEG paroxysmal discharges during slow sleep coincident with an arousal, changes in respiratory patterns, and occasional tonic seizures in patients with refractory epilepsy and cognitive and behavioural deterioration.
Methods: We studied 30 patients of ages ranging from 5.5 to 19 years (mean 12.5 years). There were 19 females. All patients underwent several whole-night video-EEG recordings. All except one patient presented frontal lobe epilepsy (one patient presented occipital lobe epilepsy). Mean age of seizure onset was 2.9 years.
Results: During slow sleep paroxysmal generalised, focal (frontal or occipital), or unilateral discharges were present. These paroxysms occurred at the same time as an arousal and irregular breathing repeatedly during slow sleep altering the organisation of sleep cycles. We consider these events as true seizures even with their infra-clinical expression. Other types of seizures were also present in all patients: diurnal (atypical absences, tonic and tonic-clonic seizures) and nocturnal (mainly tonic seizures). Cognitive decline and behavioural problems were present in all patients. MRI was abnormal in 50% of the patients. Patient follow-ups ranged from 2 to 15 years. All patients were on polytherapy. Except for 2 patients, all had a poor outcome with persistent seizures and progressive cognitive deterioration.
Conclusion: We consider that the characteristics of this group of patients including the electro-clinical findings, cognitive deterioration, poor response to antiepileptic drugs and poor outcome may represent a previously undescribed form of nocturnal frontal lobe epilepsy.

016
High-dose Methylprednisolone Therapy in 13 Children with Electrical Status Epilepticus during Sleep
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Purpose: Syndrome of electrical status epilepticus during slow-wave sleep (ESES) is not rare in children with epilepsy. High-dose intravenous corticosteroid seems to be effective in such patients (Okuyaz C. et al. Pediatr Neurol 2005;32:64-67.). The purpose of the present study is to demonstrate the efficacy and tolerability of intravenous high-dose methylprednisolone (HDMP) therapy in a Chinese group of 13 children with ESES.
Methods: 13 children with ESES on 24-hour EEG monitoring, March through September 2004, were treated with HDMP. Among the 13 patients, 6 had Landau-Kleffner syndrome, 5 had epilepsy with continuous spikes and waves during slow sleep (CSWS), and 2 had a variant-type of benign rolandic epilepsy. High dosage (15~30 mg/kg.d) of methylprednisolone was intravenously injected for 3 consecutive days, and a total of three regimens was administrated with a 4 day interval between treatments. The original antiepileptic drug therapies were kept unchanged. Clinical observation and another 24 hour EEG monitoring were recorded 2~4 weeks after the above therapeutic scheme finished.
Results: ESES pattern on EEG disappeared in 7 cases leaving only scattered epileptic discharges. Among the 6 children still with an evident ESES pattern, the frequencies of discharges significantly diminished in 4, and were almost unchanged in 2. Clinical improvement was notable in 11 cases including 1 without an obvious EEG recovery. No vital adverse reactions were recorded.
Conclusion: HDMP is an alternative effective and safe therapy for children with ESES. This work was partly supported by the Key Clinical Project□20010912□from the Ministry of Public Health of China.

017
Lesion on MRI Predicts Seizure Outcome in New-Onset Temporal Lobe Epilepsy in Childhood
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Purpose: There is a paucity of prospective data on outcomes for children with new-onset temporal lobe epilepsy (TLE).
Methods: We ascertained and studied a cohort of 77 children with new-onset TLE during 1991-93. 63 had definite TLE and 14 had possible TLE (Harvey AS et al Neurology 1997;49(4):960-968). Patients were followed prospectively with formal review at approximately 7 and 14 years from seizure onset. Only 2 were lost to follow-up. 62 patients sustained the diagnosis of TLE over time. Age at seizure onset was 0.2-14.8 years. 17/62 had significant antecedents. FSIQ ranged from 48-127. Lesions were identified at recruitment in 26 (MRI 56, CT 5, no imaging 1) and included hippocampal sclerosis in 9, tumour in 8 and dysplasia in 6.
Results: 18 are seizure free (SF) and off treatment, having not had seizures for 5-15 years. Duration of TLE in the SF group ranged 1-8 yrs, the children being treated with 0-3 drugs. 44 are not seizure free or have progressed to epilepsy surgery (NSF). The children were treated with 1-10 drugs. 15 NSF patients experienced 22 non-terminal remissions of 1-7 years duration. All children with lesions on MRI were NSF ($p<0.001$). Infant onset, family history, initial seizure frequency, early seizure remissions and EEG features were not predictive of seizure outcome.
Conclusion: A lesion on MRI is highly predictive of intractable TLE and potential need for surgery. There is a group of children with 'benign TLE' having normal intelligence, infrequent seizures and no lesion on MRI who outgrow their epilepsy.

018
Clinical Spectrum of Paediatric Patients with Mesial Temporal Lobe Epilepsy: Hippocampal Sclerosis and Post-Surgical Outcome
C.W. Fung[1], R.C. Scott[1], B. Harding[1], K. Chong[1], T. Cox[1], D. Saunders[1], W. Harkness[1], J.H. Cross[1]

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Purpose: To characterise the clinical spectrum of mesial temporal lobe epilepsy: hippocampal sclerosis syndrome (MTLE-HS) in children and to identify predictors of post-surgery seizure freedom.

Methods: A retrospective review of all children who had anterior temporal resections for MTLE-HS between 1992 and 2001 was carried out. Patients were classified into 2 groups according to the presence or absence of history of febrile status epilepticus in childhood (F/status+/ F/status-). Clinical parameters, magnetic resonance imaging (MRI), histopathology and seizure outcome post surgery were reviewed. A good outcome from surgery was defined as seizure-freedom.
Results: 15 children with F/status+ and 22 with F/status- were identified. F/status- patients had short febrile seizures, non-febrile status epilepticus, head injury or no risk factor. The F/status+ group had a higher IQ (p=0.033) than the F/status- group. Other clinical parameters were not significantly different between the two groups. Unilateral tonic/dystonic or clonic movement correctly lateralised the lesion in 87% of cases. Analysis of outcome showed that patients with a history of febrile status (p=0.017), those with typical MRI features of HS (p=0.004) and those with typical histopathological features of HS (p=0.01 alone or p=0.006 when combined with MRI findings) of MTS predicted a good outcome. IQ did not predict outcome (p=0.406).
Conclusion: At least 2 phenotypes of paediatric MTLE-HS exist. Children with a history of febrile status epilepticus tend to have higher IQ and typical MRI/histopathological features of HS. This phenotype has better seizure outcome after surgery.

Monday 29th August 2005
15:30 - 17:00
Salle 242AB
Platform Session
Epilepsy Surgery at Risk

019
Volumetric Radiofrequency Ablation for Minimally Invasive Therapy of Intractable Epilepsy Associated with Sessile Hypothalamic Hamartoma
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Purpose: Hypothalamic hamartoma (HH) is intrinsically epileptogenetic. The seizures become intractable even by various therapies, especially in cases of large sessile types. We applied radiofrequency ablation (RFA) combined with other modalities to develop minimally invasive treatment.
Methods: To avoid injury by RFA to the adjacent hypothalamus and important structures, we introduced stereotactic or navigator-guided localisation of the electrodes after image-based volumetric simulations prepared preoperatively. Illustrative cases are presented. Case 1: A 13 year old boy with a large sessile HH. He presented with refractory epilepsy, mental retardation, and aggressiveness, which did not improve with partial resection and gamma knife (GKS). RFA targets with multiple electrode trajectories were generated in the hamartoma under volumetric stereotaxy with image fusion. Case 2: A 26 year old man with refractory epilepsy and severe mental retardation. He underwent three surgeries yielding partial resection and conventional irradiation. The residual HH was shaped like a bent plate, attached widely to the floor of the third ventricle. The posterior two thirds of the hamartoma was ablated under direct microscopic inspection via the transcallosal subchoroidal approach with the aid of a neuronavigator.
Results: In both cases, immediate and dramatic seizure remission was obtained without neurological complications.
Conclusion: RFA can be applied as a minimally invasive and radical therapy for HH-associated intractable epilepsy. Its effect is immediate and is advantageous especially for large or irregularly shaped HH difficult to treat by conventional surgery or GKS.

020
Stereotactic Disconnection Surgery of Hypothalamic Hamartoma with Intractable Gelastic Epilepsy
J. Homma[1], A. Fujimoto[1], T. Ueno[1], H. Masuda[1], M. Fukuda[1], S. Kameyama[1]

1) Epilepsy Centre, Nishi-Niigata Chuo National Hospital, Niigata, Japan

Purpose: Management of hypothalamic hamartoma with intractable gelastic epilepsy remains controversial. We have been using stereotactic thermo-coagulation surgery on hypothalamic hamartoma since 1997. To clarify the usefulness of this treatment, our total experience with 5 cases is reviewed.
Methods: Subjects comprised 5 patients with hypothalamic hamartoma treated using stereotactic thermo-coagulation in our institution between October1997 and February 2004. In 3 cases, chronic intracranial electroencephalography was performed using depth electrodes implanted in the hypothalamic hamartoma. Attempts were made to induce gelastic epilepsy by electrical stimulation of the hamartoma. After magnetic resonance imaging-guided targeting of the boundary between hamartoma and normal hypothalamus, a radiofrequency coagulation needle was inserted and thermal energy delivered. The coagulation needle provided a spherical lesion of 5 mm in diameter under conditions of 74?C heating for 60s, and a combination of multiple spherical lesions provided an adequate plane of disconnection.
Results: In all cases, hamartoma was located in the third ventricle with sessile attachment to the wall. No intra-operative complications were encountered other than a single case involving acute and transient panidrosis with hot flushes during coagulation. Marked reductions in seizure frequency were obtained in all cases, with 3 patients becoming seizure-free immediately after the operation. Transient postoperative symptoms were seen, with pyrexia in 4 cases and hyperphagia in 2 cases. No mortality or permanent morbidity was associated with the use of this procedure.
Conclusion: Results from these 5 cases suggests satisfactory seizure outcome and acceptable morbidity following stereotactic thermo-coagulation surgery for hypothalamic hamartoma.

021
Role of Frameless Stereotactic Endoscopic Disconnection in the Treatment of Hypothalamic Hamartomas with Refractory Epilepsy: Results from 33 Patients
E. Procaccini[2], G. Dorfmuller[1], M. Fohlen[1], C. Bulteau[1], O. Delalande[1]

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Purpose: Hypothalamic hamartomas (HH) associated to refractory epilepsy frequently require surgery in order to prevent encephalopathy. We describe the results from our series (33 patients).
Methods: 24 males and 9 females were operated on between January 1997 and April 2004. Types of seizure experienced: gelastic (32), dacrystic (3), partial (13), tonic (17), atonic (6), generalised tonic clonic (3), infantile spasm (1). Preoperative examination revealed no motor deficits, mental retardation (19), behavioural disturbances (13) and endocrinological abnormalities (12). MRI always demonstrated an T1W - isointense and T2W - hyperintense diencephalic lesion. 49 surgical procedures were carried out. Every patient but the first underwent disconnective surgery (pterional route: 7; frameless stereotactic endoscopic route: 13; both: 12).
Results: All patients but one experienced recovery/remarkable improvement (Engel class I: 48.5%; II: 3%; III: 45.5%; follow up mean value: 1y 7m). In those patients affected by Type II HH (treatment of choice according to Delalande's classification: endoscopic disconnection) recovery was achieved in 90% and dramatic improvement in 10%. Patients presenting with Type III HH (recommended procedure: endoscopic disconnection followed by pterional approach) gained recovery in 35.3% and improvement in 60%. Postoperative neuropsychological and endocrinological tests showed improvement in the majority of patients. Surgical

complications were described only following open surgery (2 cases: persistent hemiplegia, transient hemiparesis and oculomotor palsy).
Conclusion: Our data confirm the efficacy of disconnective surgery and strongly support frameless stereotactic endoscopic approach in the presence of favourable anatomical conditions.

022
Central Region Resections for Intractable Epilepsy Associated with Taylor Type Focal Cortical Dysplasia: is a Seizure-free Outcome Possible after Resection Without Functional Compromise?
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Purpose: A seizure-free outcome after resection of Taylor-type focal cortical dysplasias (TTFCD) depends on a complete resection of the dysplastic cortex. In eloquent areas, such complete resection may be difficult to achieve and carries a risk of unacceptable permanent functional deficit.
Methods: Over a 4-year period, 11 patients (5 men, 6 women) aged 7 to 41 years (mean: 19.6 yrs) underwent presurgical investigation for early onset intractable sensorimotor epilepsy and were found to have a TTFCD in the central region. In 8 cases, standard MRI was normal or showed subtle nonspecific abnormalities, but a 18FDG PET scan demonstrated focal hypometabolism in all cases. Stereo-EEG recordings were performed in all cases and found continuous rhythmic spike activity within the hypometabolic gyrus which was also the site of spontaneous seizure onset. The TTFCD was precentral in 6 cases, within the central sulcus in 2 and post-central in 3. Surgical resection of the dysplastic cortex was guided by imaging, SEEG results, intraoperative neuronavigational guidance and cortical stimulations.
Results: Postoperatively, a motor deficit occurred in 4 cases and resolved completely within one to three weeks. A mild and transient sensory deficit occurred in the 3 cases with post-central resection. With a follow-up ranging from 4 to 54 months (mean: 22 months), 7 patients were completely seizure-free after surgery and 1 had a generalised seizure on medication removal only. An early failure was observed in 3 patients, their seizures recurring within one week after surgery. All were re-operated using cortical stimulations and dysplasia was found in the additional removed tissue. All 3 have been completely seizure-free since surgery without additional functional deficits.
Conclusion: Complete resection of TTFCD located in the central region is possible with an excellent seizure outcome and no permanent morbidity. Early failure due to incomplete resection of a TTFCD should lead to reoperation even in eloquent areas.

023
Functional and Seizure Outcome Following Resections in Primary Sensory-motor Cortex
R. Chamoun[1], A. Alaraj[1], C. Bouclaous[1], M. Mikati[1], Y. Comair[1]

1) American University of Beirut

Purpose: The management of intractable epilepsy secondary to lesions located in the primary sensory-motor cortex (PSMC) remains a neurosurgical challenge. Our purpose is to show that, in selected cases, surgical resections can be performed: the immediate postoperative neurologic deficit observed is not permanent and seizure-freedom can be achieved in a significant number of patients.
Methods: 24 patients with the diagnosis of intractable epilepsy secondary to lesions in the PSMC were surgically treated between 1997 and 2003. Tumours were found in 13, vascular lesions in 6 and cortical dysplasia in 5. Average postoperative follow-up period: 4.6 years.
Results: Following selective motor resections (including resections in the hand motor area), severe motor deficit occurred in the immediate postoperative period. Gradual improvement started one month postop on average. Substantial improvement was found at 6 months of follow-up. Long term sequelae included impaired fine hand movements and toe movements. Following sensory resections, severe sensory deficit occurred in the immediate postoperative period. Long term sequelae included impaired position sense. 18 of 24 patients were seizure-free at the latest follow-up.
Conclusion: Selective surgical resections allow excellent to good seizure outcome in most patients with lesions in the PSMC. The proposed mechanisms for functional recovery will be discussed, including reorganisation within the ipsilateral PSMC, substitution of the ipsilateral PSMC by the non-primary motor areas and recruitment of the contralateral PSMC

024
Factors Associated with Post-Surgical Outcome of Landau-Kleffner Syndrome
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1) Rush University Medical Center and Rush Medical College

Purpose: Landau-Kleffner Syndrome (LKS) is a rare disorder that may be amenable to surgical therapy with multiple subpial transection (MST). The goals of this study were: 1) to identify the frequency with which MST results in the recovery of functional language, defined as the ability to speak in complex sentences after a post-surgical period of at least two years; 2) to determine whether presurgical improvement of language disturbances with prednisone can predict a favourable post-surgical recovery of language functions.
Methods: A retrospective study of 24 consecutive children with a classic form of LKS (14 boys and 10 girls). Age of onset of LKS: 4.2±1.5 years; age at surgery: 7.0±1.9 years. 20 children had undergone a trial with prednisone. Side of surgery: left, n = 16, right, n = 8. All children underwent neuropsychological evaluation of receptive and expressive language functions before surgery and at various points after surgery. Last post-surgical neuropsychological testing: 47±31 months after surgery. Neuropsychological scores presented as age equivalents (in months).
Results: At the last speech evaluation carried out at our centre, 16 children (67%) had regained the ability to speak in complex sentences. However, only 9 children (37.5%) were in regular class and 20 (83%) were still receiving speech therapy. For the entire group of 24 patients, MST yielded a significant improvement in the age equivalent scores of receptive (baseline 18±20.4 months vs. post -op 76±33.2, $p < 0.0001$) and expressive language tests (baseline 16.6±19 months vs. post-op 74±29.2, $p < 0.0001$). Patients who underwent MST in the 'presumed' non-dominant hemisphere were more likely to speak in sentences at 6 months ($X^2 = 6.6$, $p = 0.01$) and in complex sentences at the last formal speech evaluation ($X2 = 6.5$, $p = 0.01$). Among the 20 children who underwent a pre-surgical trial with prednisone, 9 exhibited a significant improvement in language disturbances, and were significantly more likely to speak in sentences at 6 months after surgery ($X2 = 8.4$, $p = 0.004$) and with complex sentences at the last evaluation ($X2 = 6.2$, $p = 0.013$.
Conclusion: MST can result in functional recovery of language functions in two-thirds of patients. A presurgical therapeutic response to steroids is associated with a more favourable post-surgical language recovery.

Monday 29th August 2005
15:30 - 17:00
Salle 251
Platform Session
Drug Therapy - AED Trials

025
Analysis of First and Second-line Agents for the Treatment of Convulsive Status Epilepticus in Childhood
B.G.R. Neville[1], R.F.M. Chin[1], C. Peckham[1], H. Bedford[1], A. Wade[1], R.C. Scott[1]

1) Institute of Child Health, London, United Kingdom

Purpose: Although rectal diazepam is an appropriate pre-hospital treatment for convulsive status epilepticus (CSE), it is uncertain whether seizure termination in A&E is more likely with intravenous lorazepam than with rectal diazepam. It is also unclear whether seizure termination is more likely with intravenous phenytoin than rectal paraldehyde when administered as a second line agent. From a prospective population based study, we report on the safety and efficacy of rectal diazepam or intravenous lorazepam, and rectal paraldehyde or intravenous phenytoin in the treatment of childhood CSE.
Methods: Excluding neonates, children aged < 16 years with CSE within North London were enrolled using a multi-tiered notification system. In children with CSE not treated in the pre-hospital setting, seizure termination and risk of respiratory depression were assessed amongst those receiving different therapies. Differences with associated confidence intervals between treatment groups were determined through StatXact v4.0.1 and are presented.
Results: Initial treatment with lorazepam was associated with a greater likelihood of seizure termination than treatment with diazepam (16/36 vs 6/49 respectively, 95% CI 11% - 54%, p= 0.005) without an increased risk of respiratory depression (7/36 vs 8/49, 95% CI 17-27%, p = 0.8). Second line treatment with phenytoin was associated with a greater likelihood of seizure termination than treatment with paraldehyde (10/11 vs 9/22, 95% CI 12-79%, p=0.01).
Conclusion: Intravenous lorazepam should be preferred to rectal diazepam as first-line therapy for children that have not received pre-hospital treatment. When first-line therapy has failed, intravenous phenytoin should be preferred to rectal paraldehyde as second-line rescue therapy.

026
Cross-over Comparison of Efficacy and Safety of Midazolam Nasal Spray and Diazepam Rectal Solutions in Seizure Exacerbations
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Purpose: To compare midazolam (MDZ) nasal spray and diazepam (DZP) rectal solutions as acute treatments for seizure exacerbations.
Methods: A randomised open-label cross-over treatment of six seizure exacerbations in residential patients of an epilepsy centre. All patients had refractory symptomatic partial or generalised epilepsy and occasional seizure exacerbations (status epilepticus or flurries of seizures), requiring acute seizure treatment. A research nurse introduced the study to patients, families and caregivers and evaluated the results. Success rate, time between administration and cessation of clinical seizure activity, side-effects, perceived ease of use and preference for either treatment were the primary study end-points.
Results: After informed consent 24 patients were included in the study. 3 patients dropped out due to protocol violations or lack of seizure exacerbations. A total of 124 events occurring in 21 patients were evaluated, 19 patients contributed 6 events, 2 patients 5. MDZ nasal spray and DZP rectal solutions were administered 61 and 63 times respectively, abolishing seizure activity on 49 and 55 occasions, respectively. Time between administration and seizure termination was equal for both drugs (4.6+/-5.2 and 4.5 +/-3.9 min. resp.) Short lasting nasal irritation or sneezing was reported as side effect of MDZ on 17/61 occasions, but was validated 'not severe' in the final questionnaire. The nasal spray was validated significantly easier to use in the questionnaire ($p<0.001$). At the end of the study 16 out of 21 patients preferred continuation of MDZ nasal spray for the acute treatment of seizures.
Conclusion: MDZ nasal spray is as effective as DZP rectal solutions in the acute treatment of seizure exacerbations. Most patients and caregivers preferred the nasal spray because of the ease of administration and social acceptability. The study was financially supported by the Dutch Epilepsy Fund NEF (Grant 01-02).

027
New Analogue of Levetiracetam Brivaracetam and its Efficacy in the Photosensitivity Model
D.G.A. Kasteleijn-Nolst Trenite[1], D. Parain[2], P. Masnou[3], P. Genton[4], B.J. Steinhoff[5], E. Hirsch[6]

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Purpose: One of the interesting ligands with 4-substitution in the lactam ring of levetiracetam (LEV), has been selected for studying in photosensitive patients; brivaracetam has a strong affinity to the levetiracetam binding site and is about 10 times more potent than LEV. A comparison with LEV will be made, since LEV has been studied in the photosensitivity model.
Methods: During a three day period patients underwent standardised intermittent photic stimulation at fixed time points according to a standardised protocol. After the first baseline day, single oral dosages of brivaracetam were given. Dependent on the pharmacodynamic results, dosages were lowered or increased. All pharmacokinetic parameters were computed from the blood samples collected up to 72 hours post-dose. Mood scales (POMS and ARCI 49) were administered.
Results: Complete abolishment of the photoparoxysmal response (PPR) was found after intake of brivaracetam in 14 of the 18 evaluable patients (78%). Of all doses tested (80, 40, 20 and 10 mg), the 80 mg dose appeared more efficient (time to maximal response and duration of response). The pharmacokinetic and side-effect profile was similar to that in healthy volunteers. A small increase in sedation (ARCI-49) was noticed 3 hours after administration of 80 mg of brivaracetam. Compared to levetiracetam, the efficacy of ucb 34714 in this model is clearly more potent. Phase IIb studies are underway.
Conclusion:

028
Efficacy and Safety of Levetiracetam 3000 mg/d as Adjunctive Treatment in Adolescents and Adults Suffering from Idiopathic Generalised Epilepsy with Myoclonic Seizures
P. Verdru[1], A. Wajgt[2], J. Schiemann Delgado[3], S. Noachtar[4]

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Purpose: This trial was performed to evaluate the efficacy and safety of levetiracetam (LEV) 3000 mg/d when given as adjunctive treatment in adolescents (≥ 12 years) and adults (≤ 65 years) suffering from idiopathic generalised epilepsy with myoclonic seizures.
Methods: 39 centres in 13 countries participated in this double-blind, multicentre, randomised (1:1), placebo-controlled trial in which 122 patients were randomised. To be eligible, patients had to experience at least 8 days with myoclonic seizures during the 8-week baseline period and had to be treated with one concomitant AED. Patients were uptitrated over 4 weeks and treated at a stable dose over 12 weeks (evaluation period). Seizure activity was recorded by the patients in a seizure diary and evaluated by the investigators using the ILAE classification. Tolerability was assessed using adverse event reporting,

ECG, standard clinical examinations and laboratory analyses including plasma concentrations of AEDs and LEV. Entry into a long-term follow-up trial was offered to patients who had benefited from the treatment. The primary efficacy endpoint was the responder rate (≥ 50% reduction in days with myoclonic seizures during the treatment period versus baseline).
Results: 121 patients were included in the ITT analysis (PBO: n=60; LEV: n=61). Responder rate was 58.3% under LEV and 23.3% under PBO (p=0.0002). The corresponding odds ratio [95% CI] was 4.77 [2.12; 10.77]. 13 patients on LEV versus 2 patients on PBO were seizure-free during the evaluation period. The most common AE was headache (23.3% in PBO; 21.6% in LEV). One PBO and 2 LEV patients prematurely discontinued due to AE prior to the end of the evaluation period.
Conclusion: Levetiracetam proved to be highly efficacious in the treatment of refractory patients with idiopathic generalised epilepsy experiencing myoclonic seizures. LEV's outstanding tolerability profile was also confirmed.

029
Comparison of Efficacy and Tolerability of some New Antiepileptic Drugs from Long-term Studies
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Purpose: Metanalysis of key double-blind studies, have compared the short-term efficacy and tolerability of new antiepileptic drugs (AEDs). However, AEDs are usually administered for several years. The aim of the present study was to compare long term efficacy and tolerability of these drugs.
Methods: From more than 400 open studies conducted to evaluate the efficacy and tolerability of gabapentin (GBP), lamotrigine (LTG), oxcarbazepine (OXC), levetiracetam (LEV), and topiramate (TPM), we selected 27 long-term (at least one year of treatment) studies according to the following criteria: 1) the percentage of patients acquiring six month-seizure freedom (SMSF), 2) and/or percentage of patients withdrawing for adverse effects (WAE), 3) and/or the percentage of patients continuing treatment (CT) after three or more years. 21 of these studies were prospective evaluations conducted on patients with inadequately controlled partial-onset seizures and 6 were retrospective.
Results: The highest number of SMSF patients (13%), was observed in a prospective study performed with LEV. The highest number of WAE patients (32%) was observed in a prospective study with TPM. The highest percentage of CT patients were found in a retrospective study with TPM (30.2% after 4 years of treatment) and in a prospective study with LEV (32% after 5 years).
Conclusion: In our knowledge, this is the first attempt to compare the long-term efficacy and tolerability of some new antiepileptic drugs from open, long-term studies. Several methodological problems (the heterogeneity of the population studied, poor quality of some studies, different kind of evaluations, etc) are discussed.

030
Efficacy and Safety of Adjunctive Oral Lacosamide for the Treatment of Partial Onset Seizures in Patients with Epilepsy
E. Ben-Menachem[1], V. Biton[2], D. Jatuzis[3], B. Abou-Khalil[4], P. Doty[5], D. Rudd[5], S.P. 667 Study Group[5]

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Purpose: To investigate the efficacy and safety of oral lacosamide (LCM) as adjunctive therapy in subjects with uncontrolled, partial onset seizures in a multicenter, multinational, randomised, double-blind, placebo-controlled trial (SP667).
Methods: After an 8-week baseline, subjects (n=418) were randomised (1:1:1:1 ratio) to placebo, 200, 400, or 600mg/day (given bid). Subjects were titrated over 6 weeks to the randomised dose in 100mg/day/week increments. Treatment was maintained for 12 weeks. Efficacy was evaluated by intent-to-treat analyses of seizure frequency (maintenance vs baseline). Safety was evaluated by adverse event (AE), ECG, vital signs, and clinical laboratory data.
Results: LCM (400 and 600mg) significantly reduced seizure frequency (p = 0.0023 and 0.0084, respectively). The percent reduction in seizure frequency over placebo was 28.4% (400mg) and 21.3% (600mg). The 50% responder rates for placebo, LCM 400mg, and 600mg were 22%, 41% and 38% (respective p-values compared to placebo 0.0038 and 0.0141). LCM 200mg exhibited a 14.6% reduction in seizure frequency over placebo (p=0.1010) and a 50% responder rate of 33% (p=0.0899). Treatment-emergent adverse events (TEAEs) were most common in the central and peripheral nervous system. TEAEs that appear to be dose-related include dizziness, nausea, fatigue, ataxia, diplopia, vision abnormal, and nystagmus. No effects were observed on other safety variables including body weight.
Conclusion: Data from this randomised, double-blind, controlled trial showed that lacosamide (400 and 600mg/day) produced a statistically significant reduction in partial seizures in patients with epilepsy and support further development of lacosamide as an antiepileptic drug.
Study supported by: Schwarz Biosciences Research Triangle Park, NC, USA, Manheim, Germany.

Monday 29th August 2005
15:30 - 17:00
Salle 241
Platform Session
Neuropsychology

031
Emotion Recognition in Adolescents with Temporal Lobe Epilepsy after Epilepsy Surgery
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Purpose: Deficits in emotion recognition (ER) seem to be associated with amygdala/hippocampal pathology. So far, investigations have focused on individuals with psychiatric disorders, mainly psychosis. Recently, similar deficits have been reported in patients with chronic temporal lobe epilepsy (TLE) and hippocampal sclerosis. No data has been published on ER in paediatric TLE patients.
Methods: Patients with drug resistant symptomatic unilateral TLE and age younger than 18 years at epilepsy surgery were included. Patients had to be seizure free. Evaluation was not performed less than twelve months after surgery. All subjects performed three different tests: (a) face morphing task using stimuli from the Ekman and Friesen set of slides. (b) emotion labelling task using a similar set of slides, (c) affective prosody task with short sentences spoken in English in different moods by different actors. The following emotional categories were evaluated: sadness, anger, happiness, disgust and fear. Performance of the patient group was compared to healthy age matched control subjects. Variables investigated included age at seizure onset, duration of epilepsy until surgery, side of seizure onset and interval between surgery and testing.
Results: 27 patients, 14 girls and 13 boys, could be included. Mean age at surgery was 12 years 5 months, mean age at testing was 18 years 4 months, mean interval between surgery and testing was 5 years 9 months. 15 patients had left hemispheric seizure onset. Preliminary analysis revealed that patients with right hemispheric pathologies performed significantly poorer in regard to perception of fearful facial expressions. No deficits in prosodic emotional perception could be found.
Conclusion: Despite successful surgery at a young age and seizure freedom, significant ER deficits were found, warranting specific

training programs for afflicted patients in order to prevent social dysfunction.

032

Impact of Childhood Epilepsy on Quality of Life: A Qualitative Investigation using Focus Group Methods to Obtain Children's Perspectives on Living with Epilepsy

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Purpose: Epilepsy is the most common serious neurological condition in childhood and is often associated with negative consequences in terms of Quality of Life. As people's perceptions of their quality of life are unique, it is essential to elicit concerns directly from the individual rather than proxy informants. This study therefore aims to investigate the impact of childhood epilepsy on quality of life directly from the child's perspective.
Methods: Focus group techniques and qualitative analysis were utilised. 22 children between 7 years 4 months and 12 years 6 months (11 females, 11 males) were stratified by age (7-8, 9-10, 11-12 years old) into five focus groups and two semi-structured interviews.
Results: Data were transcribed and analysed using grounded theory techniques to generate themes and categories. Themes were presented using the children's language. Two major themes were identified, 'things to do with growing up' and 'things to do with epilepsy', with five and four sub-themes respectively.
Conclusion: Focus groups provided a valid method for investigating the children's perceptions. The main issues for the children were social impact, peer acceptance, academic difficulties, fear of seizures, and taking medication. No significant age-related differences were found. A conceptual model illustrates these findings, and comparisons are made to previous research with adolescents using similar methodology.

033

Predictive Value of the Individual Wada Memory Scores on the Post-surgical Memory Changes in Epilepsy Patients

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Purpose: Surgery for refractory epilepsy brings significant relief to patients but may cause memory impairment. The risk of postoperative memory loss can be determined by the Intracarotid Amobarbital Procedure (IAP) (Milner et al, 1962). Patients who passed the first, ipsilateral to the epileptogenic focus injection and thus demonstrated adequate memory in the contralateral hemisphere, are considered good surgical candidates for anterior temporal lobectomy. However, evidence regarding the contribution of the second injection in predicting postoperative memory changes remains non-conclusive (eg, Setoaian et al, 2004; Lee et al 2005).
Methods: 104 candidates for epilepsy surgery underwent the IAP procedure at the Sourasky Medical Centre during the years 1997-2004 to determine their unilateral memory capacity. Results of bilateral Wada memory scores in 32 patients that have subsequently undergone anterior temporal lobectomy were analysed. Memory score after each injection was correlated with the difference score between pre- and post-surgical standardised neuropsychological memory tests.
Results: There were no patients with significant memory decline after surgery. Wada memory scores of the hemisphere ipsilateral to the epileptogenic focus (second injection) were significantly negatively correlated with post-surgical memory changes in all patients ($p=0.05$). The lower the Wada ipsilateral memory score, the higher the post-surgical memory abilities in these patients. This effect was particularly strong in patients with right epileptogenic focus ($p=0.0007$). No significant correlation was found between Wada contralateral memory scores (first injection) and post-surgical memory changes.
Conclusion: The second injection of IAP remains an important test for predicting graded memory deficits after epilepsy surgery.

034

Neuronal Cell Density in the Hippocampal Subfields and Memory Function: The Gyrus Dentatus as a Significant Predictor in Human Memory

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Purpose: The hippocampal formation is essentially involved in the formation of conscious memories for facts and events and mesial temporal lobe epilepsy affecting the hippocampus is associated with memory deficits of varying severity. The aim of the study was to investigate the correlation between neuronal cell density in the hippocampal subfields and memory function.
Methods: We studied the degree of declarative memory dysfunction in 27 human subjects, suffering from unilateral mesial temporal lobe epilepsy, using the possibility to access memory performance of each isolated hippocampus by intracarotid amobarbital testing. Subsequently, surgical treatment for medically intractable seizures was performed and the hippocampal specimens were available for neuropathological analysis. Multiple regression and partial correlation analyses were employed to identify the association between neuronal cell loss within different hippocampal subregions with memory deficits.
Results: The internal limb of the dentate gyrus, a developmentally distinct subregion of the hippocampal formation known to generate new neurons throughout life, was identified as a highly significant predictor for the patient's ability to learn and recall memories ($r = 0.887$, $p<0.001$).
Conclusion: Our results correspond to animal studies, proposing that memory formation critically depends on the capability of the hippocampus to maintain and recruit new neurons into the dentate gyrus.

035

Recognition of Facial Expressions of Emotions in MTLE: Analysis of 122 Consecutive Patients

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Purpose: In a previous study (Meletti et al Neurology 2003) we observed that patients with focal epilepsy associated with damage to the mesial temporal lobe region could be impaired in recognising facial emotions. Subjects with seizures starting early in life and with right hemisphere involvement were particularly defective in facial emotion recognition (ER). In this study we analysed a larger group of patients with mesial temporal lobe epilepsy (MTLE) including patients with bilateral mesial temporal lobe damage.
Methods: 122 MTLE consecutive patients were evaluated. On the basis of neuroradiological (1.5 or 3 tesla MR) and neurophysiological evaluations (video EEG) patients were grouped as follows: right MTLE (n=60); left MTLE (n=50); bilateral MTLE (n=12). 65% of the patients had MR evidence of hippocampal sclerosis (HS); 35% had different lesions involving the anterior-medial temporal lobe region. 87% of the patients had a drug-resistant epilepsy. 50 healthy volunteers served as the control group. ER was tested asking the patients to couple the target facial expression with one of the following verbal labels: happiness, sadness, fear, disgust, anger.
Results: Mean accuracy score in ER was 96.5% for the control group. Left MTLE group showed a similar performance: accuracy of 93.1%. On the contrary right MTLE mean accuracy score was 82.4% ($p <$

0.05, from controls and left MTLE). Bilateral MTLE group showed the poor ER skills with a 67.3% accuracy score ($p < 0.01$). We then analysed single subject performance evaluating how many subjects in each group was fallowing below 2SD from the control mean: 100% of bilateral MTLE patients; 60% of right MTLE patients; 14% of left MTLE patients. Analysis of the recognition accuracy of the single facial emotion categories confirmed that bilateral and right MTLE group were particularly defective in the recognition of the facial expression of fear.
Conclusion: MTLE patients with evidence of bilateral or right-side medial temporal lobe damage show impairment in emotion recognition skills, ranging from a severe to moderate deficit. Future studies should address the mechanisms underlying defective recognition of facial expressions.

036
Verbal Memory Impairment in Children with Focal Epilepsy
B. Jocic-Jakubi[1]

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Purpose: Mild or moderate interictal impairment of verbal learning and memory was reported in patients with left temporal electroencephalographic (EEG) foci, but other authors did not lateralise memory impairment. Because of different data in the literature we investigated the influence of both localisation and lateralisation of epileptic foci on verbal memory.
Methods: The results of 'selective reminding test' (SR test) of 80 children aged 7 16 years with focal epilepsy were compared with results of 80 healthy school children controls. We then compared neuropsychological performance on verbal memory testing, with two groups of children with focal epilepsy: those who have the EEG epileptogenic focus in the left (L) hemisphere (n=38) , and those who have a right (R) sided epileptogenic focus (n=42). We also compared scores on verbal memory testing between two groups of children with EEG focus localised temporal (T) (n=36) vs extratemporal (ExT) (n=44). The effects of type of seizures, number of seizures and age at seizure onset were also examined.
Results: We found statistically significant differences between the results for the experimental and the control group. Group difference was found when we compared results of T vs ExT group ($p<0.01$) only for the CLTR component of SR test. A statistical significance was found comparing TR vs TL group ($p< 0.03$) and TL vs FL ($p< 0.02$) for the CLTR component. In all compared groups, children with a left temporal focus had low scores on verbal memory testing. Age at seizure onset (under 7 years) and complex seizures were related to low performances on verbal memory testing (for all components of the SR test: sigma R, LTR, STR ,LTS, CLTR), and the number of seizures was a significant predictor for LTR, STR and CLTR components.
Conclusion: Children with focal epilepsy have a verbal memory deficit. There is a significant relationship between EEG focus localisation and lateralisation and severity of verbal memory impairment. Because the CLTR component of the SR test is mostly impairment we can conclude that children with focal epilepsy have more difficulties in retrieval from long term memory. Age at seizure onset and type of seizure are very important predictive factors for cognitive functioning in children with focal epilepsy, while the number of seizure is a less important factor.

Monday 29th August 2005
15:30 - 17:00
Salle 253
Platform Session
Late Breaking News

037
Inflammation Exacerbates Neuronal Injury in the Developing Rat Brain after Status Epilepticus
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Purpose: Prolonged febrile seizures and status epilepticus (SE) have been implicated as predisposing factors for temporal lobe epilepsy and/or hippocampal sclerosis. We have previously shown an age specific pattern of neuronal injury following lithium-pilocarpine (LiPC) induced SE. Here, we assess the contribution of varying degrees of inflammation in the immature rat brain.
Methods: Rat pups of postnatal age 7 days (P7) and P14 were subjected to the lithium-pilocarpine model of SE. Lipopolysaccharide (LPS) was injected i.p., two hours prior to the induction of seizures: SE+LPS 50µg/kg (SE+LPS50), SE+LPS 100µg/kg (SE+LPS100), and control groups either received no LPS (SE group) or LPS100µg/kg, but no pilocarpine. Rats were killed after 24 hrs, and the brains examined using eosin fluorescence as a marker of neuronal injury.
Results: At P7, the number of eosinophilic neurons in CA1 was dramatically increased in the groups that received LPS prior to SE: SE 9.2±1.7, SE+LPS50 80.9±5.9 and SE+LPS100 82.3±4.3. At P14, SE resulted in 55.7±12.9 injured neurons vs. 122.4±19.6 in SE+LPS50 ($p<0.05$), and 159.2±14 in SE+LPS100 ($p<0.05$). No eosinophilic neuron was observed in any of the LPS100 groups.
Conclusion: We have previously demonstrated that prolonged LiPC SE in rat pups does not result in any injury at P7 or in substantial hippocampal neuronal injury beyond area CA1 at P14. Inducing an inflammatory response resulted in CA1 injury at P7. At P14, the inflammatory response exacerbates injury to the CA1 pyramidal cells. Presence of an inflammatory process could be a key variable accounting for the differences in vulnerability to seizure-induced injury between animal models and humans.

038
The T-type Calcium Channel Mutations Associated with Childhood Absence Epilepsy Increase Plasma Membrane Expression
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Purpose: Overactive T-type Ca2+ channels (T-channels) likely contribute to childhood absence epilepsy (CAE). In addition, many single nucleotide polymorphisms (SNPs) were discovered in the gene encoding the T-channel Cav3.2 subunit, which can be presented as a susceptibility gene in CAE. Our working hypothesis is that these Cav3.2 SNPs/mutations might lead to a gain of channel function that would predispose the thalamocortical circuit to oscillate and thereby triggering absence seizures. Since a detailed electrophysiological study of these Cav3.2 SNPs has recently revealed that only ~30 % of these mutant channels showed electrophysiological properties supporting a gain of function activity (Vitko et al. J. Neurosci. 2005, 25:4844-4855), we have explored whether expression at the plasma membrane of these mutant channels was altered.
Methods: The SNPs were introduced in an epitope-tagged Cav3.2 subunit that allow quantification of their plasma membrane expression (Dubel et al., J. Biol. Chem. 2004, 279:29263-29269).

Results: We report that these Cav3.2 SNPs significantly enhanced the amount of Cav3.2 channels at the plasma membrane. More importantly, the ratio of membrane expression over total expression (measured in permeabilized cells) was also significantly increased for the mutant channels, indicating the CAE-specific SNPs of the Cav3.2 subunit favour trafficking to the plasma membrane.
Conclusion: This study demonstrate that in addition to changes in the electrophysiological parameters observed for some CAE-specific SNPs, a common gain of channel function for all the CAE-specific SNPs would primary rely on an increase in Cav3.2 subunit expression at the plasma membrane.

039

Resistance to Antiepileptic Drug Treatment can be Counteracted by Inhibition of P-Glycoprotein in a Rat Model of Temporal Lobe Epilepsy

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Purpose: Medical intractability, i.e., absence of any response to antiepileptic drug (AED) therapy, is an unresolved problem in many patients with epilepsy. Mechanisms of intractability are not well understood, but may include alterations of pharmacological targets and poor penetration of AEDs into the brain because of increased expression of multiple drug resistance proteins, such as P-glycoprotein (P-gp; ABCB1), capable of active brain extrusion of various drugs, including AEDs.
Methods: We have recently used a rat model of temporal lobe epilepsy to examine whether AED responders differ from nonresponders in their expression of P-gp in the brain (Volk et al., Brain 128, 1358-1368, 2005). In this model, spontaneous recurrent seizures (SRS) develop after a status epilepticus induced by sustained electrical stimulation of the basolateral amygdala. Prolonged treatment of epileptic rats with phenobarbital resulted in responders and nonresponders. P-gp expression was studied by immunohistochemistry, showing a striking P-gp over-expression in nonresponders compared to responders in limbic brain regions, including the hippocampus. The P-gp over-expression was confined to brain capillary endothelial cells which form the blood-brain barrier. Because phenobarbital is a substrate of P-gp, this overexpression in nonresponders is likely to reduce drug penetration into affected brain regions. For direct proof-of-principle, we selected a new group of phenobarbital nonresponders and administered the selective P-gp inhibitor tariquidar (XR9576) in combination with phenobarbital in these rats.
Results: This combined treatment resulted in a striking suppression of SRS compared to treatment with phenobarbital alone.
Conclusion: These data therefore substantiate the multidrug transporter hypothesis of drug-resistant epilepsy and strongly suggest that P-gp inhibitors may be a novel treatment option to prevent or counteract AED resistance in epilepsy.

040

Molecular Genetic Dissection of Seizure-Type-Related Susceptibility Loci of Idiopathic Generalised Epilepsy

K.P. Lenzen[1], A. Heils[1], A. Hempelmann[1], J.F. Prud'Homme[1], R. Nabbout[1], O. Dulac[1], G. Rudolf[1], F. Zara[1], A. Bianchi[1], R. Robinson[1], R.M. Gardiner[1], A. Covanis[1], D. Lindhout[1], U. Stephani[1], C.E. Elger[1], T. Sander[1]

1) On behalf of the European Consortium on the Genetics of Idiopathic Generalised Epilepsy

Purpose: Idiopathic generalised epilepsy (IGE) accounts for 30% of all epilepsies. The etiology of IGE is genetically determined and an oligogenic inheritance is most likely in families with several affected members. The present genomewide linkage scan aims to dissect seizure type-related susceptibility loci in 93 European IGE-multiplex. Multipoint nonparametric linkage (NPL) analysis of the entire family sample yielded significant evidence for linkage on chromosome 13q31 and suggestive linkage evidence in the chromosomal regions 5q31, 11q13 and 19q13.
Methods: To dissect seizure type-related susceptibility loci, we performed linkage scans in two distinct family subgroups that were multiplex for either idiopathic absence epilepsy (IAE) or juvenile myoclonic epilepsy (JME) and generalized tonic-clonic seizures on awakening.
Results: In 40 IAE-multiplex families, suggestive linkage evidence was obtained on chromosomes 7p14, 11q13 and 13q31. In 21 JME-families, empirical suggestive evidence for linkage was found in the region 19q13 and confirmatory linkage evidence on 6p12 near the JME-related EFHC1 gene. The present genomewide linkage scan revealed a complex pattern of linkage signals that differed in their composition, depending on the predominant seizure type in the families.
Conclusion: Susceptibility loci on 7p14, 11q13 and 13q31 seem to confer susceptibility to absence seizures, whereas loci on 6p12 and 19q13 preferentially predispose to myoclonic and generalized tonic-clonic seizures on awakening.

041

Hippocampal Slerosis in Refractory Temporal Lobe Epilepsy is Associated with Gluten Sensitivity

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Purpose: Previously celiac disease (CD) and gluten sensitivity (defined as the presence of anti-gliadin antibodies and positive immunogenetics) has been associated with cerebellar degeneration and epilepsy with occipital calcifications. Hippocampal sclerosis (HS) in temporal lobe epilepsy (TLE) is a potentially progressive disorder with unknown aetiology, and autoimmunity has been implicated in TLE+HS as one of the possible mechanism leading to HS. The prevalence of CD in patients with epilepsy is not well established, none of the studies has addressed the issue of gluten sensitivity in syndrome specific approach to epilepsy.
Methods: We measured CD associated antibodies (anti-gliadin, anti-tTG and anti-EMA) and celiac type HLA (DQ2 and DQ8) in 48 consecutive patients with therapy resistant localisation-related epilepsy. The patients were categorised TLE+HS (N=18), TLE-HS (N=18) and extratemporal epilepsy (N=18) based on ictal eletro-clinical characteristics and high resolution MRI. Patients with suspected CD or gluten sensitivity underwent duodenal biopsies.
Results: Seven patients were gluten sensitive, all of these patients had TLE+HS whereas none of the patients without HS were gluten sensitive ($p< 0.0002$). In duodenal biopsies three of the patients had histological evidence of CD and four had inflammatory changes consistent with early developing CD without villous atrophy. None of the seven patients with gluten sensitivity had clinical signs of ataxia and there was no MRI evidence of cerebellar degeneration or occipital calcifications.
Conclusion: The present study demonstrates a previously unrecognized association between gluten sensitivity, CD and TLE with hippocampal sclerosis. The association was very robust in this well characterised group of patients; thus gluten sensitivity should be added to the list of potential mechanism leading to intractable epilepsy and HS.

042

Effectiveness of a Commercially Available Blue Lens in Photosensitive Epileptic Patients: The Results of a Large Multicenter Italian Study

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Purpose: Photosensitivity can represent a serious problem in epileptic patients because its seizure-elicitation role and induction of unpleasant subjective sensations. The pharmacological treatment of photosensitivity is often ineffective. In the literature, non pharmacological treatment using blue sunglasses has been shown to be effective and safe in photosensitivity control, but large series of patients have never been studied.
Methods: This multicenter study was conducted in 12 epilepsy centers of northern, central, southern and insular Italy. A commercially available lens, obtained in a previous trial, was used to test consecutively enrolled photosensitive pediatric and adult epileptic patients. Only type 4 photosensitivity (Photoparoxysmal Response, PPR) was considered in the study. A standardized methodology was used for photostimulation. All examinations were recorded on split-screen video-EEG and the results were always evaluated by one of the authors, being everyone an expert electroencephalographer working in the centers participating in the study.
Results: Six hundreds and ten patients were tested. Four hundreds patients (66%) were female, 396 (65%) were under 14 years of age. Three hundreds and eighty-one subjects (62%) were pharmacologically treated at test time. Z1 lenses made PPR disappear in 463 (75.9%) patients, while PPR was considerably reduced in additional 109 (17.9%) of them. PPR remained unchanged only in the remaining 38 (6.2%) patients. There were no significant differences in PPR disappearance among focal epilepsies, generalized epilepsies and epileptic encephalopaties. Yet, there were no significant differences between treated and untreated patient and between adult and pediatric cases.
Conclusion: This type of lens evidence great effectiveness in PPR control in a very large number of patients. The use of this lens can improve the quality of life of photosensitive epileptic patients. Moreover, in some cases, a pharmacological treatment could be avoided.

Monday 29th August 2005
15:30 - 17:00
Salle 243
Platform Session
Basic Science 1

043

Two Different Convulsants (Kainic Acid and Picrotoxin) Lead to both Seizures and Spreading Depressions

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Purpose: During neuronal discharges potassium is released into the extra-cellular space. In this study we examined picrotoxin- and kainic acid (KA)-induced seizure-associated changes in extracellular potassium ([K+]o) in the cortex and hippocampus to compare two structures often studied in epilepsy models.
Methods: Under anaesthesia, surface EEG electrodes were implanted over the frontal hind limb cortex and, in some rats, into the hippocampus. A dural window was prepared over the right frontal cortex and sealed. The next day, rats were paralyzed and artificially respired and a potassium sensitive microelectrode was introduced into the right frontal cortex or hippocampus. Picrotoxin or KA was then injected (iv).
Results: After picrotoxin, EEG spindles caused small increases in cortical [K+]o. Seizure activity led to immediate potassium increases, reaching 10 to 12 mM and followed, in 50% of the animals, by a spreading depression (SD) with a ceiling level of 40-50 mM. Hippocampal measurements revealed no effect of spindles on [K+]o. With seizure, [K+]o-rises occurred after a prolonged delay. No SDs were seen. After KA, there were electrographic generalised non-convulsive discharges and spike-wave discharges. In connection with the first discharges, there was sometimes a SD in the hippocampus, reaching 40-50 mM. During subsequent discharges, in hippocampus and cortex, [K+]o rose slowly on only 50% of occasions. Small [K+]o-rises independent of seizures occurred in both structures.
Conclusion: As judged by potassium changes, picrotoxin discharges are intense (cortex more than hippocampus) and KA discharges are mild. The association of seizures and SDs provides a link between epilepsy and headaches/migraine in both models though in different areas of the brain.

044

A Possible Role of Cell Cycle Re-entry in Epileptogenesis as Observed in the Hippocampus of EL Mice

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Purpose: We demonstrated that there was DNA fragmentation in the hippocampus of epileptic mutant EL mice, where neuronal cell loss was not found even after frequent seizure history during development. An altered equilibrium between proapoptotic Bax and antiapoptotic Bcl-2 correlated with increased DNA fragmentation without cell loss. The level of neurotrophic factors in the hippocampus showed a significant increase in earlier developmental stages before exhibiting frequent seizures. In addition, the abundance of trophic factors could also facilitate the induction of cell division-related processes. In the present study, we used EL mice to examine how cyclin and the corresponding cyclin dependent kinase (CDK) family are related to cell proliferation during development.
Methods: We examined developmental changes of cyclin/CDK family during cell cycle by Western blotting in the hippocampus in both EL mice and their control animal, DDY mice.
Results: Western blot analysis demonstrated a significant increase in the levels of cyclin B/CDK-1 protein (G2/M checkpoint) in EL mice compared to the control DDY. In EL, the levels of cyclin B and CDK-1 were increased predominantly after frequent seizures.
Conclusion: It is concluded that in EL mice, during development and particularly after repetitive seizures, re-entry of the cell cycle is promoted possibly because of the abundance of neurotrophic factors which induce the expression of cyclin B and CDK-1. DNA fragmentation without cell loss and cell cycle re-entry may work together in the process of epileptogenesis during development.

045

Diuretics Block Human Epileptiform Activity in Vitro

G. Huberfeld[1], L. Wittner[1], S. Clemenceau[3], E. Dezamis[3], M. Baulac[2], R. Miles[1]

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Purpose: Post-operative human temporal tissue with hippocampal sclerosis generates interictal-like activity in vitro. Spontaneous synchronised discharges emerge from the subiculum, de-afferented by the cell loss in CA1, which implicate depolarizing effects of GABA in some pyramidal cells (Cohen I et al. Science 2002; 298:1418-21). Chloride homeostasis is clearly perturbed, possibly due to a reduced expression of the chloride cotransporter KCC2 which extrudes chloride. We tested the effects on epileptiform activity of blocking another transporter, NKCC1, by low doses of the diuretic bumetanide. We hypothesised that blocking NKCC1, which loads cells with chloride, would restore chloride homeostasis.
Methods: Slices of human temporal lobe tissue containing the subiculum (400 µm) were prepared after surgery. Field potentials and unit activity were recorded in vitro using multiple extracellular electrodes and intracellular recordings obtained with sharp electrodes.
Results: Spontaneous interictal activity was recorded from the subiculum (n=7 patients). Bumetanide, perfused at 6-8µM, a dose which blocks NKCC1 but not KCC2 (Holtzman EJ et al. Am. J. Physiol 1998;275,550-64) suppressed epileptiform activity in 7/7 cases over 40-50 minutes. Furosemide, another loop diuretic, which inhibits KCC2 specifically at 25µM (Payne) J. Physiol 1997;273:1516-25), did not change epileptiform activity (n=2). KCC2 expression in single cells, identified by biocytin labelling, was detected immunocytochemically and correlated with the depolarizing or hyperpolarizing nature of GABA responses.
Conclusion: This action of Bumetanide reinforces evidence that depolarizing GABAergic responses are involved in human epilepsies. It supports a therapeutic role for molecules modulating chloride homeostasis in epilepsies related to de-afferentation processes.

046

Mechanisms of Drug-resistance in an Experimental Model of Cortical Malformation: Effects of Neuronal Dysplasia, Seizures and their Combination

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Purpose: Multi-drug transporter proteins in a dysplastic human epileptic brain might contribute to resistance to antiepileptic drugs (AED). We studied the intrinsic and seizure-induced expression of MDR1 and MRP1/2 in rat brain with cortical malformations due to prenatal exposure to methylazoxymethanol (MAM). We addressed also the relevance of these changes for reducing AED brain uptake.
Methods: Cortical dysplasia was induced by intraperitoneal MAM injection in pregnant rats. Pilocarpine (PILO) was injected in rats to provoke status epilepticus (SE) and spontaneous seizures (SS). MDR1 and MRP1/2 expression was assessed by RT-PCR, immunohistochemistry and western-blot analysis in dysplastic and normal brain (± PILO). NeuN and FITC-albumin immunostaining were used to detect ectopic neurons and the morpho-functional status of the vasculature. Phenytoin and ondansetron levels in plasma and brain were measured by HLPC-UV.
Results: MDR1 level (but not MRP1/2) was increased 2-3 fold in brain vessels within dysplastic brain areas only. SE and SS in MAM rats determined an additional 2-fold increase in MDR1 in neurons and glia. Increased tortuosity and altered morphology of brain vessels was found in dysplastic hippocampi but no obvious BBB damage. Brain-to-plasma ratio of phenytoin was not modified in MAM rats while SE provoked a 30% decrease in phenytoin brain uptake in naïve rats.
Conclusion: MDR1 expression is increased in vessels of MAM-induced dysplastic brain regions and it is additionally enhanced in neurons and glia by epileptic activity. Seizures in dysplastic brain may determine the attainment of sub-therapeutic levels of MDR1 substrates, including phenytoin.

047

Epileptic Seizures in Transgenic Mice with Attenuated M-channel Activity

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Purpose: We investigated whether M-channel attenuation in transgenic mice leads to epileptiform activity and may serve as an animal model for a dominantly inherited form of human generalised epilepsy associated with M-channel mutations.
Methods: Attenuation of M-channel activity in mouse brain was achieved by conditional expression of a dominant negative KCNQ2-subunit. Electrocorticograms (ECoGs) were recorded telemetrically using implantable radiotransmitters. They were combined with infrared camera recordings of mouse behaviour. Recordings were done during a period of three weeks, one week post surgery. ECoG traces were inspected visually in comparison to simultaneously recorded behavioural patterns. Data were sampled during day and night phases from at least three randomly selected days. Selected traces were digitally filtered (low-cut 0.3 Hz and high-cut 30 Hz) and analysed by conversion into power spectra. Frequency components of traces were calculated by conventional fast Fourier transformation. Each group of mice comprised 8 to 11 animals.
Results: We examined transgenic mice which expressed a dominant negative KCNQ2 subunit in most neurons of the mouse central nervous system. Expression during early postnatal development was accompanied with a loss of e.g. hippocampal neurons. Expression at later stages of development did not lead to obvious changes in neuronal morphology. The mutants showed spontaneous seizure activity to varying degrees, ranging from partial seizures without secondary generalisations to occasional spontaneous generalised tonic-clonic seizures lasting 15 - 30s. Mostly, high-amplitude sharp-wave activity at low frequencies was observed.
Conclusion: Our transgenic mice are a valuable model for studying the pathophysiological role of M channels in epilepsy.

048

Epileptic Outcome is Correlated with Protection in Temporal Cortices: Evidence from Neuroprotection Studies with a New Drug, RWJ333369, in The Lithium-pilocarpine Model

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Purpose: Hippocampus and temporal cortices are involved in temporal lobe epilepsy but their respective roles are not known. Therefore we studied the epileptic outcome and neuronal damage in lithium-pilocarpine rats treated with RWJ333369 (RWJ).
Methods: Status epilepticus (SE) was induced with lithium-pilocarpine. RWJ (30, 60, 90 or 120 mg/kg) was injected intraperitoneally at 1 and 8 h after SE onset. Injections of RWJ were repeated twice daily for 6 days. The reference group received diazepam instead of RWJ. Rats were video-recorded for occurrence of spontaneous recurrent seizures (SRS) and sacrificed after two months of epilepsy or after five months if no SRS occurred.
Results: Forty-five percent of rats treated with 90 or 120 mg/kg RWJ did not develop SRS five months after SE. Latency to SRS was increased (52-84 days after SE) in 44% of RWJ treated rats at 120 mg/kg, 19% at 90 mg/kg and 30% at 60 mg/kg. Latency to SRS was similar to diazepam-treated rats (12-15 days) in 11% of rats at RWJ 120 mg/kg, 36% at 90 mg/kg, 70% at 60 mg/kg and 100% at 30 mg/kg. There was a significant direct correlation between the epileptic

outcome and the number of neurons surviving in the deep layers of entorhinal and piriform cortices but not in hippocampus or amygdala.
Conclusion: RWJ is the first drug we have tested that was able to delay or prevent SRS occurrence in this model of epileptogenesis. Latency to the first SRS was correlated with neuronal damage in temporal cortices suggesting their major role in epileptogenesis.

Supported by Johnson & Johnson Pharmaceutical Research & Development, LLC

Tuesday 30th August 2005
15:30 - 17:00
Salle Maillot
Platform Session
Clinical Neurophysiology - Progress in Neurophysiological Investigations of Ictal and Interictal Epileptic Networks

049
Ictal Magnetoencephalography of Eleven Symptomatic Epilepsy Patients
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Purpose: There is little knowledge of ictal magnetoencephalography, because of the rare chance to examine the ictus. Therefore we report the feature of ictal magnetoencephalography and the relationship of the irritative area on the interictal magnetoencephalography and the initial onset area of the ictal one.
Methods: The twenty seconds of magnetoencephalography prior to the clinical ictus was collected manually from 11 symptomatic epilepsy patients. These patients consisted of 5 temporal lobe epilepsy, 2 arteriovenous malformations, 2 cavernoma, 1 ulegyria, and 1 metastasis. The data was analysed by the two methods; the equivalent current dipole method and the spatial filter method. The results of the equivalent current dipole analysis of ictal magnetoencephalography were displayed on MRImage as the magnetic source image. The results of the spatial filter method (synthetic aperture magnetometry virtual sensor analysis) were showed as the initial onset area in the brain. We compared the results with the localisation of the irritative area of interictal spikes.
Results: Repeated spikes were observed only from 3 patients, and theta waves were observed from 5 patients in this series. Ictal magnetoencephalography of two cavernoma were not clear from the background activity on magnetoencephalography. The initial onset area was located in the irritative area in 8 patients analysed by the spatial filter.
Conclusion: Ictal magnetoencephalography of temporal lobe epilepsy was inclined to compose theta rhythm. In cases of lesional epilepsy, the initial onset area was situated in the localisation of equivalent current dipoles of interictal magnetoencephalography.

050
MEG Analysis of High Frequency Activity (80-120Hz) in Patients with Temporal Lobe Epilepsy: Preliminary Results
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Purpose: The aim of this study was to examine high frequency activity (80-120Hz) recorded by MEG in patients with temporal lobe epilepsy. Its eligibility to reveal correctly localising time intervals compared to spike localisation was investigated.
Methods: 5 patients with monofocal temporal lobe epilepsy were examined using high frequency MEG (Magnes II, 4D-Neuroimaging, 74 channels, sampling rate 1041.7Hz, 400Hz lowpass cutoff filter). Spectral power in the 80-120Hz band was calculated. Local power maxima above the 97th power quantile indicated epochs which were then used for dipole localisation (BTI software, equivalent current dipole, sphere volume conductor). The resulting localisations were then selected using standard quality criteria (correlation 0.97, confidence volume 3cm3). As a comparison, spikes were identified in data recorded using a comparable sensor position. For both spike and power maxima indicated localisation groups median and 5-95-interpercentile distance, denoting centre and scattering, were calculated and compared.
Results: 52% of all epochs with high frequency maxima yielded dipoles meeting the quality criteria (maximum in single patient: 74%, minimum: 29%). Distance between the localisation group centres amounted to an average of 1.61cm (minimum 0.43cm, maximum 2.89cm), scattering amounted to an average of 2.64, 2.58, 2.61cm for spike localisations and 3.48, 3.15, 3.66cm on x-, y- and z-axis for high frequency indicated localisations.
Conclusion: The results suggest that local maxima of high frequency activity (80-120Hz), detected by MEG, indicate epochs containing dipolar patterns that are seen to be able to localise epileptic foci. It shows evidence for high frequency activity involvement in the generation of interictal epileptiform activity.

051
Automatisms Related to Diaschisis Between Intention for Action and Temporo-insular Networks in Mesio-temporal Lobe Epilepsy
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Purpose: The clinical usefulness of ictal SPECT is mainly based on the ability to correctly lateralise and localise the epileptogenic zone (EZ). Some productive symptoms (dystonic posturing, secondary generalisation) were associated with hyperperfusion in subcortical areas. In return, little effort was made to clarify behavioural correlates of hypoperfusion. This study was designed to clarify the significance of frontal hypoperfusion during temporal lobe (TL) seizures and assess whether ictal automatisms of TL epilepsy (TLE) are related to hypoperfusion of frontal areas usually involved in the intentional aspect of action.
Methods: We studied 24 patients with refractory MTLE with hippocampal sclerosis using substraction ECD-SPECT coregistered to MRI (SISCOM). All patients are seizure free 4 years after a temporal lobectomy. SISCOM of 3 groups of patients were studied: group 1 (n=8) had motionless staring with or without aura, group 2 had in addition automatisms (n=9) and group 3 had in addition dystonic posturing. Comparisons were made by paired t-test with the software package PLAMAIVIC of the Society Medasys. Further analysis was done by Kruskal-Wallis test upon semi-quantitative measurements of ictal blood flow (BF) changes in 20 regions of interest.
Results: Occurrence of automatisms was associated with significant hypoperfusion bilaterally (group 2) or ipsilaterally (to EZ, group 3) in prefrontal cortex, pre-SMA and the underlying pericingulate cortex, contralaterally in the cerebellum (group 2 and 3) and retrosplenial cortex (group 2). Dystonic posturing was associated with contralateral posterior putaminal hyperperfusion. Differences of seizure duration among groups didn't act as covariables.
Conclusion: We identified ictal hypoperfusion in restricted prefrontal and frontal mesial regions during automatisms in MTLE. These areas were activated in previous fMRI studies of the intentional component of motor planning.

052
Tuberous Sclerosis Complex (TSC): A Comparison of High Resolution EEG and MEG
G.J. Huiskamp[1], F.E. Jansen[1], O. Van Nieuwenhuizen[1], M.D. Bourez-Swart[1], E. Boere[1], T.A. Gebbink[1], K.L. Vincken[1], A.C. Van Huffelen[1]

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Purpose: The determination which of the many tubers in patients with tuberous sclerosis (TSC) is epileptogenic is difficult. We investigated the correspondence of epileptiform activity recorded with EEG and MEG and the location of tubers in 19 patients with TSC and epilepsy.
Methods: HR EEG, HR MEG and 1.5T MRI scans were performed. Epileptic discharges in EEG and MEG recordings were selected separately offline by three observers. Observer agreements < 0.40 were rejected from source localisation. MUSIC analysis for dipoles with free orientations was performed using CURRYV 3.0 software. Distances from the maximum of the MUSIC metric for both EEG and MEG and the border of the closest tuber were calculated and compared.
Results: In 9 patients unifocal epileptiform activity and in 9 multifocal epileptiform activity was recorded with EEG, with kappa values >0.40 in 12 patients. MEG recording revealed unifocal epileptiform activity in 11 patients and multifocal in 9, with kappa values >0.40 in 14 patients. Source localisation was performed in 12 patients. MEG sources were closer to tubers in the majority of the patients. 3 patients underwent epilepsy surgery, of whom 2 are seizure free in consistence with resection of the MEG related tuber.
Conclusion: MEG analysis is at least as accurate as EEG analysis in identifying the epileptogenic source in TSC. A unifocal epileptogenic zone in relation to one tuber was identified in one third of the patients. Clear identification of the epileptogenic zone may offer opportunities for epilepsy surgery in patients with TSC who were previously considered intractable.

053
Ictal EEG in West Syndrome: From the Onset to the Outcome
S. Binelli[1], S. Franceschetti[1], E. Freri[1], T. Granata[1], G. La Porta[1], F. Panzica[1]

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Purpose: To verify the value of the ictal EEG pattern associated with spasms in West syndrome (WS) in predicting the localisation of following focal epilepsies.
Methods: Between 1992 and 2002, we diagnosed WS in 82 patients in whom we recorded at least one cluster of spasms. Among these patients, we selected 10 cases who had a Video-EEG recording of seizures persisting more than 2 years after the onset. We compared the first and the following EEGs in order to detect focal or lateralised ictal EEG patterns. To better characterise the dynamics of the EEG changes and to compare the ictal waveforms of different seizures in the same patient, we applied autospectra, coherence and phase analysis on selected EEG samples.
Results: The follow-up was 6.8±2.7 years. At the onset, spasms were symmetrical in 3 infants, asymmetrical or associated with focal clinical features in 7; the ictal EEG was unilateral in 3, bilateral in 7 (including focal fast activity in 6). During the follow up, seizures (focal or tonic) continued to present in cluster in 5 children but were isolated in the remaining 5. In all but 1, a clearly focal ictal activity was detectable.
Conclusion: Our data demonstrate that ictal activity preserves, during the follow-up, a consistent location, which was already detectable during the spasms. The focal ictal features were congruous with ictal clinical symptoms and became more evident in the course of time. These observations may be relevant in the early evaluation of surgical strategies to treat severe, early onset, epileptic encephalopathies.

054
Reorganisation of Motor Function in Central Epilepsy
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Purpose: The aim of this study was to explore the reorganisation of cortical motor areas in epilepsy patients who present an epileptogenic network located in the central region.
Methods: We explored 6 right-handed epilepsy patients with focal motor seizures and 6 young healthy right-handed subjects using transcranial magnetic stimulation (TMS) to map the cortical representation of Abductor pollicis brevis muscle (APB) on both sides. The coil was moved by steps of 1.5 cm over the subject's head. At each location, four MEPs were delivered at 1.2 times the resting motor threshold. The mean peak-to-peak MEP amplitude was measured at each site. The area of representation was measured and the optimal point was calculated for APB on each side.
Results: In healthy subjects, the area of APB representation was similar for both hemispheres, and the optimal points were symmetric. Clinically, no patients displayed motor deficit from epileptic seizures. In these patients, asymmetric shape of APB representations and discrepancies in surface areas could be observed between both hemispheres. In some patients, the APB representation in the epileptic hemisphere was more widespread. In patients with dysplasia, the optimal point was not centred in the representation area but off-centred compared to the healthy hemisphere.
Conclusion: We conclude that abnormal excitability of an epileptogenic region induces a reorganisation of neighbouring cortical motor areas. This plasticity can be investigated by a noninvasive TMS method. We hypothesised that this cortical reorganisation would reduce the risk of motor deficits that could follow neurosurgery in rolandic regions.

Tuesday 30th August 2005
15:30 - 17:00
Salle 252A
Platform Session
Psychiatry

055
Association between Cognitive Functioning and Mental Health Problems in Children with Epilepsy
J.K. Austin[1], S.M. Perkins[1], D.W. Dunn[1], P.S. Fastenau[2]

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Purpose: Children with epilepsy have high rates of mental health problems and cognitive deficits. Although IQ has been associated with mental health problems, the role of specific cognitive deficits is not known. Purposes of this study were: a) to explore the relationships between cognitive functioning and mental health problems over time and b) to determine if gender moderates this relationship.
Methods: Subjects were 165 children (84 boys and 81 girls) with epilepsy ages 9 to 14 years. Data were collected twice over 2 years. Children completed structured interviews (self-concept and depression symptoms) and individualised cognitive testing to measure verbal/memory/executive function (VME), rapid naming/working memory (RN/WM), and psychomotor skills (PSY). Parents completed structured interviews (behaviour problems). Data were analysed using repeated measures analysis of covariance. Covariates were child age, age of seizure onset, caregiver education, seizure type, medication use and seizure control.
Results: Relationships were stable over time. Higher levels of VME and RN/WM were associated with more positive self-concepts and fewer behaviour problems and depression symptoms. Higher PSY levels were related to fewer depression symptoms. The relationship between RN/WM and self-concept and depression was moderated by gender with the relationship being significant for girls but not for boys.

Conclusion: Higher levels of cognitive functioning were generally associated with fewer mental health problems. Some relationships were not independent of gender, which might reflect that girls are more bothered by cognitive problems than boys.

056

Conversation Analysis Might Add to the Differentiation of Non-epileptic from Epileptic Seizures

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Purpose: It can be extremely difficult to communicate with patients with non-epileptic dissociative seizures. To understand their peculiar conversational behaviour and to identify clinically helpful features in the verbal communication of these patients, we explored doctor-patient interaction using conversation analysis, an established qualitative linguistic approach.
Methods: We compared 13 patients with dissociative seizures and 14 patients with epileptic auras (both diagnosed using longterm video-EEG monitoring), representing theoretically most different patient groups. 27 in-depth open interviews were conducted with the medical doctor refraining from directive questioning. Interviews were recorded and transcribed. Transcriptions of dissociative vs. epileptic seizures were analysed. The first linguistic analysis used an iterative approach to identify features characteristic for the patients' description of their seizures. Secondly, the frequency of these features was assessed in all interviews in a post hoc comparison.
Results: Comparing descriptions of dissociative seizures with epileptic auras, we found that patients with dissociative seizures tended not to denote their subjective seizure semiology as relevant (10/13 vs 3/14 in epilepsy patients). Often it was necessary to prompt this description which lacked conceivable effort and detail. There was a tendency to evade further exploration ('resistance to focussing') in 9/13 dissociative patients compared to 3/14 epilepsy patients. Patients with dissociative seizures tended 'not to know', and showed significantly more and longer pauses in the narratives of their fits.
Conclusion: These finding from interviews might explain why healthcare professionals find it confusing and tedious to communicate with patients with dissociative seizures. From these findings it is possible to recommend certain changes of explorative techniques. The power of the above features to predict diagnosis, however, awaits further hypothesis-driven and quantitative study.

057

Ictal Fear vs Panic Attacks: A Preliminary fMRI Study of Autobiographic Episodic Memory

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1) Bethel Epilepsy Centre, Ev. Krankenhaus, Bielefeld, Germany 2) Psychiatry, Ev. Krankenhaus, Bielefeld, Germany

Purpose: Clinically it can be difficult to differentiate episodes of ictal fear from panic attacks. We aimed to describe differences between these episodes of similar symptoms by comparing their neuronal representations using functional MRI (fMRI).
Methods: We studied 5 epilepsy patients with ictal fear and 7 non-epileptic patients with panic attacks. We obtained the history of episodes of ictal fear or panic attacks and of common fear (in situations of everyday life). Key words were used to trigger memory retrieval. Using a 1.5 T MRI scanner, fMRI were performed in a blocked design with memory of ictal fear/panic attacks, memory of common fear, and rest as conditions. We used standard fMRI postprocessing for comparisons within and between groups ($p < 0.05$).
Results: Episodic memory of common fear led to a left hemispheral fMRI activation pattern in the overall group. Comparing common fear between the groups, we found an increase in right fronto-orbital areas in patients with panic attacks. Again in the overall group, episodic memory of pathological fear showed right frontal activation. Comparing memories of ictal fear with memories of panic attacks directly, we found a bilateral increase of activation of occipito-temporo-mesial areas in epilepsy patients - and increased activation of right fronto-lateral and -mesial as well as temporo-mesial areas in patients with panic attacks.
Conclusion: Patients with ictal fear seem to engage secondary cortical visual areas and left frontal areas during memory of their attacks - possibly pointing to a more detailed processing. Patients with panic attacks engaged temporo-frontal (i.e. limbic-paralimbic areas) more on the right - hypothetically representing fast and shallow processing associated with the fear response.

058

Psychosocial Adjustment after a First Seizure: The Process of Losing and Regaining Control

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1) The University of Melbourne, Victoria, Australia 2) Comprehensive Epilepsy Program, Epilepsy Research Centre, The University of Melbourne, Austin Health, Victoria, Australia

Purpose: The aim of this study was to perform a phenomenological investigation into the psychosocial impact of a first seizure in adulthood, and to elucidate the processes underpinning psychological adjustment to this event.
Methods: This investigation formed part of a larger longitudinal phenomenological study undertaken at the First Seizure Clinic of Austin Health, a Melbourne hospital with a large Comprehensive Epilepsy Program. 50 patients were assessed 1- and 3- months after a first seizure using a purpose-developed semi-structured interview with high inter-rater agreement (87%).
Results: Perceived loss of control was a key theme spontaneously reported by patients 1-month after the first seizure, characterised by increased vulnerability, awareness of mortality, fear of seizures and mood disturbance. Patients were subsequently classified as experiencing either a 'pervasive' (n=28) or 'limited' (n=22) loss of control. Both groups described attempts to regain subjective control over the initial 3-months, typically by identifying and addressing what they conceived to be the cause of the seizure (74%), and viewing the seizure as an isolated event (50%). More extensive efforts at restoring psychological control were made by the pervasive group (chi-sq=25.7; $p<.0005$). Seizure recurrence (n=11) appeared to spark further subjective loss of control, and was associated with ongoing mood disturbance (54%) and anxiety about further seizures (46%).
Conclusion: These findings indicate that a first seizure in adulthood involves an unexpected and potentially traumatic loss of control for many patients. The initial three months is a critical period during which most patients spontaneously undertake a process of rebuilding their subjective sense of control. Acknowledgements: This research has been supported by The University of Melbourne, Austin Health, and GlaxoSmithKline, Australia. It is currently funded by a 2004 Australian Research Council Linkage-Project Grant with GlaxoSmithKline, Australia.

059

Preventing Depression in Adolescents with Epilepsy

Z. Martinovic[1]

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Purpose: To test the possibility of preventing depression among adolescents with newly diagnosed epilepsy.
Methods: Adolescents with newly diagnosed epilepsy were screened with a questionnaire for the risk factors of depression, Beck depression inventory (BDI) and Center for Epidemiological Study on Depression Scale (CESDS). Patients with increased risk were randomised in two groups: treatment group with short behavioural cognitive interventions (BCI) and control group with the treatment as usual (TAU). All epilepsy patients received optimal antiepileptic drug therapy and kept a seizure diary throughout the study. Ratings of

depression with BDI and Hamilton depression scale (HAMD), and quality of life scale (QUOLIE 31) were measured at baseline and during the follow-up lasting 6-9 months.
Results: Of 104 adolescents screened, a diagnosable depression was evident in 9 (8.6%) and increased risk of depression in 30 (28.8%) patients (mean age 17.4 years, 18 females and 12 males). The BCI and TAU subgroup consisted of 15 patients each who were age and sex matched, and comparable in relation to the initial BDI or CESDS scores. A diagnosable depression during follow-up occurred only in 3 patients of the TAU subgroup. Subthreshold depressive disorder was significantly improved during follow-up when BDI and CESDS scores were lower in the BCI subgroup compared to the TAU subgroup ($p<0.05$). QUOLIE 31 score was significantly correlated with mood improvement and achievement of seizure-free state.
Conclusion: The results encourage further studies to assess the selective preventive interventions in depressive disorders in adolescents with epilepsy.

060
Children with Attention Deficit/Hyperactivity Disorder and Epileptiform Abnormalities
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Purpose: This study investigated relationships between epileptiform abnormalities and ADHD symptoms in children with attention-deficit/hyperactivity disorder (ADHD).
Methods: 270 children with ADHD diagnosis (223 male, 47 female, aged between 6 to 14 years, mean age 9.4, sd 2.7) were assessed. At least one routine EEG was performed on all the patients. Evidence of epileptiform abnormalities, seizure risk, ADHD subtypes, and comorbid disorders were analysed. The EEGs were coded as either epileptiform or nonepileptiform. The mean observation period was 3.7 + 1.2 years.
Results: Epileptiform abnormalities were registered in 22 patients (8.1%). Generalised epileptiform activity was noted in 8, focal in 8, and mixed in 6. ADHD predominantly inattentive type was observed in 8 of 21 children. There was a comorbidity of epilepsy in 11 patients, conduct disorder in 5, Tourette's syndrome in 4, learning disability in 4, depression/anxiety in 4. Psychostimulants were administered to 20 patients. 11 of them were also treated with AEDs due to epilepsy comorbidity without experiencing seizure exacerbation. One child who did not receive psychostimulants had no symptoms of inattention following effective antiepileptic medication. No seizure occurrence was noted in any of the 11 patients who had epileptiform EEGs but no epilepsy comorbidity.
Conclusion: Our data suggest that ADHD predominantly inattentive is more common among children with ADHD and epileptiform EEGs. Epilepsy, conduct disorder, Tourette's syndrome, learning disability and depression/anxiety are frequent comorbid disorders. Epileptiform abnormalities do not necessarily indicate a considerable risk of developing seizures and are not associated with an increased seizure risk.

Tuesday 30th August 2005
15:30 - 17:00
Salle 252B
Platform Session
Paediatric Epilepsy 2

061
Probable Symptomatic (Cryptogenic) Epileptic Spasms with Onset after the Age of One Year Associated with Temporal or Temporo-Frontal EEG Anomalies, Electroclinical Aspects and Outcome in Children
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Purpose: The aim of the study was to analyse electro-clinical aspects and outcome of children suffering from epileptic spasms beginning after one year of age without an obvious underlying pathology.
Methods: Of 65 children with spasms onset after one year of age having undergone 24 hour polygraphic video-EEG recording (January 1994 - December 2004) 23 fulfilled the inclusion criteria: spasms recorded, absence of obvious underlying aetiology (metabolic, genetic and cerebral MRI studies). Video-EEG recordings were analysed in detail. Clinical data were evaluated retrospectively.
Results: Age at final evaluation 8.5+3.9 yrs (4-17); age at onset of spasms 19.5+12.4 mths (12-52), follow-up 5.3+2.8 yrs (2.3-10). Family history of epilepsy: 0/23. Normal psychomotor development in the 1st year of life: 23/23. Language disturbances/behaviour problems: 15/23. EEG: normal background activity (23/23), temporal or temporo-frontal slow wave and/or spike focus (unilateral 1/23, bilateral independent 22/23). Spasms: in clusters (23/23), asymmetrical (3/23), tonic component (19/23). Other seizure type: atypical absence seizures, isolated or related to cluster of spasms (23/23), tonic seizures (0/23). Response to treatment (complete cessation of seizures): VGB (2/23), HC (7/18), ACTH (1/4), ketogenic diet (0/6), callosotomy (0/3). Persistence of spasms: 13/23.
Conclusion: We present 23 children with probably symptomatic (cryptogenic) late onset epileptic spasms. They don't represent West syndrome (onset > 1 year, no hypsarrythmia, no psychomotor deterioration) nor Lennox-Gastaut syndrome (no tonic seizures nor typical EEG findings). Temporal or temporo-frontal EEG anomalies and atypical absence seizures suggest involvement of the temporal lobe in the pathophysiology of spasms despite absence of recorded typical temporal lobe seizures.

062
Electro-clinical Characterisation of Infantile Seizures
C.M. Korff[1], D.R. Nordli, Jr.[1]

1) Epilepsy Center, Children's Memorial Hospital, Chicago, Illinois, USA

Purpose: To describe the electro-clinical correlates of infantile seizures.
Methods: We reviewed video-EEG studies of 449 infants (1 month-2 years). Of these, 69 had seizures and 101 distinct seizures were systematically analysed, both clinically and electrographically. Seizures were classified using a modified version of the 1981 ILAE system. Ictal EEG features were noted according to onset lateralisation, location, and pattern; spread; and termination. Seizure classification was compared with EEG patterns.
Results: There were 13 distinct seizure types. EEG correlates are shown in parentheses. 25 were spasms (electrodecrements (88%)); 16 were spasms associated with a focal seizure, either tonic (9 cases), tonic-clonic (4) or clonic (3) (electrodecrements (94%) in addition to the admixed focal seizures); 14 were versive with behavioural arrest (unilateral ictal onset (93%), posterior quadrant (50%), regional evolution (71%), fading termination (79%)); 11 were partial clonic,

(repetitive spikes (73%), contralateral fronto-central regions (67%), restricted spread (100%), rapid fading termination (64%)); 11 were partial tonic (EEG onset, propagation, and termination variable). Diffuse tonic-partial clonic (4); tonic-clonic with secondary generalisation (3); pure behavioural arrest (1); generalised (12); and hypermotor seizures (1) were also captured.
Conclusion: The EEG ictal correlates of most infantile seizures are predictable. Important exceptions are tonic, behavioural arrest with version and spasms associated with focal seizures. These show more heterogeneous electrographic correlates which can not be reliably predicted by the seizure semiology. In such cases, video-EEG recording of ictal events might be of particular relevance. Moreover, the identification of distinct electrographic patterns might help identify specific epilepsy syndromes. Acknowledgements: Dr C. Korff was supported by a grant from the Eugenio Litta Foundation, Vaduz, Liechtenstein.

063
Change of Seizure Semiology in the Developing Temporal Lobe
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Purpose: Seizure semiology in adults with mesial temporal lobe epilepsy (TLE) is quite stereotyped manifesting with behavioural arrest and automatisms. A greater variability of semiology including motor seizures has been reported in young children with TLE. The aim of our study was to examine objectively the effects of localisation and age on semiology of seizures originating from the developing temporal lobe.
Methods: We performed a video analysis of 428 archived seizures from 100 consecutive children (50 girls; 64 mesio-temporal lesion; age 10 months to 17.4 [mean 9.45±4.76] years) selected by post temporal lobectomy seizure-free outcome, and classified them by a recent semiological seizure classification (Lüders et al. Epilepsia 1998;39:1006-13.). Seizure components were divided into two groups depending on the presence of motor manifestation. Tonic, clonic, myoclonic, hypermotor components, and epileptic spasms were categorised as motor seizure components (MSCs). The group of non-motor seizure components included hypomotor and psychomotor attacks. Ratio of MSCs was calculated in each patient using the following formula: number of MSCs/all seizure components.
Results: Ratio of MSCs was significantly lower among patients with mesial TLE ($p=0.001$, Mann-Whitney test). Spearman rank correlation showed a linear and inverse correlation of the ratio of MSCs with age at monitoring ($r= -0.382$, $p<0.001$). Univariate analysis of variance (ANOVA) revealed that both the age of patients ($p<0.001$) and mesial localisation ($p=0.019$) independently correlated with the ratio of MSCs.
Conclusion: Our findings support the hypothesis that the process of human temporal lobe maturation significantly impacts on clinical seizure semiology.

064
Familial Occipitotemporal Lobe Epilepsy and Migraine with Visual Aura
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Purpose: Epilepsy and migraine often co-occur. Our aim was to describe the clinical, EEG and MRI characteristics of a family with occipitotemporal lobe epilepsy associated with migraine with visual aura (MA) and to speculate on the neurobiological substrate of both conditions.
Methods: 88 members of a Belgian pedigree participated. All completed a validated questionnaire for epileptic seizures and 27 of them for migraine. We interviewed 21 persons, and performed interictal EEG in 14, brain MRI in 13 and brain CT in 1.
Results: 15 of the 88 members and 1 deceased member had clinically definite or possible epileptic seizures characterised by a high incidence of visual and temporal lobe simple partial seizures, variable age of onset, low incidence of epileptic EEG features, normal MRI and usually good prognosis. 6 of these 16 patients (38%) had a history of MA ($p=0.0043$). The seizures and the migraine attacks occurred temporally independent in all. 1 had severe migraine attacks after seizures. 3 described light flashes both as epileptic and migraine aura, that were identical in 2 of them. Age of onset and remission of both epilepsy and MA were similar in 3 and 2 patients, respectively.
Conclusion: The association and the clinical characteristics of epilepsy and migraine in this family suggest an autosomal dominant gene mutation resulting in transient disequilibrium of neuronal ion concentration causing both epilepsy and MA in the occipitotemporal lobe.

065
Social and Economic Burden of Paediatric Epilepsy in Ireland: A Prospective Study
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Purpose: To estimate the burden of paediatric epilepsy on the family and Irish health care system and to establish whether there is a relationship between epilepsy profile and this burden.
Methods: The sample was drawn from a population of children with epilepsy attending a tertiary paediatric neurology clinic in Dublin. Data was collected prospectively on healthcare resource use, out of pocket payments and time lost from school and work. Diary cards were collected at 3 monthly intervals.
Results: Complete data was available on 127 children aged 15 months to 16.7 years (median 8.8), 54% were male and 52% lived in a rural setting. 61% had cryptogenic or symptomatic epilepsy, 63% had partial seizures and 53% had frequent seizures (>10/month). The annual cost of epilepsy was significantly higher for those with cryptogenic/symptomatic epilepsy (€9,248) and frequent seizures (€9,145) relative to idiopathic epilepsy (€2,600) and no/infrequent seizures (€3,951) ($p<0.0001$). Children with frequent seizures had a higher risk of being hospitalised ($p=0.03$) and lost more days from school ($p<0.0005$). 50% of families contacted the paediatric liaison nurse, and 12% made more than 5 contacts. 5% of children attended their GP while 37% of families had independently sought complementary medicine.
Conclusion: The economic and social burden of paediatric epilepsy is substantial and relates to the epilepsy syndrome and frequency of seizures. In this prospective study, a large dependence in epilepsy liaison nurse support was found, an area that requires extra resources. A large number of families also sought advice from non medical sources.

066

Genetics of Photosensitivity - is Photosensitivity a Suitable Endophenotype for Idiopathic Generalised Epilepsies?

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Purpose: Although many dozens of molecular genetic linkage and association studies have been conducted, the identification of mayor genetic effects and their aetiopathophysiological principles leading to idiopathic generalised epilepsies (IGE) seems to be still far. We are particularly challenged by two principal difficulties in the genetic dissection of complex diseases - genetic heterogeneity and complex inheritance. An alternative concept to approach these difficulties in genetic studies of IGE involves the use of specific neurobiological characteristics of the disorder as additional phenotypes that might reflect more closely the underlying genetic effect.
Photosensitivity or photoparoxysmal response (PPR) is a common and highly heritable electroencephalographic (EEG) trait evoked by standardised intermittent photic stimulation (IPS) during EEG recording. PPR is a frequent finding in IGE – it is found in up to 90% of IGE patients - compared to 8% in the healthy population. Thus the molecular genetic dissection of this specific EEG trait, i.e. endophenotype, seems to be a suitable approach to overcome the difficulties in the molecular genetic dissection of IGE.
Here we present the results of a genomewide linkage scan, designed to map susceptibility loci for PPR and to explore its genetic relationship with IGE. We included 60 families of German origin with at least two siblings affected by PPR. Our study reveals two PPR-related susceptibility loci, correlating with the family history of IGE. MOD-score analyses provided significant evidence for linkage to the region 6p21.2 in families with predominantly pure PPR and photosensitive seizures and suggestive evidence for linkage to the region 13q31.3 in families with a strong IGE background. The locus on 6p21.2 seems to predispose to PPR itself, whereas the locus on 13q31.3 also confers susceptibility to IGE. Ongoing linkage and association studies have to reveal if the molecular genetic dissection of photosensitivity will finally lead to the identification of genes also involved in the pathogenesis of IGE.

Tuesday 30th August 2005
15:30 - 17:00
Salle 242AB
Platform Session
Issues in Epilepsy Surgery

067

Epilepsy Surgery in Mentally Retarded Patients: Pathoanatomical Diagnoses

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Purpose: Epilepsy surgery has been questioned for patients with mental retardation (MR). However, there are few studies of differences in underlying pathologies in patients with or without MR who undergo surgery for epilepsy.
Methods: The Swedish National Epilepsy Surgery Register includes data on all epilepsy surgery procedures in Sweden since 1990. Data from 1990-1999 was analysed with respect to resective epilepsy surgery, IQ and pathoanatomical diagnoses.
Results: Of 427 patients 70 (16%) had MR which was moderate in 52 (IQ 50-70), median age (m.a.) 16, and severe in 18 (IQ<50), m.a. 7 while 357 patients had IQ>70, m.a. 30. Mesial sclerosis was found in 41% for IQ>70, m.a. 33, 28% for IQ 50-70, m.a. 24 and 22% (4) for IQ <50, m.a. 8. Cortical dysplasias were 14.4% for IQ>70, m.a. 28, 28.8% for IQ 50-70, m.a. 9 and 56% for IQ<50, m.a. 3. Lesions were 19.9% for IQ>70, m.a. 27, 11.5% (6) for IQ 50-70, m.a. 27.5 and 0 for IQ<50. Low-grade tumours were 9.5% for IQ>70, m.a. 21 years, 3.8% (2) for IQ 50-70, m.a. 36 and 1 (5.6%) for IQ<50, age 15 years.
Conclusion: MR was present in 16% of the operated patients. Mesial sclerosis was most common if IQ>70 in contrast to cortical dysplasias, which were most common if IQ<50. There were no lesionectomies if IQ<50 and few low grade tumours in the MR group. Even if aetiologies differs in different age groups, it seems that surgery for lesions and tumours are underrepresented in the MR group.

068

Normal MRI Does Not Affect Seizure Free Outcomes after Epilepsy Surgery: Results of 176 Surgeries

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Purpose: To determine the effect of normal MRI findings on seizure free outcomes following epilepsy surgery.
Methods: We reviewed the results of epilepsy surgeries performed in Milwaukee from 1991 to 2001. In 362 evaluations of epilepsy, we found 214 surgical resections. We found 176 cases with valid MRI results, surgery locations, and 6 month seizure-free outcomes. We divided patients into seizure-free versus non-seizure-free at their 6 month assessment. Surgery locations were defined as lobar or multi-lobar. MRIs were collapsed into normal or abnormal results. We performed an analysis using Pearson's chi-squared technique on the relationship between normal versus abnormal MRI results and the patient's seizure outcome, including analysis by surgery location.
Results: Of the 176 surgeries performed, 136 were temporal and 22 were frontal. Seizure freedom occurred in 103 of temporal resections (75%) and 8 of frontal resections (37%). Abnormal MRIs were found in 92 temporal resections (67%) and 15 frontal resections (68%). Seizure freedom was no different in patients with normal versus abnormal MRIs (p=0.991). Seizure freedom rates for temporal resections were 70% in normal MRI versus 77% in abnormal MRI (p=0.43). Seizure freedom rates for frontal resections in normal MRI were 42% versus 33% in abnormal MRIs.
Conclusion: Normal MRI in the evaluation of localisation-related epilepsies did not influence seizure-free rates in our surgical experience. Previous studies suggest the presence of MRI abnormalities improves surgical outcomes and we have previously reported abnormalities of prognostic significance. Patients presenting for epilepsy surgery should not be discouraged that normal MRI findings may influence their outcome.

069

Cost-effectiveness of Epilepsy Surgery in a Cohort of Patients with Medically Intractable Partial Epilepsy

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Purpose: In a multicentre cohort, intractable epilepsy patients, candidates for resective surgery, were followed in order to compare surgical and medical therapy in a cost-effectiveness analysis.
Methods: Adult patients with a partial medically intractable epilepsy, potentially operable were eligible and followed every 6 months over two years at least. The effectiveness was defined as one year without a seizure. We assessed the incremental cost-effectiveness ratio for the first two years after surgery with a societal perspective. The long-term costs and effectiveness were extrapolated over the patients lifetime with a Markov model. Indirect costs and quality-of-life (QOLIE-31, SEALS) were also measured. Data were compared before and after surgery.
Results: 289 patients were included (105 with surgery, 164 medically treated, 7 not eligible, 13 lost of follow-up). Disease was more severe in surgical than in medical patients: seizure frequency, depressive disorders and cognitive impairment were greater. One and two years after the surgery, respectively 80% and 78% of patients were seizure free. During the year before inclusion and the year after surgery, direct costs were mainly due to hospitalisation, respectively 40.6%, (1756€/4323€) and 31.4%, (1963€/6253€). The total direct cost raised during the second year after surgery, with the cost of antiepileptic drugs predominating. One additional year without a seizure cost 29433 € one year after surgery, and 13180 € two years after surgery. In a long-term perspective, the surgery became cost-effective after 8 years.
Conclusion: Surgical therapy was cost-effective in a middle-term despite the lack of indirect cost considerations.

070

Self-assessed Change in Quality of Life after Surgery for Mesial Temporal Lobe Epilepsy

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Purpose: Traditionally, outcome after epilepsy surgery is measured in terms of seizure type and frequency. Patients with epilepsy do not only suffer from usually infrequent and unpredictably occurring seizures, but also from continuous psychosocial limitations in daily performance. We intended to investigate postoperative seizure control and its correlation with different aspects of quality of life (QOL), in a one centre series of selective amygdalohippocampectomies performed for mesial temporal lobe epilepsy.
Methods: 128 of 140 consecutive patients (91.4%) who underwent surgery returned a questionnaire (similar and adjusted to the ESI-55) at a minimum of 18 months after surgery, in order to assess different aspects of individual functioning.
Results: In 110 patients satisfactory seizure reduction was achieved (ILAE-classification 1-3: 85.9%); unsatisfactory results in 18 patients (ILAE 4-6: 14.1%). Of 110 patients with satisfactory seizure control 100 patients (90.9%) stated that their overall quality of live (QOL) was good or even very good after surgery. With unsatisfactory seizure control only 9 of 18 (50%) reported good or very good QOL after surgery ($p=0.01$). Moreover, 99 of 110 patients (90.0%) claimed improvements in QOL after epilepsy surgery. Self-assessment of more detailed neuropsychological functions revealed a significant correlation of cognitive and amnestic functioning with seizure control ($p<0.001$). Mood was significantly better with satisfactory seizure relief ($p<0.001$). Physical capabilities ($p= 0.03$) and social situation ($p=0.04$) showed significant trends towards better results with satisfactory seizure relief. No correlation was found between age, sex or duration of epilepsy and self-assessed QOL. Reduction of anti-epileptic medication post-operatively was associated with better QOL. However, QOL was dependent on the situation regarding job and family, but we did not find a significant correlation between these socio-economic aspects and seizure outcome after surgery.
Conclusion: The individual overall benefit after epilepsy surgery is difficult to assess. Definitely, seizure control correlates with patient satisfaction, but also other factors seem to have an impact on QOL after epilepsy surgery, which should not be neglected in the evaluation of patients undergoing functional neurosurgery.

071

Autonomic Cardiac Control in Refractory Temporal Lobe Epilepsy: Preoperative Heart Rate Variability in Relation to Surgery Outcome

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Purpose: The risk of sudden unexpected death (SUDEP) is high in refractory epilepsy and in particular among epilepsy surgery candidates, which may be due to impaired autonomic cardiac control. Our objective was therefore to assess heart rate variability (HRV), as a measure of autonomic cardiac control, presurgically in epilepsy surgery candidates, and to relate the findings to the outcome regarding seizures after epilepsy surgery.
Methods: We used spectral analysis to analyse prospectively preoperative HRV in 21 consecutive patients with temporal lobe epilepsy who were planned for epilepsy surgery. The presurgical HRV based on ambulatory 24 hr ECG recordings was analysed in relation to seizure control at one year after surgery.
Results: Before surgery, the HRV was significantly lower in the patients with ultimately poor outcome (Engel class II-IV; n=10) compared with patients with good outcome after surgery (Engel class I; n=11): Total power ($p=0.01$), very low frequency power ($p=0.03$), low frequency power ($p=0.03$) and high frequency power ($p=0.05$). HRV among those with a good outcome did not differ from that of healthy controls.
Conclusion: Patients with a favourable outcome regarding seizures after surgery differ in preoperative HRV measures from those with a poor outcome. Reduced HRV has been suggested to be associated with an increased risk of SUDEP. Our data thus indicate that surgery candidates with a good outcome may a priori have a lower risk of SUDEP and suggest that the lower incidence of SUDEP reported after successful surgery may not necessarily be a consequence of the operation.

072
Mortality in Refractory Epilepsy: 'Surgically Successful' versus the Rest
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Purpose: To compare mortality rates in patients with refractory epilepsy with or without successful surgical outcome and those rejected for epilepsy surgery.
Methods: Case records of 1105 patients with refractory epilepsy, evaluated from 1990 to 2003, were analysed. Patients were divided into: group A: with successful post-surgical outcome (Engel score: I) [n=313, mean age: 34.0, SD 12.7 years, M:F 144:169], group B: with poor unsuccessful post-surgical outcome (Engel score: II - IV) [n=85, mean age: 25.5, SD 6.4 years] and group C: rejected for epilepsy surgery [n=707, mean age: 36.5, SD 7.1 years].
Results: A total of 31 patients (2.8%) with refractory epilepsy died, of which 24 deaths were related to epilepsy and 22 were due to SUDEP. 20 men died compared with 11 women, but the difference was not statistically significant ($p = 0.12$). 3 patients from group A died compared with 6 from group B and 22 from group C. Epilepsy related deaths and SUDEP were - group A: 0, 0; group B: 6, 4; group C: 18, 17 respectively. The death and SUDEP rates per person-year followed up in each subgroup were: group A: 1/535, 0; group B: 1/81.3, 1/97.6; group C: 1/59.7, 1/77.2 respectively. Death rates per person-year of follow up were significantly different in 3 subgroups (Chi squared = 19.11, df = 2, $p = 0.0001$), with group A being significantly different from group B (Fisher's exact test $p = 0.36$) and group C (Fisher's exact test p □ 0.001), both 2-sided and adjusted for multiple corrections.
Conclusion: Mortality is reduced following successful epilepsy surgery in patients with refractory epilepsy. SUDEP is the most important cause of death among these patients.

Tuesday 30th August 2005
15:30 - 17:00
Salle 251
Platform Session
Drug Therapy - Safety Issues In AED Therapy

073
Variability of Lamotrigine Levels in Women on Oral Contraceptives and During Pregnancy using Frequent Monitoring with a Blood Spot Method
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Purpose: It is described that lamotrigine (LTG) clearance may increase in women on oral contraceptives (OC) or during pregnancy. These changes may have significant clinical consequences. We have developed a 'blood spot method' for the analysis of 13 antiepileptic drugs (AEDs) and 2 metabolites in blood spots and have used it for more than four years. We applied this method in clinical practice to monitor LTG levels in female patients on OC and during pregnancy.
Methods: With the 'blood spot method' patients themselves apply finger puncture blood, obtained by means of an automatic lancet, on filter paper. The method includes extraction of AEDs from an 8 mm punch of dried blood on filter paper containing 14.9 ul of blood, followed by HPLC and GC-MS analysis.
Results: We will present through LTG levels during two cycles in patients on OC, who took blood spot samples themselves every other day. Surprisingly, during the OC free week, LTG levels increased rapidly up to 50% of LTG levels during the three weeks on OC. We also present the variability of through LTG levels in patients during pregnancy and the perinatal period using frequent blood spot sampling. LTG clearance may increase until twice the pre-pregnancy values within three months and decrease to pre-pregnancy levels within two weeks after delivery.
Conclusion: The blood spot method proved to be valuable for frequent monitoring of LTG levels during pregnancy and use of OC. The results underline the importance of further studies on the clinical consequences of LTG fluctuations in such situations.

074
Variability of Carbamazepine Concentrations in Elderly Nursing Home Residents
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Purpose: Carbamazepine is used by approximately 1.0-1.5% of all elderly nursing home residents in the USA. Monitoring plasma carbamazepine concentrations is often employed to guide therapy, but the variability of routinely collected total carbamazepine concentrations under steady dosing conditions has never been evaluated.
Methods: This was an observational study of 22 elderly nursing home residents (= or > 65 years) from 14 nursing homes with 3 or more carbamazepine concentrations on the same dose for at least 4 weeks. Residents were not taking any inferring comedications.
Results: The mean age of the residents was 78.2 years (range, 65 to 97 years) and 77% were women. The mean daily dose of carbamazepine per resident was 10.3 mg/kg. The total carbamazepine concentrations within an elderly nursing home resident varied as much as two-fold despite no change in dose. The resident with the smallest variability had no change in concentrations, and the resident with the greatest variability had a minimum concentration of 6.6 ug/ml and a maximum concentration of 12.9 ug/ml.
Conclusion: Despite a constant dose, total carbamazepine concentrations may vary two-fold throughout a six month period, and measurement of single total carbamazepine concentrations should not be solely used to guide therapy.

075
Cancer Deaths in People with Epilepsy: A Study of Two Different Cohorts of People with Epilepsy.
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Purpose: The study developed out of the hypothesis that people with epilepsy have an altered pattern of cancer mortality due to the administration of antiepileptic drugs (AEDs).
Methods: Three groups of people were recruited in the sample: 1) persons (presumably with severe epilepsy) admitted to a residential care centre for epilepsy (Chalfont; National Society for Epilepsy) (n=1416); 2) persons (presumably with less severe epilepsy) who applied for a driving license (DL) (n=4534) and 3) controls for group 2 comprising persons with limb disabilities (n=4610). They were followed up from 1 January 1975 to 31 December 2003 through the National Health Services Central Register and causes of death noted from death certificates. Standardised mortality ratios (SMRs) were calculated from national mortality data for various causes of death including neoplasms.
Results: Excess mortality from all causes was demonstrated (SMR: 2.37; 95%CI: 2.19-2.57) in the residential centre but not in the DL-epilepsy cohort (SMR: 0.95; 95%CI: 0.90-1.01). SMRs for cancer deaths were elevated in all age groups in the residential centre-cohort (SMR: 1.41; 95%CI: 1.17-1.68) but were elevated only in age groups < 45 y in the DL-epilepsy cohort (SMR: 1.32; 95%CI: 0.86-1.94). The excess cancer mortality comprised of breast (SMR: 1.80; 95%CI: 0.86-3.31), liver gall bladder and pancreas (SMR: 2.35; 95%CI: 1.22-4.71) and oesophagus and stomach (SMR: 1.78; 95%CI: 1.02-2.90) cancers in the residential centre cohort and of brain neoplasms (SMR: 3.75; 95%CI: 2.77-4.96) in the DL-epilepsy cohort.

Conclusion: SMRs for certain cancer sites are elevated in people with severe epilepsy due to a combination of factors including AEDs and life style factors.

076
Higher Incidence of Components of Polycystic Ovary Syndrome in Young Women with Epilepsy Treated with Valproate Versus Lamotrigine
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Purpose: To evaluate the development of components of polycystic ovary syndrome (PCOS) in women with epilepsy (WWE) ages 17 to 40 initiating either valproate (VPA) or lamotrigine (LTG) therapy for epilepsy.
Methods: Eligibility criteria for this prospective, randomised, open-label, multicenter study (LAM30007) included age 13-40 years, regular menstrual cycles; no concurrent hormonal medications; no prior LTG or VPA; and either newly diagnosed (<2 weeks prior anti-epileptic drug (AED) use) or inadequately controlled epilepsy (only 1 chronic AED≥3 months). Subjects were randomised to VPA or LTG and were treated for 12 months. Serum androgen levels were measured every three months and urinary pregnanediol glucuronide levels weekly for two 3-month periods. Components of PCOS were defined as development of hyperandrogenism (HA) or ovulatory dysfunction (OD) during the study. A post hoc analysis was conducted in a total of 323 17-40 year old women of the ITT population (159 LTG, 164 VPA).
Results: A greater proportion of women in the VPA group developed components of PCOS when compared to women in the LTG group (33% VPA vs. 22% LTG; p=0.022). This difference was based on results from the 17-25 age group (41% VPA vs 22% LTG, p=0.008), whereas the incidence was similar in the treatment groups if VPA was started after age 25 (24% VPA vs 22% LTG).
Conclusion: This large, multiethnic, prospective, randomised study shows that components of PCOS are more likely to develop in WWE receiving VPA than LTG, but only if the medication is started earlier in life.

077
Mental Development of Infants Born to Mothers with Epilepsy
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Purpose: Mental development of infants exposed in utero to antiepileptic drugs (AEDs) may be impaired. Our objective was to prospectively evaluate mental development of such infants.
Methods: A developmental paediatrician estimated the mental developmental quotient (MEDQ) for all infants of mothers with epilepsy who were prospectively followed up in this registry at one year of age. We used Developmental Assessment Scales for Indian Infants (Indian adaptation of Bayley Scale of Infant Development). Maternal and neonatal characteristics including AED usage were abstracted from the records.
Results: We examined 341 infants (mean age 15.28 + 4.3 months) between 1998-2004. Mothers had generalised (45.9%) or localisation related (49.7%) epilepsy; 54.8% were on monotherapy and 26.7% were on polytherapy. Infants' mean MEDQ was 89.57 + 29.34. The MEDQ was highest for no AED exposure (92.25 + 26.69) lesser for monotherapy (90.72 + 29.45) and least for polytherapy (85.35 + 31.78) groups. Those exposed to phenobarbitone or valproate monotherapy had lower MEDQ (89 + 17 and 88 + 34) compared to phenytoin or carbamazepine monotherapy groups (93 + 34 and 92 + 29) but the difference was not statistically significant. Infants of birth weight < 2.5 kg had lower MEDQ (83.35 + 31.78) than others (90.16 + 29.13). Maternal age, epilepsy type, seizures during pregnancy, and use of folic acid did not have any significant influence on MEDQ.
Conclusion: Infants exposed to AEDs in utero had a trend towards lower mental development, particularly those exposed to phenobarbitone or valproate, but the statistical significance needs further confirmation with a larger cohort.

078
Genetic Variation in the GABA C Receptor may Predispose to Vigabatrin (VGB) Induced Visual Field Defects
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Purpose: Irreversible visual field constriction due to the anticonvulsant vigabatrin (VGB) occurs in 14-70% of patients. Data from our cohort of 98 patients treated with VGB suggests this effect is unrelated to maximum dose, duration or cumulative dose. We investigated if common variation in the genes involved in the pharmacology of vigabatrin predisposed to retinal toxicity.
Methods: Five candidate genes involved in the pharmacology of VGB were identified (GABRR1, GABRR2, ABAT, GAT1 and GAT3) and using a haplotype based tagging SNP approach we found 26 tags sufficient to capture common variation (MAF>5%) across these genes. Patients on a stable dose of VGB for 6 months with reliable Goldmann visual fields (n=70) were enrolled. Visual constriction was estimated by calculating the mean radial degrees (MRD) and relationship between tSNPs and MRD was assessed using linear regression at a single SNP, haplotype, and global haplotype level.
Results: A significant association was found between a tSNP in Rho 2 subunit of GABA C receptor (rs2273508 C/T) and development of constriction (homozygous major allele: MRD=45.7 degrees; heterozygous: MRD=37.7 degrees (p=0.027). Only one patient homozygous for minor allele).
Conclusion: Vigabatrin accumulates in the retina and increases GABA levels. High dose GABA can reverse chloride currents at GABA receptors causing toxicity. We have shown that genetic variation in one of the subunits of the GABA C receptor may predispose to retinal toxicity. Given the possibility of a false positive result, we are replicating the association in a separate patient cohort of greater size.

Tuesday 30th August 2005
15:30 - 17:00
Salle 241
Platform Session
Adult Epileptology - Epidemiology

079
Limoges' Questionnaire for Investigating Epilepsy: One Decade on: Outcomes and Prospects from an Analysis of 2,313 Questionnaires from Africa
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1) Unit of Biostatistics and Clinical Research, Limoges University Hospital, Limoges, France And Institute of Neuroepidemiology and Tropical Neurology (EA 3174), Limoges, France 2) Institute of Neuroepidemiology and Tropical Neurology (EA 3174), Limoges, France 3) List on http://www-ient.unilim.fr

Purpose: Epilepsy affects 50 million people across the world, most of whom live in Africa, where few studies have been able to harvest and analyse standardised data from people with epilepsy (PWE). Limoges' questionnaire for investigating epilepsy has been used in 13 African studies since 1995. Eight of these studies (61.5%) were motivated by this tool. The aim of our work was to analyse the results collected and to suggest modifications that can be made to the original questionnaire.
Methods: Data was collected from PWE, confirmed by a neurologist, in twelve countries. Undernutrition was estimated by anthropometric

indices according to age and gender. An opinion survey was carried out among medical users in order to collect information about their experiences and expectations.
Results: The database contains 2,313 questionnaires. The median prevalence of epilepsy in Africa is estimated at 15%. 35.7% of PWE have not (and had never been) treated. Undernutrition affects 25.4% of people under fifteen. Clinical aspects and past history will be described. Risk factors of not being treated or of being malnourished will be detailed. Results from opinion survey will be given.
Conclusion: This questionnaire proved its usefulness in tropical countries. Even if the questionnaires included are not representative of the general population, they represent a huge collection of data from Africa, significantly facilitating the testing of certain hypotheses. The questionnaire could be expanded to include additional modules (such as psychosocial impact, quality of life, malnutrition). Corrections will be proposed to the scientific community.

080
Epilepsy in Laos PDR: Prevalence, Parasitic Aetiology and Aspects of Control
D.S. Tran[1], P. Odermatt[4], F. Vongprachanh[3], C. Simmala[1], L. Oanh[1], P. Huc[2], S. Ly[1], P. Vongphachanh[1], M. Luong[2], T. Angerth[1], M. Strobel[1], P.M. Preux[2]

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Purpose: Between 2002 and 2005 we conducted clinical, epidemiological and public health studies in Lao PDR in order to estimate the prevalence of epilepsy in the population, its risk factors and the availability of treatment.
Methods: A door-to-door survey was conducted in a rural district of central Laos (province of Vientiane) including 4310 villagers followed by a case control study (1 case of epilepsy was matched to 4 controls). The accessibility of anti-epileptic drugs (AE) was st
Results: In the prevalence study 33 cases of active epilepsy were diagnosed (prevalence of 7.7 per 1000). Epilepsy in family history (OR=6.0; CI95%=1.3–28.3), head injuries (OR=4.4; CI95%=1.1–18.9), absence of latrine in household (OR=2.7; CI95%=1.0–6.9) and reari
Conclusion: The importance of these results for the management of epilepsy in Laos PDR will be discussed. (project funded by French Ministry of Foreign Affairs, CORUS program).

081
Prevalence of Epilepsy Associated with Neurocysticercosis: A Community-based Study in South India (Comprehensive Rural Epilepsy Study – South India - CRESSI)
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Purpose: To study the prevalence of seizure disorders associated with neurocysticercosis (NCC) is a rural community in South India, endemic to NCC.
Methods: Prevalence of epilepsy was studied by a door-to-door survey in 22 villages, geographically clustered in one region in Andhra Pradesh, a province in South India. All cases ascertained clinically had a plain and contrast CT scan. The imaging criteria for diagnosis of NCC were that proposed by Del Brutto et al (2001). Seizures associated with the transitional phase of NCC are considered to be acute symptomatic (provoked) seizures and seizures associated with active, viable cysts, or inactive, calcified parasites, or both, are categorised under unprovoked seizures.
Results: Of the 74,086 people surveyed, 462 people were identified to have 2 or more seizures, a crude prevalence of 6.2 per 1000 population. At the time of the analysis 379 (82%) patients had a CT scan. 73 scans (19%) showed imaging features consistent with NCC. Cysticercal cysts in the transitional phase were seen in 11 (3%) scans and viable cyst(s) and/or calcification were seen in 62 (16%). NCC accounted for 47% of identifiable aetiology. Crude prevalence rate for NCC-related seizure disorder was 0.98 per 1000 population. The crude prevalence of NCC-related acute symptomatic seizures was 0.14 per 1000 and the remote symptomatic epilepsy related to NCC was 0.84.
Conclusion: Prevalence studies of epilepsy in countries endemic to NCC are likely to be contaminated by the acute symptomatic seizure disorder associated with transitional phase of NCC, thus likely to project higher prevalence rates.

082
Epilepsy in Arabian Population: Results of Registry and Long-term Follow-up.
R.M. Zaidan[1]

1) King Khaled University Hospital, King Saud University, Riyadh, KSA 2) Neurology Division, Department of Medicine

Purpose: This prospective study with long term follow up was conducted in an academic institution: 1) to determine the clinical electroencephalography characteristics and neuro-imaging correlations in adult patients with epilepsy; 2) to study the outcome and prognosis of epilepsy in an Arabian population.
Methods: More than 1000 adult patients with epilepsy (males and females including many familial cases) were included in the study. Clinical assessment, EEG/video EEG and neuroimaging was done on all of them. They were followed up in our institution for a long period: 10 to 20 years. Particular attention was given to the female with multiple pregnancies on treatment.
Results: All categories of epilepsy in adult patients were seen. Partial and partial complex epilepsy represent the majority of cases. In these categories results support, in our opinion, a proposal of new considerations in clinical terminology. Analysis of abnormalities on EEG recording in patients with generalised epilepsy lead us to consider focal origin becoming very fast generalised rather than being a remnant of generalised discharges. The majority of patients had very good or good control with successful discontinuation of treatment. A minority of our patients had uncontrolled epilepsy. Finally, the majority of women with epilepsy who had multiple pregnancies had no major complications. (Details are available and will be presented in the meeting).
Conclusion: Epilepsy registries appear to be an important tool in the study of epilepsy, and long term follow up discloses important information in our population that may be used, in our opinion, in the terminology, pathophysiology, management and prognosis of epilepsy.

083
Predictive Factors of Mortality and Poor Outcome on Discharge among Adult Patients in Status Epilepticus: A Six-year Review in a Tertiary Government Hospital
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Purpose: To investigate the clinical profile, aetiology, seizure type, duration, and electroencephalographic features among adult patients in status epilepticus and to identify predictive factors of mortality and poor outcome on discharge.
Methods: 97 adult patients diagnosed with status epilepticus in a tertiary hospital were investigated . Outcome was assessed using the Modified Rankin Scale, with score of 0-2 as good outcome and 3-6 as poor outcome. Data were analysed employing chi-square tests (p value < 0.05) and multiple logistic regression analysis.
Results: Mean age of patients was 41.72 + 17.18 years. There were 44 males and 53 females. 63% had status epilepticus secondary to neurologic causes; the majority are post-gliotic. 71% presented with generalised tonic-clonic seizures. Seizure duration of more than 1 hour was present in 29% of patients. Mean Glasgow coma score on admission was 8 (range 3-15). Abnormal EEG was present in 79%; findings were predominantly mild to moderate generalised slowing

and epileptiform discharges. 38 (39%) patients had a poor outcome on discharge. Mortality was noted at 36%. On univariate analysis, the following factors were correlated with poor outcome on discharge: 1) age >40 years (p=0.018); 2) hospital stay >10 days (p=0.05); 3) concomitant neurologic disease (p=0.019); CNS infection (p=0.031); cerebrovascular disease (p= 0.014); 4) concomitant infection (p=0.00001); 5) EEG pattern of severe generalised slowing (p=0.029) On univariate analysis, the following factors were correlated with mortality: 1) age >40 years (p=0.017) 2) hospital stay. 10 days (p=0.022) 3) GCS score <8 (p=0.011) 4) concomitant neurologic disease (p=0.029) 5) post-CP arrest >5 min (p=0.001). On multiple logistic regression analysis, the presence of cerebrovascular disease and concomitant infection were correlated with poor outcome on discharge. More than 10 days hospital stay, GCS score <8 and post-CP arrest of >5 minutes were correlated with mortality. Both age of >40 years and the presence of concomitant neurologic disease were correlated with mortality and poor outcome on discharge.
Conclusion: Age and the presence of concomitant neurologic disease could influence both the mortality and morbidity of patients with status epilepticus.

084
Mortality in a Cohort of Patients with First Unprovoked Tonic-clonic Seizure
M.A. Leone[1], A. Solari[2], E. Beghi[1], The FIRST Group[1]

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Purpose: To evaluate mortality rate in a cohort of patients with a first unprovoked seizure.
Methods: The first seizure trial group (FIRST) provided a multicenter, randomised, open trial comparing immediate to delayed treatment in patients with a first unprovoked epileptic seizure to assess the effects of the earliest possible treatment on the long-term prognosis of epilepsy. Starting in February 1988, we recruited 419 patients with a first, witnessed, primarily or secondarily generalised tonic-clonic seizure. The exclusion criteria were acute symptomatic seizures, progressive neurologic disorders, alcohol or drug addiction, and overt psychiatric illness. Patients were followed for 3098 person years. Centres were asked to assess if the patients were alive or dead through telephone or clinic visits. 15 patients (6 women, 9 men) died during the follow-up. Standardised mortality ratios (SMR) were calculated applying to each patient the sex-, age-, and calendar year-specific mortality rate of the Italian population.
Results: The entire cohort had a mortality rate higher than that of the Italian population (SMR= 2.8, 95% confidence limits= 1.6-4.6). The SMR was 5.4 (2.0-11.7) for women and 2.1 (1.0-4.0) for men. The SMRs were higher for the younger decades: 7.7 (2.1-19,7) for 0-19 yrs, 2.7 (0.3-9.8) for 20-39; 1.9 (0.4-5.6) for 40-59; 2.5 (0.9-5.5) for patients 60 yrs or older.
Conclusion: Mortality rate in patients with a first unprovoked tonic-clonic seizure is higher than that of the general population. The SMR was highest in the youngest age groups, in keeping with other reports of mortality in patients with epilepsy.

Tuesday 30th August 2005
15:30 - 17:00
Salle 253
Platform Session
Social Issues

085
Factors Influencing Quality of Life (QOL) in People with Epilepsy
A.B. Guekht[1], T.V. Mitrokhina[1], A.V. Lebedeva[1], F.K. Dzugaeva[1], L.E. Milchakova[1], O.B. Lokshina[1], A.A. Feygina[1], E.I. Gusev[1]

1) Department of Neurology and Neurosurgery, Russian State Medical University, Moscow, Russia

Purpose: To assess the influence of different factors on health-related QOL in adults with epilepsy in Moscow, Russia.
Methods: Evaluation of 242 patients (98 untreated and 144 previously inadequately treated) was performed with QOLIE-31. Partial cryptogenic or symptomatic epilepsy was diagnosed in 214 patients; 28 with idiopathic generalised epilepsy. After one year of proper therapy the follow-up assessment was carried out. Remission has been achieved in 59.1% of patients. Multiple regression analysis was performed to assess the influence of different factors on QOL.
Results: The following significant factors influencing QOL were revealed: frequency of seizures (the most important parameter) and duration of disease. Frequency of seizures influenced most subscales of QOL. QOL of patients with rare seizures (1-2 per year) was significantly lower than that of patients in remission: 47.47+/-5.27 vs. 52.71+/-3.43, p=0.0001. The following risk factors for poor QOL (less than 45 points by QOLIE-31 scale) were identified: frequency of seizures more than 2 per month (OR = 19.55, 95% CI: 16.33-101.23), decrease of frequency and/or severity of seizures less than 50% on proper treatment (OR = 23.14, 95% CI: 37.12-67.11), prolonged (more than 3 years) inadequate therapy (OR = 43.14, 95% CI: 40.12-146.11).
Conclusion: Frequency of seizures is the most important factor influencing QOL in adults with epilepsy (recently diagnosed and previously treated), and we defined the extent of influence on QOL before and after adequate treatment. QOL is an important factor for the assessment of the outcome of therapy.

086
The RARE Program: An Example of Self-sustained Epilepsy Management in Rural Mali
G. Farnarier[1], K. Nimaga[2], P. Genton[3], O. Doumbo[4], D. Desplats[5]

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Purpose: Uncontrolled epilepsy has major physical and social consequences in rural developing societies. In order to create a possibility for rural populations to access medical care for epilepsy, a comprehensive, self-sustained pilot program was established in several rural districts of Mali, the RARE (Réseau Action-Recherché sur l'Epilepsie, research-action network on epilepsy), with the aim of providing a realistic and efficient tool of management for the largest possible population of patients with epilepsy.
Methods: The AMC (Association des Médecins de Campagne) is a group of 80 general practitioners who agreed to settle in rural areas with the initial help of a EU-sponsored program organised by Santé-Sud, a Marseille-based NGO. Six of them volunteered to build up a network for the management of patients with epilepsy. One was chosen as the 'head of network' (KN), and a Franco-Malian executive team was set up to organise teaching seminars and control practical aspects, including the delivery of anticonvulsants. All patients with epilepsy were included in a prospective database with follow-up at 4-month intervals over the first 3 years of management.
Results: Since the initiation of this program in 2003, two week-long seminars have led to an adequate level of knowledge on epilepsy among the RARE participants, which was quantified by repeated examinations. Over 800 patients were newly included and treated, and extensive data has been collected prospectively.
Conclusion: The six local RARE participants intend to diffuse their knowledge among the other members of the AMC and the number of treated patients will be increased.

087
Developing Approaches to Reducing Stigma of Epilepsy: Findings from a Rapid Appraisal of Epilepsy Care in China
A. Jacoby[1], W. Wang[2], J. Wu[3], T.V. Dang[4], H.N. Thanh[4], C. Begley[5], R. Reis[6], H. De Boer[7], L. Prilipko[8], D. Chadwick[1], G. Baker[1]

1) University of Liverpool, Liverpool, UK 2) Beijing Neurosurgical Institute, Beijing, China 3) Beijing Anti-Epilepsy Association, Beijing, China 4) Hanoi School of Public Health, Hanoi, Vietnam 5)

University of Texas, Houston, US 6) University of Amsterdam, Amsterdam, The Netherlands 7) Stichting Epilepsie Instelligen Nederland, Heemstede, The Netherlands 8) WHO, Geneva, Switzerland

Purpose: As part of an international collaborative research project aimed at reducing stigma of epilepsy in developing countries, we have conducted a rapid appraisal of the situation of people with epilepsy living in China. The purpose of the appraisal was to explore prevailing beliefs about epilepsy and to describe current health care provisions for epilepsy.
Methods: Searches of available secondary data sources; interviews with people with epilepsy (PWEs), family and community members.
Results: Based on the GCAE Demonstration Project, prevalence of epilepsy is 7/1000; meaning there are around 9 million PWEs living in China, of whom around half do not receive appropriate treatment. Significant numbers use traditional Chinese and folk medicines, acupuncture and fetishes. Epilepsy is generally considered a mental disorder. Among PWEs, perceived causes of epilepsy were excitement and strain, poor sleep and fatigue, fear and playing 'too crazy'. Lay community members attributed epilepsy to psychological pressures and stimulation by spirits. Epilepsy is seen as a potent source of stigma by PWEs and family members and so is often not disclosed to others.
Conclusion: PWEs and families bear both psychological and economic burdens of epilepsy. Both they and lay communities lack basic knowledge about epilepsy, its causes and treatment. These findings have informed a detailed ethnographic study now in progress in two areas. Presented on behalf of the CREST (Collaborative Research on Epilepsy Stigma) Study Group: Professor Charles Begley, Professor Gus A Baker, Ms Hanneke de Boer, Professor David Chadwick, Dr Dang Vu Trung, Ms Nguyen Thanh Huong, Professor Ann Jacoby, Dr Leonid Prilipko, Dr Ria Reis, Ms Dee Snape, Professor Wenzhi Wang, Professor Jian-zhong Wu. CREST is funded by the US National Institutes of Health.

088

Do First Seizure Clinic Patients Benefit from a Psychosocial Support Programme?

R.J. Panelli[1], S. Moore[1], C. Kilpatrick[2], Z. Matkovic[2], W.J. D'Souza[3], T.J. O'Brien[4]

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Purpose: Research documents a frequent association between epilepsy and psychosocial problems. This study examined the effect of peer-support on anxiety, depression, and satisfaction with information provided, in patients attending two First Seizure Clinics.
Methods: A prospective pragmatic randomised controlled trial compared usual care with usual care plus peer-support program. Participants 16 years and over with no known prior diagnosis of epilepsy, completed clinical and psychosocial measures at baseline (n=245) and 3 months (n=156).
Results: For baseline participants (age 37 ± 16, gender 65% male) diagnoses included epilepsy 33.5%, provoked or single seizures 33.5%, syncope 14.3%, and other (mostly diagnosis uncertain) 18.8%. The Hospital Anxiety and Depression Scale (HADS) estimates of clinical anxiety for the total group were 25% at baseline and 26% at 3 months. Clinical depression estimates for the group were 12% at baseline and 10% at 3 months. Notably, depression scores were significantly higher in the diagnostic category 'other', compared to all other diagnoses combined at baseline (p=.037, one-way ANOVA). There were no significant differences in anxiety or depression scores between control and intervention groups over 3 months. However, 70% of the intervention group valued the support program.
Conclusion: First Seizure Clinic patients demonstrate anxiety and depression rates above Australian community norms (approximately 10% anxiety, 6% depression). Psychosocial assessment may assist diagnosis and management decisions. Although patients value peer-support information, HADS measures do not indicate a positive effect of such a programme on anxiety or depression levels.

089

Illness Intrusiveness and Quality of Life in Epilepsy: Comparison of Treatments

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Purpose: Chronic illnesses are associated with multiple stressors that compromise quality of life (QOL). Implicit in many of these stressors is the concept of illness intrusiveness; illness-induced disruptions to lifestyles, activities and interests that compromise QOL (Devins et al, Int J Psychiatry Med 1983; 13:327-343). This study tested the illness intrusiveness theoretical framework in epilepsy and compared the impact of pharmacological and surgical treatments on illness intrusiveness and QOL.
Methods: Cross-sectional data were obtained and compared among three groups of a total 145 patients with epilepsy: (a) 40 patients admitted for pre-surgical evaluation to epilepsy monitoring unit; (b) 52 patients treated pharmacologically; and (c) 53 post-surgical patients.
Results: Illness intrusiveness differed across epilepsy patients with the differences primarily related to the degree of seizure control. The degree of illness intrusiveness significantly varied inversely with seizure control. Seizure freedom, whether achieved with surgical or pharmacological treatment, was associated with maximal reduction of illness intrusiveness scores. Increased illness intrusiveness was significantly associated with decreased QOL and increased depressive symptoms. Patients who perceived higher levels of control over diverse domains of life experiences reported more positive QOL and psychosocial outcomes. Path analysis supported the validity of the illness intrusiveness theoretical framework in epilepsy.
Conclusion: The most robust benefits of decreased illness intrusiveness in epilepsy occur when treatment leads to complete seizure control. Therefore every effort should be made by health care providers to achieve seizure freedom with pharmacological or, if necessary, surgical treatment, to reduce illness intrusiveness and thereby improve QOL.

090

Evaluation of Socio-economic Factors Causing Discontinuation of Epilepsy Treatment: A Study in an Urban Epilepsy Clinic in India

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Purpose: In India, the prevalence of epilepsy is 4.15-7.03 per 1000 population. In the developing countries, the major problem of epilepsy treatment lies in the treatment gap, due to discontinuation of treatment from various adverse socio-economic factors. The objective of the study was to evaluate the rate of discontinuation and related socio-economic factors leading to discontinuation causing breakthrough seizures.
Methods: Out of 1,450 epilepsy patients who were followed up at 3 month intervals, 550 patients (M=282, F=168) discontinued their treatment (from January 2000 to January 2005). All had breakthrough seizures on more than 2 occasions. Socio-economic factors were evaluated in respect to the treatment vis a vis income, unemployment, negative attitude towards epilepsy, availability of drugs locally, co-morbid psychiatric, other illnesses, polytherapy and social illusion about epilepsy.
Results: Discontinuation of treatment in 37.9% of total patients led to breakthrough seizures. The discontinued groups had an average annual cost of treatment and income of Rs 5,500 ($110) and Rs 12,800 ($256) amounting to 40% of their total income. However, continued groups', annual cost of treatment and income were Rs 4,500

and Rs 24,400, amounting to only 18% of total income (P<0.001). Amongst the discontinued group, 90% discontinued for cost factors, 15.45% due to unemployment, 20% from frustration and despair, 16.36% due to non-availability of medicine locally, 12.72% had false beliefs about spiritual factors, 10% for family problems and marital disharmony. Of this discontinued group, 10% got polytherapy against 6.66% of the continued group (P>0.10), co-morbid psychiatric illnesses were in 3.63% against the 3.33% of the continuing group. (p>0.10).
Conclusion: This study showed a significant number of patients (37.9%) discontinued therapy due to unawareness regarding the problems of discontinuation, cost and income disparity, unemployment, social illusion and frustration, uniform availability of drugs. To tide these shortcomings, uniform availability of cheaper antiepileptic drugs with adequate information, and communication regarding the disease are to be ensured.

Tuesday 30th August 2005
15:30 - 17:00
Salle 243
Platform Session
Basic Science 2

091
Transgenic Rats Harbouring a CHRNA4 Mutation Exhibit Characteristic Seizure Phenotypes of Nocturnal Frontal Lobe Epilepsy
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Purpose: To generate transgenic animals harbouring a mutation identified in human nocturnal frontal lobe epilepsy (NFLE) and investigate if generated animals demonstrate the corresponding phenotype. The mutation chosen was S284L, a missense mutation of the CHRNA4 gene encoding alpha 4 subunit of nicotinic acetylcholine receptor (nAChR).
Methods: Rat cDNA of Chrna4 bearing c.856T>C:c.857C>T mutations were constructed to generate an amino acid exchange homologous to human S284L. The mutant cDNA preceded by the PDGF promoter sequence was introduced in rat oocytes by a microinjection method. Transgenic animals were generated according to a standard protocol. Seizure and behavioural phenotypes were observed by video monitoring with simultaneous EEG monitoring.
Results: Two strains were found to harbour the transgene; one of which, called 'S284L-TG' was used for further experiments. The birth ratio of transgenic animals was consistent with Mendel's low. mRNA of Chrna4 with the mutations was readily expressed in the transgenic animals. No difference was observed between S284L-TG and its littermates in growth, longevity, reproductivity or gross motor activities. S284L-TG exhibits characteristic seizure phenotypes of human NFLE. In accordance with the electrophysiological characteristics of the mutant nAChR, the seizure susceptibility of S284L-TG to nicotine was reduced.
Conclusion: The transgenic rat, S284L-TG gave compelling evidence that abnormality of nAChR solely can cause NFLE. In addition, the animals can be a useful epilepsy model distinguished from conventional ones for investigating the molecular mechanisms of human epilepsy.

092
Neurocytoskeletal Features in Lafora Disease Null Mutant Mice
J. Machado-Salas[1], P. Guevara[2], J. Guevara[2], I. Martínez[1], R. Durón[1], D. Bai[1], S. Ganesh[3], K. Yamakawa[3], T. Suzuki[3], K. Amano[3], E. Cornford[1], A.V. Delgado-Escueta[1]

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Purpose: To study the structural features of neurons, specially their cytoskeleton, in homozygous null mutant (deficient in Laforin) and wild type mice.
Methods: We developed Laforin deficient knock-out mice by deleting the Laforin domain coding region of the EPM2A gene (Hum Mol Genet 2002, 11: 1252-1262). Wild type and homozygous null mutant mice were periodically sacrificed. Their encephalons were fixed in glutaraldehyde and processed with light-microscopy, immunocytochemical and electron-microscopy techniques. Monoclonal antibodies were used against neurofilaments M and L (NFM/NFL), Apaf-1, Caspase 3 and Cytochrome C. Tunel stain.
Results: We observed cell death at 2 months of age, when Lafora bodies (LB) were scarce and ultramicroscopic. At 9 months, LB (Ubiquitin and AGEP positive) were abundant, but seldom seen in degenerating neurons. Apoptosis images and apoptosis related immunostaining were negative. Cerebellar and Pontine reticular formation (PRF) neurons showed decreased and/or distorted immunocytochemistry reactions to NFL/NFM, and neurite and neurofibrillary fragmentation. Large neurons from the PRF showed hyperdense, intracellular bands (coalescence of neurofilaments??) and somata deformation. Some images appeared compatible with neurofibrillary tangles. Clusters of fragmented and malformed neurites resemble neurite (senile) plaques.
Conclusion: In our model, LD appears to be a neurodegenerative disorder, involving non-apoptotic cell-death. Ubiquitin-positive LB suggest inadequate presence of misfolded proteins, targeted for degradation. Early and prominent formation of neurofibrillary tangles and senile-plaque-like structures supports the view of a neurodegenerative process. Our findings do not support a primary role for LB in causing cell death and neurological impairment. (Supported by NINDS grant 5RO1NS042376-03).

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Mechanisms of Epileptic Activity in a Model Nervous System (Buccal Ganglia, Helix Pomatia)
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Purpose: Epileptiform activity in the snail nervous system corresponds in every respect to epileptiform activity in mammalian nervous systems, including man. Thus, basic mechanisms have been studied in the buccal ganglia of the snail Helix pomatia as a model nervous system in experimental epileptology.
Methods: Identified giant neurons in structurally and functionally intact buccal ganglia were intracellularly recorded under in-vitro conditions. Epileptiform activity was induced by bath application of pentylenetetrazol or etomidate. A Wilhelmy-system was used to study pressure in an artificial membrane monolayer.
Results: Paroxysmal depolarisation shifts (PDS) developed dose-dependently from endogenous pacemaker potentials in the single neuron. Threshold of alterations was about 1/40 of the concentration needed to induce PDS. Several further neuronal properties were altered showing a corresponding threshold: (1) increase in membrane resistance, (2) block of voltage dependent K+-currents, (3) block of chemical synaptic potentials (with epileptogenic concentration of the drugs: incomplete block of EPSP and complete block of IPSP). Dose-dependency of alterations corresponded to the dose-dependent insertion of the epileptogenic drugs into an artificial phospholipid monolayer. Insertion increased intra-membranous pressure with a threshold concentration of about 1/40 of the epileptogenic drug concentration. Synchronization of PDS resulted mainly from non-

synaptic exocytosis which can be induced by strong and lasting depolarisations accompanied by an increase in intracellular [Ca2+].
Conclusion: It is suggested that epileptiform activity results from a membrane pollution by amphiphilic substances which enter the neuronal membrane, increase intra-membranous pressure and by this transform endogenous pacemaker potentials into PDS

094
Damage, Neuron Loss and Alterations in the Cerebellum of Rodents Submitted to the Pilocarpine Model of Epilepsy.
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Purpose: This investigation aimed to study the physiological and structural properties of Purkinje neurons (PN) in the model of temporal lobe epilepsy induced by pilocarpine in rodents. Spontaneous firing properties, aminoacid concentrations and the density of Purkinje neurons and their dendrite spines were studied.
Methods: Patch clamp recordings (loose patch) were performed to investigate spontaneous firing properties of PN. The neurochemistry evaluation of the cerebellum was obtained by a high performance liquid chromatography (HPLC) technique. A video system (Sony Ex wave HAD) coupled to a light microscope (Nikon Eclipse E 600) was utilized to quantify cellular and spine density.
Results: In this study, we show significant differences in the spontaneous firing rate pattern of PNs recorded in animals with temporal lobe epilepsy (TLE). The concentrations of all tested aminoacids decreased significantly in the chronic phase of the pilocarpine model of temporal lobe epilepsy. PN loss was observed in the silent and chronic phases of the model. Status epilepticus per se was sufficient to generate neuron loss, which was aggravated after the beginning of spontaneous recurrent seizures. However, spine density did not change in animals with temporal lobe epilepsy.
Conclusion: Taken together, the results showed different levels of alterations and damage to the cerebellar circuitry. As PNs are considered the main element in the cerebellar cortex this may represent a larger cascade of events in the whole cerebellum induced by temporal lobe epilepsy.

095
Deregulation of Cyclin Dependent Kinase 5 in Hippocampal Sclerosis
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Purpose: Hippocampal sclerosis (HS) is amongst the most common causes of chronic medically refractory epilepsy in adults. Histologically HS is characterised by segmental neuronal loss and gliosis. While neuronal loss is important to the pathophysiology of hippocampal sclerosis, the molecular mechanisms underlying this remain uncertain. Cyclin dependent kinase 5 (cdk5) is a serine-threonine kinase important in normal cortical development. Recent work has shown that deregulation of cdk5 by p25, the calpain mediated cleavage product of the cdk5 activator p35, occurs in several cell death paradigms including apoptosis, necrosis and excitotoxicity. As each of these modes of cell loss is thought to contribute to the neurodegeneration seen in HS, we hypothesised that there would be abnormalities of the cdk5 pathway in this condition.
Methods: Surgically resected cases of HS with adjacent histologically-normal temporal lobe, surgically resected cases of hippocampi without significant neuronal loss and hippocampi removed post-mortem from patients with chronic epilepsy were examined for cdk5 and p35/p25 using immunohistochemistry, confocal microscopy and Western blots.
Results: We consistently found an excess of p25/p35 immunoreactivity within the hippocampal subfields that exhibit accelerated neuronal loss and that the ratio of p25 to p35 is higher in HS compared to normal temporal lobe tissue. Hippocampi not affected by neuronal loss demonstrated uniform staining with p25/p35 antibody and a higher ratio of p25 to p35 in the temporal lobe rather than the hippocampus.
Conclusion: Our results suggest that the p25-cdk5 complex might be important in mediating neuronal death in hippocampal sclerosis and demonstrate a possible novel convergence of developmental and degenerative pathologies.

096
Serum Antibodies in Patients with Epilepsy
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Purpose: To determine the prevalence and pathogenicity of autoantibodies in the serum of patients with epilepsy.
Methods: Serum from 139 patients with epilepsy (26 with a priori immune-mediated disorder, 46 seizure-associated syndromes referred as possible immune aetiology, and 67 from a prospective cohort of drug-resistant epilepsy), were compared with healthy and disease controls (n = 150). Sera were assayed for antibodies to voltage gated potassium (VGKC) and calcium channels, glutamic acid decarboxylase (GAD), neuronal (alpha 7) acetylcholine receptors (nAChR), ganglioside, cardiolipins, antinuclear antibodies and dsDNA.
Results: Raised titers of serum VGKC antibodies were detected in 16 out of the 139 (11%) seizure patients. Of these, 9 presented with an acute or subacute encephalopathic illness associated with cognitive problems and/or confusion. Elevated titers of anti-GAD antibodies (>10 units, U) were found in 5 patients (3.6%), all of whom had chronic drug resistant epilepsy. 2 of 8 Rasmussen's encephalitis (RE) patients tested, had antibodies to nAChR. Electrophysiological studies were performed on sera with VGKC and nAChR antibodies and demonstrated significant inhibition of their respective channels.
Conclusion: We have identified three seizure associated antibodies each related to different clinical phenotypes: GAD antibodies and a chronic drug resistant epilepsy, VGKC antibodies and an acute/subacute encephalopathy, and nAChR and RE. The VGKC and nAChR antibodies were demonstrated to have a functional effect on ion channels involved in neurotransmission in the CNS. The identification of specific and relevant antibodies along with their associated clinical phenotypes is likely to have important management implications for this sub-group of epilepsy patients.

Wednesday 31st August 2005
15:30 - 17:00
Salle Maillot
Platform Session
Imaging

097
Functional MRI Analysis of the Pre-ictal State
P. Federico[1], R.S. Briellmann[2], D.F. Abbottt[2], A.S. Harvey[2], G.D. Jackson[2]

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Purpose: The mechanism underlying the transition from interictal to ictal discharges is poorly understood. One possibility involves the brain changing into a facilitating state promoting seizures. Non-linear mathematical analysis of EEG frequency components has confirmed the presence of a pre-ictal state in focal epilepsy, however, spatial

resolution was limited. We report on fMRI analysis of the pre-ictal state in 3 patients with focal epilepsy.
Methods: We studied 3 sleep-deprived patients with intractable partial epilepsy. All subjects had habitual seizures in the scanner while continuous blood oxygen level dependant (BOLD) fMRI images were acquired. The pre-ictal BOLD changes were analysed by block design analysis comparing BOLD signals for the one minute immediately prior to seizure onset to a span of one minute beginning either five or three minutes prior to seizure onset.
Results: One typical partial seizure was captured in each patient. Each patient showed highly significant, focal BOLD signal changes. In patient #1, a striking pre-ictal BOLD signal increase was seen over the ipsilateral (left) frontocentral region, maximal at the seizure focus. No significant BOLD signal decreases were observed. Patient #2 showed a robust pre-ictal BOLD increase over the contralateral (left) frontal region as well as a focal BOLD decrease, near the seizure focus (right). In patient #3, a pre-ictal BOLD increase was seen in the premotor area contralateral to the presumed seizure focus on the right. Notably, this BOLD increase co-localised with the site of hyperperfusion seen on an ictal SPECT study. No significant BOLD decreases were seen in this patient.
Conclusion: Highly significant BOLD fMRI signal changes occur before the onset of seizures. These can be localised to the site of seizure onset, as well as to normal brain regions, suggesting that the BOLD signal changes and their underlying mechanisms are complex. Thus, fMRI analysis of pre-ictal BOLD signal changes supports the presence of a pre-ictal state.

098
Blood Oxygen Level-dependent (BOLD) Responses in Partial Epilepsy with Focal and Bilateral Synchronous Spikes
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Purpose: To determine the blood oxygen level–dependent (BOLD) responses to focal and bilateral synchronous epileptic discharges in the thalamus and cerebral cortex in patients with partial epilepsy.
Methods: We performed EEG-fMRI studies on 64 patients who had active interictal spiking during routine or telemetry EEG. Details of the EEG recording and MRI acquisition are given in Bénar et al., 2003 and Aghakhani et al., 2004.
Results: The 40 patients who had EEG spikes during scanning were divided into two groups: patients with unilateral or bilateral independent spikes (n = 29), and patients with bilaterally synchronous spikes (n =11). According to the location of spikes, 40 different analyses were performed in the first group, with significant BOLD responses in 18 studies (45%). In the second group, all patients had a significant BOLD response. A thalamic response was seen in 55% of the studies with bilateral synchrony compared to 28% of the studies with focal spikes only. The fMRI responses were also more widespread over the cerebral hemispheres in patients with bilateral synchrony. Cortical activation (positive BOLD) represented the dominant response in the patients with focal spikes and had a better correlation with spike location than cortical deactivation (negative BOLD). In patients with bilateral synchrony, deactivated areas were as important as activated regions.
Conclusion: We showed evidence of thalamic involvement in partial epilepsy during interictal discharges. This involvement is more common and widespread when bilateral synchrony is present, suggesting a role for the thalamus in the occurrence of bilateral spiking discharges.

099
Ictal SPECT Compared to MEG in the Presurgical Evaluation of Epilepsy
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Purpose: To compare ictal single photon emission tomography (SPECT) and magnetoencephalography (MEG) localisation of partial epilepsy.
Methods: As part of a prospective MEG and multimodality imaging in epilepsy surgery project, consecutive epilepsy surgery candidates at the UAB Epilepsy Center were selected for whom MEG and ictal SPECT localisation was attempted between July 2001 and November 2004. MEG was recorded with a 148 channel whole-head system. Epileptiform spikes and sharp waves were analysed with a single equivalent current dipole model. Ictal SPECT was performed with injections (within 30 seconds of seizure onset) of 20-40 mCi of 99mTc-hexylmethylene phenyloxaloacetae (HMPAO). SPECT subtraction was performed on 32 patients.
Results: A total of 49 imaging sets were analysed (46 patients with mean age=24, range 1-61, female=23); 3 patients had 2 studies because of initial failed surgical resections. Extratemporal lobe epilepsy was present in 35 (71%) and temporal lobe epilepsy in 15 (29%). The sensitivity for localising study in both ictal SPECT was 71% and MEG was 71%. In 21 cases the ictal SPECT and MEG demonstrated lobar concordance. In 2 cases ictal SPECT and MEG showed lateralisation discordance. MEG was localising when ictal SPECT was negative in 14 cases. Ictal SPECT was localising when MEG was negative in 12 cases. Only 2 cases had both negative ictal SPECT and MEG.
Conclusion: These results demonstrate a complementary clinical utility with ictal SPECT and MEG in the presurgical evaluation of partial epilepsy.

100
Usefulness of PET-MRI Registration in Cryptogenic Extratemporal Focal Epilepsy of Children
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Purpose: The success of cortical resection for intractable focal epilepsy is highly dependent on the accurate delineation of the epileptogenic zone (EZ). Although positron emission tomography (PET) with deoxy-2 [18F] fluoro-D-glucose (FDG) is a precious tool to localise the EZ in symptomatic epilepsy, its sensitivity decreases in case of extratemporal foci with no lesion detectable on MRI, a frequent situation in the paediatric population. The aim of the present study was to analyse the clinical usefulness of FDG-PET registered to high resolution 3D T1 MRI in children with intractable cryptogenic extratemporal epilepsy.
Methods: 20 children with extratemporal cryptogenic epilepsy (M:F=10:10; mean age at PET 9y (4-16); mean age at seizure onset 10y) underwent both FDG-PET and high resolution 3D-T1-MRI. Surface EEG and clinical data localised the EZ with a high probability in 19 patients (11 frontal, 4 parieto-occipital, 3 insular, 1 parietal). FDG-PET was coregistered to MRI using rigid body transformation. The non-coregistered and coregistered images of FDG-PET (respectively PET and PET-MRI) were visually analysed in order to detect potential areas of hypometabolism.
Results: The PET images showed a conclusive area of hypometabolism in only 7 out of the 20 children. The PET-MRI

images confirmed these results in all and permitted the detection of hypometabolic gyrus in 12 of the remaining 13 patients. The location of this hypometabolic area was concordant with that of the electro-clinical data in 18/19 patients. Finally, the PET-MRI coregistered images helped to identify a subtle gyral abnormality that had not been previously ascertained on MRI in 12/13 children.
Conclusion: FDG-PET coregistered to MRI is very useful in children with so called cryptogenic extratemporal epilepsy, to localise the EZ that is most often associated with a subtle gyral abnormality.

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Magnetic Resonance Evidence of Mesial Temporal Sclerosis in Sporadic Benign Mesial Temporal Lobe Epilepsy
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Purpose: To determine the occurrence of magnetic resonance imaging-detected mesial temporal sclerosis (MTS) in patients with sporadic BMTLE.
Methods: The study group consisted of 101 consecutive unrelated patients (56 female, mean age 37.3+17.4; range 5 to 81) with BMTLE, who rarely or never had seizures at long-term (< 2 years) follow-up. The diagnosis of TLE was mainly based on typical temporal auras and/or interictal EEG discharges with a maximum over the temporal lobes. In all patients, brain MR images were obtained using sequences and slices to optimise visual detection of mesial temporal structures.
Results: A familiar history of febrile convulsions or epilepsy was observed in 37% of the patients. 22% had a personal history of simple febrile convulsions. The mean age at seizure onset was 23.2+17.4, the mean duration of epilepsy was 17.1+15.7. 40 patients out of 101 (39.6%) had MRI evidence of MTS. In detail, 19 had left MTS, 20 had right MTS, while in the remaining patient there was evidence of bilateral MTS. There was no difference between patients with or without MTS in mean age at onset (MTS 23.0+18.4; normal MRI 16.2+8.9) and mean duration of epilepsy (MTS 15.8+11.8; normal MRI 16.7+15.1). Hyperintense FLAIR and T2 signal with or without mesial temporal atrophy was observed in 27 of these 40 individuals. MRI abnormalities correlated with the epileptogenic focus seen on the interictal EEG recording.
Conclusion: These results indicate that MRI evidence of MTS is often encountered in BMTLE. Our findings reinforce the belief that MTS is not necessarily related to seizure severity, and that other factors, both genetic and environmental, play an important role in determining seizure severity in patients with TLE.

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Localisation of the Epileptogenic Zone in Adults by 3D Image Registration of [C-11]-Flumazenil-PET and MRI: Comparison with Subdural EEG Recordings
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1) University of Munich, Munich, Germany 2) Technical University of Munich, Munich, Germany 3) University of Mainz, Mainz, Germany

Purpose: [11C]-Flumazenil-PET (FMZ-PET) has been reported to localise the seizure onset zone. The aim of the study was to correlate localisation of reduced GABA-receptor binding by FMZ-PET with the results from invasive EEG recording, using 3D image registration of FMZ-PET and MRI.
Methods: We investigated 18 patients with temporal (n=5) and extratemporal (n=13) epilepsy. In all patients the epileptogenic zone was identified by invasive monitoring with subdural grid and strip electrodes. Analysis of FMZ-PET images was performed by automated quantitative analysis and visual inspection by four different observers. The exact anatomic relationship between subdural electrodes and FMZ-PET findings was determined three-dimensionally by image coregistration and volume rendering of MRI, CT and FMZ-PET scans.
Results: Automated quantification of FMZ-PET localised the epileptogenic zone correctly in 6 of 18 (33%) patients and revealed false positive findings in 13 patients (72%). Consensus of visual evaluation detected the correct seizure onset zone in 9 patients (50%); false positive findings were reported in 8 cases (44%). Colour-encoded 3D rendering of coregistered MRI and FMZ-PET data helped to identify the correct epileptogenic zone in 4 additional cases (22%) and ruled out false positive findings in 5 patients (28%). The results were similar in temporal and extratemporal epilepsies.
Conclusion: The localising value of FMZ-PET is poor in adults with medically refractory focal epilepsy. FMZ-PET localised only one third of the epileptogenic zones identified by invasive EEG. 3D rendering of coregistered images improved interpretation of FMZ-PET studies in 50%.

Wednesday 31st August 2005
15:30 - 17:00
Salle 252A
Platform Session
Genetics 2

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Impaired Mitochondrial Glutamate Transport in Autosomal Recessive Neonatal Myoclonic Epilepsy
F. Molinari[1], A. Raas-Rothschild[2], M. Rio[1], A. Kaminska[3], G. Fiermonte[4], F. Encha-Razavi[1], F. Palmieri[5], P. Plouin[6], T. Attié-Bitach[1], A. Munnich[1], P. Rustin[1], L. Colleaux[1]

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Purpose: Severe neonatal epilepsies with suppression burst pattern are epileptic syndromes with onset either neonatally or in the first months of life. These disorders are characterised by a typical EEG pattern, namely suppression-burst (SB), in which higher voltage bursts of slow waves mixed with multifocal spikes alternate with isoelectric suppression phases.
Methods: Homozygosity mapping in an inbred Israeli family with 4 children presenting an EEG with severe intractable myoclonic seizures, microcephaly and abnormal ERG-VEP, localised the disease causing gene on 11p15.5.
Results: Sequencing analysis of the SLC25A22 gene (or GC1), one of the two mitochondrial glutamate/H+ symporters, identified a missense mutation (p.Pro206Leu) which co-segregated with the disease and altered a highly conserved amino-acid. To estimate the prevalence of GC1 mutations, we analysed 29 patients with epilepsy and SB pattern and identified a second mutation (p.Gly236Trp) in a child with very similar clinical features. This result suggests that GC1 mutations may account for a significant number of cases of severe epilepsy with SB associated with microcephaly and ERG abnormalities. Functional analyses of the P206L mutation showed that glutamate oxidation in patient cultured skin fibroblasts was strongly defective and reconstituted proteoliposomes showed defective [14C] glutamate uniport and [14C] glutamate/glutamate exchange by the mutant protein. During human development, SLC25A22 is specifically expressed in the brain, within territories proposed to contribute to the genesis and control of myoclonic seizures.
Conclusion: These findings provide the first direct molecular link between glutamate mitochondrial metabolism and myoclonic epilepsy and suggest potential insights into the pathophysiological bases of severe neonatal epilepsies with suppression-burst pattern.

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New EF-Hand Containing Gene EFHC2 on Xp11.4: Evidence for Association with Juvenile Myoclonic Epilepsy

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Purpose: 6 juvenile myoclonic epilepsy (JME) families were recently described in which missense mutations in the gene EFHC1 cosegregate with the epilepsy phenotype. JME belongs to the idiopathic generalised epilepsy (IGE) syndrome group. Other IGE subtypes include childhood absence epilepsy (CAE), juvenile absence epilepsy (JAE) and epilepsy with generalised tonic-clonic seizures (EGTCS). We cloned a EFHC1 paralog, EFHC2 and performed an association study to test whether genetic variation of the EFHC2 confers susceptibility to JME and other common IGE subtypes.
Methods: The EFHC2 gene was cloned in-silico and verified through RT-PCR amplification of its full length ORF. 654 IGE patients, among them 247 JME patients (99 males, 148 females), and 662 population controls (308 males, 354 females) were recruited. Genotyping of the SNPs in the EFHC2 gene was performed using a TaqMan nuclease assay.
Results: The X-chromosomal gene EFHC2 is expressed in the brain. EFHC2 protein has almost identical domain structure with EFHC1; both peptides share a.a. similarity. In males but not females, the frequency of the T allele of the SNP rs2208592 (S430Y) was significantly increased in the JME patients (14.4%) compared to the controls (7.2%; $p = 0.030$; OR = 2.17). The allelic association was even stronger for JME patients without absence seizures ($p = 0.014$; OR = 2.46).
Conclusion: Considering the similarity between EFHC1 and its paralog EFHC2, it's interesting that the EFHC2 turns out to be tentatively associated to JME susceptibility, especially (with a even higher significance) to the 'pure' JME without absence. Our data await replication in independent association studies.

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Novel Juvenile Myoclonic Epilepsy Mutation in Myoclonin 1/EFHC1 in One Large Family from Honduras

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Purpose: In 2004, Suzuki et al. showed that missense mutations in myoclonin 1/EFHC1 in 6p12.1 segregated with epilepsy and diffuse polyspike wave-traits in affected members of 6 multigeneration Hispanic JME families. (Nat Genet. 2004;36(8):842-9). We searched for myoclonin 1/EFHC1 mutations in 11 Honduran families with juvenile myoclonic epilepsy (JME).
Methods: Eleven families were ascertained through a proband with JME as defined by 1989 Epilepsy Syndromes ILAE Classification. EEGs were performed in probands, unaffected and affected family members. Clinical and EEG data were validated by at least two epileptologists. Polymerase chain reaction amplified all 11 exons of EFHC1 and mutation analysis was performed with heteroduplex analysis and sequencing.
Results: A novel stop mutation segregated with epilepsy in one three generation 35 member family. The proband had awakening myoclonias and grand mal tonic-clonic seizures at 13 years and pyknoleptic absences that started at 6 years. Myoclonias and diffuse EEG 4-6 Hz polyspike wave complexes were documented in the proband during CCTV/EEG. Non-proband affected family members had grand mal seizures only. The stop mutation (the amino acid change), domain site and calculated penetrance of the mutation in this Honduran pedigree will be presented at the meeting. Ten other JME families did not show any mutation in Myoclonin/EFHC1.
Conclusion: A novel stop mutation in myoclonin 1/EFHC1 was found in one large three generational Honduran family ascertained through a proband with JME preceded by childhood absences. These results provide further proof that myoclonin 1/EFHC1 is the epilepsy and polyspike waves causing gene of JME in 6p12.1.

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Familial Mesial Temporal Lobe Epilepsy Associated with a Deletion Mutation in the Chorea-Acanthocytosis Gene

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Purpose: Chorea-acanthocytosis (CHAC) is an autosomal recessive disorder caused by mutations in VPS13A on chromosome 9q21, and characterised by neurodegeneration and acanthocytosis. Seizures are not uncommon in CHAC, but have not been well characterised.
Methods: We studied 4 French-Canadian kindreds with CHAC. EEG, video-telemetry, MRI, blood smears, biochemical and genetic tests were performed.
Results: 12 patients had clinical features of CHAC. 8 had epilepsy and this was the presenting symptom in 6. The epileptic aura consisted of déjà vu, fear, palpitations, vertigo, and visual hallucinations. EEG with video-telemetry confirmed ictal and interictal temporal epileptic abnormalities. In three families, patients were homozygous for a deletion of exons 70-73 of VPS13A, and exons 6-7 of GNA14. In family 4, two patients were compound heterozygotes for the deletion and a 4242+1G>T splicing mutation. Of all patients with the deletion 77% had seizures, as compared to 42% in the general CHAC population. 2 other patients in family 4 were homozygous for the splicing mutation and did not have seizures.
Conclusion: Patients with CHAC have a tendency to develop temporal lobe epilepsy (TLE) and this may be the presenting feature. Treatment of epilepsy in CHAC patients represents a challenge, since seizures may be difficult to control and some anti-epileptic drugs may worsen the involuntary movements. The higher prevalence of epilepsy in the patients with the deletion suggests that this particular mutation may be more strongly associated with the epilepsy phenotype. CHAC represents a single gene disorder that can result in the TLE phenotype.

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Familial Mesial Temporal Lobe Epilepsy Maps to Chromosome 4q

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Purpose: Familial mesial temporal lobe epilepsy (FMTLE) is a heterogeneous syndrome, including a relatively benign condition characterised by simple partial (SPS) and occasional complex partial seizures (CPS). Intense and frequent déjà vu phenomenon is the most common aura and in many patients is the only manifestation. Autosomal dominant (AD) inheritance has been proposed but no linkage has been established. Here we report results of genetic analysis in a family with ADFMTLE.
Methods: We identified a 4-generation kindred with several affected members meeting criteria for FMTLE and enrolled 22 individuals who

gave informed consent. Every individual was personally interviewed and examined; EEG and MRI studies were performed on 3 affected subjects. DNA was extracted from every enrolled individual. We performed a genome-wide search using an 8 cM panel and fine mapping was performed in the regions with a multi-point lod score > 1.
Results: Inheritance was consistent with AD mode with reduced penetrance. Ten individuals were classified as affected with FMTLE and we also identified several asymptomatic individuals who had affected offspring. Seizure semiology included SPS with déjà vu feeling, CPS and, rare secondarily generalised tonic-clonic seizures. EEG recordings were normal. No structural abnormalities, including hippocampal sclerosis, were detected on MRI. Genetic analysis detected a group of markers with lod score > 3 on chromosome 4q spanning 7 cM region.
Conclusion: We report identification of a genetic locus for FMTLE. The identification of a disease causing gene will contribute to our understanding of the pathogenesis of temporal lobe epilepsies.

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Pure Childhood Absence Epilepsy Associated with a Gain-of-function Mutation in CACNA1A Affecting G-protein Modulation of P/Q-type Ca2+ Channels
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Purpose: Childhood absence epilepsy (CAE) is one of the most common types of genetic (idiopathic) epilepsy. Several loss-of-function mutations have been described in three different genes encoding subunits of the P/Q-type Ca2+ channel which were associated with a complex phenotype including ataxia and absence epilepsy in mouse or man. To investigate if this channel may also be genetically altered in individuals suffering only from epilepsy, we sequenced the CACNA1A gene in nuclear families affected by classical forms of idiopathic generalised epilepsy, in which linkage did not exclude CACNA1A mutations.
Methods: Standard genetic techniques (linkage and sequencing), and whole cell patch clamping of wild type (WT) or mutant α1A-2 co-expressed with α2δ and β2e subunits of the human P/Q-type channel co-expressed in tsA201 cells was performed.
Results: We identified a novel mutation (R2162H) cosegregating with a CAE trait. The mutation is located in a highly conserved region involved in G-protein-mediated inhibition of P/Q-type channels, which is considered a key mechanism for regulating presynaptic Ca2+ levels. Electrophysiological analysis revealed identical standard gating characteristics of WT and mutant channels. However, investigating the inhibition of these channels by G-protein βγ-subunits (G□□), activated by use of GTP□S, we observed a significant acceleration of G□□ dissociation by R2162H (τ = 57±12 compared to 118±10 ms for the WT, 0 mV, $p<0.001$).
Conclusion: These results are consistent with a facilitation of synaptic transmission by the mutant P/Q-type Ca2+ channel. They can well explain the epileptic phenotype by a novel gain-of-function pathomechanism, clearly distinct from a loss-of-function of this channel which is associated with both ataxia and epilepsy.

Wednesday 31st August 2005
15:30 - 17:00
Salle 252B
Platform Session
Paediatric Epilepsy 3 -Neonatal Seizures and Status Epilepticus in Children

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A Peculiar Type of Epilepsy in Children with Bilateral Lesions of Thalamus and Basal Ganglia
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Purpose: Bilateral lesions of the basal ganglia and thalamus occur in children as a consequence of birth asphyxia or neonatal shock. In a previous study, we were able to define three different degrees of MRI lesion patterns (Krägeloh-Mann I et al. Dev Med Child Neurol 2002;44:477-484). Since pathogenesis and timing of the lesion are homogeneous, this could serve as a model to study the impact of brain lesions on the manifestation of the epilepsy. Therefore, we investigated the relationship between lesion pattern, epilepsy and EEG findings in these children.
Methods: Eight children presenting with bilateral lesions of the thalamus and basal ganglia and a follow-up of more than five years were included in the study. MRI and EEG data were systematically reviewed by patient-blinded raters.
Results: The only child with a mild lesion (involvement of basal ganglia and thalamus only) had no seizures, and EEG was normal. 4 children with additional involvement of the pericentral region (classified intermediate) had epilepsy which was considered controlled. All showed multifocal benign rolandic spikes in the EEG. 3 children with additional involvement of the hippocampus (classified severe) had an active epilepsy with unilateral, sometimes alternating clonic seizures. EEG showed multifocal rolandic spikes with severe activation during sleep in all of them.
Conclusion: This small cohort of children with a well defined homogeneous brain lesion shows a peculiar seizure and EEG pattern including features typical for benign rolandic epilepsy. In addition, a clear correlation between the extent of the lesion and the severity of epilepsy is evident.

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Epilepsy Following Hypoxic-ischemic Encephalopathy: Clinical and EEG Follow-up
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Purpose: Hypoxic-ischemic encephalopathy (HIE) is a major cause of morbidity and mortality in full-term infants. The survivors with HIE were prospectively studied to evaluate the predictive value of clinical and EEG examinations on their neurological outcome.
Methods: 40 full-term infants with HIE were assessed during the neonatal period. HIE status was scored within the first 48 hours of life. Neurological status, cranial ultrasound and EEG findings were analysed. All infants were followed until aged 5 years for the incidence of epilepsy, developmental delay (DD) and cerebral palsy (CP).
Results: Seizures occurred in 7 patients (17.5%). Epilepsy was associated with CP and/or DD. Seizures were classified as infantile spasms (3 infants), complex focal (2), and generalised tonic-clonic (2). Analysis of HIE severity showed grade I HIE in 15, grade II HIE in 20, while 5 infants had grade III HIE. Interictal EEGs recorded in the neonatal period and during follow up were normal in 65%, moderately abnormal in 22.5% (intermediate patterns) and severely abnormal in 12.5% (low-voltage background activity, spike-wave discharges). Ultrasound scans of the brain were normal in 40%, moderately abnormal in 40% (mild periventricular densities or small intraventricular haemorrhage) and severely abnormal in the remaining

20% (widespread echogenic features in the thalami, basal ganglia, white matter, and cortex). Epilepsy developed in all infants with grade III HIE and severely abnormal EEG and in none with grade I HIE and normal EEG ($p<0.01$). However, epilepsy developed in 50% (4 of 8) of infants with severely abnormal ultrasound scans and in 18.75% (3 of 16) of infants with moderately abnormal scans. Cerebral palsy developed in 10 infants and in 7 of them it was associated with epilepsy (70%).
Conclusion: Infants with grade III HIE, severely abnormal early EEGs and focal brain lesions are associated with the greatest risk for developing epilepsy.

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Long-term Risk of Epilepsy Following Febrile Seizures
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Purpose: The long-term risk of epilepsy following febrile seizures is unsettled, especially in subgroups of children with a family history of seizures, pre-existing brain damage, or suboptimal birth history.
Methods: We evaluated the occurrence of epilepsy for up to 26 years of follow-up in a cohort of all persons born in Denmark (1977-2002). We obtained information on febrile seizures and epilepsy by linking the cohort with the National Hospital Register. Cohort members were followed from birth until onset of epilepsy, death, emigration, or 31 December 31 2002, whichever came first.
Results: In the cohort of 1.6 million persons, we identified 51,546 persons with febrile seizures and 17,470 persons with epilepsy. Persons with a history of febrile seizures carried a higher rate of epilepsy throughout the entire period of follow-up, but the rate ratio was particularly high shortly after the first febrile seizure. Cerebral palsy, family history of epilepsy, low Apgar score, low birth weight and preterm birth increased the cumulative incidence of epilepsy in general, but did not modify the rate ratio of epilepsy following febrile seizures. The rate ratio of complex partial epilepsy was virtually the same as the rate ratio of generalised-onset epilepsy following febrile seizures.
Conclusion: Although febrile seizure was associated with a higher rate of epilepsy, most children (94%) had not developed epilepsy at the age of 25 years. The rate ratio of epilepsy following febrile seizures did not depend on well-known risk factors for epilepsy, and it was not specifically related to complex partial epilepsy.

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Clinical Characteristics and Outcome of Convulsive Status Epilepticus (CSE) and Prolonged Seizures in Children
P. Metsaranta[1], A.L. Kuusela[1], K. Eriksson[2]

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Purpose: Treatment strategies for acute convulsive seizures and CSE have become more aggressive as our understanding of seizure pathophysiology has increased. Our purpose was to explore differences in background factors, treatment and outcome between prolonged seizures lasting less or more than 30 minutes (=conventional time limit of CSE) in children.
Methods: We retrospectively reviewed medical records and intensive care unit treatment charts of all children (aged 1 month to 16 years) who had been admitted to the Paediatric Emergency Room or Paediatric Intensive Care Unit of Tampere University Hospital, between January 1993 and December 2002, due to acute convulsive seizure episode lasting more than 5 minutes. All data available was analysed, including e.g. seizure duration and anticonvulsant medications.
Results: There were 187 cases of CSE and 152 prolonged seizures lasting less than 30 minutes in 234 children with mean follow-up time after the index seizure episode being 2.0 years. Previous epilepsy was present in 30.1% and 20.4% of the cases, respectively. CSE associated significantly with acute and remote symptomatic aetiologies (vs idiopathic or febrile aetiology, $p<0.001$). Eleven (5.9%) CSE and 39 (25.6%) seizures lasting 5-29 minutes ended spontaneously ($p<0.001$). The treatment delay (time from the beginning of seizure to the start of anticonvulsive treatment; usually rectal diazepam administered often by paramedics or parents) was 20 minutes in SE group and 7 minutes in the other group ($p=0.08$). During follow-up, mortality in these two groups was 1.7% and 0.4%, respectively. New epilepsy occurred in 12.8% and 20.0% of the patients. Other neurological morbidity (incidence 3.7% and 3.3%) was associated with acute aetiology ($p=0.004$) but not with seizure duration.
Conclusion: The aetiology of the seizure episode was the major determinant of neurological outcome and it was different in CSE group from the 5- to 29-minute seizure group. Only a few CSE resolved spontaneously. Rapidly induced treatment may prevent seizure prolongation but the outcome even in prolonged seizures in children seems to be good.

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Ethnicity, Socioeconomic Status and the Incidence of Convulsive Status Epilepticus in Childhood
R.F.M. Chin[1], R.C. Scott[1], C. Peckham[1], H. Bedford[1], A. Wade[1], B.G.R. Neville[1]

1) Institute of Child Health, London, UK

Purpose: Data from population based studies suggest that the incidence of convulsive status epilepticus (CSE) is higher in non-white compared to white patients. However, ethnicity effects may be related to socioeconomic factors. The study with the highest reported incidence of CSE was conducted in a predominantly black, economically deprived population. Thus, we hypothesised that the incidence previously reported in non-white patients may in part reflect the effect of socioeconomic status.
Methods: Subjects were enrolled as part of a two year prospective population based study, the North London Convulsive Status Epilepticus in Childhood Surveillance Study. Excluding neonates, children aged < 16 years with CSE within North London were identified using a multi-tiered notification system. Home post codes of children were used to assign to each child an Index of Multiple Deprivation 2004 score of socioeconomic status. Poisson multivariate regression analysis was used to investigate the relationships between incidence of CSE and age, socioeconomic status and ethnicity.
Results: 176 children were enrolled. Black children were as likely (OR 1.3, $p=0.2$) but Asian children were 2.1 times more likely ($p<0.0005$) to have CSE compared to white children. For each one point increase in IMD 2004 (worsening socioeconomic status) there is a 3% cumulative increased risk of CSE irrespective of ethnicity ($p=0.003$). In addition, the incidence of CSE in each ethnic group was significantly related to socioeconomic status but this effect was least in Asian children ($p=0.05$).
Conclusion: The relationship between ethnicity and CSE is complex and is likely to be related to both genetic and socioeconomic factors.

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Determinants of Duration of Convulsive Status Epilepticus in Childhood
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1) Institute of Child Health, London, United Kingdom

Purpose: Morbidity and mortality associated with convulsive status epilepticus (CSE) increases with increasing seizure duration. Identification of factors associated with longer duration of CSE may provide the foundations for development of interventions that could improve the outcome of CSE by reducing seizure length. From the North London Convulsive Status Epilepticus in Childhood Surveillance Study, we report on factors associated with CSE lasting > 60 minutes compared to those lasting 30-60 minutes.

Methods: Excluding neonates, children aged <16 years with CSE were identified using a multi-tiered notification system involving a research collaborative network of paediatricians from all North London hospitals. Forward stepwise multiple logistic regression analysis was used to investigate which clinical factors were associated with CSE lasting >60 mins.
Results: 240 cases of CSE were enrolled. Lack of prehospital treatment (OR 2.4, p=0.03, 95% CI 1.1-5.3), treatment with >2 doses of benzodiazepines (OR 3.6, p=0.001, 95% 1.7-7.9) and longer interval between onset of CSE and arrival in A&E (OR 1.05, p=0.003, 95% CI 1.02-1.08) were independently associated with CSE lasting >60 mins.
Conclusion: Children who receive prehospital treatment have a reduced seizure length and therefore it is possible that widespread prehospital treatment would reduce the likelihood of a 60 minute seizure. Children that fail to respond to 2 doses of benzodiazepine are likely to have CSE refractory to benzodiazepines and should not receive further doses. If pre-hospital treatment is not available then rapid transport to A&E, and earlier intervention, may also reduce the likelihood of such seizures.

Wednesday 31st August 2005
15:30 - 17:00
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Platform Session
Paediatric Epilepsy Surgery

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Tuberous Sclerosis Complex: Results of Surgery
F. Renaldo[1], P. Kahane[2], M. Bourgeois[3], P. Viviana[2], C. Chiron[4], E. Landré[5], F. Chassoux[5], J. Motte[6], B. Echenne[7], A. Arzimanoglou[1]

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Purpose: In patients with tuberous sclerosis and epilepsy, seizures are often refractory to medical treatment and surgical intervention is increasingly envisaged as an alternative. If seizures can be localised to a single tuber surgery is sometimes limited to a resection of the tuber. Certain patients may need a larger resection. Most of the available data comes from small series of patients and the most appropriate pre-surgical evaluation procedure remains to be defined.
Methods: We report on the epilepsy profile, pre-surgical evaluation and results of surgery in 22 patients, treated surgically in French epilepsy centres. Age at seizure onset varied from day 3 to 7 years, with epilepsy having started before the age of 12 months in 14 patients. Infantile spasms were reported in 9. Five patients had only one tuber visible on MRI, the majority of the remaining having more than 4. Interictal EEG discharges were considered bilateral in 3, left in 11 and right in the remaining 8 patients. Investigation with depth electrodes was considered necessary in 14 (6 with grids and 8 with stereotactic intracerebral EEG monitoring).
Results: Lesionectomy associated to a larger cortical resection (tailored or lobectomy) was preformed in 18, the remaining 4 having had a simple lesionectomy. Post-surgical follow-up on report was less than 24 months in only 5 patients. 3 patients presented post-surgical permanent complications (mild motor deficit; quadranopsia; bacterial meningitis with severe sequelae). Seizure outcome was good in 18. From those submitted to lesionectomy alone, 2 are seizure-free and 2 others are classified either as Engel III (worthwhile seizure reduction or IV (no improvement). From those submitted to lesionectomy plus cortical resection, 12 are considered as Engel I (11 Engel Ia), 1 as Engel II (rare seizures), 2 as Engel III and 3 as Engel IV. 6 out of 8 investigated with SEEG are seizure-free.
Conclusion: We conclude that patients with TSC and drug resistant epilepsy may benefit from epilepsy surgery even when presenting with multiple cortical tubers, provided that the pre-surgical evaluation can clearly evidence coherent anatomo-electro-clinical correlations. Prospective studies, integrating recent functional neuroimaging techniques, are needed to validate the indication for epilepsy surgery at an early age.

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Epilepsy Surgery in Children: Results from an International Survey
S.A. Harvey[1], G. Mathern[1], D. Nordli[1], H. Cross[1]

1) Paediatric Surgery Subcommission of the ILAE Neurosurgery Commission

Purpose: While resective surgery is becoming an accepted treatment for infants, children and adolescents with refractory epilepsies of different aetiologies, it is undertaken at a limited number of centres with possibly differing approaches to selection and surgery. The literature on paediatric epilepsy surgery concerns single aetiologies, surgical procedures, patient groups or centres. Our aim was to better understand the current clinical populations being treated and the procedures being used worldwide.
Methods: Members of an international working group on paediatric epilepsy surgery completed a web-based survey (http://www.epilepsysurvey.harvey.md/survey.html) during March 2005 on surgery undertaken in the calendar year 2004. Ten epilepsy surgery centres from around Europe, the USA and Australia participated, reporting data for patients 18 years and younger, including palliative procedures and neurostimulation. Data were collected on patient demographics, epilepsy and developmental findings, imaging findings, operative details including re-operations, complications and histology.
Results: Data were collected on 218 children who underwent 268 epilepsy surgical procedures. Preoperative investigations included video-EEG (73%), MRI (79%), PET (21%), SPECT (19%), fMRI (10%) and Wada (10%). Lesions were present on preoperative MRI in 177 (81%), being solitary and discrete in 103 (51 temporal, 29 frontal) and diffuse or multiple in 74; developmental tumours and malformations accounted for 70% of lesions. Median age at seizure onset was 1.5 years, median age at surgery was 8 years and median delay to surgery was 4.2 years. Approximately half the sample had developmental or learning problems. Preoperative seizure frequency was daily in 64% and weekly in 21%. There were 192 operative procedures, including 34 hemispherectomies and 8 callosotomies 141 (65%) children had a single-stage operative procedure and 29 children had 2- stage or repeat surgery performed. 35 patients had previous epilepsy, tumour or VNS surgery. VNS was performed in 30 and radiosurgery in 2. 38 (17%) children had intracranial EEG monitoring.
Conclusion: Knowledge of the current application of paediatric epilepsy surgery, the commonality and differences in approaches, and the areas of uncertainty and controversy, will help focus clinical guidelines, research undertakings and resource allocation in the field. It is anticipated that prospective data collection with a refined survey instrument will be initiated.

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Epilepsy Surgery in Infants Younger than Three Years
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1) Fondation Ophtalmologique Rothschild, Paris, France

Purpose: To describe our surgical experience with infants treated for refractory partial focal or hemispheric epilepsy.
Methods: We present a population of 73 infants (37F, 36M, mean age: 17 months, 2–35 months), who underwent epilepsy surgery at our institution between 1990 and 2003, with a follow-up of at least 1 year. Pathology included malformation of cortical development (n=51), Sturge-Weber angiomatosis (10), hypothalamic hamartoma (5), cortical tuber (4), and hypoxic-ischemic injury (3). Surgical procedures consisted of: 1) focal resection (n=28), preceded in a high percentage by intracranial EEG recording, 2) hemispherotomy (n=40)

and 3) intraventricular endoscopic disconnection (single or repeated) of hypothalamic hamartoma (n=5).
Results: In the focal resection group, the frontal lobe was predominantly affected (13 of 28 cases), followed by temporal, parietal, occipital or multilobar localisation. 71% had a favourable outcome (Engel class I + II), 57% were seizure-free, whereas 7% had no improvement. In the hemispherotomy group, 86% had a favourable outcome, with 81% being seizure-free. 11% had a worthwhile seizure reduction with improvement in cognitive abilities, whereas 1 infant showed no improvement. The underlying pathology in all infants with Engel III + IV outcome following hemispherotomy (14%) was hemimegalencephaly. In 5 infants, a hypothalamic hamartoma was disconnected through an endoscopic transventricular approach. 2 infants were seizure-free, whereas 3 showed a worthwhile improvement.
Conclusion: Our encouraging results, comparable to our experience in older age groups, favour an early referral for surgery in carefully selected cases, particularly with regard to cognitive development in this critical period of life.

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Surgery for Drug-resistant Epilepsy in Children: Anatomo-Electro-clinical Features and Seizures Outcome in a Series of 65 Patients Operated on Without Intra-cerebral Evaluation

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Purpose: Surgery is an early therapeutic option for drug resistant epilepsy, particularly in children where a positive outcome may improve cognitive development and psychosocial adaptation. The aim of our study is detailing the features of 65 children operated on in our Centre after a non-invasive evaluation.
Methods: In 63.1% (65 cases) of the 103 pts under the age of 16 years operated on in our Centre from 1996 to March 2004, surgery was realised on the basis of non-invasive data: clinical history, seizure semiology, inter-ictal +/- ictal EEG features and MR evaluation. There were 36 males and 29 females, age: 8 months-16 years (mean 8.7+/-4.9), epilepsy onset: birth-15 years (mean 3.6+/-7.8), epilepsy duration: 6 months-14 years (mean 5.2+/-2.8), seizure frequency: monthly 19 pts, weekly 8pts, daily 9 pts, pluri-daily 29 pts. Ictal video-EEG recordings were obtained in 47 pts; MR examination was positive in 63 cases.
Results: Surgery was right sided in 31 pts and left in 34, and involved temporal (37 pts), frontal (13 pts), parietal (2 pts) occipital lobes (1 pt), being multilobar in 12 cases. A simple lesionectomy was realised in 15pts (subtotal in 3), in 48 pts lesionectomy (subtotal in 17) was associated with corticectomy. Pathology was: neoplastic in 29 pts (DNt: 14; ganglioglioma: 10; other: 5); malformative in 26 pts (FCD: 10, tuberous sclerosis: 9, other: 7); degenerative in 5 pts; cryptogenic in 5 pts. Overall results (Engel, 1993): class I: 52 pts i.e. 80% (Ia: 46); class II: 1 pt; class III: 6 pts; class IV: 6 pts. Further analysis will be presented relating outcome with all the variables listed above.
Conclusion: Our results suggest that a positive outcome could be obtained in a consistent percentage of pts after a relatively short non-invasive diagnostic protocol.

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Posterior Cortex Refractory Epilepsy in Children

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Purpose: To describe the epilepsy features and surgical options of children and adolescents with occipital, parieto-occipital and temporo-occipital refractory epilepsy.
Methods: 18 patients aged 2-19 years were submitted to full presurgical evaluation.
Results: Epilepsy onset ranged from 2.5 months to 14 years. Posterior cortex lesions were defined by MRI in 16 patients, including malformations of cortical development in 4, destructive lesions due to perinatal or postnatal brain injury in 8, Sturge Weber syndrome in 1, and neuroglial tumours in 3. Bilateral lesions were observed in 4 cases, and dual pathology (hippocampal sclerosis) in 3 cases. Typical ictal symptomatology included visual auras, amaurosis, vomiting, eye/head deviation, blinking, headache and behavioural changes. Progression into typical temporal lobe seizures with distal automatisms were recorded in 5 cases. Bilateral asymmetric motor events (epileptic spasms or tonic seizures) were observed in 3 cases. Reflex photogenic focal seizures were recorded in 2 cases. Atypical absences and generalised paroxysmal discharges were noted in 4 children. Resective surgery was performed in 12 patients, including lobectomy or cortical resection in 9 and lesionectomy in 3. 8 patients with a follow-up longer than 1 year have a good or excellent surgical outcome (Engel class I).
Conclusion: Epilepsy surgery has been proven highly successful in a significant proportion of children and adolescents with posterior cortex refractory epilepsy.

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Outcome of Epilepsy Surgery in Children 1-16 Years of Age

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1) University Hospitals, Freiburg, Germany 2) Epilepsy Centre Kork, Kehl-Kork, Germany 3) University Hospitals, Heidelberg, Germany 4) University Hospitals, Tübingen, Germany

Purpose: To evaluate the results of resective surgical procedures for drug-resistant focal epilepsy in childhood.
Methods: 103 consecutive children who underwent resective epilepsy surgery at University of Freiburg between January 1998 and September 2004 were included in the study. Data regarding presurgical evaluation, aetiology of the epilepsy, localisation and type of surgery were analysed retrospectively. Seizure outcome was assessed at fixed intervals 6, 12, 24, 36, 48 and 60 months after surgery and classified according to Engel et al.
Results: Prior to surgery, all children were evaluated with non-invasive long-term video-EEG telemetry. 33 children also had invasive monitoring with implanted electrodes, 29 had intraoperative electrocorticography. A cortical resection was performed on 95 children (46% temporal, 33% monolobar extratemporal, 21% multilobar), 4 had a selective amygdalohippocampectomy, 4 a functional hemispherectomy. The most frequent aetiologies were cortical dysplasia (56%) and tumour (24%). Unexpected neurological deficits occurred in 3 patients (2 pareses, 1 partial aphasia). Depending on the point in time during follow-up, 66-86% of children were completely seizure-free (Engel class Ia), 73-90% remained free of disabling seizures (class I). Only about 5% of patients did not benefit from the surgery (class IV). The best outcome was achieved in patients with temporal resections, but also more than 70% of patients with multilobar resections had a class I outcome over the entire follow-up period.
Conclusion: Our results confirm that surgery is a valid therapeutic option for drug-resistant focal epilepsy in the paediatric age group. This holds true also for patients with large extratemporal resections.

Wednesday 31st August 2005
15:30 - 17:00
Salle 251
Platform Session
Adult Epileptology - Hormones

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Fertility in Women with Active Epilepsy
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Purpose: Studies suggest that fertility among women with epilepsy is decreased. The purpose of this study was to assess fertility in women with active epilepsy (WWAE) with emphasis on effects related to valproate (VPA) treatment.
Methods: We identified from the prospective, population based pregnancy registry of Kuopio University Hospital (pop. 250,000) all women who had given birth between 1989 and 2000 and had active epilepsy (N=79). Altogether 20 women were on VPA monotherapy during pregnancy. We compared the fertility related factors of these women with the healthy pregnant population (N=16,599) during the same time period.
Results: Altogether 4.7 per 1000 pregnancies involved WWAE. The average number of children was equal in WWAE compared to controls (2.1+/-1.1 vs. 2.2+/-1.2). The time needed to conceive did not differ between all WWAE (5.0+/-6.8 months), women using VPA (6.4+/-6.2) and controls (5.4+/-9.4). Women using VPA had higher body mass index than controls (24.9+/-5.3 vs. 22.8+/-4.0, p=0.09) but did not have more menstrual disturbances than controls. None of the women using VPA had needed infertility treatments. Delivery was induced in 55% of women using VPA and in 17% of controls, p<0.0001.
Conclusion: The number of children is equal in WWAE and controls. Valproate does not seem to increase difficulties in becoming pregnant in WWAE. According to the epidemiological data from our area, the prevalence of epilepsy in fertile aged women is 0.58%. In our population 4.7 out of 1000 (0.47%) pregnancies involve active epilepsy, which means that if we only exclude patient with severe comorbidity, fertility in WWAE is not decreased.

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Complications of Pregnancy and Delivery in Women with Epilepsy
K. Sindhu[1], S.V. Thomas[1], B. Ajaykumar[1], P.N. Sylaja[1], P.B. Sulekhadevi[2], S. Jacob[2]

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Purpose: Medical professionals and the public are concerned about the complications of pregnancy and delivery for women with epilepsy (WWE). Our aim was to prospectively ascertain the occurrence of these complications in a cohort of WWE.
Methods: All complications from the beginning of pregnancy, delivery and the first 48 hours of the postpartum period were prospectively recorded according to the protocol of this registry, for all cases, and were compared with similar statistics (for women without epilepsy) from a large teaching hospital. Their foetal malformations are discussed elsewhere.
Results: Between 1998 and 2004, there were 643 completed pregnancies in this registry. (Mean age 25.7 + 4.43 years; generalised epilepsy 46%; localisation related epilepsy 54%; primigravida 53%). Their complications are compared with those of 18,272 pregnancies managed in the teaching hospital (in brackets). Spontaneous abortions 4.2% (2.38%); medical termination of pregnancies 2.64% (7.71%); anaemia 0.62% (0.22%); gestational diabetes 1.56% (3.09%); pregnancy induced hypertension 3.89% (6.45%); antepartum haemorrhage 0.93% (1.64%); preterm labour 1.87% (6.12%); obstructed labour 0.62% (3%); Caesarean section 33.4% (29.5%); assisted delivery 2.8% (2.68%); post partum haemorrhage 0.31% (0.64%); peripartum seizures 1.4% (0.04%); intrauterine death 1.56% (2.2%); fibroid uterus or ovarian cyst 2.33% (0.53%); other medical illness 2.5% (2.15%); TORCH infection 0.31% (0.01%), birth weight < 2.0 kg 4.19% (7.66%).
Conclusion: Spontaneous abortions, anaemia, ovarian cyst, fibroid uterus, and seizures in the peripartum period were more common among WWE while several other complications were less common. Caesarean section and assisted delivery were more frequent among WWE. There is no undue risk to pregnancy and childbirth in most WWE.

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Reduced Bone Mass and Increased Fracture Risk in Postmenopausal Women with Epilepsy: A Case-control, Monotherapy Study
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Purpose: Increased fracture risk and reduced bone mineral density have been reported in patients with epilepsy, and especially in postmenopausal women. This may be related to seizures, but also to the use of antiepileptic drugs and life style.
Methods: 27 patients on AED monotherapy for >4 years and 25 age-matched controls underwent a structured interview and bone mineral density (BMD) examination with dual-energy X-ray absorptiometry (DEXA). BMD and T-scores were calculated from lumbar spine (L2-L4), collum femoris, proximal and distal forearm, and the whole body.
Results: Mean age was 63.6 and 63.7 yrs in patients and controls, respectively. AEDs used were: carbamazepine 16, lamotrigine 3, PB 4, valproate 2, phenytoin 1, gabapentin 1. 21 of 27 (74%) patients and 10 of 25 (40%) controls had experienced fractures (p<0.02). BMD was reduced in patients vs controls in all regions except lumbar spine. Mean T-scores for the 25 matched pairs showed lower values for patients in all regions. The reduction in T scores was more pronounced in carbamazepine treated with a maximum T-score difference between groups of 0.8 in proximal forearm. 15 of 27 (56%) patients and 7 of 25 (28%) (p<0.05) controls had osteoporotic T values (T-score below – 2.5) in one or more of the five investigated regions.
Conclusion: Postmenopausal women with epilepsy have decreased bone mass and an increased risk of osteoporosis and fractures. Reduced bone mass was especially pronounced in women on carbamazepine therapy. However, we cannot as yet exclude the possibility that other AEDs may also influence bone health.

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Catamenial Epilepsy and Reproductive-endocrine Disorders in Women with Epilepsy Starting during Puberty
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Purpose: Catamenial course of epilepsy (CE) is more common among patients with reproductive-endocrine disorders (RED) than in women with epilepsy only. Adolescent girls with epilepsy manifested during puberty (EMP) have an elevated risk of developing of RED. It could be proposed that CE may serve as a clinical indicator of RED in those girls. We aimed to evaluate reproductive-endocrine health and CE in patients with EMP.
Methods: 43 women (12–34 years old) with EMP participated in this study. Interrelation between seizure exacerbation and phases of menstrual cycle (MC) were investigated for four months. By means of investigation of serum reproductive hormones and ovarian

ultrasonography two groups of patients were defined: women with epilepsy only (WWE – 19 cases) and women with epilepsy and RED (ERED – 24 patients). 13 patients were AED free.
Results: Catamenial exacerbation of seizures was found in 46.5% of patients and occurred three times more often among patients in the ERED group than in the WWE group (66.7% versus 21%). MC disturbances occurred 3.5 times more often in patients with RED ($p>0.001$). RED was almost equally distributed among treated and AED free groups (56.7% and 53.8%, $p>0.05$); RED was found more often among patients on VPA therapy ($p>0.2$).
Conclusion: The risk of RED development is high among the patients with EMP and it doesn't depend on AED treatment. RED is equally distributed in both treated and AED free groups.

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Sexual Dysfunctions and Blood Hormonal Profiles in Males Suffering from Refractory Focal Epilepsy
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Purpose: To evaluate the incidence of sexual dysfunction in males suffering from refractory focal epilepsy, and to establish a hormonal profile with which to identify the possible hormonal changes typical for each individual type of sexual dysfunction.
Methods: We analysed the sexual functions and blood hormone levels in 40 male patients (age 18-44 years, with an average age of 27.6 ± 5.6 years) with refractory focal epilepsy. According to the evaluation, 22 of the patients suffered from temporal lobe epilepsy (TLE); 14 suffered from frontal lobe epilepsy (FLE); and 2 from occipital lobe epilepsy (OLE). In 2 patients, the localisation was not precisely determined. We used the Czech version of a structured questionnaire called the 'International Inventory of Erectile Function' (IIEF) to assess each patient's sexual functions. The subscales of this questionnaire separately evaluate erectile function (IIEF I), orgasmic function (IIEF II), sexual desire (IIEF III), intercourse satisfaction (IIEF IV), and overall satisfaction with sex life (IIEF V). In all of the patients, we performed the following blood tests: quantitative assessment of blood levels of prolactin (PRL); total testosterone (total-T); free androgen index (FAI); sexual hormone binding globulin (SHBG); estradiol (E2); dihydroepiandosterone sulphate (DHEAS); progesterone (PRG); follicle stimulating hormone (FSH); and luteinizing hormone (LH). These quantitative laboratory data were correlated with other clinical variables and with the results of the IIEF. Chi-quadrate and Wilcoxon tests were used for the statistical analysis. P value <0.05 was considered to be statistically significant.
Results: At least one of the types of sexual dysfunction defined by the IIEF (IIEF I, II, and III) was found in 22 of the 40 patients (55%). Erectile dysfunction (IIEF I) was found in 6 out of 40 patients (15%); orgasmic dysfunction (IIEF II) in 6 out of 40 patients (15%); and loss of sexual desire (IIEF III) in 16 out of 40 patients (40%). According to other subscales of the IIEF, 22 out of 40 patients (55%) were not satisfied with sexual intercourse (IIEF IV) and 20 out of 40 patients (50%) were not satisfied with their sex lives overall (IIEF V). None of the subscales of IIEF correlated significantly with the age of the patients or with the duration of their epilepsy. In patients suffering from at least one of the sexual dysfunctions (IIEF I, II, or III) we found a statistically significant increase of FSH and SHBG, and a decrease of DHEAS and FAI in comparison to patients with normal sexual functions. In patients suffering from erectile dysfunction, we found the same changes, as well as a significant increase of E2. In patients suffering from orgasmic dysfunction, we found a statistically significant decrease of DHEAS. In patients suffering from loss of sexual desire, we noticed a significant increase of SHBG, and a decrease of DHEAS and FAI. All of the patients suffering from orgasmic dysfunction were being treated with carbamazepine in monotherapy or combination therapy. In patients with at least one type of sexual dysfunction (IIEF I, II, or III), a higher proportion of valproate treatment in monotherapy and/or combination therapy in comparison to carbamazepine was found.
Conclusion: Our study showed a relatively high incidence of sexual dysfunction and dissatisfaction with sexual intercourse and sex life in males with refractory focal epilepsy. The most frequent dysfunction in these patients was the impairment of sexual appetite. The aetiology of sexual dysfunction in these patients is probably multifactorial, and the antiepileptic drug treatment may play a key role in their origin. However, our study indicates some specific hormonal changes related to various types of sexual dysfunction, which are not related to antiepileptic drug treatment.

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Polycystic Ovarian Syndrome (PCOS) among Women with Epilepsy: Is it Related to Anti Epileptic Drugs or Epilepsy?
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Purpose: Women with epilepsy have a higher incidence of reproductive dysfunction (RD), which may be due to either epilepsy per se, or its pharmacological treatment. We aimed to evaluate various patient subgroups for the occurrence of menstrual disturbances and PCO/PCOS in women with epilepsy on various AED monotherapy, women in an untreated epilepsy group, and women with bipolar affective disorder treated with sodium valproate.
Methods: Four groups of 40 women each with newly diagnosed epilepsy treated with Phb, DPH, CBZ, SV monotherapy were evaluated clinically and with ultrasound abdomen by neurologist and an ultrasonologist. The latter was blind to patient's medication. This procedure was repeated after 12 months and compared with another group of women with untreated epilepsy and 20 subjects with bipolar affective disorder on SV.
Results: 190 women were evaluated. Women with epilepsy on sodium valproate monotherapy had an occurrence of PCO in 37.5% (15 out of 40), which is significantly higher when compared with patients on carbamazepine (20%) and phenobarbitone (16%). Occurrence of PCO was no different among the untreated group compared with carbamazepine and phenobarbitone monotherapy or even with the general population. Women with epilepsy on valproate monotherapy had a statistically higher occurrence of PCOD with menstrual disturbances and obesity when compared with those on SV for bipolar affective disorders
Conclusion: Sodium valproate monotherapy in women with epilepsy has a higher incidence of reproductive dysfunction in the form of polycystic ovaries compared to other standard AED's and also those treated with SV for bipolar affective disorders. This confirms that SV and epilepsy jointly result in polycystic ovarian syndrome. Woman with epilepsy during the reproductive age group should be screened periodically for PCOD, especially those on valproate.

Wednesday 31st August 2005
15:30 - 17:00
Salle 241
Platform Session
Adult Epileptology

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Acute Symptomatic Seizures Secondary to Cerebral Toxoplasmosis Associated with HIV Clade C Virus
N. Shobha[1], P. Satishchandra[1], A. Mahadevan[1], D. Anitha[1], P.N. Jayakumar[1], V. Ravi[1], S.K. Shankar[1]

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Purpose: Toxoplasmosis is one of the common opportunistic CNS infections associated with HIV. It is generally a late complication of HIV and occurs when CD4 cell counts fall below 200/ml. Acute symptomatic seizures are seen in 15-40% of patients with cerebral toxoplasmosis. Our aim was to evaluate patients of cerebral

toxoplasmosis with HIV Clade C infection who manifested acute symptomatic seizures.
Methods: Case records of all HIV Clade C associated toxoplasma patients seen at NIMHANS were reviewed. Diagnosis of toxoplasmosis was based on clinical, serological, imaging and pathology.
Results: 62 patients with CNS toxoplasmosis were evaluated from 1993-2003 (10 years). 22 (35%) patients presented with seizures. 14 (63.6%) presented with simple partial seizures, 8 (36.4%) patients had generalised tonic clonic seizures. 19 of these 22 patients (86.4%) had CT brain, 1 (4.5%) had MRI scan, 1 underwent both CT and MRI , one had no imaging but diagnosis confirmed at autopsy. CT showed granuloma in basal ganglia 8 (36.4%), in the cerebral cortex 14 (63.6%), involvement of white matter 4 (18.2%), cerebellar granuloma 3 (13.7%), granuloma in brain stem 1, thalamic hypodensity 1, meningeal enhancement 1, cerebral edema 3, hydrocephalus in 1, cerebral atrophy was observed in 2 patients. MRI showed similar findings. 14 (63.6%) patients received 3 weeks pyrimethamine and sulphadiazine. 13 (59.1%) patients expired. Autopsy is available for 10 patients (45.4%), necropsy in 1. Nine patients are being followed.
Conclusion: 35% of the 62 CNS toxoplasmosis patients seen over 10 years at NIMHANS had acute symptomatic seizures. 59% of them expired. Neuropathology data will be presented. Early diagnosis and prompt treatment is required to reduce this mortality.

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Convulsions in Patients Suffering from Infections of the Central Nervous System and the Relation with Disease Outcome
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1) Department of Infectology and Neurology, University of Montenegro, KCCG, Podgorica

Purpose: The aim of the research is to determine the presence of convulsions during infections of the CNS as well as the correlation between them and the outcome of the disease.
Methods: The group consists of 105 patients of both sexes and of different ages: 85 with the bacterial purulent meningoencephalitis (BPME) and 20 with viral encephalitis (VE). Detailed clinical, laboratory and microbiological examinations, including CT, MR and EEG were carried out.
Results: Within the observed group of patients suffering from BPME, convulsions were manifested in 36.7%, and VE in 80% of patients. Comparing the observed group with the outcome of the disease, the majority of convulsions were found within the group of patients with fatal outcome (51.7%), recovered with sequelae in 38.9%, with complete recovery in 26.3% patients with BPME. Convulsions were registered in patients with fatal outcome (30%), in the group of complete recovery (30%) and in the group that recovered with sequelae (20%) in patients with VE. Generalised convulsions (GC) were found in 31.1% of patients, and partial in 5.6% of those affected by BPME; GC were registered in 50% of patients, and partial in 30% of those that suffered from VE. Of the 84.4% of patients affected by BPME and accompanied by generalised convulsions – according to the outcome of the disease - convulsions were mostly manifested within a group of patients who died (93.3%). Of 37.5% of those affected by VE, who manifested partial convulsions, 66.66% of patients died.
Conclusion: The analyses of the obtained data proved that there was no direct influence of the convulsions on the outcome of the disease ($p>0.05$) in patients affected by BPME, while the convulsions manifested in patients with VE significantly influence the outcome of the disease ($p<0.05$) and represent a worse prognostic result. A correlation between different kinds of convulsions and the outcome of disease ($p>0.05$) in patients with BPME is not proved, while the partial convulsions have a bad impact on the outcome of disease in patients with VE ($p<0.05$).

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Tramadol-related Seizures
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Purpose: Tramadol use has been associated with seizures. Detailed epilepsy data of reported cases is lacking and whether this association is primarily related to a proconvulsant effect of tramadol, an interaction with other drugs or due to a patient-related predisposition to seizures is unclear.
Methods: Prospective analysis of adult patients attending a hospital-based first-seizure clinic. Patients with seizures that occurred while taking tramadol were identified. Patients with prior seizures were excluded. Tramadol dose, concurrent drug use, epilepsy risk factors and EEG results were analysed.
Results: Of 605 patients 46 (8%) were on tramadol at the time of their first-ever seizure. Doses in excess of the recommended upper limit (400 mg/day) were taken by 28% of patients (median 300 mg/day). Concurrent antidepressant use was identified in 28 patients (20 selective serotonin reuptake inhibitors, 6 tricyclic antidepressants and 2 both). Antidepressant use was significantly greater in the tramadol-related seizure group versus patients with first-ever seizure not on tramadol (61% versus 17%, $p<0.001$). 9 patients (20%) had risk factors for epilepsy (8 head injury) and 4 patients had a first-degree relative with epilepsy. Epileptiform abnormalities were seen in 7 patients (15%, 4% focal, 11% generalised).
Conclusion: Seizures associated with tramadol were not infrequently encountered. A significant proportion of patients were on concomitant antidepressants, taking high tramadol doses or had risk factors for epilepsy suggesting variables other than a primary proconvulsant effect of tramadol at recommended doses contributed to the occurrence of a seizure. In many cases seizures may have been avoided by strictly adhering to prescribing guidelines.

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Status Epilepticus in Advanced Liver Disease
A. Primavera[1], L. Marinelli[1], D. Audenino[1]

1) Department of Neurosciences, University of Genova, Italy

Purpose: Status epilepticus (SE) has been reported in only a few cases with advanced liver diseases (ALD). The aim of our study is to evaluate the prevalence of SE, its aetiology and clinical manifestation in patients with ALD.
Methods: 150 patients waiting for liver transplantation because of different chronic liver diseases during the last three years entered the study. Patients with previous neurological disorders and the terminally ill were excluded. The severity of liver disease was staged according to Child-Pugh (C-P) score. All patients underwent a standardised neurological examination, EEG and MMSE. The type of status epilepticus and possible precipitating factors were evaluated.
Results: Case material included 88 men and 62 women, aged 50.36 ± 7.9 (mean ± sd). The C-P score corresponded to class A in 8 cases, class B in 92, and class C in 50. Primary liver diagnosis was viral hepatitis in 115 patients, alcoholic liver disease in 22, primary biliary cirrhosis in 6, and other advanced diseases in 7. Signs or history of encephalopathy were found in 104 patients. MMSE mean value was 27.7 ± 1.7. SE were found in 4 patients (2.7%). In 3 cases status epilepticus was related to coexisting hepatic encephalopathy, while in the other case was due to an haemorrhagic hemispheric lesion. In this patient EEG showed triphasic waves with a frequency exceeding 1/s. A further patient presented focal recurrent seizures during antibiotic therapy.
Conclusion: We confirmed that although rare, status epilepticus is a possible manifestation of ALD. In any case an organic origin must be ruled out.

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Relationship between Cerebral Malaria and Epilepsy: A Case-control Study in Libreville, Gabon
E.B. Ngoungou[1], J. Koko[2], Y. Assengone-Zeh[3], M. Ndong Launay[4], E. Engohang[5], M. Moubeka-Mounguengui[4], P. Ndouongo Kouna[4], P.M. Loembe[3], P.M. Preux[1], M. Kombila[6], M. Druet-Cabanac[1]

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Purpose: Cerebral malaria is one of the most serious complications of plasmodium falciparum infection. It is a potential cause of epilepsy in tropical areas but little information is available to quantify it. The purpose of this study was to evaluate the relationship between CM and epilepsy in young subjects in Gabon.
Methods: A case-control study was carried out on a sample of Gabonese subjects aged 6 months to 25 years and hospitalised between 1990 and 2004 within 3 hospitals of Libreville. In this study CM was defined according to the WHO clinical and biological criteria. Epilepsy was defined according to the epidemiological definition (ILAE) and confirmed by a neurologist.
Results: 592 subjects (296 epilepsy cases and 296 controls) were included. 36 (26 epilepsy cases and 10 controls) had a CM antecedent. The odds ratio to develop an epilepsy with a CM antecedent was 3.4 [CI95%: 1.6-7.4] p<0.001. But CM (coma alone) did not represent a statistically significant risk factor compared to CM (convulsions-coma associated) OR= 3.9 [CI95%: 1.7-8.9] p<0.001. Other risk factors were identified: epilepsy family antecedent OR= 6.0 [CI95%: 2.4-14.1] p<0.0001 and febrile convulsions OR= 9.2 [CI95%: 4.0-21.1] p<0.0001. Sickle cell disease represented a protective factor OR= 0.3 [CI95%: 0.1-0.7] p<0.001.
Conclusion: This study shows that epilepsy-related CM is an important problem but under-recognised. It emphasises the need for studies to better appreciate the role of convulsions during CM and sickle cell disease.

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Epilepsy in Patients with Congenital Cytomegalovirus Infection
Y. Suzuki[1], K. Ogawa[1], T. Nagai[2], Y. Mogami[1], Y. Toribe[1]

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Purpose: To define the features of epilepsy associated with congenital cytomegalovirus (CMV) infection, and to determine the risk factors predictive of epilepsy.
Methods: We retrospectively reviewed the clinical data at birth, development of epilepsy, EEG findings and neuroimagings (CT and MRI) in 19 children (male 10, symptomatic 14) with congenital CMV infection who were referred to us between 1981 and 2004.
Results: Ten (53%) patients had developed various types of seizures (epileptic spasms 2, partial seizure 7, and myoclonic seizure 1) at a mean age of 25 months (range 2-67 months). During the course of disease, 4 children with West syndrome, including 2 whose partial seizure evolved to epileptic spasms after one year of age, developed other types of seizures. At the time of the last follow-up (mean 93 months), seizures remained uncontrolled in 6 patients. With the exception of gestational age, there were no significant differences between the children with epilepsy and those without epilepsy regarding gender, birth asphyxia or symptoms at birth. Of the neuroradiological abnormalities, however, the presence of ventricular dilatation, calcification and migration disorder were significantly associated with the development of epilepsy.
Conclusion: In patients with congenital CMV infection, a variety of epileptic seizures occurred. Our data suggest that neuroimagings might be more helpful in the identification of infected children who are at risk of the development of epilepsy.

Wednesday 31st August 2005
15:30 - 17:00
Salle 253
Platform Session
Drug Therapy - Treatment Issues in Emerging Countries

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Prevalence of Medically Refractory Epilepsy: A Community-based Study in South India (Comprehensive Rural Epilepsy Study – South India - CRESSI)
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Purpose: To study the prevalence of medically refractory epilepsy in a rural community in South India.
Methods: Prevalence of epilepsy was studied by a door-to-door survey in 22 villages, geographically clustered in one region in Andhra Pradesh, a province in South India. Treatment gap was also determined. All the cases ascertained clinically were prescribed conventional antiepileptic drugs (AED) and were followed at regular intervals. We modified defined daily dose (DDD) values assigned by the World Health Organization (WHO) to suit the body weight of the local population. To calculate the dosage of AEDs, we used the ratio of the prescribed daily dose (PDD) to the modified DDD. No therapeutic drug monitoring was done. All patients were started initially on monotherapy, when failed, were changed to alternate monotherapy. When the patients failed on two monotherapy trials, they were put on two or three AEDs. Any patients who did not achieve seizure freedom within 2 years of AED therapy were considered to have medically refractory epilepsy.
Results: Prevalence study identified 462 patients with epilepsy (crude prevalence – 6.2 per 1000). Treatment gap on the prevalence data was 81.5%. Of the 396 patients who could be followed for > 2 years, 122 (31%) patients did not achieve seizure freedom for > 2 years. Thus the crude prevalence of medically refractory epilepsy was 1.65 per 1000 population. Of the 274 (69%) patients who achieved > 2 years of seizure freedom, 237 (59.8%) patients achieved seizure freedom with monotherapy, 35 (8.8%) achieved seizure freedom with duotherapy and 2 (0.5%) with polytherapy.
Conclusion: In this community-based study the proportion of patients with medically refractory epilepsy was similar to the studies in developed countries. The AED response was also similar.

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Dapsone for the Treatment of Patients with Drug-resistant, Partial-onset Seizures: An Open-label Trial
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Purpose: To assess the efficacy and safety of dapsone as adjunctive therapy in adult patients with drug-resistant partial-onset seizures.
Methods: 22 adult patients with drug-resistant partial-onset seizures receiving two or more anti-epileptic drugs (AEDs), were included in the study. After a three month follow-up baseline period, patients received dapsone 100 mg per day for a three month evaluation period. Seizure frequency during the evaluation period was compared with the previous 3 month baseline period values. Plasma concentrations of dapsone and other AEDs were determined to evaluate potential drug interactions. Adverse reactions associated to dapsone add-on were also recorded.
Results: 16 of 22 patients (72.7%) reduced their seizure frequency by more than 50% as a result of dapsone treatment, in comparison to baseline values. 3 subjects remained seizure free during the entire

dapsone treatment period. Dapsone did not significantly affect plasma concentrations of any of the concomitant AEDs during the study. The reported adverse events were: mild methemoglobinaemia (50%), headache (31.8%), paleness (27.3%) and somnolence (4.5%).
Conclusion: This open-label study of adjunctive dapsone therapy at 100 mg/day shows that dapsone is safe, effective and well-tolerated in adults with drug-resistant partial-onset seizures. A randomised, placebo-controlled, double-blind trial of adjunctive dapsone therapy in patients with refractory partial-onset seizures is warranted and currently ongoing to further substantiate the use of dapsone as adjunctive therapy for drug-resistant epilepsy.

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A World Health Organisation Demonstration Project on Community Control of Epilepsy in 6 Rural Areas of China
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1) Beijing Neurosurgical Institute, Beijing, P.R.China 2) Mental Health Division, WHO, Switzerland 3) International Bureau for Epilepsy, The Netherlands 4) National Hospital for Neurology and Neurosurgery/Institute of Neurology, London, UK

Purpose: In order to develop and test a model on managing and treating people with convulsive forms of epilepsy at primary health level in rural areas of China, a demonstration project supported by funds from WHO was carried out in 6 provinces in China between 2001 and 2004.
Methods: 6 provinces in China were selected to attend the demonstration project. This project was composed of three parts as follows: 1) epidemiological estimation; 2) service delivery which covered the issues of diagnosis, phenobarbital treatment, following-up patients and referral networks. 3) educational, social and community intervention.
Results: The epidemiological survey showed the prevalence rate of epilepsy in the rural areas was 7.0%, and the prevalence of active epilepsy was 4.6%.The treatment gap in patients with active epilepsy was 62.6%. By the end of June 2004, a total of 2455 patients with generalised convulsive seizures in 6 demonstration areas were screened and entered the treatment group. The patients were treated by those town clinical physicians who were trained the method of using phenobarbital. The result of observations during 24 mouths revealed that 30.3% of patients had been seizure-free; for 24.6% of patients the number of seizures decreased □75% as compared with the state 6 months before entering the group. About 26% of people had mild side effects, 3.7% had middle, and only 0.3% of the patients had severe side effects when increasing the dosage of phenobarbital in the first 3 months.
Conclusion: This study verified that the protocol of 'Epilepsy management at primary health level' was suitable in rural areas of China. The trained physicians could master the formulated method to treat patients with epilepsy using phenobarbital.

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Reducing the Global Burden of Epilepsy: A Comparative Cost-effectiveness Analysis of Anti-epileptic Drugs in Low- and Middle-income Regions
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Purpose: Despite the negative impact of epilepsy on public health, there remains a yawning treatment gap in most regions of the world. In order to stimulate new investment into its appropriate management, there is a need to clearly demonstrate that interventions for epilepsy are not only effective and sustainable, but also affordable.
Methods: WHO has embarked on a new initiative to assemble databases on the cost-effectiveness of key health interventions in 14 epidemiological sub-regions. Costs and effects of older and newer anti-epileptic drugs (AEDs) provided in primary care were compared to an epidemiological situation representing the untreated natural history of epilepsy. Effectiveness was expressed in terms of DALYs averted (i.e. reduced burden) and costs were expressed in international dollars.
Results: Across nine developing WHO sub-regions, extending AED treatment coverage to 50% of primary epilepsy cases would avert between 150-650 DALYs per one million population (equivalent to 13-40% of the current burden), at an annual cost per capita of I$ 0.20-1.33. Older first-line AEDs (phenobarbitone, phenytoin) were most cost-effective on account of their similar efficacy but lower acquisition cost (I$ 800-2,000 for each DALY averted).
Conclusion: A significant proportion of the current burden of epilepsy in developing countries is avertable by scaling-up the routine availability of low-cost anti-epileptic drugs. Critical factors in the successful implementation of such a scaled-up level of service delivery, apart from renewed political support and investment, relate to appropriate training and continuity of drug supply.

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Organisation of Epilepsy Care Services at a Tertiary Care Teaching Hospital
B. Vengamma[1]

1) Sri Venkateswara Institute of Medical Sciences, Tirupathi, India

Purpose: Most with epilepsy living in rural India do not receive any treatment, or drop out from treatment prematurely. Given the fact that 70-80% of people with epilepsy can lead normal lives if properly treated, it is time to investigate solutions for reducing the treatment gap.
Methods: Monthly camps for epilepsy patients were started in February 1999, by Indian Epilepsy Association, Tirupati for, the systematic evaluation, counselling, monitoring, and distribution of appropriate antiepileptic drugs for one month duration to all participants.
Results: As on January 2005, 72 monthly camps have been conducted with 350 to 375 poor patients attending each camp. Data obtained from 330 patients (mean age 23 ± 12 years; 200 males; follow-up duration 5 years) were analysed. Mean duration of epilepsy was 85 ± 86 months; 95% belonged to a low socio-economic group of daily wage earners and farmers in drought prone and backward areas. Primary generalised tonic clonic seizures were the commonest (51%), followed by simple partial seizures (30%), complex seizures (16%) and other types (4%). The majority (95%) of patients had a single type of seizures. 58% of the patients were followed-up regularly. Of these, 65% had good seizure control (seizure free interval of >2 years); 88% of patients on DPH/PB had good seizure control.
Conclusion: Identification of the factors responsible for the treatment gap, their rectification, proper counselling and making drugs available and accessible can help in rational and effective management of epilepsy and improving quality of life.

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Addressing the Treatment Gap: A Pilot Programme of Access to Anticonvulsants in Rural Mali
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Purpose: The cost and accessibility of anticonvulsants and medical care are far beyond the reach of rural populations in developing countries. Programmes based on free access to drugs initiated in developed countries have limited duration and impact.
Methods: Following 1) the country doctors programme creating independent medical practices in rural areas (organised by Santé-Sud, a NGO based in Marseille, France, and financed by the EU), and 2) a preliminary pilot study of epilepsy with free delivery of phenobarbital (PB) in selected rural areas, our group initiated in 2003 a long-term project delivering generic PB. Valproate (VPA), bought at production cost, was added in September 2004, and carbamazepine is under discussion. A special grant by Sanofi-Aventis allows us to follow patients individually over the first 3 years of treatment.
Results: On 31 December 31 2004, 686 patients had been included in the program (84 onVPA).

Conclusion: Long-term success is possible only if there is no contamination of the existing drug market and if the drugs are used to their best potential. This requires: 1) total control of delivery, from factory to final purchase by patients, through special import procedures, local storage and delivery on demand to prescribing doctors; 2) an adequate level of knowledge on indications/safety of AEDs by local physicians, ensured by yearly seminars; 3) an economically sound structure, with a slight margin added at the various steps and an affordable end price for the patients, estimated at below 5-10% of the local per capita GNP.

Wednesday 31st August 2005
15:30 - 17:00
Salle 243
Platform Session
Basic Science 3

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Cell Swelling Precedes and Accompanies Electrographic Seizures: An Impedance Study
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Purpose: The cellular processes that take place during the transition from pre-seizure state to seizure remain to be defined. In this study in awake, paralysed rats, we provide evidence of the participation of cell swelling in this process using an electrical impedance measure of changes in extra-cellular intracranial volume.
Methods: Animals were prepared with extradural surface EEG/impedance electrodes and a venous catheter. On a subsequent day, animals were paralysed and ventilated and were treated with either picrotoxin, kainic acid or fluorocitrate in doses that can induce epileptiform discharges. EEG and cerebral impedance were recorded continuously for up to 90 minutes.
Results: Increases in baseline impedance were induced by kainic acid (12.9 +/- 1 ohms) and smaller increases by picrotoxin (4.4 +/- 1.2 ohms), and epileptiform discharges were usually preceded by small, accelerated increases in impedance. Fluorocitrate had no effect on baseline impedance but discharges were preceded by increased impedance. Increases in overall impedance appeared to correlate with increases in power of non-ictal low and high frequency EEG activity. Seizures were accompanied by increases in impedance (kainate 3.7 +/- 0.5, picrotoxin 13 +/- 2.8, fluorocitrate 0.3 +/- 0.1 ohms) and all treatments induced transient, relatively large, increases in impedance (range 3.8-13 ohms) associated with unilateral reductions in low frequency EEG, possibly periods of spreading depression.
Conclusion: Cerebral cells swell prior to epileptiform discharges and swelling may contribute to the transition to seizure but cell swelling alone does not determine transition to seizure. Spreading depression-like events occur in these models.

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Focal Delivery of Gap Junction Blockers in the Tetanus Toxin Model of Epilepsy in Rats
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Purpose: To investigate the role of gap junctions, and assess the efficacy and tolerability of focal delivery of gap junction blockers in a model of refractory cortical epilepsy in rats.
Methods: Epilepsy was induced by injecting 50ng of tetanus toxin into the motor neocortex of rats as previously described (Nilsen, Epilepsia 2005:46;179-187). Using a cannula placed at the seizure focus during surgery, the effect of gap junction blockers delivered directly to the epileptic focus was assessed in freely moving non-sedated animals. 4microlitres of 150mM Carbenoxolone (n=3), 50mM Meclofenamic acid (n=5) or 0.9% saline were injected (n=9). No additional sedation was required, and EEG and behavioural parameters were monitored throughout, and analysed using the Mann Whitney U-test ($p<0.05$), with each animal (pre-drug) serving as its own control.
Results: Tetanus toxin induced mild frequent and consistent focal seizures as reported previously. A reduction in seizure frequency was seen following both Meclofenamic acid (%time seizing:17.2+/-5.8(SEM) at 20-30mins vs 58.3+/-3.7 1hr predrug; $p=0.018$) and carbenoxolone (9.3+/-3.5 at 20-40mins vs 69.4+/-7.0 predrug; $p=0.05$), with no observable side effects. By 40-50 minutes seizures returned to baseline. Saline had no effect.
Conclusion: Gap junctions are thought to be important in the propagation and maintenance of seizures, but systemic toxicity limits in-vivo investigations. Focal application of two different gap junction blockers results in an immediate reduction in seizure frequency. Whether the duration simply reflects drug dispersion, or other mechanisms requires further study. These experiments support further investigation of gap junction blockers and/or longer-term focal drug delivery strategies for refractory focal epilepsy in man.

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Voltage-Depth Analysis of Initial Slow Wave Seizure Onsets in a Rat Chronic Model of Epilepsy
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Purpose: Seizures having low voltage fast (LVF) onsets are usually generalised and accompanied by an initial slow wave (ISW) in hippocampal and cortical areas. To investigate the source of these seizure onsets, voltage-depth profile analysis of the ISW was performed using a movable microelectrode array.
Methods: Wideband, 0.1Hz-5kHz recordings were made in freely moving pilocarpine treated adult Wistar rats with recurrent spontaneous seizures. An array of 12 microelectrodes with 0.5-1.0mm horizontal separation were positioned sagittally above the neocortex 2.0mm from midline. As the array was moved at 0.4 mm steps vertically down through neocortical, subcortical and hippocampal structures, one or more seizures were recorded at each step. The peak of ISW at seizure onsets recorded from a fixed neocortical microelectrode formed a reference to temporally align all other seizures.
Results: Relative to skull screws above cerebellum, ISW showed initial negative or positive-negative polarity during recordings of seizure onsets in the neocortex, but at the DG granule cell layer was positive. ISW showed no phase reversal in any microelectrode penetrating neocortical cellular lamina, grey-white matter borders, caudate nucleus or ventricular space. ISW amplitude decreased while approaching the hippocampus and showed phase reversal in DG. ISW preceded changes in multiple unit neuronal activity during seizure onset.
Conclusion: The absence of ISW phase reversal in the neocortex and instantaneous ISW appearance at all microelectrodes simultaneously with an apparent source in the hippocampus is not consistent with normal conduction and synaptic delays associated with propagation of seizure activity. Therefore, the source of this commonly recorded seizure onset pattern remains unknown.

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Expression of Multidrug Resistance Gene 1 P-glycoprotein (MDR1) in Intractable Epilepsy with Different Aetiologies: A Double-labelling and Electron Microscopy Study
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Purpose: To study clinical characteristics, pathological features, expression patterns of MDR1 and GFAP in intractable epilepsy patients with variable aetiologies and to analyse the relationships between clinical and pathological findings.
Methods: 26 patients (15 males, 11 females, age range 4-25 years, mean age 22.92 years, SD 11.19 years) with intractable epilepsy were included in this study. The clinical characteristics were considered, and the pathological changes as well as the expression of MDR1 and GFAP in surgically resected brain tissues of each subject were examined under light and electron microscopy. Relationships between clinical and pathological aspects were studied.
Results: All patients presented a long-lasting, refractory epilepsy, mostly of the partial type, due to different causes, such as trauma, vascular injuries, encephalitis, cortical dysplasia, cavernous angioma, and Sturge Weber disease. Neuronal degenerative damage, reactive proliferation of astrocytes, as well as over-expression of GFAP and MDR1 appeared as common pathological features in all cases.
Conclusion: In this study, the detection of MDR1 by electron microscopy allowed us to precisely define its cellular location in reactive astrocytes and to exclude the presence of the antigen in other cellular types. In all cases, pathological features, at both light and electron microscopy, are similar, independent of different clinical presentations and aetiology.

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Influence of Infantile Status Epilepticus on Subsequent Susceptibility to Brain Ischemic Injury in Rats
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Purpose: Status epilepticus (SE) frequently occurs in childhood, while ischemic stroke is the most frequent neurological insult in adulthood. The purpose of this study was to determine the effect of SE induced in PN15 male rats, on susceptibility to subsequent transient focal cerebral ischemia induced in adulthood.
Methods: SE was induced by exposure to flurothyl ether (FE) or systemic of kainic acid (KA, 3.5 mg/kg i.p.) and confirmed electroencephalographically. Rats which did not develop SE were used as respective controls. Five weeks later, the now adult rats were subjected to 1 or 2 hour long middle cerebral artery occlusion (MCAo) using the intraluminal filament technique. 24 hours later rats were sacrificed and a measurement of the volume of brain infarction was performed.
Results: In rats submitted to 1 hour long FE SE in infancy, the volume of infarction after 1 hour long MCAo in adulthood was significantly reduced compared to rats exposed to FE without SE. A hypoxic-preconditioning-like effect was ruled out because no arterial blood hypoxia was observed after SE. In rats previously submitted to KA SE, the volume of infarction after 1 hour long MCAo induced in adulthood was significantly larger compared to their respective controls.
Conclusion: Our results show that an early SE can influence the outcome of a focal ischemic insult induced in adulthood. Prolonged SE induced by KA worsens the outcome while FE SE has a neuroprotective effect. The extent of the infarct might be related to the duration and cause of SE. Supported by NIH grants NS20253 (SLM), EY11053 (DMR) and K12NS48866 (SLM), by the Heffer Family Medical Foundation (SLM), and by a grant from C.U.R.E. Foundation (JV).

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Angiogenesis is Associated with Hippocampal Remodelling in Human Temporal Lobe Epilepsy
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Purpose: An important vascularisation is frequently observed in chronic epileptic foci, particularly in cases of severe lesions and neuro-glial reorganisation. We attempted to provide evidence of an angiogenesis in chronic foci of adult patients with intractable temporal lobe epilepsy (TLE). To approach the mechanisms of this vascular reorganisation, we looked for the kinetic of angiogenic processes in murine models of TLE.
Methods: Human subjects: hippocampi were obtained in 30 patients who underwent surgery for intractable TLE (with various aetiologies and different degrees of neuronal loss) and in 4 non-epileptic, autopsied patients (NE). Animal models: the lithium-pilocarpine model was applied to 20 rats and 20 mice. Hippocampi were used for immunohistochemistry and western blotting to check the expression of angiogenic factors or their receptors and markers of immature endothelial cells.
Results: In humans, microvessels were more numerous in the hippocampus of TLE patients than in NE hippocampi. Particularly in case of hippocampal sclerosis, neo-microvessels were positive for various markers of immature endothelial cells in injured areas and in the dispersed dentate granular layer. In most patients, VEGF was strongly expressed by pyramidal and granular neurons and also by astrocytes. In animals, angiogenic factors were rapidly detected by hippocampal neurons and glia after experimental seizures.
Conclusion: Angiogenic processes appear to be concomitant to the neuro-glial reorganisation that occurs in lesional epilepsy of adults. Even if VEGF expression reflects a protective mechanism triggered by the seizure itself, the neo-vascularisation could participate in the pathological remodelling of the chronic focus.

Monday 29th and Tuesday 30th August 2005
13:15 – 14:15
Poster Session
Genetics

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Association Study of Five Sodium Channel Genes in Epilepsy and Antiepileptic Drug Response
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Purpose: Voltage-gated neuronal sodium channel genes are candidates for susceptibility to epilepsy and variation in antiepileptic drug (AED) response. This study examines associations of the genes SCN2A, SCN3A, SCN8A, SCN1B and SCN2B with several types of epilepsy and AED response.
Methods: Using both resequencing and HapMap data, we selected, using the haplotype r2 method, 25 tagging single nucleotide polymorphisms (tSNPs) representing common variation across these genes. These tSNPs were genotyped by TaqMan assays in 439 North Western European patients with epilepsy and 364 controls. We assessed genotypic, allelic and haplotypic association with the following seven phenotypical categories: all epilepsies, idiopathic generalised epilepsy, symptomatic epilepsy, cryptogenic epilepsy, AED response according to two different classification systems, and

combined response to AEDs with a major action on sodium channels (phenytoin, carbamazepine, lamotrigine and oxcarbazepine). For each gene, we corrected for the seven different phenotypes and for the number of SNPs tested.
Results: Several tests reached statistical significance before correction for multiple testing. After correction, the association of SCN3A haplotypes with all epilepsies and cryptogenic epilepsy remained significant at a significance level threshold $p \leq 0.007$.
Conclusion: Our results suggest a possible association of the SCN3A gene with different types of epilepsy. Association studies of the other genes did not show any statistically significant results. However, our stringent correction for multiple testing may cause nominally significant results to become negative. Replication in a large, independent patient cohort is warranted before any result can be confirmed.

p146
Pharmacogenomics of Epilepsy: Multiple Independent SNP Studies may be of Limited Value in Predicting Response to Drug Treatment in Small Cohorts of Epilepsy Patients
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Purpose: Pharmacogenomics is the study of genetic influences on the response to drug treatment and is pertinent to disorders such as epilepsy in which more than 30% of patients fail to respond to current medications. We have commenced a pharmacogenomic investigation in a cohort of epilepsy patients attending our tertiary referral centre.
Methods: 400 epilepsy patients have been included in the study to date (118 idiopathic generalised, 270 localisation related, 12 unclassified). Genomic DNA was extracted from venous blood and single nucleotide polymorphisms (SNPs) investigated by PCR and restriction digest. Patients were categorised as responders (seizure free for at least 12 months) or non-responders by review of case notes and seizure diaries. Allele and genotype frequencies were compared by logistic regression analysis.
Results: A total of 170 (42%) patients were classified as responders and 230 (58%) as non-responders. The prevalence of recognised SNPs in the MDR1, SCN1A, SCN2A, GABBR1, IL1B, 5HTT and KCNJ10 genes was correlated with outcome. Only the R19K polymorphism in the SCN2A gene showed a significant association with response to treatment, with variant genotypes present in 8% of responders and 16% of non-responders (odds ratio 2.07, 95% CI 1.08-3.97, p=0.024). All other analyses were without significant findings.
Conclusion: Performing studies of single SNPs in small cohorts of adult epilepsy patients appears to be of limited value in predicting response to drug treatment. Large-scale investigations of variations across entire genes in less heterogeneous populations of patients may be required before the pharmacogenomics of epilepsy can be unravelled.

p147
Monitoring of Treatment Response in Patients with TLE by Gene Expression Analyses
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Purpose: The purpose is to study possibilities of obtaining valid and reproducible expression values of drug regulated mRNAs in peripheral blood cells of epilepsy patients. The hypothesis is that mRNA expression reflects the genetic background in epilepsy patients. Thus studies of expression profiles may elucidate the patient's disposition for epilepsy and the risk of a patient to develop drug resistance.
Methods: MRNA analyses are limited to patients with temporal lope epilepsy. Focus is on identification of mRNA expression levels that are related to the efficacy of certain anti-epileptic drugs. Children with a well-characterised temporal lope epilepsy diagnosis are identified among patients at the Danish Epilepsy Centre. In order to limit the expected high variation in gene expression profiles among patients mRNA analyses are restricted to patients undergoing only one out of five established medicinal treatments. For each patient blood samples are collected for mRNA extraction and subsequent expression analysis. An additional blood sample is collected for storage in a bio bank with the prospect of future elucidation of the genetic background.
Results: Children have been characterised in terms of seizure control, adverse drug reactions, manifestation of the epileptic syndrome, epilepsy familiar disposition, primary cerebral abnormalities, metabolic disorders and behavioural deficits. Based on these data 78 children were identified. Among these a cohort with full seizure control (n=15) and a cohort without seizure control (n=49) were defined. The experimental design of five medicinal treatments defines five groups within each cohort.
Conclusion: Patients fitting the inclusion criteria were identified.

p148
Kinin B1 Receptors, Not B2, Play an Essential Role in the Development of Experimental Temporal Lobe Epilepsy
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1) Universidade Federal de São Paulo, Sao Paulo, Brazil 2) Max-Delbruck Zentrum fur Molekulare Medizin

Purpose: The importance of kinin receptors in the development of temporal lobe epilepsy (TLE) has been investigated by our group. As recently reported [Arganaraz GA et al. Brain Res. 2004; 1013(1):30-39], animals lacking kinin receptors showed antagonist behaviours regarding to TLE establishment. In the present work, we investigated the expression of the remaining kinin receptor in each knockout mice strains, B1KO and B2KO, at different disease phases (acute, silent and chronic).
Methods: B1KO, B2KO and their wild-type (WT) mice strains (n=12, per group) were previously treated with scopolamine methylnitrate (1 mg/kg) followed by a pilocarpine injection (320 mg/kg). Behaviour parameters were monitored to determine different stages of TLE progression. After hippocampal RNA extraction, mRNA expression was evaluated by Real Time-PCR using specific primers for both kinin receptors.
Results: B1KO mice in the acute (0.85 ± 0.28; p=0.32), silent (0.83 ± 0.23, p=0.30) and chronic phases (0.61 ± 0.49) (p=0.64) showed no differences in B2 receptor mRNA expression when compared with their control animals (normalised to 1). In contrast, in B2KO mice, we observed an increased B1 receptor mRNA expression in treated animals (1.97 ± 0.14 and 1.83 ± 0.21, for acute and silent, respectively, $p<0.001$; and 1.35 ± 0.13, for chronic animals; $p<0.05$) when compared with their control group.
Conclusion: Our results suggest that kinin B1 receptor, not B2, is an impaired and essential factor to the development of epilepsy of both kinin receptor knockout mice strains.

p149
Gene Expression Profile in Knockout Mice for Kinin B1 Receptor after Pilocarpine-induced Epilepsy
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Purpose: Recent reports have shown the importance of kinin receptors in the development of temporal lobe epilepsy (TLE). In order to understand the genetic role of kinin B1 receptor in epilepsy, we used a knockout mice strain for kinin B1 receptor (B1KO) submitted to pilocarpine model of TLE to investigate gene expression pattern in acute phase of the disease.

Methods: B1KO mice strain (n=12, per group) was previously treated with scopolamine methylnitrate (1 mg/kg) followed by a pilocarpine injection (320 mg/kg). B1KO control group was treated with saline. After 3 h of status epilepticus, hippocampi were removed and hippocampal RNA extraction was performed. Effects of pilocarpine-induced epilepsy on the expression profile of the cerebral genes were investigated. The gene expression pattern was achieved by using a mouse brain cDNA microarray consisting of 1176 gene sequences (Atlas Mouse 1.2 array - Clontech).
Results: As results, we found that in pilocarpine-treated B1KO mice the most prominent gene cluster had growth factor genes such as BDNF (brain-derivated neurotrophic factor), NGF (nerve growth factor), FGF15 and FGF6 (fibroblast growth factor) in a central position. Downregulation of these genes indicated less intense neuronal activity and injury after pilocarpine injection. Downregulating of apoptosis-related genes, specially caspase 3 and 9 were also observed in B1KO pilocarpine-treated animals.
Conclusion: In conclusion, this work indicates an overriding participation of kinin B1 receptor and growth factors in epilepsy establishment and provides a working model for the involvement of the kallikrein-kinin system in neuronal cell death.

p150
Alterations in KCNJ4 Potassium Ion Channel Gene Expression in Human Temporal Lobe Epilepsy
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Purpose: The purpose of this research was to evaluate the possible molecular pathogenesis of intractable temporal lobe epilepsy (TLE). The potassium ion channel gene KCNJ4 encodes one of the subfamilies of Kir channels, Kir 2.3 subunit, which may play an important role in modulating neuronal excitation. Interference in its function or expression would cause disturbance of ionic concentrations, thus lead to seizure activity.
Methods: Our research program used reverse transcription polymerase chain reaction (RT-PCR) and western blot analysis to measure the expression alterations of KCNJ4 mRNA as well as its protein product Kir2.3 channel in temporal cortex samples from patients who had undergone temporal lobectomy surgery for intractable epilepsy (n=12). Nonepileptic brain tissue served as control (n=10).
Results: The expression of KCNJ4 mRNA and its protein product were significantly decreased in the epileptic brain over autopsy control ($p<0.05$).
Conclusion: These results suggest that this variation in KCNJ4 expression could be a potential aetiological agent for TLE, and might offer a novel target for anticonvulsant therapy.

p151
Serial Analysis of Gene Expression in the Hippocampus of Patients with Temporal Lobe Epilepsy
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Purpose: Hippocampal sclerosis (HS) constitutes the most frequent neuropathological finding in patients with medically intractable temporal lobe epilepsy (TLE). The cellular and molecular events leading to permanent structural and functional changes characteristic of this hippocampal pathology are incompletely understood. The development of epilepsy surgery opened new prospectives for epilepsy research, providing histopathologically well characterised hippocampal human specimens, which can be analysed using molecular biological techniques.
Methods: Serial analysis of gene expression (SAGE) was used to get a global view of the gene profile in the human hippocampus in control conditions and in epileptic conditions associated with HS. Libraries were generated from control hippocampus, obtained by rapid autopsy, and hippocampal surgical specimens from patients with TLE and the classical pattern of HS.
Results: More than 50,000 tags were analysed (28,282 control hippocampus; 25,953 HS) resulting in 9,206 (control hippocampus) and 9,599 (HS) unique tags (genes), each representing a specific mRNA transcript. Comparison of the two libraries resulted in the identification of 143 transcripts that were differentially expressed. These genes belong to a variety of functional classes, including basic metabolism, transcription regulation, protein synthesis and degradation, signal transduction, structural proteins and genes of unknown identity of function.
Conclusion: The database generated by this study represents the first inventory of gene expression in the human hippocampus, identifies new high-abundant genes associated with altered hippocampal morphology in patients with TLE and serves as a reference for future studies aimed at detecting hippocampal transcriptional responses under various pathological conditions.

p152
PTEN Mutations are Not a Major Cause of Familial Temporal Lobe Epilepsy
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Purpose: Mutations in the PTEN (phosphatase and tensin homologue deleted on chromosome 10) gene cause Cowden Syndrome in humans, an autosomal dominant syndrome associated with cancer and epilepsy. PTEN knockout mice have seizures and hippocampal gliosis, phenotypically similar to humans with temporal lobe epilepsy (TLE) and hippocampal sclerosis (HS). As familial TLE (fTLE) is an autosomal dominant epilepsy syndrome associated with hippocampal abnormalities, PTEN is a plausible candidate gene for fTLE. We thus screened for PTEN mutations in a cohort with fTLE.
Methods: We recruited 41 families with varying fTLE syndromes, including fTLE with and without HS, fTLE with a family history of febrile seizures, autosomal dominant partial epilepsy with auditory features where LGI1 mutations were absent, TLE associated with heterogeneous focal epilepsy syndromes, and familial partial epilepsy with variable foci. One affected member diagnosed with TLE from each family was selected for genetic analysis. We also identified 4 individuals with sporadic TLE and a personal or family history of cancer. The coding and promoter regions in PTEN were screened via single-strand conformation polymorphism (SSCP) in all 45 subjects. Variants detected by SSCP were confirmed by sequencing, and their frequency compared with healthy controls.
Results: One intronic single nucleotide polymorphism was found at the same frequency in fTLE cases and healthy controls; it was unlikely to affect gene expression or function. Mutations in the coding or promoter regions of PTEN were not detected in familial or sporadic TLE cases.
Conclusion: We conclude that mutations in PTEN are not a major genetic cause of fTLE.

p153
Tumour Necrosis Factor Alpha Gene Polymorphisms in Mesial Temporal Lobe and in Idiopathic Generalised Epilepsies
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Purpose: Mesial temporal lobe epilepsy (MTLE) has been associated to the occurrence of febrile seizures (FS) (Baulac S et al., Lancet Neurol 2004; 3: 421-30). The presence of elevated cytokine levels in plasma and/or CNS in FS patients and the genetic involvement in FS pathogenesis (Virta M, et al., Epilepsia 2002; 43: 920-3; Nakayama J et al., Neurology 2004; 63: 1803-7) lead us to hypothesize a possible involvement of cytokine polymorphisms in MTLE. The purpose was to evaluate if two single nucleotide polymorphisms (SNPs) in the promoter region of TNFA (-308G>A and -238G>A) could be differentially distributed among patients with MTLE.
Methods: 94 epilepsy patients, 26 with MTLE, 33 with juvenile myoclonic epilepsy (JME) and 35 with other idiopathic generalised epilepsies (IGE) were studied and results compared to a control group of 222 healthy individuals from the same origin. TNFA genotyping was assessed by melting curve analysis with fluoroscein-labelled hybridization probes after PCR amplification.
Results: TNFA-308G>A and -238G>A polymorphism frequencies were homogeneously distributed among MTLE patients either comparing with IGE, JME and controls. The -308A allele was underrepresented in the JME comparing to all other groups frequencies. This finding was suggestive when IGE group was considered (7.1% in JME vs 19.7% in IGE, p=0.031 (Pearson's Chi-square).
Conclusion: Converse to our previous findings pointing to a possible linkage disequilibrium between EMJ1 susceptibility locus and TNFA -308 and -238 promoter polymorphisms, this association was not observed in MTLE patients. Nevertheless a direct functional effect of these SNPs in MTLE should not be ruled out. These first results require replication in a larger series of patients. Work supported by a BICE - TECNIFAR Grant for Epilepsy Research.

p154
A Missense Single Nucleotide Polymorphism (RS2228292, E718D) in CLCN2 Associated with Absence Epilepsy
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Purpose: The aim of this work was to evaluate CLCN2 as a candidate gene for absence epilepsy (AE).
Methods: A resource of 82 nuclear pedigrees (with 185 affecteds) and 302 parent-child trios with AE was ascertained. Parametric and non-parametric linkage analysis using microsatellites (D3S3609 and D3S3583) spanning CLCN2 was performed. 15kb of genomic DNA including all coding exons, 1kb of the predicted promoter region and 1kb of the 3' region of CLCN2 was re-sequenced in 24 patients. A previously identified missense polymorphism (rs2228292) was found and subsequently genotyped in the entire resource. Intrafamilial association analysis was performed using the pedigree transmission disequilibrium test (PDT). Three previously identified epilepsy-associated mutations (597insG, IVS2-14del11, and G2144A) were screened for in the nuclear pedigrees.
Results: At the chromosome 3q27-q28 CLCN2 locus, the maximum heterogeneity LOD score (HLOD) was 1.17 (alpha=0.34), assuming autosomal dominant inheritance and a penetrance of 0.5. PDT analysis showed suggestive evidence for transmission disequilibrium of the rs2228292 minor allele in the entire resource (AVE-PDT chi-sq = 4.516, p=0.034). The variants 597insG, IVS2-14del11, and G2144A were not found in the pedigrees.
Conclusion: The results from the linkage and association analyses suggest that the CLCN2 gene may harbour susceptibility alleles in a subset of patients with AE. The missense SNP, E718D, may be a functional variant or in linkage disequilibrium with an unidentified functional variant. It changes a conserved residue close to the previously identified functional mutant, G715E (G2144A, Haug K et al. Nat. Genet. 2003; 33: 527-532).

p155
Absence Epilepsy: Evaluation of Linkage Disequilibrium and Allelic Association in GABRB3, GABRA5, and GABRG3 on Chromosome 15Q11-13
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Purpose: Linkage analysis in 82 nuclear pedigrees found suggestive evidence of linkage to the GABA(A) receptor gene cluster (GABRB3, GABRA5, and GABRG3) on chromosome 15q11-13. The aim of this study was to establish the pattern of linkage disequilibrium (LD) in this chromosomal region and perform SNP-based association analysis.
Methods: A resource of 82 nuclear pedigrees (including 185 affected) and 279 trios with absence epilepsy (AE) was ascertained. An LD map based on 35 SNPs (minor allele frequency >0.01) typed in 31 trios was constructed with the program HaploBlockFinder. Further LD structure analysis was then performed with the program HaploView. Twenty-eight tagSNPs were genotyped in the entire resource. Intra-familial association analysis was carried out using the pedigree transmission disequilibrium test (PDT).
Results: Linkage analysis using four microsatellites (GABRB3(CA), 155CA2, A55CA1 and D15S156) was performed using GeneHunter 2.1 assuming a disease allele frequency of 0.005 and penetrance values of 0.001, 0.5, 0.5. A maximum HLOD score of 1.75 was found (alpha=0.42) at marker A55CA1. PDT showed no evidence of association of AE with SNPs or SNP haplotypes in GABRA5 and GABRG3. In GABRB3 SNPs in introns 4 and 7, rs1432007 and rs1897356, showed association ($p<0.05$) in the entire resource. Analysis of the pedigrees alone showed association ($p<0.05$) with 2 different SNPs in intron 3: rs2162241 and rs970408. Haplotype-based association analysis of these two SNPs together showed association in the entire resource (p=0.03).
Conclusion: LD block structure in the GABA(A) receptor gene cluster has been characterised and suggestive evidence for association between GABRB3 and AE found.

p156
Digenic Inheritance in Photosensitive Idiopathic Generalised Epilepsy
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Purpose: The interplay of multiple genetic factors, as opposed to monogenic inheritance, is suspected to play a role in many idiopathic generalised epilepsies. This leads to a digenic or oligogenic inheritance model, which although rather simplified, may explain at least some of the clinical observations. The model is based on the assumption that the expression of a specific type of epilepsy depends partly on the interaction of two or more independent genetic factors.
Methods: We have used photosensitivity as a clinical marker for such a genetic factor.
Results: We examined two families in which the clinical phenotype in the offspring can be explained by a combination of a photosensitivity trait and an epilepsy trait that segregated independently of each other.

Conclusion: These cases demonstrate the need to evaluate family histories in more detail in order to uncover potential clinical markers for genetic factors in complex epilepsies.

p157
Genetic Studies in Families with Epilepsy and Photosensitivity
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Purpose: To improve the genetic characterisation of photosensitivity studying photosensitive epilepsy patients and relatives exhibiting photosensitivity, without seizures or having a history of spontaneous seizures.
Methods: Three families with photosensitive epilepsy patients were studied. Patients and relatives were assessed by means of a standard IPS protocol: 1-60Hz BW flash (see Kasteleijn-Nolst Trenité et al., Neurophysiol Clin 1999, 29:318-324 for methodology and terminology). The genetic study was conducted on the analysis of chromosome 6p21q region. A mutation analysis the cystatin B gene was performed to discard the possibility of progressive myoclonic epilepsy of Unverricht-Lundborg.
Results: Family 1: 2 patients with JME (brothers). Proband, female, with photosensitivity (PSW). Brother without. Mother had EEG/OR during IPS. Brother (without seizures) with EEG SW/OR, IPS induced. Daughter (a niece from proband) had GSW IPS induced; another son (nephew) had febrile seizures. Families 2 and 3 had the same clinical picture: proband with JME and relatives free of seizures. Family relatives have IPS EEG induced changes. Neither long expansions of the dodecamer repeat or exonic mutations were found. However, two different short expansions of the dodecamer repeat on cystatin-B gene were found in each of the probands of these two families, transmitted by the unaffected (free from EEG IPS changes) fathers.
Conclusion: The study of these families introduces three points for discussion: the role of specific genetic markers on the definition of the epilepsy phenotype in patients with photosensitivity; the identification of specific genetic markers related to EEG-IPS changes in families of patients with photosensitivity; its possible contribution to the mode of inheritance of photosensitivity in some families. Work supported by a BICE - TECNIFAR Grant for Epilepsy Research.

p158
Generalised Epilepsy with Febrile Seizures Plus: Evidence for Complex Inheritance and Overlap with Idiopathic Generalised Epilepsies
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Purpose: Generalised epilepsy with febrile seizures plus (GEFS+) is characterised by phenotypic and genetic heterogeneity. Three genes (SCN1A, SCN1B and GABRG2) have been confirmed as having a role in autosomal dominant GEFS+ families. Here, we analyse the phenotypes and clinical genetics of GEFS+.
Methods: Twenty new families with GEFS+ underwent electroclinical characterisation.
Results: 121 individuals in 20 families had seizures, 84 with previously recognised GEFS+ phenotypes: febrile seizures (FS) in 37, febrile seizures plus (FS+) in 16, FS+ with other seizure types (absence, atonic) in 7, myoclonic-astatic epilepsy in 7, and partial epilepsy with or without FS in 17 individuals. In 7 families, an additional 11 individuals had idiopathic generalised epilepsies (IGE): childhood absence epilepsy in 5, juvenile myoclonic epilepsy in 5, juvenile absence epilepsy in 1. 26 individuals had other phenotypes: tonic-clonic seizures with normal EEG in 5, Lennox-Gastaut syndrome in 1, unclassified seizures in 17, unconfirmed seizures in 3 individuals. Bilineal inheritance of seizure disorders occurred in 8 families.
Conclusion: This study expands the phenotypic spectrum of GEFS+ syndrome to include afebrile GTCS with generalised spike wave or normal EEG in the absence of FS. Partial epilepsy may occur with or without preceding FS. Our findings emphasise the inter-relationship of GEFS+ and IGE; shared genetic determinants probably account for the overlap of these syndromes in some families. Bilineal inheritance and small GEFS+ families add support for complex inheritance in a significant proportion of families.

p159
A Large Roma (Gypsy) Family with the Syndrome of Generalised Epilepsy with Febrile Seizures Plus Not Linked to the Known GEFS+ Genes
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Purpose: The syndrome of generalised epilepsy with febrile seizures plus (GEFS+) was revealed in several families and only some of them were associated with mutations of the genes of voltage-gated sodium channels or GABA (A) receptors. The purpose of the study is to describe and investigate genetically a large Roma family with GEFS+ syndrome.
Methods: A large inbred Roma family living in Southern Bulgaria with 162 family members in 6 generations was investigated. Individuals with putative seizure events were subjected to neurological and EEG examinations. Genomic DNA of these patients and their close relatives was investigated for mutations in the SCN1B, SCN1A, SCN2A and GABRAG2 genes.
Results: 25 individuals with putative epileptic seizures were identified. In 17 of them (14 male, 3 female) the seizures were assessed as epileptic and idiopathic. They were classified in the following phenotypes: febrile seizures – 6 cases; febrile seizures plus – 4 cases; afebrile generalised tonic-clonic seizures (GTCS) starting after the first decade -2 cases; Dravet syndrome - 1 case; unclassified phenotype – 4 patients with one or few GTCS in the first 2 years. In 14 of these 17 individuals the seizures were single or rare and in 10 of them they subsided without treatment. No pathogenic mutation in the above listed genes was found.
Conclusion: This is the first report of GEFS+ syndrome in a large Roma family. The phenotypic spectrum is similar to the other GEFS+ families but with male dominance and milder affection. No mutations in the known genes responsible for GEFS+ syndrome were discovered supporting genetic heterogeneity.

p160
Paroxysmal Dyskinesia, Epilepsy and Febrile Convulsions in a Large Belgian Family: Clinical Features, EEG and Imaging Findings
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Purpose: We describe clinical findings, EEG and imaging results in a family with autosomal dominant paroxysmal dyskinesia (PD), epilepsy and febrile convulsions (FC).
Methods: We identified 24 affected patients in a pedigree with 68 family members. We obtained a structured interview (n=23), DNA (n=42), interictal EEG (n=16), CT or MRI (n=11), video-EEG monitoring (n=4), video-EEG registration and ictal SPECT of a PD attack (n=1) and interictal FDG-PET (n=1).
Results: 5 had FC. 13 reported afebrile seizures: absences (n=5), complex partial seizures (n=1) and generalised tonic-clonic seizures

(n=8). PD was diagnosed in 11 patients, and was characterised by choreoathetosis (n=11) and dystonia (n=4), involving predominantly the lower limbs with varying lateralisation. Precipitating factors for PD were prolonged physical exercise, emotional stress and starvation. A tingling sensation in the legs preceded PD in 3. Median age of onset of PD was 8 years. Median duration of PD attacks was 30 minutes. Interictal EEG showed generalised epileptic abnormalities in 10. Ictal EEG during one PD attack was normal. Subtraction ictal SPECT of a PD attack involving the legs showed hyperperfusion bilaterally in the leg motor areas and basal ganglia. Interictal FDG-PET in the same patient showed hypometabolism in the leg motor areas. DNA analysis excluded linkage to known PD loci.
Conclusion: We present the largest family ever described with co-occurrence of PD, epilepsy and FC. Based on our data, we postulate an autosomal dominant mutation causing paroxysmal disturbances in the cortico-striatal pathways with phenotypic divergence, i.e. co-occurrence of PD, epilepsy and FC.

p161
Familial Focal Epilepsy with Prominent Vertiginous Symptoms: A New Form of Hereditary Focal Epilepsy?
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Purpose: To describe a new form of familial focal epilepsy characterised by prominent vertiginous symptoms.
Methods: We collected 3 nuclear families including 6 affected individuals. Each patient underwent full clinical (personal and family history), EEG (routine and sleep tracings) and neuroradiological (conventional MRI) investigation. Mutations of the epitempin (LGI1) gene were searched for in at least one affected member of each pedigree.
Results: The onset of seizures ranged between 3 and 12 years (mean: 8). The seizures were characterised by prominent vertiginous (5 cases) or complex visual (metamorphopsia) (4 cases) symptoms followed by loss of contact. Forced deviation of the head and eyes was reported in 3 cases. Interictal EEG findings demonstrated paroxysmal abnormalities localised over the parieto-temporo-occipital regions of one side. MRI findings were negative. Seizures usually occurred on a monthly or sporadic basis and were completely suppressed by one drug (usually carbamazepine) therapy. The genetic study is still in progress.
Conclusion: We propose the existence of an homogeneous form of benign familial focal epilepsy with symptoms suggesting a parietal or parieto-temporal onset. Whether this is a separate epileptic entity awaits confirmation by genetic studies and description of further families.

p162
Observations of Concordant Focal Epilepsy in Monozygotic Quintuplets
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Purpose: To review the birth in 1934 and development of the premature monozygotic Dionne quintuplets.
Methods: They were closely followed by the media in the 20th century, and we received legal consent for hospital data.
Results: Emilie, whose uncontrolled epilepsy in her teen years was kept secret, was found dead in her bed at age 20. Because there was no family history, the quints regarded her epilepsy as a form of punishment. She had right adversive seizures with secondary generalisation. The history revealed that she was left-handed, that she had a 48-hour coma during a febrile illness at age 4 years and that she had "slight asymmetry of the face with flattening on the left" whereas before adolescence, all the quints had a constitutional right-sided asymmetry. Photographs of the time also show a progressive coarsening of her face features, possibly related to treatment with phenytoin. During investigation by W. Penfield and H.H. Jasper in 1947, her EEG showed bilateral frontotemporoparietal epileptic foci predominating on the left. At autopsy, Prof. Olszewski found left temporoparietooccipital atrophy and less marked right frontal atrophy, "similar to those observed in cases of infantile hemiplegia". Later published interviews of the remaining quints suggest that all may have had later-onset epilepsy. Marie reportedly had sudden unexplained falls and was found dead in bed at age 35. Annette, Cecile and Yvonne were diagnosed with epilepsy between 1993 and 1995. Cecile and Annette's seizures began with an olfactory aura.
Conclusion: These observations in monozygotic quintuplets revealed that early and later onset of focal epilepsy may develop over a 50 year interval in all five.

p163
A New Candidate Locus for Bilateral Perisylvian Polymicrogyria on Chromosome Xq27-q28
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Purpose: Recently, familial forms of BPP have been described and a candidate locus was mapped on chromosome (ch) Xq28, distal to marker DX8103. The objective of this study was to describe clinical and linkage analysis in 3 families segregating bilateral perisylvian polymicrogyria (BPP) and to establish genotype-phenotype correlations.
Methods: We studied 3 unrelated families segregating BPP. A total of 26 individuals, including 14 patients were evaluated in this study. All family members were examined by a neurologist and subjected to high resolution volumetric MRI scans with multiplanar reconstruction. Family members were genotyped for 6 polymorphic dinucleotide repeat markers: DXS1192, DXS1227, DXS8043, DXS8091, DXS8103, and DXS1073, flanking a 10 cM interval on ch Xq27-q28. Two-point lod scores were calculated for all families combined using the LINKAGE package.
Results: Clinical spectrum ranged from normal to mild neurological dysfunction, mainly pseudobulbar paresis, such as poor articulation and poor tongue movements. All 14 patients had BPP confirmed by MRI, in different anatomical distributions: 9 patients had only BPP, 3 had posterior parietal BPP and 2 had frontoparietal BPP. Linkage analysis yield a Zmax = 3.01 at theta=0.00 for DXS8091. Haplotype analysis showed two critical recombination events that place the candidate interval within a 21.6 cM region between markers DSXS1227 and DX8091.
Conclusion: Our results point to a different candidate region on ch Xq in familial forms of BPP. In addition, our data places the candidate interval to a 21.6 cM region mapped to Xq27-q28, a more centromeric location than previously reported. Study supported by: CNPq and FAPESP.

p164
Relation between Seizures and Genotypes in Fukuyama-type Congenital Muscular Dystrophy
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Purpose: Fukuyama-type congenital muscular dystrophy (FCMD) is characterised by congenital muscular dystrophy associated with brain malformation (micropolygyria) due to a defect in the migration of neurons. A 3kb-retrotransposal insertion of the FCMD gene was found to be a founder mutation. Combined heterozygotes between this

mutation and deletion or non-sense mutations have generally a more severe phenotype than individuals homozygous for the retrotransposon. Here, we analysed the relation between seizures and genotypes in FCMD to predict prognosis of epilepsies associated with FCMD.
Methods: 34 patients who were diagnosed as having FCMD because they had the founder mutation homozygously (group A) or heterozygously (group B). Both groups had 17 patients, 8 males and 9 females. Mean follow-up period was 16 and 9 years for A and B, respectively. In all patients, EEG was examined once or twice a year and cortical dysplasia was evaluated by MRI.
Results: Seizures were observed in 11 (65%) and 12 (71%) of A and B, respectively. Mean age at onset of seizures was 4.9 and 2.8 years in A and B, respectively. In both groups, generalised tonic-clonic seizures (GTC) occurred at febrile episodes in infancy, while later complex partial seizures or secondary GTCs were developed. Intractable seizures such as Lennox-Gastaut syndrome or myoclonic seizures were only observed in 4 patients belonging to B. Cortical dysplasia was more severe and extended in B.
Conclusion: Heterozygotes developed seizures earlier than homozygotes and some of the former showed intractable seizures. Special attention is necessary for treatment of epilepsy developed in heterozygotes.

p165
Mutation Screening in Genes for Cortex Development in Patients with Cortical Malformations
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Purpose: To perform mutation screening in candidate genes (EMX2, FLN1, LIS1 and DCX) in a large cohort of patients with different types of cortical malformation.
Methods: All patients included in this study had CT or high resolution MRI scans. We divided them into three groups according to different stages of cortical development: a) group I: patients with schizencephaly, b) group II: patients with periventricular nodular heterotopia (PNH) and c) group III: patients with the lissencephaly/subcortical band heterotopia spectrum (LIS/SBH). Mutation screening was performed by single strand conformation polymorphism (SSCP), followed by sequencing.
Results: We studied 81 patients. 47 have schizencephaly, 16 have PNH and 18 have the LIS/SBH spectrum. In 6 patients with schizencephaly we detected SSCP band shifts in the EMX2 gene. We found SSCP band shifts in the FLN1 gene in 7 individuals with PNH. Only one patient with LIS/SBH showed a band shift in the DCX gene; however, 9 of them had band shifts in the LIS1 gene. To date, we have completed the sequencing analysis in 18 of the 23 patients with SSCP band shifts. Normal variants were found in 15 patients, while putative deleterious mutations were detected in only 3 individuals: 2 patients with PNH and mutations in FLN1 and 1 patient with LIS/SBH and mutation in LIS1.
Conclusion: Mutation screening in EMX2, FLN1, LIS1 and DCX genes are important to understand pathways involved in cortex development and for genetic counselling. However, most patients with cortical malformations do not have mutations in the candidate genes identified to date.

p166
Coexistence of A3243G mt-DNA and nt697 Doublecortin (DCX) Mutations in a Female with Mitochondrial Encephalomyopathy and Double Cortex
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Purpose: We describe a 13-year-old girl with mental retardation, myoclonic epilepsy, lactic acidosis, mitochondrial myopathy, sensorineural hearing loss and diffuse subcortical laminar heterotopia on MRI. The aim of this work was to study the genetic background of this neurological phenotype.
Methods: We tested the mutation A3243G in blood and muscle by RFLP analysis and by sequence analysis of mt-DNA. We created suitable PCR primers to amplify and sequence the coding region of the DCX gene.
Results: RFLP and mt-DNA sequence analysis revealed the heteroplasmic mutation A3243G in muscle and blood. In DCX gene was identified a new heterozygous insertion A mutation at nt697, that results in a frameshift after amino acid residue 232 with a premature stop codon at amino acid residue 244.
Conclusion: Although the presence of the A3243G mt-DNA mutation in this subject might be only casual, there is evidence that a mitochondrial dysfunction can be involved in this brain malformation. Cerebral malformations have been reported in some subjects with mitochondrial diseases and the A3243G mutation was described in association with polymicrogyria. An energetic defect and an alteration of calcium metabolism, both impaired in mitochondrial disorders, can determine neuronal migration disorders. Doublecortin, encoded by DCX gene, is a microtubule-associated protein expressed by migrating neurons. The 3243A-->G mutation leads to selective disruption of the vimentin network, a predominant intermediate filament protein, which seems to have a functional role in migrational events. We speculate that a contemporary dysfunction of microtubules and neurofilaments could explain the neuronal migration disorder in our patient.

p167
A Male with Focal Epilepsy, Valproate Hepatotoxicity and mtDNA G7444A Point Mutation
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Purpose: Seizures are frequent in mitochondrial cytopathies with heteroplasmic mtDNA mutations. Homoplasmic point mutations, however, are so far not known to be associated with epilepsy. We describe a patient with epilepsy, valproate hepatotoxicity and a homoplasmic mtDNA mutation.
Methods: Case report
Results: After an uneventful medical history a male (*1971) complained of visual disturbances lasting several hours and occurring almost daily since 1998. In 1999 a generalised seizure occurred followed by rare complex partial seizures. Several EEGs demonstrated generalised 6-7 Hz activity combined with multiregional spikes. A complex-partial seizure with head and eye deviation to the right with a diffuse seizure pattern was recorded. EEG during the visual disturbances revealed a rhythmic slow bilateral temporo-occipital activity. MRI and PET were normal. Initial treatment with valproate had to be discontinued due to elevated liver enzymes. This event and his mother's history of epilepsy preceding an atypical stroke and sudden death prompted analysis of mtDNA which disclosed a homoplasmic G7444A point mutation which was also found in the two healthy older sisters. Thereafter optical nerve damage could be excluded. SEP were not giant. Serum lactate and cerebral lactate (in MRS) were normal. Seizures, but not the visual disturbances were controlled by lamotrigine plus topiramate after failure of lamotrigine

monotherapy and carbamazepine, oxcarbazepine, levetiracetam in different combinations.
Conclusion: Since the G7444A mtDNA point mutation is known to cause a mild reduction of cytochrome c oxidase activity we believe that this homoplasmic mutation has a role in the pathogenesis of epilepsy in this patient.

p168
Favourable Neuro-Psychiatric Evolution in a Bright Young Man with Ring CHR20
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Purpose: To study the syndrome from adolescence to young adulthood in a bright young male.
Methods: Longitudinal clinical, electrophysiological and neuropsychological follow-up in a young man with ring chromosome 20 mosaicism (3%), from age 14-22 years.
Results: Physical examination: no dysmorphic features, bradykinesia, clumsiness, rare eye-blinks, subjective sensation of tremor epilepsy; started at age 14, focal motor simple/complex; focal with loss of consciousness only and generalised (?) nocturnal tonic clonic; frequent in adolescence, gradually becoming more rare, recently not seen nor self-reported EEG: focal (spiky potentials more often starting right frontal) and regional abnormalities (slow more often left temporal-occipital) and diffuse, often not coinciding with any clinical phenomena or corresponding to slowing or lack of responsiveness. Electroclinical correlations: more abnormalities when presented with difficult tasks; left temporal when verbal tasks; more likely clinical seizure when relaxed after testing (right frontal with motor phenomena). Last recordings: less abnormalities, more regular low voltage background. Neuropsychology: deterioration from high normal IQ in verbal and spatial memory; low results on performance scale compared to verbal tasks - fear of dementia; but good linguistic function and preserved learning curve. Thereafter fluctuating results with temporary school failure and later improvements allowing him to follow university curriculum. Neuropsychiatry: acute episode of hallucinations and psychomotor agitation during environmental stress (travel, heat, sleep deprivation); no recurrence. Schooling: deterioration in mid-adolescence, unsuccessful at 1st baccalaureate attempt, second attempt successful (notes 4/out of 5), 3rd year university mean score 9.4/out of 10).
Conclusion: What is the minimal expression of ring chr20 phenotype? Ring chromosome 20 is compatible with very high intelligence and favourable course even after refractory adolescent onset epileptic seizures, severe cognitive deterioration and acute psychiatric disorder.

p169
Genetic Evaluation of a Case with Continuous Spike-and-wave Discharges During Slow Sleep and 22q13 Deletion Syndrome
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Purpose: The syndrome of continuous spike and wave discharges during slow sleep (CSWS) is an age-related epilepsy part of the epileptic encephalopathies. Delayed language acquisition and mental retardation are specific acquired neuropsychological deficits associated with CSWS. Unknown genetic factors may participate to the epileptic phenotype.
Methods: Video-EEG recordings were performed during wakefulness and sleep. Conventional cytogenetic techniques, fluorescent in situ hybridation and molecular biologic techniques were investigated for subtelomeric deletion definition.
Results: We report the case of a child with a longitudinal follow up until adulthood with autistic-like behaviour, fixed and acquired motor speech disturbances, CSWS and a de novo 22q13 cryptic deletion detected by FISH analysis after routine cytogenetics failed to discover any visible anomaly.
Conclusion: The 22q13 deletion syndrome is a microdeletion syndrome characterised by neonatal hypotonia, global developmental delay, absent to severely delayed speech, minor dysmorphic features and seizures. 'Autistic-like' behaviour, high tolerance to pain and habitual chewing or mouthing are other features of this syndrome. This is the first report of 22q subtelomeric deletion associated with CSWS, making 22q13 a new candidate region that could be screened by FISH in CSWS and related disorders.

p170
Gene Disorders and Chromosomal Abnormalities Associated with Epilepsy
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Purpose: Cytogenetic and molecular abnormalities are associated with certain syndromic epilepsies. Non-dysmorphic patients with epilepsy are at great risk of delayed diagnosis of chromosomal or gene abnormalities.
Methods: During the last 5 years, we performed cytogenetic and molecular analysis in 41 children with epilepsy: 4 were dysmorphic and 37 non-dysmorphic. Electro-clinical phenotypes were analysed.
Results: From 4 dysmorphic patients 3 had trisomy 21 and West syndrome and 1 had Mowat Wilson syndrome (de novo frameshift mutation 1352delC (exon 8)) in ZFHX1B gene on chromosome 2q22 and generalised epilepsy. From 37 non-dysmorphic patients, one had interstitial deletion of 10q (q25.1q25.3). He presented with behavioural changes, lack of speech development, myoclonias and paroxysmal discharges. Two had Rett syndrome (25 bp deletion 881-905del25 and R 294x mutation on exon 4 of MECP2 gene) presented with speech delay, epilepsy and paroxysmal discharges. The other 2 patients had Angelman syndrome with microdelation 15 q11.2-q13 and uniparental disomy. They both had motor delay and no speech development with paroxysmal discharges but only one developed myoclonias and generalised seizures at the age of 4.5 years. Patient 6 was mentally retarded with partial complex seizures and focal discharges at the EEG. Molecular analysis revealed Fragile-X syndrome, as in his older brother without epilepsy.
Conclusion: Cytogenetic and molecular analysis should be performed in all children with epilepsy, because non-dysmorphic children also carry a higher risk of chromosomal abnormalities or gene disorders, especially if their clinical features are accompanied by mental retardation, speech delay or autistic disorders.

p171
Myoclonus and Epilepsy in Early Childhood as a Result of Different Diseases
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Purpose: Seizures in early childhood are always a problem.
Methods: We received 3 patients into the Department of Neurology. They were about 6 week old boys, born at full-term, and with normal weight and head circumference. When several hours old they began grand mal seizures, were given phenobarbital and the seizures stopped, but at 1 month old starting myoclonic seizures. We saw myoclonic seizures when the boys were asleep or stayed awake: erratic myoclonus affects face, limbs, a finger, a toe, eyebrows and one boy also had general myoclonic seizures. In the neurology status all boys had: microcephaly, absent development, dysmorphisms.
Results: On the MRI scans: the first patient had brain malformation, pachygyria and disgenesie corpus collosum; the second had cysts degeneration; the third, periventricular atrophy. EEG: all 3 patients had repetitive suppression-burst pattern without physiological rhythms. Cytogenetics inspections sent to the Medical Genetics Laboratory were: the first boy-46,XY,4p-(p14-16 pter); the second - mos 46,XY,del(4) (p16.2) [15]/46,XY[15]; the third - 46,XY,17,ps.

Treatment: the first boy – phenobarbital 10 mg/kg, but seizures were not stopped, after-VPA (depakine 30 mg/kg) and added BDZ (antelepsini 0 075 mg/kg); the seizures were stopped. The second - phenobarbital 10 mg/kg, the seizures were stopped. The third - phenobarbital 10 mg/kg, but seizures weren't stopped; after-VPA (depakine 30 mg/kg), the seizures were stopped.
Conclusion: Myoclonic seizures would have been caused by chromosome aberration (Wolf syndrome, for example), or would have been caused by early myoclonic encephalopathy.

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13:15 – 14:15
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Seizures in Patients with Human Immunodeficiency Virus (HIV) Infection
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Purpose: Neurological disorders and seizures are relatively common in patients with human immunodeficiency virus (HIV) infection and acquired immuno deficiency syndrome (AIDS). The advent of highly active antiretroviral therapy (HAART) has resulted in a reduction of the incidence of most opportunistic infections and central nervous system (CNS) disorders. Many neurological disorders have disappeared with the advent of HAART. This study aimed to study new onset seizures in HIV patients and to determine seizure frequency, aetiology and clinical aspects.
Methods: A retrospective survey of a cohort of 1720 HIV-infected patients in an Infectious Disease Unit. HIV patients with seizures were enrolled and seizure type classified. All patients received antiepileptic drugs and antiretroviral therapy. Specific therapies were added for treatable opportunistic infections.
Results: 69 HIV patients with seizures were enrolled. In 12/69 patients (17.4%) epilepsy preceded HIV-infection and 57/69 patients (82.6%) had seizures after HIV infection. Identified causes of seizures in 40/57 patients included AIDS dementia complex (ADC) in 20/57 (35.1%), cerebral toxoplasmosis (NTX) in 12/57 (21.97%), cerebrovascular disease in 4/57 (7.03%), bacterial meningitis in 1/57 (1.75%), and progressive multifocal leukoencephalopathy (LEMP) in 1/57 (1.75%). 2 patients had 2 infections associated: 1 NTX and LEMP, 1 NTX and ADC. 17/57 patients (29.8%) had no identifiable cause of seizures. Levetiracetam, phenobarbital, carbamazepine, clonazepam and oxcarbazepine were used for seizure control during the follow up period.
Conclusion: The majority of patients (36/57, 63.2%) with HIV infection and new onset seizures have secondary cerebral infections as the cause of seizures.

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Alterations in Glutamic Acid/GABA Ratios in Sera of Epilepsy Patients on Long-term Antiepileptic Monotherapy
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Purpose: Gamma-aminobutyric acid (GABA) is an important inhibitory neurotransmitter in the human brain and synthesized from glutamic acid (Glu) by glutamic acid decarboxylase (GAD). Glutamate is a predominant excitatory neurotransmitter in the central nervous system. Some antiepileptic drugs (AED) (e.g. valproic acid) are known to interfere with GABA metabolism resulting in changes of GABA concentrations in the brain and in the periphery. To find out if chronic antiepileptic medication with valproic acid, carbamazepine and newer AEDs influence the serum concentrations of glutamic acid and GABA we analysed these neurotransmitters in sera of epilepsy patients on long-term therapy.
Methods: GABA and glutamic acid were measured in sera of 126 epilepsy patients (100 focal epilepsies, 26 generalised epilepsies; 56 on monotherapy, 77 on polytherapy) and 29 healthy controls by high performance liquid chromatography (HLPC) with fluorescence detection. Furthermore, we determined the ratio of glutamic acid/GABA (Glu/GABA) to find evidence for irregularities in this metabolic equilibrium. Patients on monotherapy were split into five groups depending on the AED used: valproic acid (VA) n = 11; lamotrigine (LTG) n = 20; carbamazepine (CBZ) n = 7; oxcarbazepine (OXC) n = 11; topiramate (TPM) n = 3. The concentrations of glutamic acid, GABA and Glu0/GABA of these groups were compared with controls.
Results: In the whole epilepsy patient group (mono and polytherapy) GABA concentrations were significant lower and glutamic acid and Glu/GABA significantly higher compared to the control group. The CBZ-, LTG-, and TPM-monotherapy group showed similar results whereas in the VA- and the OXC-group GABA serum concentration was significantly higher than in the controls.
Conclusion: Our data show that there are alterations in the GABA metabolism due to medical treatment with AED; at least in the periphery. This may be useful for drug level monitoring. Moreover, measurement of GABA and Glu concentrations may reflect success of medical antiepileptic therapy.

p174
Novel Tools for Epilepsy Care and Research (EpilCare)
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Purpose: The purpose of this research is to create a specialised computer application and clinical database for epilepsy (EpilCare), which is used as a tool for supporting the daily registration and storage of clinical events in epilepsy (seizures and changes of medication). Traditionally, paper-based records have been used for these purposes.
Methods: The collection of patient-specific clinical data forms the patient database. The database contains structured terminology of seizure types, syndromes, epilepsy type, aetiology, description of the impairment(s) caused by the epilepsy and diagnostic evaluations and treatments. We have used the new 2001 ILAE diagnostic scheme consisting of five axis as the basis of describing individual data in each patient.
Results: The EpilCare application is built by MariMedical Ltd which is also responsible for the maintenance of the database. Adult and paediatric epileptologists have provided the knowledge of diagnostics and treatment of epilepsy for the basis of the application. The personnel and patients at Kuopio University Hospital Epilepsy Centre have tested EpilCare. EpilCare utilises the latest internet technologies and contains an advanced graphics user interface.
Conclusion: EpilCare is a novel method for collecting and storing clinically relevant data from patients with epilepsy. EpilCare allows a fast review of data during the clinical visit or during a phone call. The application improves the flow of information within the hospital information system. The clinical database of EpilCare allows the standardisation of patient data, and a better organisation of the patient management process. It can also be used for quality management purposes, for medical research and as an information exchange channel.

p175
Bone Mineral Changes and Antiepileptic Drugs
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Purpose: To assess the severity of bone mineral density (BMD) abnormalities in patients taking antiepileptic drugs without other risk factors for bone disease.
Methods: 73 patients and 59 control subjects were included. The inclusion criteria for patients were: diagnosis of epilepsy; aged 20 to 60 years old; at least 6 months of continuous monotherapy. The exclusion criteria were: presence of any risk factor for bone disease. BMD of lumbar spine and total femur was measured by dual energy x-ray absorptiometry. Osteopenia and osteoporosis were determined according to WHO scores. Quantitative data was analysed by Student's t-test and ANOVA. Chi-square test was used to relate osteopenia with therapy duration, type of medication and traumatic fracture history.
Results: Patient group included 44 females and 29 males, aged 20 to 58 years. 30 were on valproate, 38 on carbamazepine, 3 on lamotrigine, 2 on topiramate and 1 on phenytoin. Treatment duration was between 1 and 30 years. 18 patients had a traumatic fracture history. Osteopenia was found in 25 patients and 14 control subjects. Mean spine BMD, was significantly ($p=0.045$) lower in patients (0.978± 0.096 g/cm2), than in control group (1.016± 0.103 g/cm2). Osteopenia was not related to treatment duration, type of medication or traumatic fracture history.
Conclusion: Patients treated with an antiepileptic drug had lower BMD in spine. No relation was found between osteopenia, treatment duration and traumatic fracture history. There were no differences between carbamazepine and valproate.

p176
Low Femoral Neck Bone Mass in a Norwegian Epilepsy Cohort
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Purpose: To assess bone mass in the femur and lumbar spine in patients on long term antiepileptic drug (AED) treatment, and to evaluate possible associations between specific epilepsy-related factors and bone mass.
Methods: We performed a cross-sectional evaluation of 35 consecutive adult outpatients at a tertiary referral centre and 15 institutionalised adult patients, all having used AEDs for at least 5 years. Standard bone mass measurements (BMD) were performed by Hologic DXA in the lumbar spine (L1-L4) and left femoral neck. The values were compared to age-related reference values supplied by Hologic. Multiple linear regression analyses were performed with the patients merged with a large unselected population to test the effect of epilepsy on BMD and also for assessing the effect on patients only.
Results: Mean femoral neck BMD was significantly lower as compared with the reference ($p<0.0001$), but insignificant in total spine. 51% of the patients had a femoral neck BMD >1 SD below reference mean 8 patients (16%) had values consistent with osteoporosis (>2.5 SD below reference). The vast majority of the patients (36 patients) used a combination of enzyme-inducing and non-enzyme-inducing AEDs, making it impossible to evaluate the effect of the individual drugs. However, 7 of the 8 patients with osteoporosis were on carbamazepine. In the multivariate linear regression model, duration of AED therapy and number of previously tried AEDs were most consistently associated with low bone values.
Conclusion: More than half of the patients studied had femoral BMD values >1 SD below the reference mean, which means that their fracture-risk is at least doubled. Duration of AED therapy and number of previously tried AEDs were significant determinants of low BMD.

p177
Use of Antiepileptic Drugs in Norwegian Nursing Homes
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Purpose: Incidence of epilepsy is highest at the extremes of life, i.e. in children under age 1 and in adults above age 65. As many older patients are being treated for several diseases, and age-related physiological changes may alter the pharmacokinetics of drugs, the potential for drug-related problems is large. The aim of this study was to reveal the prevalence of those taking antiepileptic drugs (AEDs) in Norwegian nursing homes, which drugs and which doses they were given and for which reasons.
Methods: In January 2005 we examined the medical records of all the nursing home residents in two municipalities just outside Oslo, the capital of Norway. In this area, covering approximately 155,000 inhabitants, there are 19 nursing homes comprising 1053 residents: 752 (71%) females and 301 (29%) males. The average age was 84.4 years (range 40-104).
Results: 116 (11%) of the residents were treated with AEDs (73 women and 43 men). 79 (7.5%) were given AEDs due to epilepsy. 77 (66%) of the residents received one AED on a permanent basis, 14 (12%) two AEDs and 1 (1%) four AEDs. 84 (72%) were treated with first generation AEDs. 23 (20%) of those receiving AEDs were not taking these drugs on a permanent basis; they received diazepam intermittently. 16 and 14 residents used AEDs as analgesic or as psychotropic drugs, respectively.
Conclusion: 11% of the nursing home residents received AEDs, mostly old drugs. 3.4% used AEDs for reasons other than epilepsy, mainly to alleviate pain or psychiatric symptoms.

p178
Association Between Polymorphisms and Response to Carbamazepine: A Pilot Study
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Purpose: It is unknown why epilepsy patients with the same epilepsy syndrome and/or seizure type respond differently to drugs. Possibly these interindividual differences are caused by genetic differences between patients. In so-called pharmacogenetic research the relationship between drug response and the absence of polymorphisms is determined; polymorphisms are mutations occurring in more than 1% of the population. The objective of the present study was to determine the influence of certain polymorphism factors in response to carbamazepine.
Methods: Two groups of 25 patients were recruited: patients who became seizure free on carbamazepine monotherapy and patients who did not become seizure free on carbamazepine monotherapy, but did become seizure free on another AED or combination of AEDs. Blood was collected from patients by venapuncture. Relevant polymorphisms in the gene coding for the pharmacodynamic targets of carbamazepine and for disease aetiology were identified in available polymorphism databases. Genotyping of SNPs was performed using pyrosequencing and restriction fragment length polymorphism analysis. Allele and genotype frequencies in responders and non-responders were compared using the Pearson X2 test.
Results: No significant association between genotypes and CBZ response was found in our sample. However, there were some indications for association, most notably in SCN2A1.
Conclusion: Larger samples are needed to confirm the indications for association between certain polymorphisms and response to carbamazepine.

p179
Short-duration Low-dose ACTH Treatment for Cryptogenic West Syndrome
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Purpose: Mental outcomes of cryptogenic West syndrome (WS) are often unfavourable. Standard ACTH treatment is effective for WS, although it has side effects. In the present study, we assessed short-term developmental and seizure outcomes in cryptogenic WS patients treated with a new ACTH treatment protocol.
Methods: 5 patients less than 12 months old, diagnosed as cryptogenic WS, were included in this study. Our ACTH treatment protocol is as follows: synthetic corticotrophin (0.5mg (20 IU)/m2) is administered daily until the spasms and the EEG hypsarrhythmic patterns disappear. ACTH treatment is stopped without a gradual reduction.
Results: The age at onset was 5 to 8 (mean 6.8) months; all had normal development before the onset of spasms. The medications used before the ACTH treatment were valproate or zonisamide. Treatment lag was 12 to 19 (14.3) days. The duration of ACTH treatment was 7 to 12 (9.5) days. Spasms disappeared within 3 to 7 days. None of the patients had relapses. Neither severe side effects nor withdrawal syndromes were observed. The total ACTH dose was 0.17 to 0.28 (0.22) mg/kg. None of the patients had clinical seizures or developmental delay until 23 to 76 (41.5) months of age. All except one patient had no residual seizure discharge on EEG.
Conclusion: Our ACTH protocol showed a good effect on seizure and developmental outcome and is safe for patients with cryptogenic WS.

p180
Efficacy and Tolerability of a Sustained Release Versus an Immediate Release Formulation of Valproate in Childhood
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Purpose: To confirm that switching from IRF-VPA to SRF-VPA in paediatric patients improves compliance, reduces adverse effects and improves patient and family satisfaction, by means of maintaining VPA plasma levels when determined at 24 h from intake.
Methods: Prospective, non-randomised, experimental study in patients with any type of epilepsy, in monotherapy or add-on therapy with IRF-VPA, switching to SRF-VPA, at the same dose. Patients underwent physical and neurological examination. Plasma drug levels were determined previously and after the switching. The number of adverse events and seizures were also determined at 3 months after the switching.
Results: 26 patients (12 male and 14 female) with ages between 3 and 14 years (mean 9.03 years). Patients were diagnosed as follows: 6 malformative epileptic encephalopathy, 6 primary generalised epilepsy, 3 partial symptomatic epilepsy, 2 secondary generalised epilepsy, 2 childhood and juvenile absence epilepsy, 2 juvenile myoclonic epilepsy, 2 idiopathic partial epilepsy, 1 Lennox-Gastaut syndrome, 1 epilepsy with CSWS and 1 febrile seizure. 16 patients were on monotherapy, 9 on bitherapy and 1 with VPA plus 2 AEDs. 69.2% of patients were without seizures at the end of the study, compared with 42.3% at the start. The mean result of the satisfaction questionnaire given to relatives was 4.2 points (maximum 5). Only one possible adverse event was reported.
Conclusion: The use of a valproic acid SRF reduces seizure frequency, maintains plasma drug levels, improves patient compliance and minimises adverse events. Relatives are also satisfied with the switching.

p181
Advantages of Sodium Valproate Substitution with 'Chrono' Formulation in Idiopathic Epilepsies
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Purpose: In the management of children epilepsies the 'Chrono' formulation of VPA is important to assure linear pharmacokinetics. The aim of the study was to assess the efficacy and safety of valproate sustained-release formulation (VPA-SR), called 'Chrono', as monotherapy in young patients with idiopathic epilepsies, previously treated with valproate enteric-coated (VPA-EC) and changed to VPA-SR.
Methods: In the last two years 5 patients with idiopathic focal epilepsies (mean age 11.6 yrs) and 29 with idiopathic generalised epilepsies (mean age 14.5 yrs), on VPA-EC monotherapy (twice or three times daily), were switched to VPA-SR (once daily in the evening). They were prospectively followed up for mean 17 months to evaluate efficacy and tolerability with an open observational design. Plasma VPA levels were performed before the change and after 1-3-6 months.
Results: At the end of the follow-up patients who were seizure-free increased from 18 to 26 (by 44%) in total population. Improvement in seizure control was not observed in patients with refractory seizures. Mean daily VPA-SR dose was 16.7 mg/kg/die, whereas plasma VPA levels were 86.8 microg/ml. The number of side effects, particularly sleep disorders and appetite changes, decreased by 66%.
Conclusion: This clinical experience has shown no significant differences in efficacy (with improved tolerability) between VPA-EC monotherapy and VPA-SR monotherapy with similar mean daily dose and plasma VPA levels.

p182
Open Study to Evaluate the Acceptability of a New Microsphere Formulation of Sodium Valproate (Depakine® Chronosphere®) in Healthy Volunteers
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Purpose: A new microsphere formulation of slow-release valproate (Depakine® Chronosphere®; Sanofi-Aventis) has been developed to be administered sprinkled on food or swallowed with a drink. The objective of this study was to evaluate the acceptability of this new galenic formulation via its placebo form administered by the direct oral route and to evaluate satisfaction in healthy volunteers.
Methods: An open-label, randomised study was performed with 16 healthy volunteers. After three training sessions with the lowest dose, subjects received the four doses (500 mg, 750 mg, 1000 mg and 1500 mg) in a random order. Acceptability and safety were assessed by visual analogue scales; a questionnaire assessed ease of administration, ease of swallowing, the need for accompanying fluid and occurrence of signs of discomfort or adverse events.
Results: The safety of the direct route of administration was satisfactory; in particular, no misroutes, nausea or vomiting were observed. Time required to swallow and the quantity of water required increased significantly with dose. 30-50% of subjects found the formulation stuck to the teeth or tongue and required mouth rinsing. 93.8% would recommend this form for an adult for the three lowest doses and 81.3% for the highest dose.
Conclusion: This new microsphere formulation was well-accepted and safe when administered by the oral route. Adherence of the particles could be countered by rinsing the mouth. The formulation was considered convenient for use by adults. Financial support for this study was provided by Sanofi-Aventis.

p183
Valproates in Treating Adolescents with Epilepsy and Depression
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Purpose: Adolescence is the period of life when young people suffer from many changes. During our long practice we have noticed that the period of adolescence is much more complex in patients who suffer from epilepsy. This is the result of the processes of identification which are much more painful in this period of life and the dilemmas connected to maturity are more intense because of the nature of the disease, prejudice, social environment and the therapy. Depression as an integral part of puberty is much more present. We have introduced valproate as an antiepileptic but at the same time as an psychostabilizer and we have noticed that this state of depression is reduced.
Methods: This research included adolescents who were treated on our children's department of the Clinic for Mental Health. A group of 15 adolescent children, diagnosed with temporal epilepsy, was treated at our department from January to July 2004. Five of them were depressed. Hamilton's scale for depression was used throughout the process of monitoring and evaluating depression.
Results: The depressive score was mild, for the whole group at baseline, and after 6 months the score was < 8. This may indicate a therapeutic effect of valproate on adolescent depression.
Conclusion: Following our patients we have concluded that the symptoms of depression are much more reduced in patients who were treated with valproate.

p184
A Multinational Observational Study of the Effectiveness and Tolerability of First-line Monotherapy with Sodium Valproate (Depakine®) for Partial Epilepsy
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Purpose: The utility of sodium valproate in the treatment of both generalised and partial epilepsies has been demonstrated. This observational study was implemented in order to collect, under daily practice conditions, additional clinical data on the effectiveness and tolerability of sodium valproate used as first-line monotherapy in patients newly or recently diagnosed with partial epilepsy.
Methods: The study included 1192 adults and 792 children (6-15 years) newly or recently diagnosed with partial epilepsy recruited in 19 countries. Treatment was initiated with sustained release sodium valproate (Depakine® Chrono®; Sanofi-Aventis) given orally at the dose considered appropriate by the investigator. The mean dose was 864 mg. Seizure control and occurrence of adverse events were assessed after six-months of treatment.
Results: The retention rate in the study at six months was 90.0%. At this time, 77% of subjects were seizure-free (83.7% of children £ 15 years and 72.7% of adults). The best outcome was observed for patients with simple partial seizures (82.1%) and with seizures of idiopathic aetiology (83.2%). Adverse events possibly related to treatment were observed in 10.2% of patients, leading to treatment modification for 1.7%. The most common adverse events reported were gastrointestinal, weight gain, neurological and skin disorders. The proportion of subjects with abnormal neurological examination at six months was 87.5% compared to 83.9% at inclusion.
Conclusion: Sustained release sodium valproate is effective and shows acceptable tolerability as a first-line monotherapy for children and adults with partial epilepsy. Financial support for this study was provided by Sanofi-Aventis.

p185
Effect of AEDs on Blood levels of Homocysteine
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Purpose: Hyperhomocysteinemia can occur in persons with antiepileptic treatment. We wanted to investigate homocysteine levels in blood in such patients, with a specific aim to compare old and new antiepileptic drugs regarding their tendency to develop increased blood levels of homocysteine.
Methods: Blood samples were consecutively taken from patients with epilepsy at a neurological polyclinic in Sweden. The samples were analysed in a similar fashion. Levels above 15 micromol/l homocysteine were regarded as clearly pathologic, levels between 12 and 15 micromol/l as border line pathologic and levels below 12 micromol/l as normal. Factors like concomitant diseases and nutritional status were disregarded in this first phase of the study.
Results: Blood samples from 113 patients were analysed. 24 of these had clearly pathologic levels (21%) and 24 patients had border line levels (21%). Men were slightly more prone to demonstrate abnormal levels (29 men/19 women). Patients on monotherapy treated with the old AEDs showed that 48% (23/48) had homocysteine levels over 12 micromol/l, and most interestingly had 21% (10/48) of patients in monotherapy treated with the new generation of antiepileptic drugs (lamotrigine, gabapentine and topiramate) a level of homocysteine over 12. (5 borderline och 5 over 15 micromol/l.)
Conclusion: We address the importance of recognising increased blood homocysteine in patients with antiepileptic treatment, especially the modern drugs. We propose that all patients with AEDs should be supplemented with folic acid, as this may not have any serious neurotoxic effects, contrary to former beliefs.

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Levetiracetam in Idiopathic Generalised Epilepsies
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Purpose: Idiopathic generalised epilepsies (IGE) represent 20-30% of all epilepsies. Valproate (VPA) is effective in IGE, but 15-25% of patients either do not respond or experience adverse events (AEs) requiring drug withdrawal. Lamotrigine (LTG) is effective but can worsen myoclonic seizures. The aim of this study was to evaluate levetiracetam (LEV) in IGE.
Methods: Adults (18-63 years) with IGE in whom previous treatment with ≥1 of LTG, VPA or topiramate was ineffective or withdrawn due to AEs, were assigned add-on therapy with LEV and followed for ≥1 year.
Results: 12 patients (10 juvenile myoclonic epilepsy [JME], 2 generalised tonic-clonic seizures [GTCS]) were followed for 12-46 (mean 22) months. LEV was initiated at 1000 mg/day given in two divided doses and uptitrated (mean dose 2300 mg/day). 2 GTCS patients and the 2/10 JME patients with tonic-clonic seizures, all on LEV 2000 mg/day, became seizure-free; the GTCS patients for ≥1 year. In the remaining 8 JME myoclonic patients, 3/8 (37.5%) became seizure-free, 4/8 (50%) had >75% seizure reduction and 1/8 (12.5%) no seizure reduction. 4 JME patients received LEV as monotherapy (main dose 2500 mg/day; 3 for >1 year), 1 had a generalised seizure requiring VPA to be added to his regimen. LEV was generally well tolerated; mild sedation initially occurred in 3/12 (25%) patients but improved after several weeks.
Conclusion: In this small study, LEV was highly effective in controlling GTCS and myoclonic seizures.

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Levetiracetam Reduces Interictal Activity Frequency and Duration in Patients with Primary Generalised Epilepsy
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Purpose: Levetiracetam (LEV) is highly effective as an add-on treatment for refractory partial epilepsies. Recent evidence from case reports and small patient series indicates LEV also reduces seizure frequency in patients with generalised epilepsies. This study investigates the EEG effects of LEV, add-on or monotherapy, in adults with idiopathic generalised epilepsy (IGE).
Methods: 8 adult patients with treatment-resistant IGE were assigned to LEV (mean maintenance dose 2000 mg/day; range 1000-3000 mg/day) as add-on therapy (n=4) or converted to monotherapy (n=4). Interictal activity was monitored using continuous EEG and analysed to determine spike-wave frequency, duration of spike-burst, and longer burst activity. The mean interval between baseline and final EEG examination was 149 days (range 8-473 days).
Results: Median spike-wave burst length decreased from baseline by an average of 72% for all patients ($p<0.05$). Patients on add-on therapy showed 23% burst length reduction and those converted to monotherapy 90% reduction. Improvement was more marked during the day. Maximal burst-length was considerably reduced in 7/8 patients (mean reduction 67%; $p<0.05$). Spike-wave frequency (spikes/hr) for all 8 patients was reduced by a mean of 53%. The 4 patients converted to LEV monotherapy showed considerable improvement with a 90% reduction in spike frequency and maximal burst length.
Conclusion: This study showed for a first time a consistent long-term reduction of interictal epileptic activity with LEV. Reduction in duration of spike-wave bursts additionally supports a clinically relevant antiepileptic effect. Our results support the concept that LEV is an effective alternative in primary IGE. Supported by funding from UCB

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Open-label Pragmatic Study on Levetiracetam in the Treatment of Juvenile Myoclonic Epilepsy
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Purpose: Valproate is the first-line drug in the treatment of juvenile myoclonic epilepsy (JME). However, a number of patients are refractory or may exhibit adverse effects to valproate. Levetiracetam has been reported to be effective in JME. The aim of this multicentre, prospective, open-label study is to evaluate the efficacy and tolerability of levetiracetam in JME.
Methods: Levetiracetam was given as add-on treatment in JME adult patients resistant or intolerant to previous AEDs, or as a first treatment in newly diagnosed patients. Three periods were considered: baseline (three months); levetiracetam titration (two weeks) up to 1000 mg/day; long-term phase (up to two years), during which levetiracetam could be increased up to 3000 mg/day.
Results: 43 patients were enrolled (35 F, mean age 27+8). 8 patients were newly diagnosed. Main concomitant therapies were valproate (14), lamotrigine (10), valproate+lamotrigine (4). Mean study duration was 18+10 months. 16 (37%) patients were seizure-free over the study period, 18 (41%) were without myoclonias, and 30 (69%) did not have generalised tonic-clonic (GTC) seizures. Mean monthly frequency of days with myoclonias and GTC seizures were reduced after levetiracetam (respectively: 5.9+6.4 vs 2.1+5.5 [p=0.004], and 0.5+0.9 vs 0.2+0.6). 5/10 patients showed a suppression or a marked reduction of photosensitivity. 5 patients dropped out because of lack of efficacy or GTC seizures, and 1 because of pregnancy. 5 patients complained of minor side effects, which did not cause discontinuation.
Conclusion: This study suggests that levetiracetam may be particularly effective and well tolerated in the treatment of newly diagnosed or refractory JME.

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Short and Long-term Efficacy of Levetiracetam Adjunctive Therapy in Children with Refractory Partial Epilepsy
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Purpose: To evaluate the short- and long-term efficacy of levetiracetam (LEV, Keppra®) as adjunctive therapy in children (4-16 years) with partial-onset seizures (PS) inadequately controlled on 1-2 concomitant antiepileptic drugs.
Methods: This was a multicentre, double-blind, randomised, placebo-controlled, parallel-group, 14-week study; and an open-label, long-term, follow-up study. Eligible patients having ≥8 PS during an 8-week baseline were randomised to LEV 20 mg/kg/day or placebo. Titration of LEV over 4 weeks to a target dose of 60 mg/kg/day was followed by 10 weeks' evaluation at this dose, then either an optional open-label extension phase (allowing dose adjustment of LEV) or a 6-week withdrawal period.
Results: 216 patients were randomised and 198 provided evaluable data. With LEV, percentage reduction in log-transformed PS frequency was 26.8% ($p = 0.0002$) over placebo. The percentage of responders (≥50% reduction in weekly PS) with LEV was 44.6% (45/101), compared with 19.6% (19/97) for placebo ($p = 0.0002$). 7 (6.9%) LEV and 1 (1.0%) placebo patients remained seizure-free during the entire treatment period. 183 out of 192 patients who completed the short-term phase entered the long-term phase and 168 provided evaluable data; 72 are still ongoing. Mean treatment duration was 16 months and 123 patients received LEV >1 year. Seizure control was maintained during the long-term phase. 19 patients remained seizure-free for ≥6 months and 12 patients were seizure-free for ≥1 year.
Conclusion: LEV adjunctive therapy is efficacious in both short- and long-term treatment in children with treatment-resistant PS. Supported by funding from UCB Pharma Inc, USA

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Levetiracetam as Monotherapy in Newly Diagnosed Benign Rolandic Seizures in Children: An Open-label Pilot Trial
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Purpose: To evaluate the efficacy and tolerability of levetiracetam as monotherapy in children with benign epilepsy with centrotemporal spikes (BECTS) for whom carbamazepine or valproate were not effective or tolerated.
Methods: Children were recruited based on the following inclusion criteria: 1) age 3 years and over; 2) diagnosis of frequently recurrent secondarily generalised benign rolandic seizures based on clinical and wake/sleep EEG criteria; 3) CT/MRI normal findings; 4) normal neurological and mental evaluation; 5) inefficacy and/or no tolerability to previous therapy with carbamazepine or valproic acid as monotherapy; 5) informed consent by parents and/or caregivers. Exclusion criteria were: 1) poor compliance by parents/caregivers; 2) progressive neurological and/or systemic disease. LEV was titrated up

to 500 mg once a day (preferably in the evening) and the previous drug was tapered off.
Results: Up until now, 14 children (6 females, 9 males), aged between 4.5 and 12 years (mean 9.4 years), were recruited into the study. After a mean follow-up period of 8.7 months (range 1-14 months), 12 patients were seizure-free. Mean serum level of LEV was 4.1 microg/ml (range 1.3-9.0). In 1 patient, seizures recurred 4 months after starting therapy, and they are now assuming 1000 mg of LEV per day. In another girl aged 5 years, LEV was tapered off due to seizure recurrence at 1 gr/day of LEV. Neither laboratory nor cognitive/behavioural adverse side effects were reported in our patients.
Conclusion: Preliminary data from a still ongoing open-label, pilot trial suggest LEV to be a potentially effective and well-tolerated therapy against recurrent secondarily generalised idiopathic rolandic seizures, alternative to carbamazepine or valproic acid.

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Levetiracetam as Add-on Therapy in Idiopathic Focal Epilepsies
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Purpose: In Germany sulthiame represents a first-line drug for idiopathic focal epilepsies (IFE). In refractory cases clonazepam, valproate and ethosuximide are used with varying success and steroids as a last resort. Case reports and small studies report levetiracetam (LEV) as of benefit in IFE (Rolandic-epilepsy, Landau-Kleffner-syndrome, continuous spike-wave syndrome [CSWS]). This study investigated LEV as an add-on therapy for patients with treatment resistant IFE.
Methods: Children with treatment resistant IFE taking ≤2 antiepileptic drugs (AEDs) were treated with LEV (mean dose 40 mg/kg/day) as an add-on therapy. Efficacy was assessed by the number of patients continuing LEV, seizure reduction, EEG changes (during sleep) and cognitive, behavioural and linguistic performance.
Results: 39 patients (21 male, 18 female) aged 2-12 years with IFE (6 Rolandic-epilepsy, 4 Landau-Kleffner-syndrome, 4 CSWS, 9 atypical IFE with seizures and cognitive/behavioural problems, 11 with idiopathic and symptomatic epilepsy, 5 no seizures but cognitive/behavioural problems) were treated for 1 month to 2 years with LEV. 26/39 (67%) patients continued LEV; 13/39 (33%) patients discontinued (10 insufficient efficacy, 3 side effects). 13/39 (33%) patients with seizures initially showed ≥50% seizure reduction; 3/39 (7.7%) became seizure-free. 14/39 (36%) showed improvements in cognitive, behavioural or linguistic problems and 20/39 (51%) had reduced EEG discharges. Reduction of positive effect occurred in 7 children leading to discontinuation in 1 patient. 14/39 (36%) experienced side effects, most commonly sleepiness.
Conclusion: LEV represents an extension of therapeutic options for IFE. Being well tolerated with a low rate of severe side effects, LEV treatment should be considered before steroids.

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Early Therapeutic Response to Levetiracetam
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Purpose: Levetiracetam (LEV, Keppra®) is used as add-on therapy in adults for the treatment of localisation-related epilepsies. LEV shows very good tolerability and high efficacy in patients with refractory epilepsy and we have observed a quick response to LEV in terms of seizure reduction or seizure-freedom. In this investigation, we studied changes in seizure frequency and characteristics during the first 15 days of LEV treatment in patients with frequent seizures.
Methods: Adults (aged 18-68 years) with localisation-related epilepsy uncontrolled on 2-3 antiepileptic drugs (AEDs), were given LEV 1000-1500 mg/day as add-on therapy titrated to a maximum of 3000 mg/day according to clinical response. Seizure frequency was recorded daily for the first 15 days of treatment. Follow-up ranged from 7-28 months.
Results: 35 patients were evaluated; duration of epilepsy was 8-41 years, aetiology was both symptomatic and cryptogenic. 15 patients with very frequent seizures (2-6 per day) were identified and followed. Seizure types in this group were: 8 complex partial, 3 simple partial, and 4 secondary generalised. A ≥50% reduction in seizure frequency was observed as early as the 2nd or 3rd day of LEV treatment. This study provides clinical confirmation of the early therapeutic efficacy of LEV.
Conclusion: Our clinical results show that LEV is effective in patients with refractory epilepsy and provides a quick response to treatment with early therapeutic results.

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Fast and Sustained Efficacy of Levetiracetam During Titration and the First 3 Months of Treatment in Refractory Epilepsy
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Purpose: Levetiracetam (LEV) is an antiepileptic drug effective from the first day of treatment. While its efficacy and tolerability were demonstrated in short-term and long-term studies, no analysis has yet been performed to assess variability in efficacy throughout the duration of the trials. This study investigated whether the efficacy of LEV was sustained in adult patients with refractory partial seizures over a 3-month period.
Methods: Treatment effect was assessed in a post-hoc analysis of pooled data from three randomised, double-blind, placebo-controlled trials (N=883). The proportion of seizure-free days (SFDs) during each week of a 3-month period after the initiation of treatment was analysed using analyses of covariance with treatment as a factor and the proportion of SFDs over the baseline as a covariate.
Results: The mean proportion of seizure-free days was greater in the LEV group than in the placebo group. The difference, which was statistically significant, was observed as early as the first week after the initiation of treatment. It was higher in the first week of treatment, and subsequently was maintained for each week over the 3-month period (all $P < 0.01$). Patients in the LEV group had on average 74% to 81% days each week seizure free, compared with 69% to 72% in the placebo group.
Conclusion: LEV is efficient in controlling seizures from the first week of drug initiation, during uptitration, and throughout the first 3 months of treatment. There is an interesting amplification of efficacy in the first week of therapy, which is intriguing and warrants further investigation.

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Levetiracetam as Monotherapy for Partial Epilepsy in Adults: A Case Series
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Purpose: To evaluate efficacy and tolerability of levetiracetam (LEV) monotherapy in adult patients with partial seizures.
Methods: Adult patients with partial epilepsy, with or without secondary generalisation and with both cryptogenic and lesional aetiology, received LEV monotherapy. Patients were either newly diagnosed or converting from add-on therapy. All patients underwent objective neurological and psychological examination, EEG, and encephalic CT/ MRI at baseline; EEG, neurological examinations and routine laboratory tests were performed 3 monthly.

Results: 37 patients (17 male, 20 female), aged 17-70 (mean 40) years, mean baseline seizure frequency 4.8/month, received LEV monotherapy 1000-3000 (mean 2300) mg/day for between 6 and 24 months. 14 patients were newly diagnosed, 23 converted from add-on therapy (1-2 other AEDs; mostly carbamazepine or valproate, also topiramate, lamotrigine). Overall responder rate (≥50% seizure reduction) was 29/37 (78%); 12/14 (86%) of newly diagnosed and 17/23 (74%) of those converting from add-on therapy. Seizure freedom was achieved in 14/37 (38%) of all patients; 8/14 (57%) of newly diagnosed, 6/23 (26%) of those converting from add-on therapy. A further 15/37 (40%) patients achieved a ≥50%-99% seizure reduction, of whom 8 (21%) achieved ≥75-99% and 7 (18%) a ≥50-99% reduction. An unsatisfactory clinical outcome was reported for 8/37 (21%) patients; 5/37 (13%) had <50% seizure frequency reduction, 3/37 (8%) discontinued with adverse events (AEs) e.g somnolence, anxiety, depression. LEV was otherwise well tolerated; with no irreversible toxic effects or clinically relevant changes in laboratory parameters.
Conclusion: In our case series, LEV showed good efficacy as monotherapy and was well tolerated.

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Long-term Retention and Efficacy of Levetiracetam in a Large Cohort of Patients with Chronic Epilepsy
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Purpose: To determine the long-term retention rate and levetiracetam (LEV, Keppra®) treatment outcome in patients with chronic epilepsy.
Methods: Patients were prospectively enrolled if LEV was commenced within 24 months of being first marketed in the UK. The following were analysed: LEV retention rate at last follow-up; LEV dosage; percentage of patients achieving seizure freedom, ≥50% seizure reduction; LEV discontinuations and discontinuation reasons.
Results: 811 patients (49% male), aged 14-79 (mean 37) years, were included. Longest follow-up was 41 months. At last follow-up, 528 patients (65%) were continuing LEV, 426 (81%) with ≥12 months follow-up. LEV dosage at last follow-up was 125-5000 (median 2000) mg/day. 143 patients (18%) attained seizure freedom any time during treatment for between 1-35 (mean 11, median 10) months. At least a further 237 patients (29%) had a ≥50% seizure frequency reduction period. 46 patients achieved LEV monotherapy, 26 had seizure-free periods of between 2-35 (mean 13, median 11) months. Seizure freedom was attained in 120/654 (18%) patients with cryptogenic or symptomatic partial and 15/68 (22%) patients with idiopathic generalised epilepsy. 269 patients (33%) discontinued LEV; due to inefficacy in 100 (14%), adverse events in 81 (10%), both in 75 (9%) and pregnancy in 3 (0.4%).
Conclusion: Nearly two thirds of chronic epilepsy patients were continuing LEV at the last follow-up. Almost 50% of patients achieved a period of ≥50% seizure frequency reduction, nearly 20% achieving a period of seizure freedom. This study, evaluating the largest single-centre patient cohort taking LEV, confirms LEV's long term efficacy and tolerability. (Supported by The National Society for Epilepsy, United Kingdom.)

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Non-fluent Speech in Patients with Partial Epilepsy: Beneficial Effect of Levetiracetam
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Purpose: Few reports indicate that some antiepileptic drugs, e.g., levetiracetam (LEV) may improve verbal fluency (Neurology 59; 1288, 2002). The objective of this study was to evaluate the clinical effect of LEV as adjunctive therapy to carbamazepine (CBZ) or phenytoin (PHT) in a series of patients with partial epilepsy and non-fluent speech.
Methods: 5 consecutive patients (3 men; 2 women), aged 35-59 years, with partial epilepsy and moderate to severe non-fluent speech due to developmental stuttering (n=3 cases) or neurogenic stuttering (n=2 cases) were enrolled in a 9 week, open-label, prospective-controlled trial. LEV was given in combination with CBZ (n=4 cases) or PHT (n=1 case), at dosages ranging from 500 mg twice daily to 1500 mg twice daily. The severity of stuttering was assessed by a verbal fluency test, and by the Patients Global Impressions Scale at baseline and after 9 weeks.
Results: No adverse effects were noticed. During use of LEV, verbal fluency improved in all patients, compared with the baseline period, from 25% to 50%. All patients rated themselves as better and with less fluency problems after LEV. After the addition of LEV, 4 patients with an incomplete control of seizures had their total seizure count reduced by more than 50%. All patients chose to keep taking LEV.
Conclusion: Our study indicated that for patients with partial epilepsy LEV may have a beneficial effect on non-fluent speech due to developmental or neurogenic stuttering. A prospective, placebo-controlled trial of LEV in this kind of verbal non-fluency is warranted.

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In-hospital Use of Levetiracetam: A One-year Retrospective Study
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Purpose: To describe the in-hospital use of levetiracetam (LEV) during 2004 in a tertiary hospital.
Methods: The charts of all patients who received LEV during hospital admission in 2004 were reviewed.
Results: LEV was administered to 50 patients. Of those, 19 had were admitted to the Epilepsy Monitoring Unit for presurgical evaluation. LEV was administered to another 11 patients who were already taking LEV and were admitted to the hospital for: increase in seizure frequency (2 patients), another medical condition (4), diagnostic procedures (3) and epilepsy surgery (2). LEV was continued in all patients except 2 (1 patient with suspected LEV induced psychosis and 1 with pseudoseizures). LEV therapy was initiated during admission in 20 patients. LEV was used as monotherapy in 5 patients, 4/5 with seizures secondary to CVA (3 on coumarin and 1 with hepatic disease). One HIV+ patient received LEV after VPA-induced rash. Seizures were controlled in all patients being discharged on LEV. In 15 patients, LEV was started as add-on treatment for repeated seizures (status epilepticus in 6). Epilepsy was cryptogenic in 6 patients and symptomatic in 9 (1 cavernous angioma, 1 haematoma, 2 abscesses, 4 tumours, 1 encephalitis). Other relevant medical conditions included hepatic transplantation (1), liver cirrhosis (2) and renal failure (2). Evolution was: seizure control (12 patients), >75% decrease in seizure frequency (1) and no response (2), without significant adverse effects. 11/15 patients were kept on LEV at discharge.
Conclusion: LEV is a useful antiepileptic drug in an in-hospital setting, providing adequate and fast seizure control without significant adverse effects in the majority of patients.

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Audit of Outcome of the first 101 Patients to be Prescribed Levetiracetam in One Practice
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Purpose: To audit 101 patients prescribed levetiracetam (LEV) for largely refractory epilepsy.
Methods: Follow up was over a maximum of 4 years. Outcome was determined in relation to reduction in seizures, seizure freedom, retention rates and side-effect profile.

Results: There were a total of 101 patients (40.6% male) with a mean follow-up, for those who remained on LEV, of 2.3years. 76.2% remained on LEV at last the review (mean dose 1311mg.) 12.9% of the total evaluated in the audit were seizure free (mean duration of seizure freedom=19.2 months) The average daily LEV dose associated with seizure freedom was 908mg (range 125mg - 2000mg). 7 of 13 seizure-free patients had idiopathic generalised epilepsy. 28 of the cohort improved by more than 50% reduction in seizure frequency (mean dose=1380mg). 6 patients who remained on LEV found that higher doses of LEV were associated with worse control. 24 patients ceased treatment, 9 because of side-effects and 5 because of lack of efficacy. 5 patients, with partial or generalised epilepsy, ceased LEV treatment, because it made their seizures worse.
Conclusion: This audit demonstrates efficacy in this cohort, with good retention rates (76.2%), seizure freedom (12.9%) and > 50% improvement (27.7%). We observed efficacy at lower doses than in clinical trials. Although LEV appeared to be broad spectrum, and was effective in both partial and generalised epilepsies, seizure exacerbation occurred in a few patients, with both partial and generalised epilepsies. This was also observed in some on higher doses following improvement with lower doses suggesting a therapeutic window of efficacy.

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Add-on Levetiracetam in Focal Drug-resistant Epilepsy: Is there any Effective Association?
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Purpose: We try to find out if any antiepileptic drugs (AED) are more effective than others in decreasing seizure frequency in focal drug-resistant epilepsy (FDRE) when levetiracetam (LVT) is added.
Methods: This prospective, observational, add-on, open study explores the efficacy (number of seizures/month) of LVT associated with other AEDs in 35 consecutive patients with FDRE. For statistical analysis we used the SPSS 12.O program.
Results: 35 patients with FDRE were included. All patients were treated with AED at maximum tolerated doses: 12 patients with one AED, 19 with two, 3 with three and 1 with four (AEDs: carbamazepine (CBZ): 18 patients; phenobarbital (PB): 13; phenytoin: 8; clobazam: 7; valproate: 5; lamotrigine: 5; topiramate: 3; gabapentin: 2. Mean duration of treatment with LVT: 9 months (range: 4-18); mean doses of LVT: 1,900 mg/d (range: 500-3,000). Response to add-on LVT: Group 1 (seizure-free) 6 patients (17%); Group 2 (reduction in seizure frequency more than 50%) 13 (37%); Group 3 (reduction less than 50%): 15 patients (42%). Group 1: 3 patients received CBZ and PB (50%), 2 patients CBZ or PB (32%). Group 2: 4 patients received CBZ and PB (30%), 3 CBZ (23%), 2 CBZ or PB in association (30%). In Group 3 only 5 patients received CBZ and 3 PB.
Conclusion: Our study suggests that LVT is significantly ($p<0.04$) more effective associated with CBZ and/or PB as add-on therapy in FDRE. Association of LVT with CBZ and PB seems to be particularly effective.

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Efficacy of Levetiracetam in a Patient with Symptomatic Epilepsy with Spontaneous and Photically Induced Seizures
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Purpose: Levetiracetam (LEV) is a new antiepileptic drug with efficacy in partial-onset seizures. We report a case of symptomatic partial complex epilepsy in which spontaneous and photically induced seizures responded clinically and electrographically to LEV.
Methods: A 60 year old male, diagnosed with adult-onset vascular epilepsy associated with photoparoxysmal responses, was treated with LEV 2000 mg/day. The patient showed both spontaneous and photically induced partial onset seizures with affective symptoms. MRI showed multiple small lacunar infarcts in the subcortical white matter. Interictal EEG revealed a nearly normal background activity, recurrent theta bursts of low amplitude in the right temporal region, and generalised polyspike discharges to intermittent photic stimulation. Clinical, EEG and video-EEG follow-up was performed.
Results: LEV produced a rapid and complete clinical/EEG response, with complete disappearance of EEG-photoparoxysmal discharges. The therapeutic effect was sustained for the 6 months follow-up.
Conclusion: This case showed a rapid and sustained effect of LEV on both unprovoked and photically induced seizures in symptomatic late-onset epilepsy.

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Levetiracetam Adjunctive Therapy in Refractory Partial Epilepsy: Long-term Efficacy and Tolerability
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Purpose: To evaluate the long-term efficacy and tolerability of levetiracetam (LEV) add-on therapy for patients with highly refractory partial epilepsy.
Methods: A prospective, open-label, add-on study with LEV for 72 weeks was conducted in 4 University neurological clinics. 40 patients with uncontrolled partial seizures (PS) were included, 19 of them with secondary generalisation (SGPS); 23 were male, 17 female, aged 19-58 years (mean 32.6 years). Epilepsy duration was 3-48 years (mean 19.9 years) and PS frequency 3-14 (mean 7.4) per month in the preceding 3 months. All patients had previously failed treatment with 3-8 antiepileptic drugs (AEDs) and were stable on 1-2 AEDs. LEV 1000-3000 mg per day was added over a 2-4 week titration period. Number and type of seizures, tolerability and side effects were recorded.
Results: 25 (62.5%) patients experienced ≥50% seizure reduction at 72 weeks and 11 (27.5%) achieved seizure freedom, 5 (12.5%) for the full 72 weeks. 61.5% were responders in complex PS, 64.3% in simple PS and ~80% in SGPS. Responder rates at 24 weeks and 72 weeks were comparable. Seizure-free days increased by 4.9 per quarter. Retention rate was high; 26/40 patients (65%) continued treatment beyond 72 weeks. 2 patients (5%) discontinued LEV because of side effects, 1 with allergic skin reaction (comedication: valproate+topiramate), and 1 with psychotic reaction (comedication: carbamazepine+topiramate).
Conclusion: This study demonstrated the long-term efficacy of LEV add-on therapy for highly refractory partial epilepsy with no development of tolerance. LEV was safe, well tolerated and rarely led to withdrawals of the treatment.

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Levetiracetam in Brain Tumour Patients: Preliminary Report
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Purpose: Epilepsy is common in patients with brain tumours. The antiepileptic drugs (AEDs) more frequently used may often have potential or substantial interactions with anti-neoplastic agents. Levetiracetam (LEV) has no known pharmacological interaction as it has no effect on liver enzymes. Therefore, it may be useful for this group of patients. We studied 12 patients affected by supratentorial gliomas in order to evaluate the safety and efficacy of LEV.
Methods: 12 patients (3 females and 9 males, aged 28-70 years, median age 48 years) were included in the study. 5 were affected by glioblastoma multiforme, 4 by anaplastic astrocytoma, 2 by low grade

astrocytoma and 1 by meningioma. Seizure types were: simple partial in 3 patients, complex partial in 2 patients, complex partial with secondarily generalisation in 5 patients, and generalised tonic-clonic in 2 patients. All the patients were on therapy with other AEDs and LEV was added on account of persisting seizures.
Results: We found a seizure-reduction of >50% in 4 patients; 5 patients were seizure-free. In 3 patients the seizure frequency was unmodified. The patients were followed for a mean period of twelve months. No adverse effects or significant changes in blood chemistry were observed in any patient.
Conclusion: Our preliminary data seem to indicate that treatment with LEV in patients with brain tumours is safe and efficacious. Further studies are necessary to confirm these data, with particular attention to interactions between LEV and antineoplastic agents.

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Use of Levetiracetam as Pre-Operative Prophylaxis in Brain Tumour Surgery Patients
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Purpose: To compare the complications of peri-operative antiepileptic drug (AED) prophylaxis in patients who underwent brain tumour surgery with and without levetiracetam (LEV).
Methods: Patients who underwent elective brain tumour surgery at the University Hospital in Cincinnati Ohio were identified from the neurosurgery database. Two separate three month time periods were reviewed (April–June 2004; prior to routine LEV use and September–November 2004; after routine LEV use). A retrospective chart review was performed to assess post-operative AED complications, postoperative seizures and length of stay.
Results: 39 patients met inclusion criteria. Mean age at surgery was 55 +/- 13 years (49% male, 51% female). 82% had malignant brain tumours. 51% had complete tumour resection, 33% had subtotal resection and 16% had a biopsy. 11 were treated with LEV (3 as monotherapy) and 27 patients were not treated with LEV (17 with monotherapy AEDs; 81% received phenytoin, 41% received valproate). AED-related adverse effects were seen in 44% of the non-LEV treated patients (15% had thrombocytopenia, 15% had encephalopathy, 7% had AED toxicity (by blood level), 4% had rash, elevated liver enzymes, hyponatremia, or bleeding complications). No patient treated with LEV had adverse effects (p=0.01, Fisher's exact test). 2 patients in the non-LEV group and none in the LEV treated group had post-operative seizures (p=NS). No difference on length of stay was seen between the two groups.
Conclusion: LEV is associated with a reduced rate of complications in brain tumour patients treated with prophylactic AEDs.

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Long-term Follow-up of Levetiracetam in Patients with HIV Infection using Highly Active Anti-retroviral Therapy
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Purpose: Levetiracetam (LEV) has a good safety and efficacy profile and no effect on drug-metabolising enzymes, giving it a low potential for interaction with antiretroviral therapy. This ongoing study is evaluating the persistence of LEV efficacy and tolerability in patients with epilepsy and HIV infection, and the interaction of LEV with antiretroviral therapy.
Methods: 7 patients with advanced HIV infection and epilepsy are receiving LEV 1000-2000 mg daily as monotherapy or add-on antiepileptic drug (AED) therapy. Blood tests, CD4 counts, viral load, general and neurological examination, EEG, and brain imaging are conducted regularly. All patients are receiving concomitant antiretroviral therapy with 3 different antiretroviral drugs.
Results: Follow-up to date ranges from 60-400 days (mean 230 days). All patients (5 on monotherapy; 2 on add-on therapy) are currently seizure-free. In all patients no changes to antiretroviral therapy have been required and HIV stage has not worsened. One patient initially receiving LEV monotherapy, who experienced worsening of seizures due to cortical atrophy near a site of cerebral ischemia, required a second AED. No patients have reported side effects with LEV.
Conclusion: Our experience is with a small group of patients but a long follow-up. In this special group, LEV appears to be effective at a low to medium daily dose and shows no interaction with antiretroviral therapy. We suggest that LEV could be used in monotherapy in patients at all stages of HIV infection, for control of seizures and to minimise the risk of antiretroviral resistance and loss of efficacy.

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Influence of Levetiracetam on Sleep Behaviour and Sleep Architecture
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Purpose: Many antiepileptic drugs have sedating side effects and can affect sleep. Adverse psychiatric effects of levetiracetam (LEV), including aggressive behavioural changes and hypervigilance, are known from several reports. In this study we wanted to examine the impact of continuous medication with LEV on sleep architecture. In the only study to have been published until now that investigated the influence of LEV on sleep, only a single dose of LEV had been administered.
Methods: 8 patients with medically refractory epilepsy received LEV as add-on therapy. They were evaluated in our sleep laboratory for two nights prior to commencement of treatment, which comprised administration of 2000mg LEV. Four weeks later the patients were re-evaluated for one night. Patients were also instructed to complete the Epworth Sleepiness Scale (ESS), the Pittsburgh Sleep Quality Index (PSQI) and to keep sleep logs for two weeks before each polysomnography (PSG). In addition, the maintenance of wakefulness (MWT) test was done.
Results: Comparing pre- and post-treatment PSG variables by applying the two-sided Wilcoxon rank test, none of the principal parameters (total sleep time, sleep efficiency, sleep latency and percentage of time spent in the different stages of sleep such as wake, S1-S4 and REM) showed statistically significant changes ($p<0.05$). There was only a tendency to a smaller percentage of REM-sleep. The patients' perception of sleep and also the scores of ESS and PSQI and the MWT remained without statistically significant changes.
Conclusion: LEV seems to be a well tolerated AED without significant impact on sleep behaviour and sleep architecture.
Acknowledgement: The study has been supported by an Educational Grant from UCB, Germany

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Effects of Add-on Treatment with Topiramate or Levetiracetam on Cognition and Health Related Quality of Life for Patients with Epilepsy
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Purpose: To compare two novel antiepileptic drugs (AEDs), topiramate (TPM) and levetiracetam (LEV) regarding efficacy, cognitive effects, Health Related Quality of Life (HRQOL) and mood in pharmacoresistant epilepsy patients.
Methods: A prospective, open-label add-on study of 59 patients aged 18-75 (mean 38.74) years assigned TPM (n=20) or LEV (n=39). Patients were examined at baseline (T1) and 3 months after first titration (T2). Cognitive AED side effects (visuo-perceptual and

psychomotor speed, mental flexibility, working memory, and word fluency) were assessed at baseline (T1) and T2. Self-report questionnaires addressed depression (BDI), anxiety (SAS) and HRQOL (31-QOLIE).
Results: Information on seizure frequency was available for 46 patients (31 LEV, 15 TPM). Intent-to-treat analysis showed improved seizure control (≥50% seizure reduction) in 71% (n=22) LEV patients versus 53% (n=8) TPM; 32% (n=10) of LEV patients and 6.7% (n=1) of TPM achieved seizure freedom. 36 patients completed follow-up at T2 (25 LEV, 11 TPM). Group and individual analysis indicated significant deterioration in cognitive performance with TPM (40% unchanged; 60% significantly deteriorated). With LEV, performance improved in 13%, was unchanged in 71%, and worsened in 16%. For mood and HRQOL, TPM patients showed increased depression scores and cognitive side effect concerns; patients on LEV showed no significant changes.
Conclusion: Consistent with previous findings this study demonstrates LEV treatment is efficient with no relevant cognitive or mood changes. In contrast, add-on TPM suggests a high risk of cognitive side effects. These findings are preliminary and long-term follow-up and inclusion of further patients may change the picture. Supported by funds from UCB GmbH

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Recovery of Explicit Memory after Switching Therapy using New Generation Antiepileptic Drugs
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Purpose: Memory impairment is recorded among epilepsy patients taking phenytoin and phenobarbital, according to the bibliography. This study was performed to investigate the possible recovery of explicit memory in patients, whose antiepileptic therapy was switched from conventional antiepileptic drugs (AEDs) to new generation AEDs.
Methods: Data were obtained from a randomised sample of 55 adults suffering from idiopathic temporal epilepsy. Patients over 60 years old and mentally retarded were exempted. We measured memory performance with tests focusing on explicit memory. We changed AED for those who were not sufficiently controlled or presented low performance values in the memory tests. Data were collected at two points in time: at screening and at the end of a 1 year follow up after modified treatment.
Results: 22 patients were treated with new generation AED, using levetiracetam and Keppra. 18 subjects were treated with topiramate, topamax. We did not change the treatment for 15 patients due to their antiepileptic providing sufficient control. All treatments were monotherapies. There was statistically significant improvement in explicit memory (overall evaluation) for the subjects treated with levetiracetam ($r = 0.64$, $p < 0.03$). Verbal and recent memory have presented even better values ($r=0.69$, $p<0.01$). Statistical improvement was also recorded for topiramate ($r=0.61$, $p<0.05$). The remaining 15 patients did not present any specific improvement ($r=0.33$, $p<0.5$).
Conclusion: These data demonstrate that patients receiving new generation AEDs, especially levetiracetam, had better outcomes on memory tests. This fact implies that for patients with memory impairment, especially due to AEDs, treatment with levetiracetam may offer recovery of explicit memory.

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Impact of Levetiracetam on Epilepsy in People with a Learning Disability
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Purpose: To explore the pattern of use and outcome of levetiracetam when prescribed to individuals with a learning disability and co-existent epilepsy.
Methods: The study identified all patients prescribed levetiracetam in a specialist epilepsy service for people with a learning disability through a retrospective case review. 63 individuals were identified: 26 male and 37 female with an age range of 14 to 59 years. Follow-up ranged from 3 months to 2 years. Outcome was measured by percentage seizure change at the final data point as compared with the baseline.
Results: Levetiracetam was prescribed to individuals with a range of seizure types: 31 generalised, 21 partial and 11 mixed partial and generalised. Polytherapy, including oral 'as required' antiepileptic prescription, was common with 16 patients receiving one, 29 two and 18 three drugs at baseline. Seizure frequency was defined as total seizures of all types per year. Mean seizure frequency at baseline was 517 per year (range 4-4745). At the final data point 7 individuals (11%) were worse, 7 (11%) had no seizure change, 12 (19%) had up to a 50% seizure reduction and 37 (59%) had over 50% seizure reduction. 3 patients were seizure free. 9 patients (14%) discontinued the levetiracetam and 54 (86%) continued.
Conclusion: Whilst open retrospective analysis should be treated with caution, this study shows that the use of levetiracetam in a population of people with chronic epilepsy can lead to a great reduction in the burden of seizures and is well tolerated.

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Neurobehavioural Effects of Levetiracetam: A Clinical Audit in Two Canadian Adult Epilepsy Clinics
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Purpose: Levetiracetam (LEV) was released in Canada as adjunctive treatment in partial epilepsy not satisfactorily controlled by conventional therapy, in July 2003. The neurobehavioural adverse effects (NAE) of LEV in the pivotal placebo controlled trials in adult refractory partial epilepsy were reported to be rare (3%) and mild. The purpose of this audit study in two Canadian cities was to determine the incidence of NAE in clinical practice. We analysed all cases started on LEV from adult epilepsy clinics in Calgary (N=86) and Ottawa (N=35) over a 16 month period prior to November 2004.
Methods: Retention, duration of treatment, reasons for discontinuation, titration schedules and maintenance doses, concurrent therapy, adverse effects and response were analysed.
Results: 64 males and 57 females, mean age 36.6 years, 108/121 with partial or secondarily generalised seizures and 13 with primary generalised epilepsy, were treated. Continuing patients were followed for a mean of 6.5 months (62/120 ≥6 months). Titration was slow (≤500mg/day/week) in 50 and ≥500mg b.i.d. in 70. LEV was discontinued in 41 (33.8%) due to side effects. Seizures increased in 6/120 (5%). NAE occurred in 28/121 (23%). Affective disorder was the most common (9%), followed by aggressive behaviour (8%), emotional lability (4%) and psychosis was the least common (1.6%). Discontinuations occurred in 17/28 with NAE and 11 continued despite NAE because of better than 50% seizure improvement. All side effects, including NAE, reversed promptly on discontinuation of LEV.
Conclusion: 1) NAE with LEV add-on therapy occurred in 23% of adults with refractory epilepsy. 2) NAE are more common than reported in controlled trials but led to withdrawal in only 17/121 (14%) of cases and reverse rapidly on withdrawal of LEV. 3) Discontinuations due to NAE did not appear to be related to dose or the speed of titration.

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Levetiracetam Therapy in Human Pregnancy: Preliminary Experience from the UK Epilepsy and Pregnancy Register
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Purpose: Levetiracetam is an antiepileptic drug (AED) indicated as adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation. The safety or otherwise of levetiracetam in pregnancy is unknown. Animal pregnancy data are encouraging but published data from human pregnancies are sparse. To date this has been limited to three outcomes from a single retrospective series. Here we report on our experience of pregnancies exposed to levetiracetam.
Methods: Prospective, observational, registration and follow-up study. Suitable cases are women with epilepsy who become pregnant while taking levetiracetam, either singly or along with other anti-epileptic drugs, and who are referred before outcome of the pregnancy is known. The main outcome measure is the major congenital malformation (MCM) rate.
Results: Full outcome data are available on 89 pregnancies. Of 25 pregnancies exposed to levetiracetam monotherapy no major or minor congenital malformations were observed; MCM rate 0.0%. For the 64 polytherapy exposures 1 had a MCM, (1.6% (95% C.I 0.3-8.7%)). 6 minor malformations were noted in the polytherapy group giving a rate of 11.3 % (95% C.I. 5.6-21.5%) for any type of malformation.
Conclusion: While the absolute number of outcomes of human pregnancies exposed to levetiracetam is low both preliminary animal studies and the data we present here are encouraging. Larger numbers are required for statistical analysis; as such it is imperative that practitioners continue to enrol patients into prospective pregnancy registers.

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Paediatric Pharmacokinetic Modelling for Sparse Lamotrigine Data using Adapt®
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Purpose: The paediatric population represents a vulnerable group with developmental, physiological and psychological differences from adults, which makes age and development related research particularly important. It is estimated that between 50 and 90% of medicinal products used in the paediatric population have never been specifically evaluated for use in that age group. Most physicians use ad hoc reasoning in the design of therapeutics and dosage regimens for these drugs in children, as there is still a lack of satisfactory models and software packages that will allow accurate predictions of drug levels with these drugs in these populations. This is of particular importance in a chronic neurological condition such as epilepsy.
Methods: In this study, the value of a sparse data model, using Adapt® software was developed for lamotrigine in a group of paediatric patients. Plasma lamotrigine levels in 20 paediatric patients (mean ± S.D., age 8.85 ± 3.47 years and weight, 32.22 ± 20.81 kg) were measured using a novel validated high performance liquid chromatography (HPLC) technique. The pharmacokinetic parameters in the four groups (lamotrigine alone, valproate co-medication group, carbamazepine co-medication group, and clonazepam co-medication group) were estimated in this study using model independent pharmacokinetic equations.
Results: The only significant difference ($P < 0.05$) was obtained between the four groups in the case of estimated volume of distribution, predicted minimum plasma concentration, estimated area under the curve and average plasma concentration. The data was also analysed using a modification of a one compartment first order absorption model with an Adapt® population simulation programme. The model included four kinetic parameters and two demographic parameters. A population mean of 0.64 ml/min/hr was estimated for systemic clearance, 1500 ml/kg for central volume of distribution and 4.15 hours for lag time.
Conclusion: Overall, the results thus obtained from the studies in this research, indicate the important need to streamline pharmacokinetic data for the use of AEDs in children. Our studies have shown that there are too many variables that could influence the plasma drug concentrations obtained and satisfactory models and there is still of lack of software packages that will allow accurate predictions of drug levels.

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Lamotrigine Serum Concentrations Throughout the Menstrual Cycle
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Purpose: It has been reported that the lamotrigine (LTG) serum concentration-to-dose ratio may decrease by 60% during pregnancy, thus deteriorating seizure control. This is most probably due to an increased plasma-clearance of LTG induced by hormonal changes during pregnancy. We wished to investigate whether hormonal fluctuations within a normal menstrual cycle also may alter LTG pharmacokinetics.
Methods: Repeated blood samples from two females (age 28 and 25), taken between day 0 of a menstrual cycle until the first day of bleeding, were analyzed for LTG, estradiol and progesterone. Intervals between samples were 1-3 days and the time from the last LTG intake was 10-12 hours. Both patients were on stable LTG monotherapy for at least three months, did not use hormonal contraception and were non-smokers.
Results: Minor fluctuations of the LTG concentrations were observed. However, there was a trend towards higher LTG levels during the follicular phases compared to the luteal phases. LTG serum concentrations (umol/l) in the two women ranged from follicular 24.8 to luteal 16.3, and from follicular 16.7 to luteal 13.1, respectively.
Conclusion: In contrast to the endocrine changes during pregnancy, the hormonal fluctuations throughout a normal menstrual cycle do not seem to alter LTG pharmacokinetics to a clinically significant degree. However, a slight reduction in LTG concentrations was present in both women in the mid-luteal phase. A much higher number of patients will be needed to reveal whether this trend represents a consistent relationship between LTG and hormone levels during the menstrual cycle.

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An Audit of Lamotrigine, Levetiracetam and Topiramate Usage for Epilepsy in a District General Hospital
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Purpose: The aim was to ascertain outcomes for people who had taken or who were still taking three 'new generation' broad spectrum antiepileptic drugs (AEDs); namely lamotrigine, levetiracetam and topiramate.
Methods: Hospital patient notes were searched on three separate occasions for people who were taking or who had taken one of the three audit AEDs approximately two years post the United Kingdom licensing of each audit AED. The same search criteria were used on each occasion.
Results: 93 exposures (20%) were in people who had primary generalised epilepsy, 57 (12%) had symptomatic generalised epilepsy and 317 (68%) had localisation related epilepsy. 96 exposures (20%) were in people who had learning disabilities. When audited 245 (52%)

had taken lamotrigine (LTG), 94 (20%) topiramate (TPM) and 129 (28%) levetiracetam (LEV). 13% of people became seizure free and approximately one third had a reduction of greater than 50% in their seizures. Two thirds of people were still taking their audit AED. In addition, approximately one third of people with a learning disability derived substantial benefit, although the rate of seizure freedom was lower.
Conclusion: All three AEDs were most successful at treating primary generalised epilepsy and least successful with symptomatic generalised epilepsy. With some reservations the data suggests that levetiracetam and topiramate are the most efficacious AEDs, but topiramate is the least well tolerated. These results mean consideration of a 'general prescribing policy' is important when using and choosing these AEDs.

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Significant Improvement on Different AED Regimens: An Audit of 559 Inpatients with Chronic Epilepsy
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Purpose: To determine which antiepileptic regimens were most effective in a special patient population with intellectual disabilities.
Methods: We investigated resident patients of the Bethel Epilepsy Centre who had mental retardation or multiple handicaps of different degrees. Inclusion criteria: a confirmed diagnosis of epilepsy (ILAE criteria); inpatients since at least 1992. These data were extracted out of the patient files: seizure frequency in 1992 and 2002 (completely/nearly seizure free; more than one per year; more than one per month; more than one per week; more than one per day) and antiepileptic medication in 1992 and 2002. A patient was considered 'improved' if changed into a better frequency class (e.g. in 1992 more than one seizure per day, in 2002 more than one seizure per week).
Results: Of 559 patients included, 226 (40%) were improved in 2002 as compared to 1992. Improved patients were on the following antiepileptic regimens: lamotrigine/valproate (49 patients), carbamazepine/phenobarbital (23), only carbamazepine (19). 70 other regimens occurred in less than 10 improved patients.
Conclusion: The study has obvious limitations: its retrospective character; it also reflects different therapy strategies by the individual epilepsy specialists; other factors besides medication may have influenced seizure activity. Strengths are the large patient number and also the long time span reported. Our results clearly point at lamotrigine as the major therapeutic innovation of the last decade and at lamotrigine with valproate as an example of rational combination therapy. Further improvements were mainly achieved by optimisation of therapy with classic antiepileptic drugs (AED) rather than by administering new AED. The rate of significant improvements in highly therapy resistant patients was surprisingly high. Even for chronic epilepsy, long term specialist antiepileptic treatment with systematic trials of nearly all available AED is worthwhile.

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Safety of Valproate and Lamotrigine Combination Therapy in Patients with Refractory Complex Partial Epilepsy: Post-marketing Experience with Different Titration Schedules
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Purpose: Comparison of adverse effects of lamotrigine (LTG) and valproate (VPA) combination therapy, in patients with refractory complex partial epilepsy with regard to different titration schedules.
Methods: Retrospective analysis of patients initiated LTG add-on therapy with pre-existing VPA therapy, for the treatment of patients with refractory partial epilepsy. We analysed efficacy and safety of treatment in different study groups. Statistical analysis was performed for alpha=0.05; results are expressed as confidence intervals.
Results: 173 patients (median age 26 years, range 18-54), were initiated with LTG add-on therapy with previous VPA therapy. Three different LTG starting daily doses were recognised: A) 12.5mg alt die (n=32); B) 12.5mg (n=97) and C) 25mg (n=44). LTG doses were escalated by 6.25-25mg every 2 weeks, until initial target dose of 100mg/d were achieved. Further adjustment was performed according to clinical response. Median achieved daily doses for LTG and VPA were 250mg and 1000 mg respectively. Seizure freedom and reduction were similar between groups. Adverse effects were significantly more frequent in group C (13/44, 29.5%, 18.2-44.2%) in comparison with group B (15/97, 15.5%, 9.6-24%) and group A (4/32, 12.5%, 5-28.1%). The most serious adverse effect was rash, leading to discontinuation of LTG in 20.45% (group C), 3.01% (group B), and no patients from group A.
Conclusion: Side effects with LTG add-on therapy are likely connected with starting doses and titration schedule rather than VPA comedication. In order to improve safety of LTG add-on therapy a starting dose smaller than recommended could be useful.

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Effect of Lamotrigine in 5 Patients with Unverricht-Lundborg Disease: Clinical Observations
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Purpose: Unverricht-Lundborg disease (ULD) is a progressive myoclonus epilepsy with tonic-clonic seizure, action myoclonus, mild ataxia, without dementia. Persistence of invalidating action myoclonus is a major problem. Some drugs can aggravate ULD like phenytoin and carbamazepine. In this study, we retrospectively analysed the effect of add-on lamotrigine (LTG) in 5 patients.
Methods: 5 patients, 3 men and 2 women, aged 20 to 50 years who had ULD confirmed by molecular biology have been referred in two epilepsy centres. Lamotrigine was given at 100 to 200 mg/d during a minimum of 6 months. All of them had valproate. The other drugs used in co-therapy were piracetam, levetiracetam and benzodiazepines.
Results: In our series LTG was not very efficient, as most patients (4/5) did not notice a change in seizure frequency. 1 patient experienced a clear exacerbation of myoclonus jerks at 200 mg/d leading to LTG decrease. At 100 mg/d exacerbation disappeared. Because of lack of efficacy, LTG was discontinued in all.
Conclusion: LTG does not appear an effective drug in Unverricht-Lundborg disease. In some cases, LTG can aggravate myoclonus jerks in a dose-dependent manner.

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Lamotrigine may be Associated with Early or Late-onset Exacerbation or De Novo Appearance of Myoclonus in Idiopathic Generalised Epilepsy
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Purpose: Lamotrigine (LTG) is widely used in idiopathic generalised epilepsies (IGE) but may aggravate myoclonic jerks (MJ) in juvenile myoclonic epilepsy (JME). De novo MJ and myoclonic status have never been reported in IGE.
Methods: In our IGE population treated with LTG, we identified 5.4% patients with exacerbation or de novo appearance of MJ.
Results: 5 patients (1 JME, 1 juvenile absence epilepsy, and 3 other IGE not further classified), received LTG monotherapy (3 patients) or add-on to valproate or phenobarbital. In 2 patients, the onset of MJ was delayed (9 and 12 months), 1 had de novo MJ and both patients developed myoclonic status leading to withdrawal of LTG. In the other 3 patients, MJ appeared during titration (range 4 weeks to 16 weeks). MJ were de novo for 2 patients and consisted of exacerbation

in 1 patient. MJ disappeared when the dose was decreased by 25 to 50%. For all patients, MJ were numerous, intense, and affected the neck and the lower limbs.
Conclusion: In patients with IGE, LTG may be responsible for de novo appearance or exacerbation of MJ. We found two distinct profiles of aggravation: a benign type during titration which responds to reduction of dosage; a severe type with a risk of myoclonic status, which required withdrawal of LTG. Although, LTG may trigger MJ, this risk is low and LTG must clearly remain a treatment option in IGE.

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Lamotrigine in Pregnancy
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Purpose: Lamotrigine (LTG) is increasingly used for women with epilepsy. Changes in LTG plasma levels during pregnancy have already been described, but the clinical significance of these changes is unknown. The aim of the observation was to identify changes in dosage of LTG during pregnancy in a routine clinical setting.
Methods: We retrospectively analysed 15 pregnancies in a series of women with epilepsy exposed to LTG monotherapy. We collected the following data: age of patients, type of epilepsy and seizures, frequency of seizures and EEG, prepregnancy daily dose of LTG and plasma level when available, changes in LTG dosage and plasma levels and seizure frequency during pregnancy.
Results: The mean age of patients was 28 years (21-36). 11 idiopathic generalised epilepsies, 3 focal epilepsies and 1 undetermined epilepsy were identified. The mean prepregnancy LTG dose was 220 mg/day (range 0-500). There were no changes in LTG daily dose during pregnancy in 7 patients (47 %). The dose was increased in 8 patients, but in only 4 patients was this due to seizure recurrence. LTG plasma levels obtained were in a broad range from 1.05 to 57.09 micromol/L. LTG prepregnancy plasma levels and measurements during pregnancy were not examined in fixed terms in all patients but on the basis of clinical need.
Conclusion: Further information is needed and a fixed schedule for examination of LTG plasma level is proposed: 1) prepregnancy, 2) end of first trimester (13th week), end of second trimester (26th week), before (39th week) and after delivery (1st day and 7th day).

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Twelve Years of Monitoring Through an International Observational Study of Pregnancy Outcomes Following Exposure to Lamotrigine
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Purpose: The international registry forms part of an epidemiologic safety programme monitoring pregnancy outcomes in women exposed to lamotrigine.
Methods: Physicians report exposure to lamotrigine during pregnancy and subsequent outcomes on a voluntary basis. Prospective reporting early in pregnancy is encouraged. Major congenital malformations (MCMs) are classified according to the Centers for Disease Control criteria and are reviewed by a paediatrician. The percentage of MCMs is calculated for prospective first trimester lamotrigine monotherapy and polytherapy exposures. Conclusions are developed by a scientific advisory committee.
Results: As of September 2004, 14 MCMs were observed among 491 monotherapy exposures giving a risk of 2.9% (14/491,95% CI 1.6% - 4.9%). This is similar to the risk in the US general population (~2.2%) and in women with epilepsy on AED monotherapy (3.2% to 4.5%). The observed risk among 101 lamotrigine and valproate polytherapy exposures was 11.9% (95% CI 6.6% - 20.2%) and was 2.9% (95% CI 1.2% - 6.5%) among 206 exposures to lamotrigine polytherapy without valproate. No consistent pattern of malformation types was observed.
Conclusion: The current data do not indicate any large association between prenatal lamotrigine exposure and an elevated risk of major birth defects, though the sample size is insufficient to allow definitive conclusions concerning specific defect types. The higher frequency of major malformations following lamotrigine-valproate polytherapy exposure was consistent with publications on valproate monotherapy, though the registry is not powered to determine the individual contribution of each medication. Supported by GlaxoSmithKline.

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Lamotrigine Induced Fatal Stevens-Johnson Syndrome
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Purpose: Lamotrigine (LTG) is a broad spectrum antiepileptic drug that blocks sodium channels, thereby inhibiting the pre-synaptic release of excitatory neurotransmitters. It has become established as a major antiepileptic drug with good efficacy against a variety of seizure types. It has a reasonable adverse effect profile, which has contributed positively to its acceptance. It rarely causes severe adverse effects. In this study we report 2 cases of fatal Stevens-Johnson syndrome, in spite of following the strict criteria of slow introduction and titration of the drug and taking care of comedication.
Methods: We treated 72 patients with LTG. 59 males, 13 females aging from 15 years to 62 years for 3 years from December 2001 to December 2004. 42 of them had primary generalised seizures and 30 patients had partial and secondary generalised seizures. LTG was introduced in all of them as an additional drug as the seizures were refractory.
Results: Patient No 1: 21 year male had suffered from secondary generalised seizures since age 10 and was on carbamazepine 1000mg/day. He was given LTG as an additional drug starting with 12.5mg BD and titrated up to 50mg BD over a period of 4 weeks. 4 weeks later he developed extensive exfoliative dermatitis and S.J. Syndrome and died 10 days later in the hospital. Patient No 2: 43 year old male had suffered from primary generalised seizures for the past 15 years and was treated with phenytoin sodium 300mg/day and phenobarbitone 120mg/day. Seizures were recurrent and intractable. LTG was started in a small dose and titrated slowly, meanwhile phenobarbitone was withdrawn. About 22 days after LTG with dose of 25mg BD he developed a severe form of S.J. Syndrome and died 6 days after admission.
Conclusion: Even though lamotrigine (LTG) is a safe and broad spectrum second line AED and can also be used in monotherapy, it can still rarely cause fatal Stevens-Johnson Syndrome and we should be careful in using this drug.

p221
Metabolic Side-effects During Valproate, Carbamazepine and Lamotrigine Therapy
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Purpose: The most common side effect of VPA is weight gain and an increase in insulin resistance associated with various metabolic and endocrine abnormalities. In the present study we have evaluated the occurrence of non alcoholic fatty liver disease (NAFLD) in epilepsy patients.
Methods: 68 non-diabetic patients (37 women and 31 men) on continuous antiepileptic therapy were consecutively recruited. 23 patients were on VPA, 22 on CBZ and 23 on LTG. Clinical visits

included laboratory controls, determined in the morning after an eight hour overnight fasting period, determination of body mass index (BMI) and ultrasound scanning performed by use of a standard technique.
Results: The BMI was 24.8±6.0 kg/m2 in the VPA group and thus significantly higher than in the lamotrigine group (22.2±2.6 kg/m2). Treatment with VPA was associated with metabolic findings indicating a higher degree of insulin resistance than under carbamazepine or lamotrigine therapy. Ultrasound measurements could demonstrate characteristics of fatty liver disease in 14 of 23 VPA (60.9%), in 5 of the 22 CBZ (22.7%) and in 2 of 23 LTG patients (8.7%). The ultrasound finding of steatosis revealed a significant positive correlation with BMI in the whole study population (R=0.592, p<0.001), as well as in VPA (R=0.645, p<0.003) and carbamazepine treated patients (R=0.645, p<0.001) A correlation with plasma insulin levels was only demonstrable in the VPA group (R=0.609; p=0.002).
Conclusion: The increased risk of NAFLD under VPA therapy might be related to the increased risk of insulin resistance. Our data show the importance of glucose and lipid control, as well as BMI and ultrasound measurements in the course of AED.

p222
Effects of Topiramate on Epileptiform Discharge Induced by Mg2+-free medium and 4-aminopyridine in Hippocampal Slice of Immature Rat
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Purpose: Topiramate (TPM) is one of the newest antiepileptic drugs. However, its action mechanism is not understood very well and the optimal dose of antiepileptic efficacy in animal seizure models is not yet determined. In order to elucidate the action mechanism and the optimal concentration of TPM that suppresses the epileptic discharge, we observed ictal and interictal discharges from immature rat hippocampal slices in Mg2+-free, 4-aminopyridine (AP) added artificial CSF with various TPM concentration.
Methods: We divided 19-23 day old Sprague-Dawley rats into 5 groups, control group (n=12) and 4 TPM groups; divided by the concentration of TPM, 6 (n=11), 20 (n=7), 60 (n=10), and 200 (n=14) μM. The rats were anesthetised and their brains were taken, soaked in artificial CSF (NaCl 125 mM; KCl 2.5 mM; NaH2PO4 2 mM; MgSO4 1.25 mM; NaHCO3 25 mM; CaCl2 2 mM; glucose 10 mM, pH 7.3-7.4). Then the brains were cut into 400 □ hippocampal slices by vibratome. The slices of control group were soaked in 200 μM 4-AP added Mg2+-free medium for 1 hour, then extracellular recordings were performed in hippocampal CA1 pyramidal region. The slices of TPM groups were soaked in the solution containing 6, 20, 60, 200 μM TPM, then extracellular recordings were performed.
Results: 1) Interictal discharges were observed in all of control group and 6, 20 μM group but the frequency was decreased as the concentration of TPM increases, 90% in 60 μM group, and 35.7% in 200 μM group. And the amplitude of TPM group was much smaller than that of the control group. The latency to the first interictal discharge after 4-AP addition was 52.7 ± 7.5 sec in control group, but was 290.2 ± 78 sec in 60 μM group, 568 ± 113.1 sec in 200 μM group. Duration of interictal discharge was 64.6 ± 10.3 sec in control group, but was prolonged to 141 ± 38.1 sec in 60 μM group (p<0.05). 2) Ictal discharges were observed in all of control and 6 μM group, but the frequency was decreased as the concentration of TPM increases, 55.6% in 60 μM, 28.6% in 200 μM group. The amplitude of TPM group was much smaller than that of control group. The latency to ictal discharge after 4-AP addition was 141 ± 15.2 sec in control group, but increased as the concentration of TPM increases, 431.8 ± 57.4 sec in 60 μM, 627.8 ± 143.5 sec in 200 μM group (p<0.05). The duration of ictal discharge was 1534.7 ± 97.9 sec in control group, but decreased as the concentration of TPM increases, and the shortest in 60 μM-treated group, 155.2 ± 65.5 sec (p<0.05). 3) Status epilepticus was seen in 58.3% of control and 27.2% of 6 μM-treated group.
Conclusion: TPM suppresses the frequency, latency, and duration of epileptiform discharge induced by Mg2+-free, 4-AP added artificial CSF in immature rat hippocampal slices, starting from 20 μM concentration and reaching the maximal effect at over 60 μM. This finding is presumably due to TPM enhancing of GABA receptor currents and/or K+ channel conductance in response to TPM.

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Neuroprotective Effect of Topiramate in Cultured Rat Primary Cortical Neurons Exposed to Oxygen-Glucose Deprivation
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Purpose: Topiramate (TPM) is a structurally novel compound which has demonstrated a broad spectrum of antiepileptic activities both in experimental and clinical studies. We tested whether treatment of TPM could reduce OGD-induced in vitro ischemic neuronal damage and what was the action mechanism of TPM.
Methods: Primary cerebral cortical cell cultures were prepared from embryonic 17 days rat. Cultured neurons were transferred to anaerobic chamber containing a gas mixture of 5% CO2, 10% H2, 85% N2 and exposed to glutamate receptor specific agonists (Glutamate, AMPA , NMDA or Kainic acid). TPM and glutamate receptor specific antagonists (CNQX, NBQX, GAMS, D-AP5) were included in the culture from the time point when OGD- or glutamate receptor agonists were treated.
Results: There were less than 5% neurons remaining 24 h after OGD treatment in control group, whereas treatment with TPM after OGD significantly increased the number of viable cells. Treatment of TPM with non-NMDA receptor antagonists (CNQX) did not show additive effects, whereas co-treatment with NMDA receptor antagonists (D-AP5) exhibited marked additive effects.
Conclusion: TPM selectively prevented AMPA-induced, but not NMDA or KA-induced neuronal death. These results suggest that TPM suppress OGD-induced neuronal death via AMPA receptor blockade, and TPM treatment may be beneficial for several brain diseases related to the excitotoxicity.

p224
Low-dose Topiramate is Effective in the Treatment for Infantile Spasms
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Purpose: Management of infantile spasms is difficult because current treatment regimens, including many anticonvulsants and hormones, are often ineffective. We conducted this study to test the effective dose of topiramate (TPM) in patients with infantile spasms.
Methods: 14 patients with infantile spasms were given TPM with an initial dose of 12.5 mg/d, and the dose was raised by 12.5 mg every 2-3 days. If the seizure frequency had not decreased after the initial 2 weeks, the dose was raised more rapidly. Titration continued for < 12 weeks or until one of the following end points was reached: a maximal dose of 24 mg/kg/d was achieved, a maximal tolerated dose was attained, or spasms were absent for 7 days. Subjects were monitored by weekly titration visits. After stabilization, spasms were monitored at 3 monthly intervals.
Results: Aetiology of the infantile spasms included cryptogenic group (n=3) and symptomatic group (n=11). Overall, 5 patients (38%) became spasm free. A > 50% reduction in spasms was observed in 11 (85%) of the 13 subjects during stabilization. The mean dose of TPM during stabilization was 7.35±4.9 mg/kg/d. 6 patients achieved

seizure control, 3 became seizure free, with a TPM dose lower than 6 mg/kg/d.
Conclusion: Seizure control was achieved in good result with a lower dose of TPM therapy (7.35±4.9 mg/kg/d) in this study than previous studies suggested (Glauser et al. 15.0 ± 5.7 mg/kg/d).

p225
Topiramate (TPM) in Children ≤2 Years with Refractory Infantile Spasms (IS) and Refractory Epilepsy (RE)
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Purpose: The special challenge of seizure control in very young children may reflect a different nature of epilepsy and more rapid clearance of antiepileptic drugs (AEDs) than in older children. We report on findings from TPM use in the very young.
Methods: Data from 3 studies involving 57 children ≤2 yrs with refractory IS or RE were analysed. Open-label TPM was added to existing therapy at 1 mg/kg/day and titrated to an optimal dosage.
Results: Study 1: TPM pharmacokinetics were evaluated in 8 children 0.76-1.84 yrs of age receiving b.i.d. TPM (7.00-8.90 mg/kg/day). At steady state, apparent oral clearance was 30.5-60.2 mL/hr/kg and half-life was 7.36-9.92 hrs in patients receiving non-enzyme-inducing AEDs, compared with 76.8-121 mL/hr/kg and 4.35-5.00 hrs, respectively, in those receiving enzyme-inducing AEDs. Study 2: Frequency of spasms and other seizures was reduced in 21 children with IS (median age, 8.8 mos; range, 0.8-25.8 mos) treated with 17.3 mg/kg/day (median) TPM; 11 patients were spasm-free ≥7 days. Study 3: 7/8 children with IS had a clinically significant response (≥50% seizure reduction). Among children with other forms of RE, seizures were reduced ≥50% in 8/20 patients. Overall, few patients experienced treatment-limiting adverse events (4/57 discontinued). Most common adverse event was irritability.
Conclusion: Children ≤2 yrs with RE who were treated with open-label TPM had fewer spasms and other seizure types. Because TPM clearance is higher in infants than in older children, higher mg/kg doses may be needed, especially with enzyme-inducing AEDs. Study sponsor: Janssen-Cilag and Johnson & Johnson Pharmaceutical Research and Development, L.L.C.

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Topiramate Treatment for Infantile Spasms: A Retrospective Analysis of 28 Cases over a 5 Year Period
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Purpose: This is a retrospective analysis of cases with infantile spasms admitted in our clinic over a period of 5 years, treated with topiramate (TPM) and evaluating the immediate and long-term effects (efficacy and safety) of this drug.
Methods: There were 28 patients with infantile spasms who received TPM as monotherapy (7 cases) or as add-on therapy (21 cases). Data were extracted from medical files and direct questioning of the parents. Blood tests, EEG, neuroimagery were performed . 5 cases with unclear anamnesis had video-EEG. TPM titration: started with 1mg/kg/day and raised by 1mg/kg/day every 7days to maximum 10mg/kg/day. Titration was stopped if seizures ceased (in some patients at 3mg/kg/day).
Results: Overall, 10 patients remained seizure-free, 8 patients had 50-80% and 6 had less than 50% reduction of seizure frequency. In 2 patients TPM had no effect. 4 of 7 patients with TPM monotherapy remained seizure-free. Long-term observation of these cases (1.5 to 4.5 yr) revealed: 6 cases remained seizure-free and 5 developed other seizure types: partial seizures (2 cases) or evolved in LGS (3 cases). In 13 cases TPM was discontinued after 3 mo. to 2.5 yr after treatment onset. Hypsarrhythmia was noted in 22 cases and in 6 was not. Few patients reported adverse events: weight loss, nervousness, behavioural problems). One patient discontinued TPM because of adverse events.
Conclusion: 1) TPM monotherapy had better results than add-on therapy in our group; these results are not statistically significant and need further monotherapy studies. 2) There was no correlation between spasm aetiology and treatment results. 3) There was no correlation between treatment response and TPM dose: best response appeared after the first 2-4 administrations. If there was no response in the first 2 weeks, further dose raising gave poor benefits. 4) TPM was well tolerated even at young ages.

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Recent Experience from Clinical Trials of Topiramate in Children
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Purpose: To assess the efficacy and tolerability of Topiramate as monotherapy (in recently diagnosed patients with epilepsy) and adjunctive therapy (in intractable childhood epilepsy).
Methods: Children > 2 years with uncontrolled seizures were included, regardless of epilepsy type. The patients were followed up to 6 months. Topiramate was started at dose 0.5 mg/kgBW/day (monotherapy) and 1 mg/kgBW/day (adjunctive). The dose could be increased by 0.5 mg/kgBW/day weekly increments, depending on the clinical response. Maximum dose was 9 mg/kgBW/day. The outcome measurement was seizure free (50%, 75%, 100% responders) and adverse events.
Results: Monotherapy trial: 22 patients were recruited (mean age = 6.5 years), median baseline seizure frequency was 8 seizures per month. The 100% seizure reduction (seizures free) was observed in 17 patients, whereas about 1 patient has shown 50% and 75% seizure reduction each. Mean Topiramate dose was 2.75mg/kgbw/day. Adjunctive trial: 40 patients were recruited (20 got TPM and AEDs, 20 got only AEDs). Median baseline seizures frequency case vs control was 35 seizures/month and 60 seizures/month. Median seizure reduction was 88.6% vs 25.0%, p=0.030. Seizure freedom was experienced by 25% patients (case) and 5% patients (controls), p=0.049. Mean topiramate dose was 8.3 mg/kgBW/day. Safety and tolerability: the common adverse events were decreased body weight, fever, and flushing.
Conclusion: In both monotherapy and adjunctive trials, topiramate was shown as an effective and safe AED for childhood epilepsy.

p228
Topiramate in Children and Adolescents with Epilepsy
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Purpose: To evaluate the efficacy and tolerability of flexible doses of topiramate (Topamax®; TPM) in children and adolescents with epilepsy independent of seizure type and epilepsy syndrome.
Methods: In this prospective multicentre observational study in- and outpatients 2–16 years of age with epilepsy were evaluated at baseline and after 12 and 24 weeks.
Results: Of 176 patients (53% male, mean age 8.9 years), 65% had partial and 29% had generalised seizures, 6% were unclassified. TPM was introduced mainly due to persisting seizures (73%) or side effects (26%) with the previous AED. The mean daily dose of topiramate at endpoint was 3.3±2.0 mg/kg body weight in monotherapy (45% of patients) and 4.5±3.8 mg/kg in combination (55% of patients). Median seizure reduction was 90%, and 40.5% of the patients remained seizure free for more than 3 months. Seizure reduction was substantial not only for partial and tonic-clonic but also for absence (77% responders) and myoclonic seizures (80% responders). The only adverse event >5% was somnolence (8.5%). Cognitive adverse events

such as language problems (4.5%), difficulties with thinking (4.5%) or concentration (2.3%) were infrequent.
Conclusion: In children and adolescents between 2 and 16 years of age topiramate was associated with a substantial reduction in seizure frequency and well tolerated. The high responder rates for both partial and primary generalised seizures including absences and myoclonic seizures support recent results about the broad spectrum efficacy of topiramate in this age group.

p229
Assessment of the Effectiveness and Safety of the First Adjunctive Treatment of Topiramate (TPM) in Patients with Refractory Epilepsy
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Purpose: The objective of the current study was to assess the efficacy of TPM in the adjunctive treatment of refractory epilepsy previously treated with other drugs in monotherapy.
Methods: The paper presents the results of a retrospective study concerning the effectiveness and safety of the first adjunctive treatment of TPM in patients with refractory epilepsy with partial and secondarily generalised seizures, previously treated with CBZ or VPA in monotherapy. The study included 62 patients. There were 33 females and 29 males, aged from 17 to 65. The initial dose of TPM (25mg) was continued for one or two weeks and then increased by 25mg per week and administered twice a day. The average total daily dose was 250mg (100-500). TPM was given together with CBZ (41 patients) and VPA (21).
Results: The final analysis included 50 patients, while in 12 subjects (19.4%) the treatment was discontinued due to the adverse effects of TPM. After the 6 month observation, 17 patients (34%) became seizure free, in 27 (54%) a reduction in seizure frequency above 50% was observed and in 6 (12%) the effects of treatment were not good enough. After the 12 month observation, 14 patients (28%) were still seizure free, in 22 (44%) a reduction in seizure frequency above 50% was observed and in 7 (14%) the effects of treatment were not good enough. 7 patients (14%) were excluded from the study due to lack of therapeutic effects.
Conclusion: The results in this group of patients with refractory epilepsy have demonstrated that TPM is an effective drug for this condition. After the one year observation, treatment with TPM as first add-on therapy with basic antiepileptic drugs (CBZ, VPA) was effective in 58% of cases with refractory epilepsy. TPM was discontinued in 19.4% of patients due to adverse effects.

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Topiramate as First-line Adjunctive Therapy of Epilepsy
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Purpose: To evaluate the tolerability and efficacy of flexible doses of topiramate (Topamax®; TPM) as first-line adjunctive antiepileptic drug (AED).
Methods: In this multicentre observational study, patients with epilepsy (12 years or older) who had failed on their first AED monotherapy were enrolled. Patients were evaluated at baseline and after 6, 16 and 30 weeks.
Results: 239 patients (58% female, mean age 42 years, range 12–89 years) were enrolled. 54% had partial and 36% had generalised epilepsy. Reasons for initiating TPM were lack of efficacy (85%) and lack of tolerability (23%) of the previous AED, mainly carbamazepine (55%) or valproic acid (40%). The mean TPM dose at endpoint was 118±60 mg/day. 53% of patients received 100 mg TPM/day or less during the study. In 35% of patients the previous AED could be discontinued. 50% of the patients remained seizure free throughout the study, 89% had a seizure reduction of at least 50%. 88.7% of the patients continued TPM after the end of the observation period. There were no adverse events (AEs) >5%. The most frequently reported AEs were dizziness (4.2%), weight decrease (2.5%) and nausea (2.1%). 3.3% of patients discontinued due to an AE. The only cognitive side effects reported were difficulty with memory (1.3%) and language problem (0.4%).
Conclusion: Topiramate as first line add-on therapy was associated with a substantial reduction of seizure frequency and a high seizure-free rate. The use of topiramate doses comparable to those recommended for monotherapy was associated with good tolerability including few CNS-related side effects.

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Topiramate Monotherapy in Patients with Epilepsy: A Prospective Multicenter Flexible-dose Study
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Purpose: To evaluate the efficacy and tolerability of flexible doses of topiramate (TPM) in epilepsy monotherapy independent of seizure type or epilepsy syndrome.
Methods: In this naturalistic prospective multicentre study, patients >12 years of age, previously untreated or unsuccessfully treated with a maximum of one antiepileptic drug were evaluated at baseline and after 6, 16 and 30 weeks. Patients were either initiated on or converted to TPM monotherapy.
Results: 243 patients (44% male, mean age 43±17 years, range 13–91 years) were enrolled. The most frequent seizure types were generalised tonic-clonic (n=154), complex partial (n=50), simple partial (n=35) and absence seizures (n=35). Of all patients, 47% were recently untreated, 68% of those received TPM as their first antiepileptic treatment. At endpoint, the median topiramate dose was 100 mg/day. 61% of the patients received 100 mg TPM/day or less. Of the 216 patients completing the study, 64% remained seizure free for at least the last 12 weeks of the study. 90% were responders with at least 50% seizure reduction. Median seizure frequency decreased from 4.0 at baseline to 1.0 at endpoint. 2.1% of the patients discontinued the study prematurely due to lack of efficacy, 7.0% due to an adverse event. Adverse events reported in >3% were dizziness (4.0%), headache (3.6%) and paraesthesia (3.2%).
Conclusion: Topiramate monotherapy in patients with epilepsy was associated with a substantial reduction of seizure frequency and a high seizure-free rate, independent of seizure type or epilepsy syndrome. Topiramate daily doses of around 100 mg were well tolerated.

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Optimising the Tolerability of Topiramate Through Reduction of Antiepileptic Co-medication
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Purpose: Topiramate (TPM) has been associated with a wide range of adverse effects including cognitive side-effects like memory and speech disturbances. The purpose of this study was to evaluate the impact of reduction of antiepileptic co-medication on the range of side-effects of TPM.
Methods: Naturalistic, observational study in Switzerland. In total, 108 patients with epilepsy with an average age of 32 (± 20) years were included by neurologists and neuro-paediatricians. During the observation period of one year patients were put on TPM and additional antiepileptic co-medication was gradually reduced, if possible.
Results: The ratio of patients on TPM monotherapy increased from 6% at the beginning to 36% at the end of the observation period. The average number of antiepileptic drugs (AEDs) per patient could be reduced from 1.6 to 1.1. 71% of the patients completed the study, with all of them continuing the TPM treatment. A comparison of the patient groups treated either with a combination therapy (TPM plus □ 1

AED) or with TPM monotherapy at the end of the study revealed a side-effect-rate of 19% and 13%, respectively. Furthermore, in the combination-therapy subgroup a variety of known side-effects was observed whereas in the TPM monotherapy group the range of side-effects was reduced to paresthesia, ataxia and amenorrhea (4.3% each). Response rates (patients with >50% seizure reduction) were 81% for the combination-therapy group and 92% for the TPM monotherapy group.
Conclusion: Compared to previous regulatory trials, this naturalistic setting demonstrated a decrease in the total side-effect rate for TPM, especially of cognitive side-effects like memory and speech disturbance. This may be associated with the reduction of adjunctive AEDs. The benefits in the tolerability profile for TPM monotherapy are not offset by a reduced efficacy.

p233
Post-launch Survey on Use and Outcome of Topiramate Treatment in Patients with Epilepsy
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Purpose: To document use and outcome of topiramate treatment for epilepsy in clinical practice following its registration in the Czech Republic.
Methods: Results of treatment with topiramate according to regular prescribing were recorded on forms during 2001-2003 to document its post-registration use, efficacy and safety in children and adults. Disease features, seizures, concomitant medications, adverse events and further prescribing were documented for 6 months.
Results: Data were collected by 50 epileptologists on 933 patients (230 children <16 years): 31.5% presented with simple partial, 50.3% complex partial, 59.2% secondarily generalised and 11.3% other seizures. At the start, 13.1% received topiramate monotherapy, while 48.3% used one additional AED, 38.6% two AEDs add-on to topiramate (mainly valproate and carbamazepine). After 6 months, these proportions were 25.2%, 50.9% and 23.9% respectively. During topiramate, seizures decreased in 83.7% of patients versus start and increased in 13.4% (2.9% no change); 64.8% of patients had achieved at least 50% seizure reduction. At the end of the survey, topiramate was chosen to be continued in 86.7% of patients, and to be stopped in 9.4% (reasons: lack of effect on seizure frequency (3.4%) or seizure course (1.9%) and adverse events (5.9%); 3.9% no data). The most common side effects were weight loss (5.0%), drowsiness (4.8%), CNS-inhibition (4.5%), lack of appetite (4.1%) and paraesthesia (3.1%).
Conclusion: In this survey, a high intention for topiramate continuation was found, possibly mediated by improved seizure control, good tolerability and/or reduced concomitant AED burden. (Funded by Janssen-Cilag).

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Quality of Life in Treatment of Epilepsy: Topiramate Compared to Conventional AEDs-Carbamazepine and Valproic Acid
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Purpose: To evaluate the use of HRQL in comparing new and conventional AEDs in patients with epilepsy.
Methods: We conducted a one year, prospective, open labelled study, which included 82 patients with refractory epilepsy. 42 received topiramate (100 mg/day), 29 were treated with carbamazepine (800 mg/day) and 11 received valproic acid (900 mg/day). HRQL-QUOLIE 89 was used as a measure of therapeutic efficacy, to compare new AEDs and conventional AEDs. Seizure reduction rate was also assessed in the three groups of patients (reduction >50%).
Results: The improvement of QUOLIE score in topiramate treated patients was 38% ($p<0.05$), where reduction of seizures >50% was achieved in 48% patients. The carbamazepine group of patients showed lower improvement of QUOLIE-89 (18%) after 1 year, but seizure reduction >50% was registered in 31% of patients. Improvement of QUOLIE score in valproic acid group was 23% after 1 year, and seizure reduction was >50% in 38% of patients.
Conclusion: Improvement of QUOLIE score was significantly higher in topiramate treated patients, compared to conventional AEDs. Our results suggest that this is probably due to reduction of seizure frequency, but also because of improvement of social, mood and cognitive functions.

p235
Topiramate (TPM) in Older Adults with Partial-onset Seizures: A Double-blind, Dose-comparison Study
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Purpose: We evaluated TPM in the first double-blind, randomised controlled trial limited to older adults with partial-onset seizures (POS).
Methods: Patients ≥60 yrs old with ≥1 POS in last 6 mos, ≥2 POS in 12 mos, and drug-naive or on 1 AED were randomised to 50 or 200 mg/day TPM titrated 25 mg/day/week. Once 50 mg/day achieved, co-therapy was tapered 25% weekly to convert to TPM monotherapy; patients were maintained on adjunctive therapy if conversion unsuccessful.
Results: In 45 patients on monotherapy, the proportion seizure free (TPM 50, 52% [11/21]; TPM 200, 58% [14/24]) and median time to first seizure (168 days) did not differ by assigned dose. Of patients on adjunctive therapy, the proportion seizure free (TPM 50, 21% [3/14]; TPM 200, 50% [6/12]) and median time to first seizure (TPM 50, 56 days; TPM 200, 81 days) favoured the higher TPM dose. Overall, 13% reported ≥1 cognitive-related adverse event (TPM 50, 16%; TPM 200, 10%). Adverse events were treatment-limiting in 7 (18%) in each group; only 2 patients (both in TPM 50 group) had cognitive-related treatment-limiting adverse events.
Conclusion: Although our sample size was too small to definitively conclude that 50 and 200 mg/day are equally effective as monotherapy, data suggest that, when initiating TPM as monotherapy in older patients, 50 mg/day TPM may be a dose at which to evaluate early response, with further titration as needed. In older patients, 200 mg/day TPM as adjunctive therapy appears to be an effective dose with monotherapy-resistant epilepsy. Study sponsor: Ortho-McNeil Pharmaceutical.

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Can Topiramate Aggravate Juvenile Myoclonic Epilepsy?
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Purpose: Juvenile myoclonic epilepsy (JME) is a condition that can be aggravated by various anticonvulsants. Aggravation of JME by topiramate (TPM) has never been reported.
Methods: A female patient had experienced myoclonic jerks (MJ) and a total of 4 GTCS with onset at age 13. The clinical and EEG traits were typical for JME. On valproate, she was totally controlled but experienced weight gain and hair loss. She was switched to TPM, with slow uptitration to 400 mg/d (8 mg/kg) because of persisting GTCS.
Results: Besides other benign side-effects (impaired memory, slurred speech, mental slowing), there was a progressive, dose-related worsening of MJ and GTCS. In parallel, the EEG showed a marked increase of interictal SW discharges. Rapid tapering of TPM resulted

in spectacular EEG and clinical improvement. The patient was then treated with a combination of lamotrigine and clobazam, and is now totally controlled (follow-up: 6 months).
Conclusion: TPM is increasingly used in idiopathic generalised epilepsies, with satisfactory results in most cases. In JME, drugs like carbamazepine and oxcarbazepine are associated with a high risk of aggravation, while other drugs like phenytoin and lamotrigine are less often, but also significantly involved. This observation points to the possibility of aggravation using TPM, which should be used with proper warning. Dose escalation must be avoided if the initial response already points to a possible paradoxical effect.

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Relationship between Topiramate Use and Ocular Angle Status: A Prospective Pilot Study
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Purpose: Topiramate is approved for the treatment of epilepsy and prophylaxis of migraine attacks. There were case reports of acute angle closure glaucoma (AACG) associated with its use. As AACG is particularly common in Asians because of a higher prevalence of narrow angle, we test the hypothesis whether topiramate narrows the ocular angle, rendering patients more likely to suffer from AACG.
Methods: Adult patients indicated for topiramate treatment were recruited. Patients with a history of glaucoma were excluded. Topiramate was titrated to a maintenance daily dose of 100 mg after 3 weeks. Detailed ophthalmic examinations were carried out at baseline and after 4 weeks of treatment. The parameters measured included best-corrected visual acuity, refraction, Goldmann application tonometry, gonioscopy, dilated fundus examination, and the latest technology of ultrasound biomicroscopy of angle and anterior segment.
Results: 8 patients (62.5% female) aged between 22 and 57 years (mean age 38.1 years) were recruited. No patient withdrew from topiramate due to adverse events or lack of efficacy. There was no statistically significant change in any parameter measured in the ophthalmic examination before and after topiramate use.
Conclusion: Short-term topiramate use was not associated with changes in ocular angle status. Our results suggest that topiramate may be associated with AACG only in certain susceptible individuals.

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Suicidal Attempt with Topiramate: A Case Report
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Purpose: Depression and psychosis have been associated with topiramate use but suicide was rarely reported.
Methods: Case report.
Results: 26 year old university graduate male patient who suffered from complex partial seizures since childhood. He was tried on many antiepileptic drugs (AEDs) but his seizures proved to be intractable. He had no history of depression or psychosis, so he was given topiramate and the dose was slowly built up over six weeks to 200mg/day. He was admitted to hospital after he cut his radial artery attempting suicide. He denied any seizure before it. He said that he became progressively depressed and hopeless and he decided to put an end to his life. He never experienced this feeling before topiramate use. Topiramate was withdrawn and the patient continued his regular AEDs. His depression subsided within weeks and has had no more depression or suicide ideations for the last five years.
Conclusion: Patients started on topiramate should be evaluated regularly for depression and suicidal ideation.

p239
Diuretics, Oral Hypoglycaemic Agents and Insulin do not Alter Pregabalin Pharmacokinetics
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Purpose: To assess the effect of concomitant diuretics, oral hypoglycaemic agents, and insulin on the pharmacokinetics (PK) of pregabalin - a ligand for the α2-δ subunit of voltage-gated calcium channels. Patients taking pregabalin may be concurrently taking diuretics, oral hypoglycaemic agents, and/or insulin. The impact of these medications on pregabalin oral clearance (CL/F) was assessed using a population PK analysis.
Methods: A population PK model for pregabalin was previously validated in healthy subjects and in patients with epilepsy or chronic pain. Using this model, a post-hoc population PK analysis was conducted to assess the impact of various diuretics, oral hypoglycaemic agents, and/or insulin on pregabalin CL/F. The dataset used in this analysis included plasma pregabalin data from 4 studies in healthy volunteers, 1 study on renal impairment patients, and 9 studies on chronic-pain patients (total N=1097). Concomitant medications of interest (number of subjects receiving pregabalin and co-medication) were: metformin (132), glibenclamide (87), glipizide (60), glimepiride (22), furosemide (77), hydrochlorothiazide (48), hydrochlorothiazide-triamterene (31), and insulin (123).
Results: All of the concomitant medications had no statistically significant impact on pregabalin CL/F. The change in pregabalin CL/F with individual co-medications ranged from –13% to +12% which are considered not clinically important. The 90% confidence intervals for each concomitant medication were within 80% to 125% of the reference value for CL/F further supporting a lack of interaction with pregabalin.
Conclusion: Based on pharmacokinetics, no adjustment in pregabalin therapy is necessary when co-administered with insulin, metformin, glibenclamide, glipizide, glimepiride, furosemide, hydrochlorothiazide, or hydrochlorothiazide-triamterene. Funded by Pfizer.

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Model-based Evaluation of the Cost-effectiveness of Pregabalin, Levetiracetam and Generic Gabapentin versus Standard Therapy as an Add-on Anti-epileptic Therapy in Patients with Refractory Epilepsy: A Spanish Perspective
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Purpose: To estimate the cost-effectiveness of pregabalin (PGB) relative to standard therapy (ST) as add-on anti-epileptic (AED) therapy in patients with refractory epilepsy in Spain, and to make a similar comparison for generic gabapentin (GBP).
Methods: Using stochastic simulation techniques, we estimated the cost-effectiveness of PGB (300mg/d) and GBP (1800 mg/d) in a hypothetical cohort of 1,000 patients (vs ST). The model used data from three randomised controlled clinical trials. Estimated mean number of seizure-free days per year with ST was 249.2. Expected number of additional seizure-free days with add-on AED therapy was calculated using monthly changes in seizures rates from controlled trials of these therapies. Model outcomes included the expected number of additional seizure-free days and quality-adjusted life-years (QALYs). Cost effectiveness was calculated as the incremental cost per additional seizure-free day and QALY gained.
Results: Compared with ST, treatment with PGB yielded an estimated 40.9 (+-5.7) (mean [+-SE]) additional seizure-free days, and a gain of 0.027 (+-0.005) QALYs over one year. Comparable figures for GBP

relative to ST were 30.5 (+-8.7), and 0.020 (+-0.007) QALYs. The costs of therapy were €1,299 for PGB and €1,029 for GBP. Incremental cost-effectiveness ratios (ICER) for PGB vs ST were (mean, 95% confidence interval) €32 (€24, €41) per additional seizure-free day, and €50,019 (€35,563; €67,946) per QALY gained; estimates for GBP were €38 (€23, €76), and €66,167 (€32,516; €158,101), respectively.
Conclusion: In patients with partial refractory epilepsy, when compared with ST, PGB demonstrated better cost-effectiveness per additional seizure-free day and QALY gained than GBP. Pfizer funded.

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Outcomes of Treatment of Partial Refractory Epilepsy: A Simulation Model
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Purpose: To develop a model of treatment outcomes for patients with refractory partial epilepsy (RPE).
Methods: We developed a simulation model to depict clinical outcomes of add-on anti-epileptic drug (AED) therapy for patients with RPE. A hypothetical cohort of 1,000 RPE patients is assumed alternatively to receive add-on AEDs plus standard therapy (ST) versus ST alone. Outcomes over one year include the number of seizure-free days and quality-adjusted life-years (QALYs). The number of seizure-days per month for patients treated with ST alone is estimated for each patient using distributions that incorporate inter-patient and intra-patient variability in seizure frequency. For patients receiving add-on AEDs, the expected reduction in the monthly number of seizure-days is estimated by applying seizure-rate reductions from clinical trials to the estimated rate for ST. During simulation, each patient is randomly stepped through the model yielding individual expected values for all measures of interest. The model is run for 100 samples of 1,000 patients each to address first- and second-order uncertainty using Monte Carlo simulation techniques. To illustrate its use, the model was estimated using efficacy and safety data from a clinical trial of a new add-on AED (pregabalin).
Results: Compared to ST alone, add-on therapy with pregabalin over one year is estimated to result in a gain of (mean [SE]) 40.8 (5.8) seizure-free days and 0.023 (0.005) QALYs.
Conclusion: When combined with data on treatment costs, this new analytical tool can provide a powerful foundation for cost-effectiveness evaluations of therapies for patients with RPE. Pfizer funded.

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Efficacy, Safety and Tolerability of Pregabalin as Add-on Treatment for Partial Seizures with or without Secondary Generalisations: Findings from the Analysis of Four Randomise Clinical Trials
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Purpose: To study the overall efficacy, safety, and tolerability of pregabalin when used as adjunctive treatment for partial seizures with or without secondary generalisations in a large patient cohort formed by combining four randomised trials.
Methods: Pregabalin's ability to reduce partial seizures was characterised using data from four similarly designed double-blind, placebo-controlled trials involving 1174 refractory patients (367 received placebo; 185, 90, and 532 received fixed doses of pregabalin 150, 300, and 600mg/day). Treatment efficacy was assessed by measuring the percent reduction in seizure frequency compared to baseline and by measuring the proportion of patients who experienced seizure reductions ≥50% (responders).
Results: Pregabalin-treated patients consistently reported significantly greater reductions in seizure frequency than those receiving placebo. Patients receiving add-on pregabalin 150, 300, and 600mg/day reported statistically significant seizure-frequency reductions of 27.1%, 43.5%, and 49.7%, respectively, compared to 3.5% by those on placebo. Seizure reductions were positively correlated with dose. Overall, 22.2%, 40.0%, and 46.1% of patients receiving adjunctive pregabalin 150, 300, and 600mg/day were responders compared to 10.1% of patients on placebo (P≤0.001). AEs associated with pregabalin treatment were generally mild to moderate and tended to resolve with treatment. In most cases, AEs did not result in discontinuations (6% of placebo and 19% of pregabalin patients discontinued).
Conclusion: Pregabalin is effective and well-tolerated as add-on treatment for partial seizures with or without secondary generalisations across the dose range with a clear dose-response relationship. Treatment with pregabalin yields significant reductions in seizure frequency with as many as 46.1% of patients categorised as responders. Pfizer funded.

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Add-on Treatment for Partial Seizures of Pregabalin is not Affected by the Concomitant use of an Oral Contraceptive or by Menopausal Status
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Purpose: Pregabalin is an alpha-2-delta ligand recently approved in the EU as add-on treatment for partial seizures with/without secondary generalisation. Using data from three trials, we investigated whether the efficacy and tolerability of pregabalin is affected by oral-contraceptive (OC) use or by menopausal status.
Methods: Data from three 12-week, double-blind, placebo-controlled trials involving 484 patients were analysed. 138 patients received placebo while 105, 42, and 199 patients received pregabalin 150, 300, and 600mg/day. Differences in pregabalin efficacy induced by OC use or by menopausal status were assessed by measuring the number of patients who experienced a ≥50% decrease (responders) in seizure frequency in each investigated group.
Results: No statistically significant differences in pregabalin efficacy were detected between OC and non-contraceptive cohorts. In the OC group, 27%, 40%, and 43% of patients treated with pregabalin 150, 300, and 600mg/day experienced ≥50% decreases in seizure frequency compared to 21%, 43%, and 53% of patients in the non-contraceptive group. Similarly, no statistical differences in pregabalin efficacy were detected between pre- and post-menopausal cohorts. In the pre-menopausal group, 22%, 46%, and 48% of patients on pregabalin 150, 300, and 600mg/day reported ≥50% reductions in seizure frequency compared to 24%, 29%, and 67% in the post-menopausal group. Pregabalin was well tolerated (8% of placebo and 18% of pregabalin patients discontinued). The most common AEs were dizziness and somnolence. AEs were generally mild/moderate.
Conclusion: The anticonvulsant efficacy of pregabalin was not affected by the concomitant use of an OC or by the menopausal status of patients. Pfizer funded.

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Efficacy, Safety and Tolerability Characteristics of Anticonvulsant Pregabalin as a Treatment for Neuropathic Pain: Findings from the Analysis of 10 Randomised Placebo-controlled Clinical Trials

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Purpose: Pregabalin is an effective add-on treatment for partial seizures with/without secondary generalisations that also has analgesic and anxiolytic properties. Using data from 10 trials, we investigated pregabalin's analgesic effect as treatment for neuropathic pain (NeP) associated with diabetic peripheral neuropathy (DPN) and postherpetic neuralgia (PHN).
Methods: Pregabalin's ability to reduce NeP in DPN or PHN patients was assessed in 10 placebo-controlled trials involving 2207 patients (796 received placebo; 406, 457, and 548 received pregabalin 150, 300, and 600mg/day). The primary efficacy measure was study-end mean pain score derived from patient recorded daily pain diaries (11-point scale; 0=no pain; 10=worst possible pain). Efficacy was also assessed by measuring the proportion of patients with pain reductions ≥30% and ≥50% by study-end.
Results: Pregabalin patients consistently reported significantly greater pain reductions than placebo patients. On average, patients receiving pregabalin 150, 300, and 600mg/day reported pain score reductions of -1.8, -2.2, and -2.6 vs -1.2 for patients receiving placebo (P<0.0001). Reductions were positively correlated with dose. 40%, 51%, and 62% of patients receiving pregabalin 150, 300, and 600mg/day reported pain reductions ≥30%, while 30% of patients receiving placebo reported comparable reductions. 26%, 34%, and 47% of pregabalin patients reported reductions ≥50% vs 18% of placebo patients. AEs were generally mild/moderate (dizziness and somnolence were most common) and led to withdrawals in 11% and 4% of pregabalin and placebo patients, thereby demonstrating that pregabalin is well tolerated.
Conclusion: Pregabalin yielded significant pain reductions; as many as 62% of patients reported clinically meaningful responses (≥30%). Pfizer funded.

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Anticonvulsant Medication, Pregabalin, Efficaciously Treats Generalised Anxiety Disorder (GAD)

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Purpose: Recent studies indicate that anxiety is prevalent among epilepsy patients and detracts from their quality of life. Pregabalin is approved as adjunctive treatment of partial seizures with or without secondary generalisation. This analysis evaluates the efficacy of pregabalin on the physical-somatic as well as the psychic symptoms of GAD.
Methods: Data from all six short-term placebo-controlled trials of pregabalin in GAD (4-6 weeks in duration) of similar design were combined to analyse three pregabalin treatment groups (low-dose = 150 mg/day; mid-dose=200-450 mg/day; or high-dose=600 mg/day) vs placebo (total N = 484). Responders to treatment were defined as those patients with ≥50% improvement on the Hamilton Anxiety Rating Scale (HAM-A) total score. HAM-A somatic and psychic factor scores were also analysed.
Results: At LOCF-endpoint, significantly more GAD patients treated with pregabalin than with placebo responded to treatment: 40.4%, 52.8%, and 50.5% of patients receiving low, mid, and high pregabalin doses were responders, respectively; 35.1% of placebo patients were responders (p<0.0001 for mid and high pregabalin doses). Pregabalin was also associated with significant improvement in HAM-A somatic- and psychic-factor scores (p≤0.05). The median duration of somnolence was 8 to 14 days in pregabalin treatment groups versus 9 days on placebo.
Conclusion: Pregabalin's rapid efficacy in relieving physical-somatic and psychic symptoms of GAD was maintained through endpoint. Pregabalin was well tolerated and the most common AEs such as somnolence were limited in duration in most patients. Funded by Pfizer.

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Safety of Zonisamide as Adjunctive Therapy in Patients with Primary Generalised Epilepsy

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Purpose: Evaluate the safety and efficacy of zonisamide as adjunctive therapy for patients with primary generalised epilepsy.
Methods: 56 patients with primary generalised epilepsy and seizures that are refractory to other AEDs (at least 4 seizures within 28 days) received up to 172 weeks of open-label zonisamide. The primary study phase (PSP, weeks 0-16): zonisamide was titrated to efficacy (100-mg increments; maximum dosage, 600 mg/day during weeks 1-8, and patients maintained a stable dose during weeks 8-16). Patients not reaching an effective dosage during PSP were eligible for the extension study phase (ESP, weeks 16-172). Safety and efficacy assessments were performed during the PSP and ESP visits and included assessment of adverse events (AEs), seizure type and frequency, and investigator and patient global assessments.
Results: PSP was completed by 48 patients (85.7%); mean age 20.6 years. Mean zonisamide dosage was 4.8 mg/kg/day and mean treatment duration was 112 days. ESP included 42 patients; mean zonisamide dosage was 4.7 mg/kg/day and mean duration of treatment was 411 days. The most common seizures types were absence (51.7%), tonic-clonic (37.9%) and myoclonic (34.5%). The frequency of all 3 seizure types decreased over the course of the study: absence (44 to 9), myoclonic (23 to 8), and tonic-clonic (19 to 7). Seizure control was rated as improved during PSP by the patients and investigators. 5 patients (8.9%) discontinued treatment due to AEs. Serious AEs (SAEs) occurred in 9 patients (16.1%); 2 had zonisamide-related SAEs.
Conclusion: Zonisamide was generally safe, well tolerated, and effective in patients with generalised seizures.

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Efficacy of Zonisamide Against Refractory Partial Seizures in an Evaluable Patient Population

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Purpose: To assess zonisamide efficacy in an evaluable population of patients with partial seizures receiving ³10 weeks' study medication during a 36-week, double-blind, placebo-controlled trial.
Methods: Following a 12-week baseline period, 351 patients (³12 years; receiving 1–3 antiepileptic drugs) were randomised (2:1:1:2) to placebo or zonisamide 100, 300 or 500mg/day. After a 6-week dose titration phase, patients entered an 18-week, fixed-dose phase. Responder rates (patients experiencing ³50% reduction in seizure frequency) and median percentage reduction in frequency of complex partial seizures (CPS), all partial and all seizures were assessed in an evaluable population, and adverse events (AEs) were assessed in all patients enrolled.
Results: 294 patients were included in the efficacy analysis. Zonisamide 500mg/day significantly reduced seizure frequency (49.8% vs 16.3%; p<0.001) and increased responder rates (50.0% vs 20.9%; p<0.001) for CPS, compared with placebo. The frequency of all partial and all seizures was also significantly reduced compared with placebo for zonisamide 300mg/day (p<0.01) and 500mg/day (p<0.0001). The responder rates with zonisamide 500mg/day were

also statistically superior to placebo (p<0.001) for all partial (48.8% vs 19.8%) and all seizures (51.1% vs 18.3%). A significant linear relationship was observed between dose and responder rates for all seizures (p<0.0001). Zonisamide was well tolerated, although withdrawals due to AEs were greater with higher doses (6.7%, 0%, 12.5% and 24.6% for placebo, zonisamide 100, 300 and 500mg/day, respectively). The most common AEs were somnolence, dizziness, headache and nausea.
Conclusion: Zonisamide is a well tolerated treatment that shows dose-dependent efficacy for refractory partial epilepsy. Funded by Eisai Europe Ltd.

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Long-term Efficacy and Safety with Zonisamide: Interim Analysis of an Open-Label Study
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Purpose: To establish the long-term safety and efficacy of zonisamide in refractory partial epilepsy.
Methods: This was a 2-year, multicentre, open-label extension of a 36-week, double-blind trial of patients (n=243) with refractory partial seizures (≥12 years; on 1–3 antiepileptic drugs [AEDs]) who had received placebo or adjunctive zonisamide 100, 300 or 500mg/day. In the extension phase, zonisamide was titrated up to or maintained at 500mg/day over 6 weeks, then adjusted according to need (100–600mg/day); doses of concomitant AEDs were also modified. Efficacy (seizure frequency and number of seizure-free days) and safety (incidence of adverse events [AEs] and discontinuations), relative to baseline (final assessment of double-blind phase), were assessed at a fixed time point, 49 months after study initiation.
Results: Zonisamide efficacy was maintained or improved with longer-term treatment; the frequency of all partial seizures decreased by 31%, 28%, 11% and 33% in patients who had received placebo, zonisamide 100, 300 and 500mg/day in the double-blind phase, respectively. Most patients (130/243; 53.5%) achieved ≥28 days of seizure freedom, with 28 (11.5%) and 17 (7.0%) patients remaining seizure-free for ≥6 months and ≥1 year, respectively. Concomitant AEDs were reduced in 27 (11.1%) patients, with 4 achieving zonisamide monotherapy. There were no unexpected AEs, the most common being headache and somnolence. Few (28/243; 11.5%) patients withdrew due to AEs and 44 (18.1%) withdrew due to lack of efficacy.
Conclusion: Zonisamide shows continued efficacy and safety with long-term use in patients with refractory partial epilepsy. Funded by Eisai Europe Ltd.

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Serum Concentrations of Oxcarbazepine Metabolite in Epilepsy Patients
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Purpose: The aim of this study was to investigate the influence of oxcarbazepine (OXC) dose and co-medication on the serum concentration of the pharmacologically active monohydroxy metabolite (MHD) in epilepsy patients.
Methods: Plasma levels of MHD were evaluated in 240 patients with epilepsy, 133 females and 107 males, mean age 38.3 years, range 17 to 82 years; 87 patients received OXC as monotherapy, 82 patients received enzyme inducing co-medication and 71 patients received co-medication considered not enzyme inducing. The MHD serum concentration in relation to OXC dose per body weight (level to dose ratio - LDR) was compared for patients receiving OXC monotherapy and for patients receiving OXC plus other antiepileptic drugs (AEDs).
Results: In our patient population, the mean OXC dose per body weight was 21.67±9.8 mg, the mean MHD serum concentration was 16.85± 8.2 mg/mL, the mean LDR was 0.82±0.3. The OXC dose per body weight was significantly correlated with MHD serum concentration ($r = 0.62$, $p < 0.001$); in co-medication with other AEDs, the LDR was significantly lower than it was in OXC monotherapy ($r = 4.73$, $p < 0.001$); the LDR for patients receiving enzyme inducing co-medication was significantly lower than it was for patients receiving co-medication considered not enzyme inducing ($r = 2.76$, $p. < 0.001$).
Conclusion: These results suggest that determination of MHD serum concentration may be useful for individualising the therapeutic regimen especially for patients using OXC in polytherapy with enzyme inducing AEDs.

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Population Pharmacokinetic/Pharmacodynamic Analysis for Oxcarbazepine in Paediatric Patients
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Purpose: Explore the population pharmacokinetics/pharmacodynamics of oxcarbazepine at doses up to 60 mg/kg/day as monotherapy or adjunctive therapy in children 1 month to <17 years with partial seizures.
Methods: Plasma samples were analysed using HPLC-UV and LC-MS/MS methods. Under monotherapy, dose group and MHD clearance were used as indicators of MHD exposure in a proportional hazards model for time to exit. Under adjunctive therapy, the average MHD trough concentration during video-EEG monitoring was used as a predictor of percent change from baseline in seizure frequency. Under both therapies, dose group and MHD clearance were used as indicators of MHD exposure in logistic regression models for the risk of adverse events (AEs).
Results: The population pharmacokinetic model based on samples from 218 patients was similar to one previously found for patients 3 to <17 years. Under monotherapy, no relation was found between MHD exposure and time to exit. Under adjunctive therapy, seizure frequency during the video-EEG measurement decreased with increasing MHD troughs. The number of AEs increased with MHD exposure in both types of studies. Under both therapies, weight-adjusted MHD clearance decreased as age increased. MHD exposure is expected to be one-half and two-thirds that of adults in patients 1 month to <4 years and 4 to ≤12 years, respectively, when treated with similar weight-adjusted dose.
Conclusion: Based on these data, young children may need up to double oxcarbazepine doses/weight compared to adults. However, dosing should be initiated at 10 mg/kg/day, and be titrated to clinical response up to 60 mg/kg/day. Supported by Novartis Pharmaceuticals.

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A Multicenter, Rater-blind, Randomised, Age-stratified, Parallel-group Study Comparing two doses of Oxcarbazepine as Adjunctive Therapy in Paediatric Patients with Inadequately Controlled Seizures
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Purpose: To evaluate efficacy, safety and population pharmacokinetics of 10 mg/kg/day (low-dose) vs. 60 mg/kg/day (high-dose) oxcarbazepine as adjunctive therapy in patients 1 month to <4 years with inadequately controlled partial seizures.
Methods: Patients had a minimum of 2 study-defined seizures (SST1) during 24-72 hour continuous inpatient video-EEG monitoring and on a stable dose of 1 to 2 antiepileptic drugs. Patients were stratified by age and randomised to receive either low-dose oxcarbazepine for 9 days or high-dose oxcarbazepine for 35 days (with 10 mg/kg/day titration at 5-day intervals). v-EEGs were collected during the last 72 hours of study. A central reader blinded to study treatment assessed seizure records. Plasma samples were collected for determination of the active 10-monohydroxy derivative (MHD).

Results: A total of 128 patients were equally randomised with 115 patients completing the study (59 low-dose; 56 high-dose). Statistically significant differences between low- and high-dose treatment groups were observed for key efficacy measures including median absolute change in SST1 frequency/24 hours (–1.37 vs. –2.00 seizures; p = 0.043). 5 patients discontinued due to AEs (2 low-dose; 3 high-dose). The most common AEs included pyrexia (13.3%) and somnolence (10.9%). The trough MHD concentration clearly differentiated for high-dose (58.4 micromol/L) vs. low-dose (9.76 micromol/L).
Conclusion: This study demonstrates the efficacy of oxcarbazepine, as adjunctive therapy in young children (1 month to <4 years) with inadequately controlled partial seizures. Oxcarbazepine was generally well-tolerated with a safety profile in line with that reported for adults and older children. Supported by Novartis Pharmaceuticals.

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Long -term Safety of Oxcarbazepine in Patients 1 Month to <17 Years of Age with Partial Seizures: A Pooled Analysis
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Purpose: To evaluate long-term safety and tolerability of oxcarbazepine therapy in patients 1 month to <17 years of age with partial seizures.
Methods: Data from nine studies were pooled and analysed: two dose-controlled short-term efficacy studies (mono and adjunctive therapy), two short-term pilot safety studies (mono and adjunctive therapy) and five long-term safety studies (one 6-month new-onset monotherapy study and four 6-month extension studies).
Results: 337 patients were enrolled with 241 patients (71.5%) <4 years of age. Seizure classifications included complex partial seizures (68.8%), secondarily generalised seizures (50.5%) and simple partial seizures (30.6%). The mean duration of oxcarbazepine exposure was 4.8 months in patients <4 years of age and 5.3 months in patients ≥4 year of age. Serious adverse events occurred in 18.4% of patients including 2 deaths (sudden death and pneumonia), not suspected to be related to study drug. 31 patients (9.2%) withdrew due to AEs (10 with convulsions and 3 with laboratory abnormalities). AEs (≥10%) included pyrexia (21.7%), vomiting (14.8%), somnolence (13.9%) and upper respiratory tract infection (12.8%). Clinically notable laboratory values at two or more consecutive visits (≥10%) included elevated lymphocytes in 14.3% of patients, likely due to high rate of viral infections. Clinically notable decreases in sodium values (<125 mEq/L) occurred in 2 patients (0.6%); neither patient prematurely discontinued. No patients withdrew due to vital signs or ECG abnormalities.
Conclusion: Studies demonstrate that oxcarbazepine was generally well-tolerated over the long-term in very young paediatric patients with a safety profile in-line with that reported for adults and older children. Supported by Novartis Pharmaceuticals.

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Efficacy and Safety of High Versus Low-dose Oxcarbazepine Monotherapy in Paediatric Patients with Partial Seizures: A randomised, Age-stratified, Parallel-group Study
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Purpose: To evaluate the efficacy and long-term safety of oxcarbazepine monotherapy in patients 1 month to 16 years with partial seizures.
Methods: Hospitalised patients with newly diagnosed or inadequately controlled seizures were stratified by age and randomised to 10 or 40-60 mg/kg/day oxcarbazepine. Patients had 2-30 seizures before entry and if receiving another antiepileptic drug, the dose was reduced 50% on day 2 and discontinued on day 3. Patients completed by finishing the 5-day treatment core phase or meeting exit criteria. Seizures were documented by continuous video-EEG monitoring and assessed by a central reader. Eligible patients continued in a 6-month open-label extension (OLE) phase.
Results: Of 92 patients randomised, 19 (20.7%) met exit criteria, 67 (72.8%) completed, and 6 (6.5%) discontinued the core phase. No significant difference in exit rates was observed between treatment groups (p=0.904). AEs were reported for 21 (45.7%) low-dose and 28 (60.9%) high-dose patients. Of 82 patients (89%) entering the OLE phase, 59 (72%) completed, 5 (6.1%) discontinued for AEs, 9 (11%) for unsatisfactory therapeutic effect, and 9 (11%) for other reasons. Most frequent AEs (>10%) included pyrexia, convulsion, upper respiratory tract infection, vomiting, somnolence, diarrhoea, nasopharyngitis and otitis media.
Conclusion: Although this study did not show a significant difference between high and low-dose oxcarbazepine monotherapy in controlling partial seizures in children over a 5-day treatment phase, most remained seizure free and exit rates were lower than expected. Oxcarbazepine was well tolerated over 6 months with a safety profile similar to that reported for adults and older children. Supported by Novartis Pharmaceuticals.

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Assessment of Oxcarbazepine Effect on Bioelectrical Brain Activity in Epilepsy
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Purpose: Oxcarbazepine (OXC) is one of the new antiepileptic drugs used as monotherapy and adjunctive therapy for simple or complex partial epileptic seizures and for generalised seizures. The aim of the study was the evaluation of OXC influence on bioelectrical brain activity in partial and generalised epileptic seizures.
Methods: A group of 106 patients aged of 4 to 33 (14.1□5.2) with simple or complex partial seizures and with generalised seizures was observed. OXC was administered in poly- and monotherapy during the 6-24 month trial. The bioelectrical activity of the brain before and after the application of OXC was analysed for all patients. EEG recordings were made using of 'Ceegraph' (Biologic, USA).
Results: During OXC therapy, which takes 6-24 months, 27 of the patients (25.5%) were seizure free. On the basis of performed EEG analysis an improvement of bioelectrical activity in over half the patients (53%) was noted. Among this group the release of generalised or focal abnormalities in 26% examined was noted and reduction of the number or duration time of epileptic discharges in 27% was found. In 43% of cases EEG recordings were unchanged. In 4% of patients deterioration was noticed.
Conclusion: The results of the study indicate that OXC is an effective antiepileptic drug applied as mono- and adjunctive therapy for both partial and generalised epilepsy. In over half the cases a decrease in the number of epileptic seizures was connected with an improvement of bioelectrical brain activity.

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Long-term Clinical Experience with Oxcarbazepine in Both Newly Diagnosed and Refractory Partial Seizures
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Purpose: To evaluate long-term efficacy and safety of oxcarbazepine as monotherapy or add-on therapy across newly diagnosed and refractory patients with partial seizures in Triveneto, Italy.

Methods: This is a prospective, open-label, post marketing surveillance study of oxcarbazepine-treated patients with partial seizures referred to Neurological Departments of Triveneto (Northern Italy*), over a period of thirty months. Data had been collected through clinical interviews and patients underwent clinical controls, blood samples and EEG, according to our follow-up purposes. * with the collaboration of the Triveneto Epilepsy Study Group.
Results: 202 adult patients with partial seizures joined the study. Baseline monthly seizure frequency was 8.5 over the preceding 3 months. Mean dose of oxcarbazepine was 1180 mg/day (range 300-3000) with mean treatment duration of 23 months. At first observation, the seizure free rate was 72.2% in newly diagnosed patients given monotherapy, 40% in patients in whom oxcarbazepine replaced another monotherapy and 10.3% in patients given oxcarbazepine as adjunctive therapy. At least 50% reduction in seizure frequency was achieved in 90.7%, 72% and 57%, respectively. In the 160 who completed the study, the seizure free rate was 61.3% with monotherapy and 28% with adjunctive therapy. 16.3% of patients reported adverse effects, mainly sedation and sleepiness; 5% discontinued oxcarbazepine because of adverse events. Efficacy increased with the duration of treatment ($p<0.0001$).
Conclusion: OXC is an effective and well tolerated antiepileptic agent when it is used in clinical practice for the long-term treatment of partial epilepsy in adults, both as monotherapy and as adjunctive therapy.

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Evaluation of the Tolerability and Safety of Oxcarbazepine (Trileptal) in the Treatment of Epilepsy: Results of a National Observational Study EPI-TRI
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Purpose: Oxcarbazepine (OXCZ, Trileptal) is a 10-keto analogue of carbamazepine designed to maintain the therapeutic potential of carbamazepine with a superior safety profile. Its effectiveness in the treatment of epilepsy in both mono and polytherapy has been demonstrated with a large number of clinical trials (1). An open-label observational study has been conducted in order to assess the tolerability and safety of oxcarbazepine (Trileptal) (OXCZ) in the treatment of epilepsy in routine clinical practice.
Methods: The study was based on a review of ambulatory patients' records and was conducted from March 2003 to September 2003. 200 neurologists from the whole region of Poland participated in this study. The study reviewed 1807 patients' records included data from 1-15 years children (24%) and adults (76%) among the population of 847 males and 958 females. Seizure type was defined according to the 1989 ILAE classification. At a follow-up visit 6-8 weeks after OXCZ was introduced the type and degree of adverse events (AEs) and possible reasons for discontinuation of the drug therapy were determined. All of the data was subjected to statistical analysis; the estimated level of statistical error does not exceed ± 2.2%
Results: Even though oxcarbazepine has been indicated for the treatment of partial seizures with or without secondary seizures among the reviewed patients' records in 73% of cases OXCZ was used in the therapy of partial seizures; in 27% OCBZ has been used in patients with primary generalised seizures. In 2/3 of the patients' records OCBZ was used as monotherapy. The average dose of OXCZ in the study group was 970 mg/day in adults and 478 mg/day in children. OXCZ was used as first-line therapy in 39% of patients, in 42% as a second-line medication, in the remaining patients, as a drug in subsequent lines of therapy. The most frequent reason for switching to OXCZ was the lack of effectiveness with the previously used drug. During this observational trial adverse events occurred in 17% of patients and were primarily CNS-related (drowsiness, headache, dizziness, fatigue). Adverse events were significantly more frequent in patients in whom OXCZ was not used in first-line therapy. Only 12% of the patients in whom adverse effects occurred required treatment discontinuation.
Conclusion: This observational study provided data of the safety profile of OXCZ used in a routine clinical practice in the initial phase of therapy. The results confirmed a good safety and tolerability profile of OCBZ, also reported in another open-label study with OCBZ in epilepsy with partial seizures(2). In only 36 (2%) of the 1807 patients adverse events caused a discontinuation of the OXCZ treatment during first 8 week of the therapy. In most of the patients the adverse events were transient and did not lead to discontinuation of treatment with OXCZ or the dose reduction. References: 1. Beydun A. Epilepsia, 2003, 44 (9) : 1160-1165 2. Derambre P, at all, (poster) EFNS Helsinki , 2003.

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Effect of Oxcarbazepine on Lipid and Lipoprotein (a) Levels in Children
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Purpose: Antiepileptic drugs may alter lipoprotein (a) and other plasma lipid levels in epilepsy patients. The aim of our study was to determine the effect of oxcarbazepine on serum total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL) and lipoprotein (a) levels .
Methods: This study was performed at the Paediatric Neurology Department of Karadeniz Technical University, Medical faculty. 13 patients (10 females, 3 males) with idiopathic partial epilepsy with a mean age of 8.6 years (range 3-14 years) were included in the study. The patients were treated with oxcarbazepine, 30 mg/kg/day, twice daily. Plasma lipid levels and lipoprotein (a) levels were studied before therapy and during the 3rd, 6th and 12th months of treatment.
Results: 3 patients were excluded because of irregular drug usage in 1, and the addition of another antiepileptic for intractable seizures in the others. There was no statistically significant differences between the pretreatment and 3rd, 6th and 12th months of the therapy.
Conclusion: Oxcarbazepine, is a new antiepileptic drug. It is a keto derivate of carbamazepine. Despite a similar clinical structure, oxcarbazepine has a different metabolic effect from carbamazepine. According to our study, we suggest that oxcarbazepine is safe for epilepsy patients who have a high atherosclerotic risk.

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Safety and Tolerability of Intravenous Lacosamide as Replacement for Oral Lacosamide in Subjects with Partial-Onset Seizures
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Purpose: Investigate the safety and tolerability of intravenous lacosamide (LCM) as replacement for oral LCM in subjects with partial-onset seizures.
Methods: 60 subjects enrolled from an open-label extension trial of oral LCM. Subjects were randomised 2:1 to iv LCM plus placebo (PBO) tablets twice daily (bid) or iv PBO plus LCM tablets bid, respectively, for 2 consecutive days. Subjects (n=30) in Cohort A received 60-minute infusions of trial medication; whereas, Cohort B (n=30) received 30-minute infusions. Safety data from Cohort A were reviewed before enrolment in Cohort B. At screening, subjects received a single-blinded infusion of iv PBO. In the 2-day treatment period, subjects received blinded trial medication every 12 hours. The dose of LCM (100 to 300mg bid) was the same as the subject's daily dose in the extension trial. Safety was evaluated with AE reports, serial ECG and vital sign evaluations, and clinical laboratory data. After the treatment period, subjects underwent follow-up evaluations, then returned to the oral extension trial.
Results: 59 of 60 randomised subjects completed the trial. No subject withdrew because of AEs. Few AEs were reported and were

comparable to those reported with oral LCM. Serial monitoring of ECG and vital signs showed no clear differences in ECG intervals, blood pressure, or heart rate between the iv and oral LCM groups.
Conclusion: In this trial, the nature of AEs reported following 60- and 30- minute infusions of SPM 927 was consistent with AEs previously reported following oral administration of SPM 927. Study supported by Schwarz Biosciences, Inc.

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Seletracetam (ucb 44212), A New Pyrrolidone Derivative, Inhibits Epileptiform Responses in Hippocampal Slices in Vitro
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Purpose: Seletracetam (ucb 44212) is a new pyrrolidone derivative, structurally related to levetiracetam (LEV; Keppra), which displays higher affinity than LEV to the LEV-binding site (the synaptic vesicle protein 2A - Lynch et al., PNAS 101, 9861, 2004). This study assessed seletracetam's activities in two in vitro models of epilepsy.
Methods: The effects on the epileptiform responses induced either by perfusion with a high K+ - low Ca2+ fluid (HKLCF), or by addition to the normal perfusion (ACSF) of 5µM bicuculline methiodide (BMI) were assessed upon field potential recordings in the CA3 area of rat hippocampal slices. Field potentials were evoked by fimbrial stimulation with constant pulses eliciting a single population spike (PS) in ACSF.
Results: HKLCF and BMI induce epileptiform field potentials in CA3 area, upon increasing PS amplitude and producing repetitive PSs, in response to single stimuli. HKLCF, but not BMI, regularly induced spontaneous bursts. Seletracetam, 1 – 10 µM, markedly decreased the HKLCF-induced increase in PS amplitude (□PS), and the amplitudes and number of repetitive PSs, with maximal effect at 3.2 µM. LEV has previously shown similar, though lesser activity, maximal at 32 µM (Margineanu & Klitgaard, Pharmacol. Res. 42, 281, 2000). Seletracetam did not reduce the rate of spontaneous bursts, similarly to LEV (Margineanu et al., Epilepsia 44, Suppl. 9, 261, 2003). Seletracetam inhibited BMI-induced □PS, with significance at 10 µM. Seletracetam, 1 – 10 µM reduced the number of BMI-induced repetitive PSs. LEV has been reported to inhibit these epileptiform markers, with maximal effect at 32 µM.
Conclusion: Seletracetam inhibited the epileptiform responses of rat hippocampal slices, with higher potency and efficacy than LEV, in two in vitro epilepsy models.

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Seletracetam (ucb 44212), A New Pyrrolidone Derivative, Suppresses Seizures in Animal Models of Chronic Epilepsy in Vivo
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Purpose: Seletracetam (ucb 44212) is a new pyrrolidone derivative, structurally related to levetiracetam (LEV; Keppra), which displays a higher affinity (pKi=7.1) than LEV (pKi=6.1) to the LEV-binding site, recently discovered as the synaptic vesicle protein 2A (Lynch et al., PNAS 101:9861-9866, 2004). This study assessed the putative anti-seizure properties of seletracetam in in vivo models of epilepsy.
Methods: Anti-seizure activity was assessed in corneally kindled male NMRI mice (25-35g; n=10), hippocampal kindled male Sprague Dawley rats (350-450g; n=8), audiogenic seizure prone male mice (20-25g; n=10) and Genetic Absence Epilepsy Rats from Strasbourg (GAERS), as well as against maximal electroshock and pentylenetetrazole-induced seizures in male NMRI mice (22-28g; n=10). CNS adverse effects were quantified in the rotarod test.
Results: Seletracetam protected against secondarily generalised motor seizures in corneally kindled mice (ED50 = 0.31 mg/kg i.p.) and hippocampal kindled rats (minimal active dose = 0.23 mg/kg p.o.). Likewise, seletracetam suppressed clonic convulsions in audiogenic seizure susceptible mice (ED50 = 0.17 mg/kg i.p.) and spike-wave-discharges in GAERS (ED50 = 0.15 mg/kg i.p.). This contrasts with a lack of protection in the maximal electroshock and pentylenetetrazole seizure tests (ED50 > 232 mg/kg i.p.). The rotarod TD50 values of seletracetam in corneally kindled mice and GAERS were 325 and 449 mg/kg i.p., respectively. Compared to the protective ED50 values, obtained in the same animals, this resulted in a high safety margin of 1048 and 3075, respectively.
Conclusion: This study showed a potent seizure protection and high CNS tolerability of seletracetam in various in vivo models of epilepsy.

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Anticonvulsant Action of Seletracetam (ucb 44212) in an Animal Model of Status Epilepticus
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Purpose: Seletracetam (ucb 44212) is a new pyrrolidone derivative, structurally related to levetiracetam (LEV; Keppra□), which displays higher affinity than LEV to the LEV-binding site (the synaptic vesicle protein 2A - Lynch et al., PNAS 101, 9861, 2004). This study examines the putative seizure-protective properties of seletracetam in an animal model of self-sustaining status epilepticus (SSSE).
Methods: SSSE was induced by 30 min intermittent stimulation of the perforant path (PPS) through chronically implanted electrodes in free running adult male Wistar rats. Seletracetam (100-300 mg/kg) vehicle or levetiracetam (500 mg/kg) were injected intravenously 10 min after SSSE induction (early treatment of established SSSE). Electrographic and behavioural manifestations of SSSE were analysed off-line.
Results: Seletracetam injected iv during the early stages of established SSSE (10 min after the end of PPS), shortened the duration of seizures in a dose-dependent manner. Total time spent in seizures after levetiracetam was 32+5 min (500 mg/kg), total time spent seizing after seletracetam was 3.5+0.7 min (300 mg/kg), 11+1.7 min (200 mg/kg) and 25+3.4 min (100 mg/kg), whereas control animals spent 32.2+5.1 min seizing. This seizure protection by iv seletracetam (300 mg/kg) was stronger than that previously reported for iv diazepam (10 mg/kg) or iv levetiracetam (300 mg/kg), and comparable to that of iv phenytoin (50 mg/kg). However, this effect was obtained at doses of seletracetam markedly higher (100-300 mg/kg iv) than those inducing protection in animal models of partial and generalised epilepsy (0.1-0.3 mg/kg ip; abstract by Matagne et al., at this congress).
Conclusion: Seletracetam displayed significant seizure-protective effects in this animal model of SSSE. Supported by VHA, by research grant NS13515 from NINDS, and by a research grant from UCB S.A.

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Eslicarbazepine Acetate (BIA 2-093): Relative Bioavailability and Bioequivalence of 50 mg/mL Oral Suspension and 200 mg and 800 mg Tablet Formulations
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Purpose: To investigate the bioavailability and bioequivalence of three different formulations of eslicarbazepine acetate (BIA 2-093): 50 mg/mL oral suspension (Test 1), 200 mg tablets (Test 2) and 800 mg tablets (Reference).
Methods: Single-centre, open-label, randomised, 3-way crossover study in 18 healthy subjects. The study consisted of three consecutive periods separated by a washout of 7 days or more. Each subject received a 800 mg single-dose of eslicarbazepine acetate on three different occasions: either 16 mL of oral suspension 50 mg/mL, 4 tablets 200 mg or 1 tablet 800 mg.

Results: Eslicarbazepine acetate was rapidly and extensively metabolised to BIA 2-005. Maximum BIA 2-005 plasma concentrations (Cmax) and area under the plasma concentration-time curve from 0 to infinity (AUC0-∞) were respectively (mean±SD) 18.1±4.6 µg/mL and 325.7±64.9 µg.h/mL for Test 1, 16.0±4.0 µg/mL and 304.2±66.0 µg.h/mL for Test 2, and 17.0±4.1 µg/mL and 301.1±60.0 µg.h/mL for Reference formulation. Point estimate (PE) and 90% confidence intervals (90% CI) for AUC0-∞ Test 1/Reference ratio were 1.09 and 1.01-1.15; for Cmax ratio, PE and 90% CI were 1.07 and 0.97-1.15. When Test 2 and Reference formulations were compared, the PE and 90%CI were 0.99 and 0.94-1.07 for the AUC0-∞ ratio, and 0.94 and 0.86-1.02 for the Cmax ratio. Bioequivalence of Test versus Reference formulations is accepted for both AUC0-∞ and Cmax because the 90% CI lie within the acceptance range of 0.80-1.25.
Conclusion: The pharmacokinetic profiles of eslicarbazepine acetate oral suspension 50 mg/mL, 200 mg tablet and 800 mg tablet formulations were essentially similar and formulations can be considered bioequivalent. Supported by BIAL (Portela & C[a] SA)

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Protective Effect of Pentoxifylline on Lithium-Pilocarpine Induced Status Epilepticus in Immature Rats
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1) Armed Forces Hospital, Riyadh, 11159, Saudi Arabia.
Purpose: Status epilepticus (SE) is among the most severe form of epilepsy and is regarded as a medical emergency associated with considerable morbidity and mortality. Permanent neuronal cell loss and cognitive impairment are most frequent neurological deficits observed in children following SE. Although several drugs are used for therapeutic and prophylactic treatment of SE, the available agents are far from satisfactory and warrant further investigation. Pentoxifylline (PTX), a potent anti-inflammatory and immunomodulating agent has been shown to exert neuroprotective effects including improved learning acquisition and reversal of impaired memory. Hence the present study was undertaken to investigate the effect of PTX in lithium-pilocarpine (Li-Pc) induced SE in immature rats.
Methods: SE (continuous seizure for a period longer than thirty minutes) was induced in 20 day old immature rats by lithium chloride (3mEq/kg, i.p.) followed (24 h later) by pilocarpine (20mg/kg, s.c.). The animals in test group received PTX (20, 40 and 60mg/kg, i.p.) 30 minutes before pilocarpine administration, whereas control animals received the same volume of saline instead of PTX. Animals were observed for tremors, stereotyped movements, seizures, SE and mortality. The motor function and cognitive behaviour of the animals were studied using rotarod, activity meter, elevated plus-maze and Morris water-maze. The animals were sacrificed and their hippocampus was isolated for histological studies.
Results: Treatment of rats with Li-Pc produced significant SE in 90% of animals along with significant motor deficit, anxiety and impairment of memory. PTX attenuated dose-dependently the incidence of SE, motor deficits, loss of memory and cognitive dysfunction. Hippocampal neuronal cell loss and sprouting of mossy fibres observed in the SE group were also attenuated in PTX treated groups.
Conclusion: Administration of Li-Pc in immature rats, produced SE (in 90% of animals) as well as significant motor deficits and cognitive impairment accompanied by loss of neuronal cells and sprouting of mossy fibres in the hippocampus. These changes were dose-dependently attenuated by PTX.

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Normalising Effect of Peony Root Extract on Pentylenetetrazol-induced Expression Changes of Seizure-related Gene Group
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Purpose: To establish fundamental therapy against epilepsy, the possibility of normalisation of PTZ-induced expression changes of the seizure-related gene group (SEZ gene group) by peony root extract was investigated.
Methods: C57BL mice were used. Expression changes of the SEZ group genes were examined using the northern blotting method. Peony root extract was prepared from peony root purchased from an authorised wholesaler of herbal drugs in Japan. The peony root extract was boiled, filtered, vacuum concentrated and pulverised (38% w/w yield). Peony root extract was administered orally using a feeding catheter at 1 g/kg continuously for 30 days.
Results: Expression changes (increased or decreased) of SEZ gene group induced by systemic injection of PTZ were normalised or showed tendency of normalisation by long-term oral administration of peony root extract. Xenopus oocyte injected with SEZ-17 RNA, one of the SEZ group RNA, showed a marked increase in intracellular calcium by extracellular application of PTZ in an examination using calcium-sensitive dye, Fluo 3, with observation by confocal microscopy. This abnormal intracellular calcium increase was completely inhibited by incubation with peony root extract.
Conclusion: The above-mentioned results indicate that peony root extract prevents abnormal adverse expression of the SEZ gene group by long-term oral administration. These results suggest the possibility of normalisation of the seizure-evoking abnormal expression changes of SEZ genes and also indicate the possibility of preventive therapy against epilepsy using peony root extract.

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Enigma of Borax as an Antiepileptic Drug
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Purpose: In a previous study (Jensen, JPA. Epilepsia 2004;45 suppl. 3: 159) the effect of borax used as an antiepileptic drug from 1912 - 1948 at Kolonien Filadelfia, Denmark, was minimal, based on a review of the medical charts. As less than 5% experienced a significant reduction in seizure activity, it is difficult to explain why borax was prescribed so often. The purpose of this study is to focus on the effect of borax in monotherapy or in combination with bromides to see if better results were obtained.
Methods: 586 medical charts of patients treated with borax from 1912 - 1948 were reviewed; 92 were found to fulfil the criteria. The average number of seizures a month during treatment was compared to the average number of seizures a month prior to treatment, whenever possible for the equivalent period of time.
Results: 14 charts contained insufficient data. In the remaining 78 cases, 22 (28.2%) showed no effect at all, and 30 (38.5%) had a reduction of seizures less than 33%. However, in a third of the cases, a significant reduction in seizure activity was observed, between 33-50% in 12 (15.4%) and between 50 and 91% in 14 (17.9%). The effect was capricious, independent of age, sex, dosage and duration of treatment. Monotherapy did not show better results. 13 (16.6%) experienced side-effects.
Conclusion: The better results prior to the introduction of more efficient drugs might explain why borax continued to be an alternative choice in the treatment of epilepsy for so many years.

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Seizure Anticipation: Are Neuro-phenomenological Approaches Able to Detect Preictal Symptoms?
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Purpose: Epilepsy patients suffer from the unpredictability of their seizures. Seizure anticipation would reduce both morbidity and mortality among patients with pharmacoresistant epilepsy. Analysis of the EEG signal using new mathematical methods have suggested that it is possible to detect a preictal state in the neuronal dynamics before the seizure onset. Do these neurodynamic changes correspond to any modifications in the patients' lived experiences?
Methods: Nine patients suffering from an intractable partial epilepsy with subjective symptoms preceding their seizures were included. Brain MRI and EEG were analysed in all patients, and video-EEG monitoring was performed for 6 patients. Description of the patient's subjective experience before seizure onset was analysed by phenomenological approaches. Symptoms were then classified among aura (ictal phenomena) if they fitted with those usually described in simple partial seizures, or, if not, among prodroma (preictal phenomena).
Results: All patients experienced auras, 5 experienced prodroma. The delay between the prodroma and the seizure was usually several hours, whereas aura occurred a few seconds or minutes before the other ictal symptoms (usually a complex partial seizure). Prodroma were continuous and progressive, whereas aura was sudden and intermittent. Prodroma are not specific symptoms, but interestingly they refer to negative symptoms whereas aura refer to positive symptoms.
Conclusion: Factors that may interfere with the patient's ability to report preictal symptoms are discussed. Future correlation between the phenomenological analysis and the simultaneous analysis of the EEG signal may provide more clues for understanding the preictal period.

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Are All Cases of Generalised Epilepsy in Adult Patients Idiopathic?
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Purpose: IGE is clinically characterised by the triad of typical absences, tonic-clonic seizures and myoclonic jerks. According to the 1985 ILAE definition there are no neuroradiological signs in IGE. Therefore, some authors state that if clinical and EEG data are consistent with IGE there is no need for imaging. It may be reasonable to perform MRI in those with refractory IGE. We sought to determine whether structural changes detectable by MRI might be present in our patients with IGE.
Methods: We focused on patients whose clinical and EEG data were consistent with IGE. We studied 14 patients in whom MRI was performed who were recruited at our tertiary epileptological centre.
Results: 7 of 14 patients had abnormal morphological findings on MRI. There was 1 patient with cavernoma of pons, 1 patient with thalamic cavernoma, 1 patient had multiple cavernomas (right frontal and left temporal), 1 patient with right frontal venous angioma, 1 patient with high intensity signal in right mezencephalon and right frontal lobe, 1 patient with a frontal cyst and 1 patient with multiple ischaemic lesions.
Conclusion: Our findings support the concept that structural changes may be associated with abnormalities in functional connectivity within the cortex and, in some cases, between cortical and subcortical structures. We are convinced that a morphological examination is necessary for all patients with obvious primary generalised epilepsy and it can happen that striking results can be found. The number of patients with structural lesions in our tertiary epileptological centre is high because of the high concentration of intractable patients.

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Facial Asymmetry in Patients with Mesial Temporal Sclerosis: Correlation with Clinical and MRI Findings
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Purpose: Unilateral emotional facial paresis has been observed in patients with temporal lobe epilepsy. We aim to assess the frequency and significance of this clinical sign in a well-defined cohort of mesial temporal sclerosis (MTS).
Methods: 55 consecutive patients with MRI findings consistent with MTS and concordant electroclinical data underwent facial motor examination at rest, with voluntary expression and spontaneous smiling. Hippocampal, amygdaloid and temporal pole volumetric measurements were performed in these patients. A T1-weighted three-dimensional gradient-echo acquisition of the whole brain was used and measures were adjusted for normal variation due to intracranial volume based on 20 age and sex matched healthy subjects.
Results: 31 patients (56.4%) exhibited facial asymmetry, in which 64.5% of these were visualised at rest, with voluntary and emotional expression, characterising facial paresis (FP). In 63.6% of patients, FP was contralateral to the side of MS, and in 61.2% was contralateral to the side of temporal pole signal abnormality. No correlation was found between the presence and lateralisation of FP and hippocampal, amygdaloid or temporal pole volumes. Simple febrile seizures as initial precipitating insult were observed in 72.7% of patients without FP while complex febrile seizures occurred in 69.2% of patients with FP ($p = 0.02$). Patients with FP presented 25.7 ± 12.1 (mean ± SD) years of epilepsy, while patients without FP had 22.6 ± 10.0 years of epilepsy history.
Conclusion: Facial paresis was significantly associated with the history of complex febrile seizures as an initial precipitating insult and a tendency for longer duration of epilepsy.

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Aphasic or Amnesic Status Epilepticus Detected on Positron Emission Tomography but not EEG
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Purpose: To describe 5 patients with ictal aphasia (4) or ictal amnesia (1), with hypermetabolism demonstrated by PET in the absence of clear ictal activity on EEG.
Methods: We obtained FDG PET scans in 5 patients with suspected ictal aphasia or ictal amnesia without demonstration of ictal activity on EEG. We reviewed clinical, EEG and imaging data, as well as outcomes with treatment.
Results: 4 patients presented with subacute onset of aphasia and 1 with amnesia, without structural abnormalities on MRI. In 3 patients with aphasia, the EEG showed left temporal irregular delta activity but no clear ictal pattern. 2 patients had other non specific abnormalities, again without evidence of ictal patterns. All patients were demonstrated to have a focus of hypermetabolism. This was left frontotemporal in the patients with ictal aphasia and bilateral hippocampal in the patient with amnesia. 3 patients who received intravenous benzodiazepines during their episodes responded transiently. With anti-epileptic drug therapy, symptoms gradually resolved and resolution of PET hypermetabolism was demonstrated, in 3 patients. 1 of these patients with ictal aphasia developed recurrent episodes of aphasia and then had two attacks of optic neuritis. Treatment with steroids and immune suppression stopped recurrences. 1 subsequent patient with past evidence of autoimmune disease had

only a partial response of aphasia to antiepileptic treatment, but a complete response with the addition of steroids.
Conclusion: PET scan should be considered as a diagnostic tool in patients with suspected ictal aphasia who fail to show clear evidence of ictal activity on EEG. A subset of patients with PET positive and EEG negative aphasic status epilepticus may have an immune basis for their manifestations and may require steroids in addition to antiepileptic drugs.

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Ictal Behavioural Patterns in Extratemporal Seizures
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Purpose: It is difficult to lateralise and localize an epileptogenic focus in extratemporal lobe epilepsy (ExTLE) by ictal semiology, long term scalp video\EEG monitoring and cranial MRI. In this study we aimed to evaluate ictal behavioural patterns in ExTLE patients.
Methods: 84 patients with EXTLE were retrospectively evaluated at the Telemetry Center. 45 (53.6%) were male, 39 (46.4%) were female. Mean age was 15.7 (2-45).
Results: We observed only one type of seizure in 64 (75.3%) and two or more types of seizures in 21 (24.7%) patients. 109 different seizure types in 84 patients were reviewed. 27 (24.8%) seizures had an aura. Automatisms were seen in 17 (15.4%) of seizures. Ictal vocalization was observed in 14 (12.8%) seizures and 5 (4.6%) patients had ictal speech. We also observed head and/or eye deviation in 43 (41.3%), turning of the whole body in 3 (2.9%) seizures. Tonic activity was seen in 50 seizures; 16 (14.7%) were symmetrical and 34 (31.2%) were asymmetrical. 53 (48.6%) patients had postictal confusion. 4 patients (4.8%) underwent invasive monitoring by the use of subdural strips or grids, and 4 patients (4.8%) underwent surgery. We localised the seizures in 40 (47.1%) and lateralised in 53 (62.4%) patients. Although cranial MRI revealed abnormalities in 28 (33.3%) patients, only 6 (5.5%) of them had the same localisation with video\EEG monitoring findings.
Conclusion: As a conclusion, the determination of epileptogenic focus in ExTLE is very difficult. The majority of patients had no MRI abnormalities or the same localisation with video\EEG monitoring findings. The value of the cranial MRI and clinical lateralisation sign for the determination of the focus in ExTLE is limited when compared with those with temporal lobe epilepsy. For definite localisation, invasive monitoring and functional neuroimaging techniques are mostly inevitable.

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Misdiagnosis of Epilepsy
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Purpose: To present 7 representative cases of misdiagnosis of epilepsy. Nonepileptic events misdiagnosed as primary epilepsy are as many as 20% to 30% of people with epilepsy. There are many imitators, ranging from convulsive syncope through to psychogenic events; conversely, symptomatic epileptic seizures may be not recognised as such.
Methods: Out of 33 patients with a primary diagnosis of epilepsy, we found 7 cases (21%) with an initial erroneous diagnosis. Diagnosis was based on careful analysis of preictal and postictal events, EEG, head-up tilt test and carotid sinus massage, ECG and blood pressure monitoring, CT, MRI, MRA.
Results: There were 6 men and 1 woman; 3 cases with syncope: micturition sy., (23 y), orthostatic hypotension, bradycardia, correlated with unknown diabetic autonomic neuropathy, (48 y) and orthostatic hypotension from dehydration syndrome, (49 y). A 29 y M, with tonic seizures unexpectedly died from miocarditis, (autopsied); a 47 y M had a MAV. A 52 y F with symptomatic epilepsy, with ictal olfactory hallucinations and cardiac autonomic deregulations, wasn't first recognised as a neurological patient, and only later was diagnosed with hippocampal lesion. A 43 y M, with polymorphous symptoms of frontal epilepsy, from callosal aneurysm, was first incorrectly diagnosed as psychogenic.
Conclusion: 1) Epilepsy may be a symptom of a disorder of the cerebral lesions with diverse aetiology. 2) Many seizure-like attacks have a cardiovascular cause. A non-invasive cardiovascular evaluation is always necessary to identify an alternative diagnosis. 3) Incomplete history-taking, the absence of eye-witness descriptions and misinterpretations of phenomena, are important causes of misdiagnosis.

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Photosensitive Epilepsy
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Purpose: Clinical evaluation of 14 photosensitive epilepsy cases by their history, EEG and clinical findings.
Methods: 14 photosensitive epilepsy cases are evaluated by their history, EEG and clinical findings. Response to the drug therapy was also evaluated.
Results: The mean age was 20.5 years and the mean duration of epilepsy was 7.2 years. All of these patients presented with a generalised multiple spike wave pattern during photic stimulation in their interictal EEG recordings. 5 patients presented myoclonic or generalised seizures during photic stimulation. Only 1 patient had a typical photosensitive epilepsy history while the others also had seizures without photic stimulation in their history. There were individuals among the first degree relatives of 2 patients and among the second degree relatives of 2 patients. 5 patients had myoclonic seizures while the others had generalised tonic clonic seizures. 8 were treated with valproic acid (1000 to 2000 mg/day). 2 out of 8 didn't respond to the therapy.
Conclusion: Photosensitive epilepsy is a rarely seen reflex epilepsy and it has a good prognosis

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Ethological Approach to Epileptic 'Automatisms' Viewed as Fixed Action Patterns Induced by a Release of Central Pattern Generators
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Purpose: Central pattern generators (CPGs) are genetically determined neuronal aggregates in the mesencephalon, pons, spinal cord, subserving, from molluscs to vertebrate, selectively adapted survival behaviours, such as locomotion, feeding, reproduction. In higher primates, CPGs are largely under 'neocortical' control.
Methods: While analysing seizures in patients undergoing presurgical evaluation, we observed behaviours suggesting that the seizure can be responsible for a jacksonian loss of control of CPGs mediating 'epileptic' automatic behaviours.
Results: We identified: motor cyclic-rhythmic behaviours, observed in hypermotor frontal seizures, and likely the expression of CPGs for

locomotion; affective behaviours, mainly related to seizures involving the 'limbic brain' and responsible for facial 'universal expressions' of basic emotion (analysed by Facial Action Code System) (Tassinari et al., Annals NYAS, 2003, 1000: 393-394) or other expressions of affective/approach, aggressive/withdrawal behaviours.
Conclusion: 1) Seizures can express innate behaviours related to CPGs usually under neocortical control. 2) Such behaviours are observed preferentially, but not exclusively, in certain seizure types (frontal, temporal). 3) However, release of the same CPG can be triggered by seizures arising in different epileptogenic areas. 4) Other non epileptic events (such as sleep disorders, psychiatric conditions) can lead to a release of the same CPG. 5) Hence a major caveat: the same semiology can be observed in different aetiologies. As by the 'carillon (musical box)' theory (Tassinari et al., in: A. Beaumanoir et al. (eds) 'Frontal lobe seizures and epilepsies in children', John Libbey, Montrouge, 2003, 43-48), the (motor) symphony occurs independently from what, who, and why opens the lid.

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Sexual Dysfunction in our Patients with Partial Epilepsy
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Purpose: Epilepsy patients have higher rates of sexual dysfunction than the general population, but patients do not spontaneously report these problems and physicians rarely inquire about epilepsy patients' sexual activity. Sexual dysfunction appears to be more common in localisation –related (partial) than generalised epilepsy, although psychological factors play a very important role.
Methods: We evaluated 74 patients (36 female, 38 male), mean age 36.2±11.8 years, with partial epilepsy (SPS, CPS with or without secondary generalisation (sGTCS)). Our patients were not treated for depressive disorder. The survey included two standardised diagnostic instruments, the Arizona Sexual Experiences Scale (ASEX) and Beck Depression Inventory (BECK). The ASEX has five questions assessing sexual dysfunction. This study examined the occurrence and correlation between sexual dysfunction and depression in patients with partial epilepsy, the relationship between sexual dysfunction and factors of epilepsy (seizure type, frequency, age, antiepileptic drug therapy, temporal versus extratemporal epilepsy). These data were analysed.
Results: Epilepsy patients included in our study have higher rates of sexual dysfunctions than found in the general population: male 26% and female 39%. The higher statistical relationship showed: frequency focal seizures (p= 0.001), age (p=0.002), depression (p= 0.004), sGS (secondary generalisation seizures, p= 0.37), antiepileptic drug therapy (p= 0.152). According to the ASEX both groups had higher scores in sexual desire and orgasm (lower scores indicate greater sexual function). There were no significant differences between men and women in distribution of sexual dysfunction. Statistical analyses in our study showed no significant relationship of sexual dysfunctions between groups of temporal and extratemporal epilepsy (p= 0.559). In the BECK women had higher depression scores then men. Details of the statistical analyses will be presented.
Conclusion: Our study demonstrated that seizure frequency, age, depression and antiepileptic polytherapy could have an affect on sexual dysfunctions. Specific evaluation, successful seizure control and psychotherapy may improve sexual dysfunctions in patients with epilepsy.

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Epilepsy in Hereditary Disorders of the Central Nervous System
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Purpose: Analysis of hereditary syndromes of progressive myoclonus-epilepsy, with special accent on differential diagnosis between mitochondrial diseases (MERRF), Unferricht-Lundborg's myoclonus-epilepsy (ULME) and Lafora disease (LD).
Methods: Clinical, genetic, morphological (muscle and skin biopsies) and ultrastructural study of 21 patients with progressive myoclonus-epilepsy (8 sporadic and 13 familial cases).
Results: 1) 12 patients (including 8 familial cases from 3 families with maternal inheritance) were diagnosed with mitochondrial disease of the MERRF or MERRF/MELAS type. In all these patients RRF features were seen on muscle biopsy. The onset ages varied from 6 to 56 years, and, in addition to myoclonus-epilepsy, cerebellar ataxia was seen in 60% of cases. 2) In 2 MERRF families we identified mutations in mtDNA in affected members and in one 'subclinical' case, thus confirming the diagnosis of mitochondrial disease. 3) The manifestations of the disease in the other 9 cases were presented by photo- and audio-sensitive myoclonus, and myoclonic jerks were usually followed by major epileptic seizures of tonic-clonic nature at a later stage of the disease. 4) Skin biopsies performed for all patients showed Lafora bodies in 2 brothers, leading to the diagnosis of LD. In 1 patient, DNA testing allowed us to identify the typical mutation (12-nucleotide expansion) in the 5' region of the CST6 gene on chromosome 21q22; this finding confirmed the diagnosis of ULME.
Conclusion: Analysis of clinical, morphological and molecular genetic features provides a firm basis for differential diagnosis of ULME, LD, MERRF and other similar disorders characterised by progressive myoclonus-epilepsy.

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Epilepsy and Multiple Sclerosis
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Purpose: This study was performed to analyse clinical characteristics of epilepsy in patients with multiple sclerosis (MS), whether there is a correlation between the semiology of seizures, EEG and magnetic resonance imaging (MRI) recordings, and to examine the response to anticonvulsant therapy.
Methods: The study group comprised 71 patients suffering from MS and hospitalised in 2004 in the Department of Neurology. There was no evidence of other potentially epileptogenic pathologies.
Results: Out of 71 patients, 5 patients (3 men and 2 women) displaying seizure activity were selected. In 2 patients, epileptic seizures formed part of the first episode of their illness. The seizures were partial with secondary generalisation in 4 patients; 1 of them presented status epilepticus. 1 patient had more than one type of epileptic seizure. Anomalies in all 5 cases were found in the EEG (periodic lateralised epileptiform discharges mostly in the temporal region). Brain MRI showed scattered T2 hyperintensities in several localizations, including the periventricular and subcortical white matter bilaterally, cortical and subcortical lesions, and in 1 patient there was an accompanying oedaema. All patients displaying seizure activity were treated with carbamazepine or valproate with good therapeutic responses.
Conclusion: The obtained data support earlier findings indicating that epilepsy occurs more frequently in patients with MS, compared to those in the general population. It may also be concluded that seizure activity may be an initial symptom of MS and seizures are usually partial with secondary generalisation. Finally, EEG-MRI seizure type correlation can be observed in SM patients

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Bilateral Hip Fractures in First Epileptic Seizure
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Purpose: Fractures due to epilepsy have two main causes: 1) falls during or after the seizure, which typically lead to fractures of exposed

body parts, and 2) fractures due to the direct effect of violent muscle activity, which is more likely located proximally.
Methods: An 82 year-old man had a first-ever, eye-witnessed, generalised tonic-clonic seizure, which led to urgent hospital admission. He was a little bit drowsy, and complained of diffuse, mild hip girdle pain. The next day, a haematoma of the left posterior thigh was noted, suggestive of hip fracture. Radiography disclosed a bilateral hip fracture with instability. The past medical history of the patient included vascular leukoencephalopathy with moderate dementia and pseudobulbar paralysis as well as cervical spondylotic myelopathy.
Results: The fracture was operated on, technically successfully, but the patient didn't recover neurologically, and died from central regulation failure on day 30.
Conclusion: Hip fractures are more frequent in patients with epilepsy seizures when compared to age-matched controls without epilepsy. In age, most of the fractures might be attributed to falls, if they are unilateral. This applies to our case, which rather resembles the rare cases of bilateral humerus fractures in epileptic seizures, and the fractures are probably due to violent muscle activity in weakened, osteoporotic bone. The emergency examination of a patient with an epileptic seizure should include screening for hip fractures, too, especially in the elderly.

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A Sleep Disorder? Hypothalamic Hamartoma Diagnosed in a 66 Year Old Woman
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Purpose: Hypothalamic hamartomas (HH) diagnosed in childhood are usually due to a typical clinical presentation with severe epilepsy including gelastic seizures, and complex endocrine features with precocious puberty. We wish to report the circumstances that led to the diagnosis of HH in an elderly woman.
Methods: A 66 yr old female patient was referred for longstanding, severe disruption of sleep and a history of GTCS since school years. She had led a normal life working on the family farm, had raised 4 children, and had menopause around age 50. GTCS with falls had hindered her schooling, but their frequency had abated over the years while on phenobarbital and later carbamazepine, with only a few episodes per year. Since early adulthood, she had been awakening repeatedly from sleep laughing or sneering, and often had difficulties falling asleep again. A CT scan was considered normal.
Results: Video-EEG monitoring recorded several gelastic episodes arising from sleep, without clear EEG changes beyond a waking reaction. Interictal EEG showed some rare isolated right temporal spikes. A HH was present on the MRI.
Conclusion: This patient had none of the usual endocrine symptoms associated with HH, a not so severe epilepsy, but the typical gelastic seizures that presented in this case as frequent nocturnal episodes disrupting sleep. Among other recently evaluated patients with HH, frequent seizures during sleep were only present in a minority of cases.

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Familial Non-conclusive Status Epilepticus Characterised by Ictal Hemiplegia
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Purpose: Familial incidence of adult onset localisation-related partial epilepsy is relatively rare compared with familial idiopathic generalised epilepsy. Furthermore, non-convulsive status epilepticus presenting with prolonged hemiplegia is an unusual manifestation.
Methods: A 39 year old woman has had recurrent episodes of transient right hemiplegia, lasting from several hours to one day. On neurological examination during the ictal period she had alert consciousness with aphasia, head and eyeball deviation to the right side, and right hemiplegia. A 37 year old sister has had same manifestation of seizures since 25 years of age.
Results: Brain MR imaging studies did not show any abnormality. EEG video monitoring of the ictal period showed continuous ictal discharge in the midline frontocentral area (suggest supplementary negative motor area) coincided with right hemiplegia. After injection of diazepam, the ictal discharge and right hemiplegia disappeared.
Conclusion: We report a familial occurrence of ictal hemiplegic seizure, which may result from continuous epileptic activity in the supplementary negative motor area.

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Seizures After Stroke in Adults
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Purpose: Cerebrovascular diseases are significant aetiological factors of epilepsy. Our goal was to analyse the frequency and correlation between epileptic seizures and the type and size of cerebrovascular lesion.
Methods: In this prospective study, we evaluated patients with stroke who were hospitalised at the Department of Neurology in Nis, between January and December 2004. Witnessed epileptic seizures occurred in 57 patients. 41 patients had ischemic and 16 patients had haemorrhagic cerebrovascular disease. Patients with a previous history of epilepsy and pulmonary diseases were excluded. Patients were evaluated and had the same investigations with anamnestic, clinical, neurological, EEG and neuroimaging (CT, MRI) variables which were compared.
Results: Of the 840 patients with stroke who were admitted to the hospital, 206 (25%) had haemorrhagic stroke, and 634 (75%) had ischemic stroke. Mean age was 54 +/- 30 years, male 33 and 24 female. 16 (7.76%) patients with haemorrhagic and 41 (6.46%) patients with ischemic stroke developed seizures after 14 days of the stroke. Partial motor seizures (PMS) were registered in 22 (38.6%) patients, partial seizures with secondary tonic-clonic generalisation (GTC) in 18 (31.6%) patients and primary GTC seizures in 17 (29.8%) patients. Status epilepticus (SE) was registered in 7 patients. 15 (26.3%) patients had EEG pathological changes (spike or sharp-waves) and 19 (33.3%) patients had focal or diffuse Theta-Delta waves. Normal EEG patterns were registered in 3 patients.
Conclusion: Patients with haemorrhagic stroke and cortical lesions are at a higher risk of developing seizures. Partial motor seizures and partial seizures with secondary tonic-clonic generalisation are a dominant feature.

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Profile of Patients with Epileptic Seizures of Alcoholic Genesis
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Purpose: It is known that long-term alcohol abuse can be connected with epileptic seizures. The aim of the study was to determine a profile of patients with epileptic seizures of alcoholic genesis.
Methods: The sample consisted 230 patients (216 or 90% males) with epileptic seizures of alcoholic genesis. The control group consisted 230 patients with seizures of 'unknown genesis'' with similar sex and age distributions. The focus was on determining: average age of patient during first epileptic seizure, alcohol abuse duration, volume of alcohol drinks, hereditary risk, type of epileptic seizures, EEG. Statistical analysis was made by appropriate statistical tests (chi square).
Results: Average age of examined patients was 46.5 (±22.5) years, and the first seizure appeared in more than 60% in the period between 31-50 years. Alcohol abuse duration before the first seizure was from 10 to 20 years in the majority of cases. In 90% of cases seizures

appeared during the abstinence period. High volume alcohol drinks were consumed by 90% of epilepsy patients. Hereditary risk was low (6.1%, opposite 8.6% in the control group) ($p>0.05$). Epileptic seizures were predominantly generalised, tonic-clonic type ($p<0.05$). EEG findings were normal in almost 90% patients, opposite 27.0% in the control group ($p<0.05$).
Conclusion: Results reflect just some aspects of the always-present problem called alcohol induced fits. Those indicate the patient's profile with 'alcoholic epilepsy': mainly male, approximate age of 46, long-term alcoholic, experiencing epileptic seizures mostly in abstinence period. EEG findings are normal, and seizures are predominantly generalised, tonic-clonic type.

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Clinical Study of Paroxysmal Kinesigenic Choreoathetosis
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Purpose: To study the clinical characteristics, electrophysiological manifestations and pathogenesis of paroxysmal kinesigenic dyskinesias (PKD) and paroxysmal non-kinesigenic dyskinesias (NPKD).
Methods: The clinical characteristics of 33 patients with PKD and 5 patients with NPKD during 1997 to 2004 were analysed and related literatures were reviewed.
Results: All the patients were young without familial history. The clinical manifestations were a sudden onset of abnormal involuntary movements in unilateral/bilateral limb or face that last only several seconds and relieved spontaneously, and which were precipitated by starting of movement. There was no impairment of consciousness and discomfort during and after paroxysm. No abnormal signs in physical examination of nervous system, EEG and head CT/MRI were found, thus these 38 patients were diagnosed as idiopathic PKD and NPKD. After oral administration of carbamazepine or dilantin, the paroxysmal symptoms with PKD were under effective control.
Conclusion: The PKD and NPKD are autosomal dominant inheritance diseases, with sporadic or idiopathic occurrence. They may occur secondary to other diseases. The pathogenesis has not been elucidated. The clinical characteristics of PKD and NPKD are abnormal involuntary movements in unilateral/bilateral limb or face while they are precipitated by movement. The PKD and NPKD are diseases with good prognosis and PKD is sensitive to antiepileptic drugs.

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Seizures after Heart Transplantation
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Purpose: Seizures were reported to be a frequent complication (6 to 36%) of organ transplantation. We analysed the incidence and aetiologies of seizures among patients with heart transplantation.
Methods: All patients presenting a seizure after heart transplantation from 2002 to 2004 in the Cardio-vascular Surgery Department, at the Pitié-Salpêtrière Hospital, were included. Immunosuppressive drug levels were monitored each day after transplantation. Patients underwent brain MRI and EEG at the time of the seizures and during the follow-up.
Results: 8 patients (4.6%) presented seizures among the 176 patients with heart transplantation. In half of them, brain MRI showed a posterior leucoencephalopathy that was associated with cyclosporine immunosuppressive treatment, although this drug was within the therapeutical level. Other causes of seizures were identified, including cerebrovascular complications, pre-existing pathology such as mitochondrial disease. No seizure was related to the surgical procedure, or to CNS infection. Neuroimaging and clinical abnormalities improved after replacement of cyclosporine by tacrolimus and the addition of antiepileptic drugs, in patients with posterior leucoencephalopathy.
Conclusion: In our study, the incidence of seizures in patients with heart transplantation is weaker than in previous reports. This may be due to improvement of the surgical procedure and the monitoring of immunosuppressive drug levels. Posterior leucoencephalopathy occurring in therapeutical levels of immunosuppressive drug has become the major cause of seizures after heart transplantation. Symptoms are reversible after prompt change of immunosuppressive agent.

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Moderate Hyperhomocysteinemia in Adults Treated for Epilepsy
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Purpose: Hyperhomocysteinemia (HHcy) is mostly discussed as a marker of the risk factor in vascular damage, mild already (up to 30 umol / l) and was often studied in patients on antiepileptic drugs (AEs). For its neuroexciting properties, Hcy is used as an epileptogenous agent; experiments in-vivo as well in-vitro revealed its relationship to NMDA glutamate receptors, also with potential neurotoxicity. However, its importance in clinical epileptology is rarely discussed.
Methods: The total plasma Hcy as well as vitamin levels (folate, vitamin B6, B12) and routine estimations including lipid spectrum were determined in the group of 123 adult patients, 68 men and 55 women, on long-term AEs inducing the cytochrome P 450. Hhcy, mostly the mild type, was diagnosed in about 30%. Out of the total group we analysed 8 patients (7 men and 1 woman) with moderate HHcy - 30.7 to 109.0 umol/l. Retrospectively we described the clinical course and therapy, neuropsychological, EEG and morphological investigation (CT, MRI). The patients were followed up for 30-60 months after Hcy normalisation achieved by vitamin therapy. Basic vascular disease risk factors were monitored. In all 8 patients, molecular genetic tests were performed.
Results: The group was characterised by concomitant factors: treating by AEs inducing the cytochrome P 450, the vitamin deficits, mainly folate and /or vit B6 and B12 and the MTHFR mutation of the gene C677 T in all cases, homozygous in 7 and heterozygous in 1case. All the patients suffered from partial and/or secondary generalised seizures accompanied by neuropsychological impairments ranging from mild to the severest degree, depending on the aetiology. No detectable or only a mild influence of Hcy normalisation was found from the point of view of epilepsy (clinically and/or EEG) as well as of neuropsychology. In the case of a generalised EEG pattern deterioration was found.
Conclusion: The results confirmed the usefulness of Hcy and vitamin levels investigations, though unresolved problems exist. The small number and retrospective following under treatment do not suggest any definite conclusions from the point of view of epileptogenicity.

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Clinical Characteristics of Temporarily Associated Epilepsy and Migraine in Adult Patients with Epilepsy
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Purpose: To determine the prevalence of migraine in patients with epilepsy, the temporal association of these two conditions and the clinical characteristics of patients having this comorbidity.
Methods: A group of 40 (15.44%) outpatients with epilepsy and migraine, out of 259 adults with epilepsy, were examined during a 30-month period. A standardised questionnaire was filled out; neurological examination, EEG, MRI were performed. Epileptic seizures and headaches are classified as generalised or focal.

Results: Among 40 patients, 85% were females. Males were significantly less involved ($p<0.001$). 32 (80%) patients had generalised seizures (GTCS). The patients less than 40 years old were found to have a significantly higher frequency of GTCS ($p<0.05$) in relation to focal seizures. 10 patients had migraine with aura. Temporal association of epileptic seizures and migraine attacks was found in 19 (47.5%) out of 40 patients. Among these 19 patients, 8 (42.1%) had preictal migraine attacks, 5 (62.5%) of these patients had migraine with aura. Postictal migraine was found in 11 patients. Postictal and interictal migraine attacks without aura were found to be significantly more frequent than those with aura ($p<0.05$).
Conclusion: Associated epilepsy and migraine are significantly more frequent in female patients. In almost half of patients the onset of migraine was temporarily linked to the occurrence of epilepsy. Two-thirds of these patients had generalised attacks, while one-third had focal seizures. Preictal migraine with aura was found to be more frequent than postictal. This might support the theory that cortical spreading depression during the migraine aura triggers an epileptic seizure.

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Sudden Unexpected Deaths In Epilepsy
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Purpose: Patient groups are increasingly concerned and questioned regarding the risk of death in epilepsy, and particularly that of sudden unexpected death (SUDEP). Many issues are still pending, including the risk factors for SUDEP.
Methods: We analysed all available relevant data on a cohort of 87 patients with epilepsy who died unexpectedly. Among these 87 patients, only 64 were eventually considered to have suffered SUDEP, whereas 7 committed suicide, 5 died from status epilepticus, 1 from a car accident, and 7 from an associated condition. Only data regarding the 64 SUDEP patients are reported.
Results: 53% were male, and there was an overrepresentation of young adults between 21 and 28 years old. Socio-professional status did not appear to influence the risk of SUDEP. The occurrence of a seizure immediately prior to death could be ascertained in only 5 patients (8%), provided that 64% of SUDEP occurred during sleep. 55% of patients suffered from complex partial seizures with secondary generalisation, 52% from drug resistant seizures, and 61% from cryptogenic epilepsy. 28% of patients were thought to be non or poorly compliant with their drug regimen. 58% presented with psychological disturbances, including patients who suffered significant emotional stress immediately prior to death.
Conclusion: Results from this preliminary study emphasise the risk of SUDEP in young adults with nocturnal secondary generalised drug resistant seizures and psychiatric co-morbidity. Further studies are warranted in collaboration with family members of deceased patients.

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Comorbidity in Epilepsy: A Prospective Study at the Epilepsy Centre, Kork
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Purpose: To investigate clinically relevant comorbidities in adult epilepsy patients who were consecutively included from May 2004 to February 2005.
Methods: We analysed the data of 399 adult patients and collected and classified all clinically relevant additional diagnoses according to the ICD-10.
Results: Only 344 patients (86%) suffered from epilepsy. Among the 55 patients without epilepsy 27 had dissociative seizures. 28 patients suffered from syncopal fits, paroxysmal movement disorders or other neurological or psychiatric conditions. 21 epilepsy patients had additional dissociative seizures (6%). The most frequent additional psychiatric diagnosis among the epilepsy patients was mental retardation (26%). Other common psychiatric diagnoses were organic and symptomatic psychic disorders (17%), depression (10%), somatoform (9.0%), affective (6.7%) and anxiety disorders (3.2%) as well as psychosis (2.6%). Common non-psychiatric diagnoses were central paresis (43%), adipositas (11%) and hypertonus (10%).
Conclusion: A high proportion of 14% of our adult in-patients had no epilepsy. The most frequent comorbidities were severe handicaps such as mental retardation and central paresis thus reflecting the patient mix in a specialized epilepsy clinic. Psychiatric comorbidity factors such as depression, anxiety disorders or psychosis which were frequently reported in other epilepsy patient surveys were relatively rare. One should be concerned about the high rates of overweight and hypertonic disorders.

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Different Types of Epilepsy and the Structure of Sleep in Patients with and without Antiepileptic Therapy
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Purpose: To establish the degree of sleep disturbance in epilepsy patients with AET and different types of epilepsy.
Methods: We performed long-term polysomnographic EEG recording in 58 patients with different types of epilepsy.
Results: 1) Sleep is more disturbed in patients with partial attacks (PA) then in patients with generalised attacks (GA) (both without AET). Patients with PA in respect to GA (both without AET) have shortened duration of sleep stage III. 2) Patients with PA in respect to GA (both with AET) have prolonged duration of sleep stage III and sleep latency. 3) Sleep disturbance is more pronounced in patients with partial simple attacks (PSA) than with partial complex attacks (PCA) (both without AET).
Conclusion: 1) Patients with different types of epilepsy have different degrees of sleep perturbation. 2) Sleep structure is more disrupted in deeper than in superficial sleep. 3) Sleep perturbation is higher in patients with PA than in patients with GA. 4) Patients with PSA in respect to PCA, have longer sleep duration but also a higher number of sleep stage shifts. 5) Sleep structure is influenced by AE therapy more in deeper then in superficial sleep stages. 6) AE therapy improves the duration of sleep more in PA than in GA, but it also increases their number of sleep stage shifts. 7) REM sleep is unfavourably influenced by AE therapy both in respect to duration and the number of episodes. 8) Sleep latency to stage I does not differ between the patients with GA and PA.

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Impairments, Disabilities and Handicap in Patients with Intractable Focal Epilepsy Compared to Patients with Terminal Organ Failure
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Purpose: Intractable epilepsy is a chronic disorder associated with severe consequences for the patients' daily life. Less is known about the individuals' own experience of the causes of impairments and disabilities and of external factors that lead to disadvantage, and this may constitute a problem for the optimal treatment. The aim of this study was to clarify these questions based on the WHO's concept of impairment, disability and handicap in comparison with patients with other severe chronic intractable conditions.
Methods: Patients referred to an epilepsy surgery program and patients with terminal liver or heart-lung failure referred to a transplantation waiting list (N=139), were systematically interviewed by use of questionnaires.
Results: The 'Psychological Impairment' of the epilepsy patients were equal to the organ failure patients concerning (lack of-) 'positive well-being', 'self-control' and 'anxiety'. 'psychosocial disability' was the same for both groups but epilepsy patients were less dependent.

Conclusion: Patients with intractable epilepsy are as anxious as organ transplant candidates, have the same low sense of positive well-being and feel the same lack of self-control.

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Psychiatric Symptoms and Risk-taking Behaviour in Youth with Epilepsy, Compared with Youth with Diabetes and Asthma
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Purpose: We have previously presented data from a population-based study showing increased psychiatric problems and risk taking behaviour in youth with epilepsy. These findings may be related to epilepsy itself, or they may be due to the youth having a chronic disorder. To explore these possibilities we compared our findings in youth having or having had epilepsy with findings in youth with asthma and diabetes.
Methods: The study was cross-sectional and based on questionnaires from youth aged 12 – 19. 20,083 questionnaires were filled out (82% responder rate). To screen for psychiatric symptoms we used the Strengths and Difficulties Questionnaire (SDQ).
Results: The percentage of pupils scoring borderline or abnormal in SDQ was higher in all grades in those reporting having or having had epilepsy and diabetes compared to those without any chronic disease (controls) and those with asthma. In 10th grade 38% of those with epilepsy and 37% of those with diabetes scored borderline or abnormal compared to 17% of the controls and 20% of those with asthma. The percentage of youth reporting risk taking behaviour was also significantly higher in these groups.
Conclusion: Youth with epilepsy and diabetes had a higher percentage of borderline and abnormal scores in SDQ, indicating a higher tendency to psychiatric disorders as compared to youth with asthma and controls. Risk-taking behaviour was also significantly more common among youth with epilepsy and diabetes The finding suggests that youth with epilepsy and diabetes may have common factors facilitating the development of psychiatric problems and risk-taking behaviour.

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Who Among Patients with Recurrent Seizures is Prone to Traumatic Intracranial Haemorrhage?
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Purpose: To characterise patients with seizures who develop traumatic intracranial haemorrhage (TIH).
Methods: We reviewed, retrospectively, all cases of TIH in patients with recurrent seizures between the years 1989-2003 (15 years), from lists provided by Soroka Beer Sheva, Sourasky Tel-Aviv, and Rambam Haifa Medical Centres in Israel. We identified patients by crosschecking ICD codes of epilepsy/seizures with codes of all types of TIH (epidural, subdural, subarachnoid, brain contusions and lacerations).
Results: 52 patients were identified. Age: 8-85 years, 44 males. 27 (52%) had additional risk factors for TIH: old age (>70 y) (n=12); alcohol abuse (n=13); anticoagulant treatment (n=3). Of 25 patients without the above risk factors, 9 (36%) suffered from a mental handicap (8 with mental retardation, and 1 had poorly controlled schizophrenia). Of the 16 patients with neither mental disease nor additional risk factors, 9 had evidence of under treatment of anti-epileptic medications.
Conclusion: Most of the patients with seizures who developed TIH have additional risk factors for TIH, are mentally handicapped or are treated with sub-therapeutic dosages of anti-epileptic drugs.

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Work Beliefs and Work Status of People with Epilepsy
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Purpose: To determine differences in work beliefs, held by people with Epilepsy, between those who work (W) and those who do not (NW).
Methods: 113 subjects 58 females, mean age 41.56 yrs old plus-minus 11.42s.d., seizure duration mean 22.88 yrs plus-minus 12.96s.d. were given a validated questionnaire (MASQ-II) to assess work beliefs. Items were scored on a Likert-type scale (1-5) where 5 was the worst response. 45/113 people worked full time, 11 part-time, 57 did not work. 35 subjects had more than 1 seizure/month, 78 had less than 1. Those who worked had fewer seizures.
Results: People who worked believed that: you don't have to have a job to be 'normal' [mean 3.02 plus-minus 1.95s.d. (W) vs. mean 2.05 plus-minus 1.50s.d. (NW), p=0.004], they have enough education [mean 1.48 plus-minus 1.06s.d. (W) vs. mean 2.73 plus-minus 1.68s.d. (NW), p=0.0001], not having a job is not the only barrier to independent living [mean 0.425 plus-minus 0.689s.d. (W) vs. mean 0.892 plus-minus 1.25s.d. (NW), p=0.01], their families did not fear job injuries [mean 1.75 plus-minus 1.52s.d. (W) vs. mean 3.57 plus-minus 1.78s.d. (NW), p=0.0001], working did not present a risk of injury [mean 1.81 plus-minus 1.42s.d. (W) vs. mean 2.75 plus-minus 1.72s.d. (NW), p=0.003], they would not hurt others [mean 2.05 plus-minus 1.47s.d. (W) vs. mean 3.01 plus-minus 1.72s.d. (NW), p=0.002], their families wanted them to work [mean 1.29 plus-minus 0.88s.d. (W) vs. mean 2.76 plus-minus 1.77s.d. (NW), p=0.0001], and that seizures would not negatively affect job performance [mean 2.37 plus-minus 1.78s.d (W) vs. mean 3.50 plus-minus 1.62s.d. (NW), p=0.001].
Conclusion: Work beliefs are important factors contributing to work status for people with epilepsy.

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Clinical and Radiological Features of the Glenohumeral Joint in a Population of Patients with Generalised Tonic-clonic Seizures
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Purpose: Generalised tonic-clonic seizures (GTC) may lead to shoulder fractures and/or luxations, as well as a predisposition to degenerative osteoarthritis (DOA) affecting the glenohumeral joint (GHJ). We aim to determine the frequency and severity of DOA in epilepsy patients and their relation to seizure frequency and epilepsy duration.
Methods: 100 patients (20 to 50 y/o), with no history of shoulder surgery, diabetes, ankylosing spondylites, syringomyelia and rheumatoid arthritis were assembled in Group I: 50 patients with frequent GTC (≥ 1/month, over 5yrs of epilepsy) and Group II: 50 patients with no history of epilepsy or shoulder complaints. All patients received a full clinical and radiological GHJ work-up, conducted by a trained orthopaedist.
Results: In Group I patients had a mean age of 34 y/o, 58% female, 86% right handed, 7.4 (1-32) GTC/month, 23.4 (9-49) yrs of epilepsy and were taking 2.6 antiepileptic drugs. In Group II mean age was 40 y/o, 52% female, 92% right handed. Group I presented with a higher incidence of both flexion amplitude and internal and external rotation reduction of the GHJ (p<0.01). GHJ ostheophitosis was found in 8% Group I and 12% Group II (p=0.5819). DOA in Group I was mild in

10 patients and moderate in 1 case. GTC frequency was higher in patients with DOA (p=0.04), but lacked significance in terms of epilepsy duration.
Conclusion: Frequent GTC seizures predispose to a decrease in flexion amplitude of the GHJ and radiological findings suggesting DOA. No statistical significance was established between epilepsy duration and clinical or radiological findings of DOA.

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Seizure Recurrence in Late-Onset Post-Stroke Seizures
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Purpose: The aim of the present study is to evaluate various epidemiological and clinical data for recurrence of late onset post-stroke seizures (PSS).
Methods: All consecutive first attack late onset post-infarct seizure patients (n= 25) who visited Kaohsiung Municipal Hsiao-kang Hospital from 1998 to 2002 are evaluated. Only patients with latency (from last stroke to the first seizure occurrence) for more than 14 days are included.
Results: The average age at first PSS is 64.6 ±15.9 years. The average latency of first PSS was 27.8 ± 36.4 months (range: 0.6 ~ 146.2 months; 16% < 30 days, 44% < 1 year, and 68% < 2 years). It was found that the recurrence group has significantly shorter latency of first PSS (9.3± 7.1 months) compared with the nonrecurrence group (51.5 ± 44.9 months) (P < 0.05). Stroke severity measured by NIHSS is found to be significantly lower in the recurrence group (8.4 ±5.8) than in the nonrecurrence (13.8 ±6.8) group (P < 0.05). There are no significant differences between the two groups in age, arterial territories, cortical involvement or various stroke risk factors.
Conclusion: The present study found that the risk of developing seizures is in the first two years after a stroke. Among the PSS patients, the recurrence group has significantly shorter latency of first PSS and lower NIHSS when compared with the nonrecurrence group. The mechanisms underlying the above findings need further investigation.

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Outcome of Pseudoseizures: 2 to 5 Years of Follow-up in 16 Patients
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Purpose: In this study we consider the outcome of all adult patients (more than 16 years old) with pseudoseizures and without epilepsy who were referred to the Epilepsy Center of our Department between 1999 and 2004.
Methods: We performed a follow-up study of 16 patients (10 women and 6 men) whose mean age was 22.4, with confirmed (ictal EEG-CCTV) psychogenic non epileptic seizures (PNES). The follow-up period after diagnosis ranged from 2 to 6 years. The information has been obtained by telephone interviews or neurological examinations.
Results: 7 patients (43.7%), 5 of whom were females, eventually became seizure-free. Among the patients who did not recover, 4 reported at least a seizure-free period after diagnosis lasting 7.3 months on average. Mean age of seizure-free patients was 19.6 years old (at the time of diagnosis) and they all received psychotherapy treatment. Among these patients, the diagnosis of PNES was made earlier than in the not seizure-free group. The outcome was better for patients with PNES with less dramatic features. A strict co-operation between neurologist and psychotherapist was possible only in 7 patients (and of these 4 were seizure-free and the other 3 enjoyed periods without seizures).
Conclusion: Early diagnosis, younger age at presentation, female sex and prolonged psychotherapy treatment appear to result in a good outcome. The acceptance of diagnosis and a good communication between neurologist and psychiatrist may also positively impact on the outcome.

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Incidence Rate of Active Epilepsy in Rural West Bengal, India: A 5 Year Longitudinal Study
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Purpose: To find out the incidence rate of active epilepsy cases in a rural community, since 70% of the Indian population resides in villages.
Methods: A team of neurologists conducted a two staged house to house survey consisting of screening of active epilepsy cases followed by clinical examination of all the screened cases within a cluster of 12 villages in a rural belt of West Bengal, Eastern, India during the first year of study (92-93), based on a validated WHO questionnaire. During the subsequent 4 years, surveillance was continued and newly diagnosed cases were recorded.
Results: On a base population of 20,842, 20,717 (M-10,972; F-9,745) subjects could be surveyed over 5 years and a total of 38 cases were identified. Five years' cumulative incidence rate stood at 183.42/100,000 and the average yearly incidence rate of epilepsy was 36.68/100,000 (95% CI 25.8-50.5). Age adjusted rate was 25/100,000 (95% CI 17.6-34.4) Based on the USA 1990 population and 52.07/100,000 (95% CI 36.7-71.6) based on the Indian standardised population. Age specific incidence rate showed a progressive decline in incidence rate over the years except for a slight surge in 5th decade.
Conclusion: The incidence rate in our study is similar to that of developed countries, ranging from 20 to 70 per 100,000 and this is against the prevalence idea that the incidence rate is high in developing countries. Interestingly, the typical late life increase in incidence rate is absent in our study, probably due to the younger age of our sample population.

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Prognosis of Newly Diagnosed Epilepsy: Preliminary Results of a Two-year Prospective Follow-up Study
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Purpose: To assess the prognosis of newly diagnosed epilepsy prospectively over a two year period in an adult patient population.
Methods: 261 patients (136 male, 17-84 years) with newly diagnosed epilepsy or new onset seizures were enrolled in this prospective observational study. The history, neurological examination, laboratory tests, EEG, provoking factors and neuroimaging findings were taken into account. Prognosis in terms of remission and mortality were determined by following up the patients each six months after the index seizure. The minimum follow-up period is 30 days and the maximum is 32 months (mean 14 months).
Results: Currently we have 5 subgroups of patients according to their follow-up periods. Group 1 (0-6 months), group 2 (6-12 months), group 3 (12-18 months), group 4 (18-24 months), group 5 (24 months and more). 66 patients had cerebrovascular disease (57 ischemic, 9 haemorrhagic), 38 had tumour related seizures. 12 had acute symptomatic, 24 had post-traumatic seizures. 81 had cryptogenic and 30 had idiopathic epilepsy. 5 had cortical dysplasia, 3 had Behçet's disease and 2 had multiple sclerosis. 16 patients presented with status epilepticus. Patients with acute symptomatic seizures had no relapse. The number of patients in the first group is 44; 5 of them had recurrent seizures. 12 of 64 patients in group 2, 16 of 68 patients in group 3, 8 of 67 patients in group 4, 7 of 18 patients in group 5 had recurrent seizures. The overall mortality rate is 4%.
Conclusion: In our study, the relevant factors for seizure recurrence were symptomatic epilepsy, epileptiform EEG abnormalities and presentation with status epilepticus.

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Predictors of Disease Course among Patients with Cryptogenic Epilepsy

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Purpose: To find predictors of the long-term treatment outcome of cryptogenic epilepsy patients.
Methods: We selected a sample of 17 male and 42 female cryptogenic epilepsy patients from a group of 250 patients with epilepsy, who had been followed in the Brno Epilepsy Centre. The patients were examined twice in five years. We studied the frequency change of seizures, the durations of seizure-free periods and the appearance of status epilepticus, with respect to gender, age at onset of disease, seizure type and the frequency of seizures in year one.
Results: 32% (19 patients in total) were seizure-free (SF) throughout the period. The treatment was more successful among patients with just SGTCS (50% SF) when compared with those with SPS and SGTCS (16% SF), with CPS and SGTCS (18% SF) or just with CPS (28% SF). Apart from the SF group, the success of treatment is negatively related to the age of epilepsy onset. High frequency of seizures in the first year of disease predicts worse course of disease (mean 0.46 seizures per month in SF group versus 9.00 per month in the group with an increased number of seizures). There are 13% SF patients in the group with seizure onset in left temporal lobe (40% on the right side).
Conclusion: Gender, age, frequency of seizures during year one and the type of seizures provide considerable predictors of treatment prognosis among patients with cryptogenic epilepsy.

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Epilepsy in Kolkata, India: Report of a Population-based Random Sample Survey

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Purpose: The study aimed to determine the prevalence and incidence of epilepsy, and among those aged 5 years or less the prevalence of febrile convulsion (FC) through a door-to-door random sample survey in the Indian city of Kolkata.
Methods: Kolkata is divided into 141 municipal wards composed of 5200 blocks. Using a table of random numbers, 160 blocks were randomly chosen, and from each chosen block 75 households were randomly selected for a door-to-door survey. This was a two-stage survey. Initially, trained field workers screened cases of epilepsy and of FC using a pre-designed questionnaire. Subsequently the neurologist performed a comprehensive clinical examination of screened positive cases and studied their investigational reports. ILAE criteria were followed to diagnose epilepsy and FC.
Results: Out of the total surveyed population of 52,377 (men 27,415, women 24,962), there were 288 cases of active epilepsy. The crude prevalence rate was 550 per 100,000 (men 584, women 513). The annual incidence rate of epilepsy was 17.2 per 100,000. FC was noted among 5.4%, i.e. 211 out of 3,927 cases of children aged 5 years or less. Neuroimaging, performed in 46% of epilepsy patients, showed solitary granuloma as the commonest structural lesion. About 26% of epilepsy patients did not receive any allopathic medicine until the time of the survey.
Conclusion: The prevalence of epilepsy and of FC in Kolkata was similar to that obtained from population-based studies in western countries. There is a considerable lack of awareness even in our urban community regarding epilepsy and its appropriate treatment.

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An Epidemiological Study of Epilepsies in Six Districts of Albania

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Purpose: The purpose of our study was to analyse the annual incidence and the prevalence in 6 districts of our country (Tirana, Durres, Elbasan, Vlora, Shkodra and Lezha) to make a comparison of the data found in these different districts.
Methods: Each patient is accepted as having epilepsy according to the H. Gastaut Classification, which has only a little modification from the International Classification of Epilepsies of 1981.
Results: In a population of 1,226,078 inhabitants of the six above-mentioned districts, there are 1499 patients (pt.) in Tirana district, 483 pt. in Durres district, 577 pt. in Elbasan district, 695 pt. in Vlora district, 451 pt. in Shkodra district and 202 pt. in that of Lezha. The prevalence of this 10 year study for the six above-mentioned districts is 3.19% (pro mille). The result of the annual average incidence for the six districts is 18 new pt. for 100,000 inhabitants.
Conclusion: 1) Analysing a population of 1,226,078 inhabitants in the six districts results in 3,907 epilepsy pt.: from them 1,499 are in Tirana district; 483 in Durres district; 577 in Elbasan district; 695 in Vlora district; 451 in Shkodra district and 202 in Lezha district. 2) The prevalence for these 6 districts is 3.19% (pro mille) annually for 6 Districts. The incidence is 18 new cases in one year for 100,000 inhabitants. These data are similar to certain other studies in Europe. 3) The epidemiological study of epilepsies is an important duty for analysing more profoundly the epilepsy pt. suffering from a chronic epilepsy, which manifests several psychic symptoms, and for improved organisation of treatment and rehabilitation, in order to enable integration in social activity.

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Epilepsy in the Elderly in Mexico in the New Millennium: 88 Cases

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Purpose: The causes of epilepsy in people over 60 years are different from causes for other ages. Identifying these causes should allow us to establish preventative measures and to diagnose early and reliably. In Mexico studies of elderly patients presenting only with epilepsy do not exist.
Methods: We analysed data from 88 patients with epilepsy, aged between 60 and 90 years, who had their initial crises in 2000, and who presented at one of 10 neurological centres in the republic of Mexico. All the patients were reviewed by a neurologist, and all had an EEG and CT scan.
Results: 46 men (52%) and 42 women were studied (average age 70.6 years, DS +/- 7.32). Crises were tonic-clonic generalised (56%), motor partials (18%), partial secondarily generalised (14%). 8% presented/displayed 2 types of crisis. The majority were treated with monotherapy (83%). The main drug used was diphenylhydantoin (47%), followed of carbamazepine (24%). 26% were cryptogenic. The most frequent causes were ischemic (42%), cortic-subcortic atrophy (14%), cysticercosis (10%) and neoplasias (5%). The neurological explanation was altered in 38%. EEGs were affected in 72%, with patterns generalised (41%).
Conclusion: Significant differences exist between this series and others involving patients of equal or similar age. One of the most significant differences was aetiology by neoplasias, observed in our

series in under 5%, compared with up to 25% by others. Another important difference was that in none of the other series was as high a rate of cysticercosis observed as in ours (10%).

p302
Epilepsy in the Elderly
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Purpose: Epilepsy affects 1-2% of the general population. An increase of epilepsy in the elderly, older than 60 years, has been reported. The objective of the present study was identifying clinical-aetiologic behaviour of epilepsy in the elderly in Consolación del
Methods: The population in Consolación is composed, according to the 2003-census, of 87,419 inhabitants, 14.30% are older than 60 years. A prospective and descriptive study of cases suffering from epilepsy in the elderly was conducted from January 2000 - January 2
Results: 212 epilepsy patients were recorded, representing 1.7% of the total elderly population; age range 61-102 years, average age 75.6 years, prevailing male sex and white race. Epilepsy was more frequent in the 70-80 years age group. Complex partial seizures w
Conclusion: Epilepsy in the elderly represents an increasing health problem. Age and cerebrovascular disorders are the main risk factors of seizures in the elderly.

p303
Twenty Years Evaluation of Mortality in France of Patients with Epilepsy Using Death Certificates
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Purpose: Evaluation of the specific mortality rates in patients with epilepsy during the last twenty years in France.
Methods: The study is based on the analysis of death certificates as filled out by French practitioners from 1979 to 1999 and collected by the National Health Medical Research Institute (INSERM). We analysed the standardised death rates, the age and sex-specific death rates as well as the regional distribution where epilepsy was the underlying, or only contributing cause of the death.
Results: As an underlying cause of death, standardised death rate in patients with epilepsy has increased from 1.5 to 1.9/100,000 with small variations between years. We note an overmortality in the male population (2 to 2.5 vs 1 to 1.4) and in the elderly for both sexes, particularly after 80 years. The mortality rate among children is very low. Moreover, it must be underlined that there are large discrepancies in some regions, especially for Brittany where a threefold, or in the North Region a twofold increase in mortality rates has been reported.
Conclusion: Death rates in France among patients with epilepsy are quite similar to those reported in other advanced countries. Nevertheless, there is an increase in reported rates over the years for males, and elderly populations are more represented. Some regions in France have three or twofold rates. The explanation of overmortality in these areas can be only speculative and a large prospective study is needed to outline the exact causes of death in patients with epilepsy.

p304
Nyctohemeral Distribution and Precipitating Factors of Seizures in 100 Patients with Medial Temporal Lobe Epilepsy
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Purpose: In order to determine the nyctohemeral distribution and precipitating factors of seizures, we analysed all seizures of 100 patients with medial temporal lobe epilepsy (MTLE) referred for presurgical assessment.
Methods: Patients had video-EEG monitoring to determine the epileptogenic zone. Patients were monitored over five days and four nights under the same conditions. They had progressive drug discontinuation, sleep deprivation, activation methods and wake-sleep cycle analysis. For each seizure, we analysed the patients' activity and behaviour 15 minutes before the seizure and in which stage of vigilance he was (wakefulness or sleep determined by EEG).
Results: Two peaks of seizure occurrence were determined: the first around 7 am and the second around 1 and 2 pm. Seizures occurred in wakefulness (determined with EEG) in more than 80% of cases. No peculiar precipitating factor was found.
Conclusion: Seizures in MTLE are particularly related to wakefulness. The first peak of seizures occurs in the awakening period that could indicate that MTLE epilepsy belongs, to some extent, to the 'awakening' epilepsies.

p305
Prevalence of Epilepsy in Thai Bao-Bac Ninh, a Region in Vietnam Affected by Neurocysticercosis
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Purpose: Taenia solium neurocysticercosis (NCC) is a major cause of seizures and epilepsy in developing countries. We conducted a prevalence study of epilepsy in a Vietnamese rural community in which T solium cysticercosis is known to be endemic.
Methods: We used the epilepsy protocol from the Neurological Institute of Limoges to evaluate the prevalence of epilepsy among 6617 residents of Thai Bao community–BAC NINH (40 km from Hanoi capital) in the year 2004. All those found to have epilepsy were subjected to an immunological test for T solium (linked immuno-electrotransfer blot: EITB). All patients with active epilepsy, having at least 2 seizures during 2 years from confirmation-date and 30 other randomised non-epileptic control subjects underwent a cerebral CT scan.
Results: 71 subjects (41 males) suffered from epilepsy (prevalence:10.7/1000 including 7.9/1000 active epilepsies), with partial seizures in 64.8%. 35 of the patients underwent a cerebral CT scan. 14 of the 35 (40%) had CT abnormalities related to NCC compared to 4 of the 30 (13%) control subjects, yielding an odds ratio of 4.3 (1.2-15.1;95% CI). Only 10 (14%) of the 71 epilepsy patients were positive in the EITB assay.
Conclusion: The prevalence of epilepsy was comparatively high, probably due to a high incidence of NCC in this region, and the role of NCC as an important aetiology was confirmed. This needs to be taken into account in public health interventions in order to reduce the role of this infection as an aetiological factor for epilepsy.

p306
Symptomatology of First Seizures in Adults: A Prospective Observational Study
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Purpose: To describe the clinical characteristics of patients presenting with a first provoked or unprovoked seizure.
Methods: In Hong Kong, patients with a first seizure are routinely admitted into hospital for initial investigation. We prospectively screened all patients admitted to the medical and neurology wards in a regional hospital within 48 hours of admission and evaluated those presenting with first seizures.
Results: Between 1 March 2004 and 31 January 2005, 827 patients were admitted for suspected seizure disorders, 84 of whom were due to a first seizure (44% female, mean age 56.5, age range 19-101). EEG was performed on 42.9% of patients within 48h of admission. Brain CT and/or magnetic-resonance imaging was obtained for 95.2%. 47 patients (56%) had provoked or acute symptomatic seizures (ASS). Among those with an unprovoked first seizure, 23 had remote symptomatic seizures (RSS), 9 idiopathic generalised seizures (IGS) and 5 cryptogenic seizures (CS). The first seizure was classified as generalised tonic-clonic seizure in 74.5% of provoked and 59.5% of unprovoked seizures ($p>0.05$). Patients with RSS were older than those with ASS, IGS or CS (mean age 69, 54, 40 and 47 years, respectively; $p=0.003$). Motor deficits on admission were more frequently seen in RSS (73.9%) than in ASS (26.7%), GIS (11%) or CS (0%) ($p=0.002$) The 7-day seizure recurrence rate was 11.9% with no difference detected between the provoked and unprovoked group ($P>0.05$).
Conclusion: Half of all adults presenting with a first ever seizure have an underlying provoking cause that may require urgent hospital admission for immediate intervention. There are few reliable clinical features to distinguish provoked or unprovoked seizures.

p307
The Mortality Risk of Suicide in Epilepsy
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Purpose: To calculate the standardised mortality ratio (SMR) for suicide in people with prevalent epilepsy in the community.
Methods: We reviewed death certificates (DCs) in England & Wales (E&W) over a one-year period (1999-2000) to estimate the number of observed deaths from suicide in epilepsy. All deaths were investigated and certified by a Coroner. The expected number of deaths was calculated by applying the year 2000 death rates for 'suicide and self-inflicted injury' (ICD-9, E950-959) of the population of E&W per age group and sex to the epilepsy population. The latter was estimated by applying the 1998 prevalence rates of treated epilepsy in E&W per age group and sex to the resident general population. An assumption was made that all deaths occurred amongst people with treated epilepsy. The SMR was calculated as the ratio of the observed to the expected number of deaths in the epilepsy population.
Results: Epilepsy was recorded on the DC of 2,042 people, of whom 11 died of suicide. Because only 20% of people with treated epilepsy who die and are certified by a coroner in E&W have epilepsy mentioned in their DC (previously shown by our group), we introduced a correction factor of 5 to calculate the total number of observed deaths as 55. The SMR for suicide in people with epilepsy of 1.8 (95% CI, 1.4-2.3). The risk was higher in women: SMR 2.9 (1.8-4.4) vs. 1.5 (1.0-2.0) in men.
Conclusion: The estimated SMR for suicide reflects a mortality risk that lies between that of an incidence and a hospital epilepsy cohort. The higher SMR in women may reflect their significantly lower mortality rate from suicide in the community.

p308
Depression in Patients with Generalised Epileptic Tonic Clonic Seizures
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Purpose: It is known that chronic illnesses such as epilepsy, are connected with depressive symptoms. The aim of this study was to determine depression level and its correlation with frequency of epileptic seizures in patients with primarily generalised epileptic tonic-clonic seizures.
Methods: We analysed 50 males and 50 females with primarily generalised epileptic tonic-clonic seizures, normal neurological status and regular CT scan. Actual age, epilepsy duration, and frequency of epileptic seizures were determined. The depression level was measured by Hamilton's Depression Scale, and data were analysed by appropriate statistical tests (F test, Pearson Correlation Coefficient).
Results: Actual age of males was 33.6±12.4, and females 31.4±11.7 years ($p>0.05$). Average age at time of first seizure was 21.3±12.4 in males, and 21.1±9.4 years in females ($p>0.05$). Average duration of epilepsy in males was 12.3±11.0, and in females 10.8±9.9 years ($p>0.05$). 17 women or 34% have had less than one seizure per year, while 15 or 30% men have had one seizure per year ($p<0.05$). Medium value of Hamilton's Scale score in males was 9.5±6.8, and in females 11.4±8.3. There was no gender significant difference according to medium value of depression level ($p>0.05$). Frequency of seizures correlated positively with depression level in both sexes, ($r = 0.64$ in females; $r = 0.51$ in males).
Conclusion: Patients with primarily generalised tonic-clonic epilepsy suffered mainly from mild depressive symptoms. Frequency of seizures shows a positive significant correlation with depression level.

p309
Mortality in Newly Diagnosed and Chronic Epilepsy Cohorts
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Purpose: Patients with epilepsy have an increased risk of death compared to the general population. We analysed two cohorts to assess the excess mortality; 890 patients with newly diagnosed epilepsy and 2689 patients with uncontrolled chronic epilepsy.
Methods: Patients diagnosed with epilepsy at the Epilepsy Unit, Western Infirmary, Glasgow, between July 1981 and May 2001 were studied. They were matched against the Death Database at the General Register Office for Scotland in August 2002. Death certificates were obtained for patients whose demographic information matched. Surviving patients were flagged prospectively on the National Health Service Central Register. All deaths reported by October 2003 were analysed.
Results: There were 93 deaths in the newly diagnosed cohort (crude death rate 10.4%) compared to 65.54 expected deaths (rate ratio 1.41; 95% CI 1.15-1.74). Standardised mortality ratios (SMR) were greatest in patients aged less than 40 years with symptomatic epilepsy (SMR 8.64; 95% CI 3.78-13.50, $p<0.0001$). There were 316 deaths in the chronic epilepsy cohort (crude death rate 11.8%), compared to 155 expected deaths (rate ratio 2.04; 95% CI 1.82-2.27). SMRs were highest in patients aged less than 40 years with cryptogenic epilepsy (SMR 6.13; 95% CI 4.43-7.84, $p<0.0001$) and symptomatic epilepsy (SMR 5.14; 95% CI 3.24-7.05, $p<0.0001$).
Conclusion: Patients with newly diagnosed epilepsy had a 40% greater risk of death compared to controls. Mortality was highest in younger patients with symptomatic epilepsy. Chronic epilepsy patients had a mortality twice that expected. This was highest in younger patients and with all epilepsy types except idiopathic generalised epilepsy. This information will be used when counselling patients with epilepsy.

p310
Relative Importance of Various Risk Factors for SUDEP
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Purpose: Several risk factors for SUDEP (sudden unexplained death in epilepsy patients) have been proposed, but results from different studies may be conflicting and the relative importance of various risk factors is never explored. The aim of this study is to determine the relevance of risk factors for SUDEP.
Methods: We performed a literature-search on 'SUDEP' in Medline, the Cochrane Library and EMBASE. Studies with an unknown number of SUDEP cases, case reports and reviews or studies of low quality (scale will be presented) were excluded for further analysis. For each analysed factor a risk factor ratio was determined (flowchart will be presented), with a higher ratio indicating a stronger risk factor.
Results: Strong risk factors for SUDEP were: young age, early onset of seizures, the presence of generalised tonic clonic seizures, male sex, and sleeping. Weaker risk factors were: being in the bedroom, lying in bed, posttraumatic epilepsy, chronic epilepsy, one or more subtherapeutic blood levels of AED and the presence of a structural brain lesion.
Conclusion: A listing of risk factors by relevance may allow us to differentiate populations at higher and populations at lower risk for SUDEP. This may be interesting for decisions which patients should be monitored while admitted in epilepsy centres and identifying groups at high risk. Future research on risk factors is still needed and should be based on a prospective database. Meanwhile, preliminary guidelines based on available literature should be developed to prevent SUDEP.

p311
Status Epilepticus in Adults and Elderly: Aetiology, Clinical Manifestation and Prognosis
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Purpose: In recent years a higher incidence of status epilepticus (SE) in the elderly has been observed. The aim of the study was to compare the type, aetiology and prognosis of SE in patients aged over 60 years and younger adults.
Methods: We analysed 121 consecutive patients with SE admitted to neurological departments between 2000-2004; 43 patients aged 18-59 years (median 49) and 78 aged 60-98 years (median 64). In all patients EEGs and/or video-EEGs and CT/MRI examinations were performed.
Results: Among the patients under 60 yrs, 22 had a positive history of epilepsy; in 21 (48.8%) SE manifested as de novo SE. Convulsive SE was identified in 29 patients and nonconvulsive SE (NCSE) in 14 (32.5%). The most common aetiology was brain tumour (25.6%) and vasogenic lesions (18.6%). On the contrary, in patients over 60 years, de novo SE appeared in as many as 72 (92.3%) patients. NCSE was diagnosed in more than half of the patients (48; 61.5%); vasogenic aetiology was markedly predominant in this group (70.5%). All these differences between the groups were statistically highly significant ($p<0.000$; $p<0.000$; $p<0.005$). 21.8% of elderly patients and 11.6% of younger patients died during hospitalisation; 40% of them were in coma.
Conclusion: In our study a considerably higher proportion of patients aged over 60 years compared to younger adults were admitted to hospital because of SE. De novo SE and NCSE were observed significantly more frequently in patients over 60 years. Protracted coma was a determinant factor of poor prognosis.

p312
Sudden Unexpected Deaths In Epilepsy
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Purpose: Patient groups are increasingly concerned and questioned regarding the risk of death in epilepsy, and particularly that of sudden unexpected death (SUDEP). Many issues are still pending, including the risk factors for SUDEP.
Methods: We analysed all available relevant data on a cohort of 87 patients with epilepsy who died unexpectedly. Among these 87 patients, only 64 were eventually considered to have suffered SUDEP, whereas 7 committed suicide, 5 died from status epilepticus, 1 from a car accident, and 7 from an associated condition. Only data regarding the 64 SUDEP patients are reported.
Results: 53% were male, and there was an overrepresentation of young adults between 21 and 28 years old. Socio-professional status did not appear to influence the risk of SUDEP. The occurrence of a seizure immediately prior to death could be ascertained in only 5 patients (8%), provided that 64% of SUDEP occurred during sleep. 55% of patients suffered from complex partial seizures with secondary generalisation, 52% from drug resistant seizures, and 61% from cryptogenic epilepsy. 28% of patients were thought to be non or poorly compliant with their drug regimen. 58% presented with psychological disturbances, including patients who suffered significant emotional stress immediately prior to death.
Conclusion: Results from this preliminary study emphasise the risk of SUDEP in young adults with nocturnal secondary generalised drug resistant seizures and psychiatric co-morbidity. Further studies are warranted in collaboration with family members of deceased patients.

p313
Predictors of New Onset of Epilepsy within 2 Years following Traumatic Brain Injury: A Population-based Follow-up Study
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Purpose: To determine risk of developing new onset of epilepsy within two years following hospital discharge with traumatic brain injury (TBI) and assess what predicts new onset.
Methods: From 1 January 1999 to 30 June 2001, 7,613 individuals older than age 14 were discharged with a diagnosis of TBI defined with ICD-9-CM codes of 800, 801, 850-854, and 959.01. Using two-stage sampling design, 3,932 (52%) were randomly selected. 54% (2118) participated in Year 1 and 1,531 (39%) in Year 2, providing a cumulative of 3,489 person-years. Sets of questions that asked if patients had been told by their doctors that they had developed epilepsy were used to assess new onset. Post TBI disability and other covariates were assessed by a standardised questionnaire. Risk of epilepsy was determined by incidence density. A multivariable log linear model was used to determine the predictors.
Results: 62 individuals (3.1%) developed epilepsy after TBI—41 within the first year and 21 the second year. The risk was 3.5% within 2 years of follow-up. Compared with the incidence of epilepsy in the US, this cohort experienced a 29-fold increased risk of epilepsy. The strongest determinants of epilepsy were severity of TBI (relative risk [RR] 1.9, 95% confidence interval [CI] 1.02, 3.41); pre-existing alcohol/drug, mood disorders (RR 2.1, 95% CI 1.2, 3.5); age between 25 and 64. Persons who developed epilepsy were highly probable to have significant disability (RR 6.9, 95% CI 2.7, 17.5).
Conclusion: This cohort experienced a higher incidence of epilepsy after TBI. Persons who developed epilepsy have an increased risk of residual disability.

p314
Late-stage Seizures in the Brain Contusion or Subcortical Haemorrhage Patients
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Purpose: Authors investigated some factors of the occurrence of late-stage seizures in brain contusion or subcortical haemorrhage patients who had no seizure episodes in the acute stage.
Methods: We retrospectively analysed data of 12 brain contusion or subcortical haemorrhage patients who have been observed for more than five months.
Results: Patients' details were as follows: mean age 51 years (SD: 16 years), 7 females and 5 males. 6 cases had late seizure (A-group) and the other 6 had no seizures (B-group). There were no statistical significances among age, gender, and late seizure occurrence. In A-group, there was 1 subcortical haematoma case, 2 brain contusion cases, and 3 arteriovenous malformation cases. In B-group, there was 1 subcortical haematoma, and 5 brain contusion. The number of surgical treatments including 1 stereotactic radiosurgery patient was 5 in A-group only. The number of prophylactic anticonvulsant treatments was also 5 in A-group only. The results that were statistically significant were (1) the period from the date of the contusion or haemorrhage to the first late seizure event, or the date of the last visit to the outpatient clinic and being seizure free between the surgical treatment (mean: 445 days [SD: 82 days]) or not (mean: 240 days [SD: 17 days]) (p=0.016), and (2) the maximal diameter of the lesion (mean: 3.8cm [SD: 1.3cm], 2.1cm [SD: 0.7cm], respectively) (p=0.019).
Conclusion: The prophylactic anticonvulsant treatment had no effectiveness. In the surgical treatment group, the authors recommend a follow-up period of about 20 months in order to detect late seizures.

p315
Auto-immune Antibodies to Voltage Gated Ion Channels in Epilepsy
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Purpose: Although the CNS is protected from circulating antibodies by the blood brain barrier, pathogenic serum auto-antibodies in CNS diseases, such as Rasmussen encephalitis, have been described in rare instances. Growing evidence indicates that antibodies to potassium channels (VGPC) are involved in limbic syndromes which are often associated with seizures, and that these patients respond to immunotherapies. This raises the possibility that autoantibodies to these and other channels or neuronal antigens may be present in epilepsy.
Methods: We retrospectively screened blood serum of female epilepsy patients (n=106) with late-onset epilepsy for auto-antibodies to voltage-gated calcium channels (VGCC), VGPC and glutamic acid decarboxylase (GAD). Demographics, medical history, and epilepsy related information was gathered.
Results: GAD antibodies were found in 4 patients, VGPC antibodies in 5 and VGCC antibodies in 1 patient. Age at first seizure and duration of epilepsy was not related to the presence of antibodies. 3 patients suffered from symptomatic epilepsy. 7 patients suffered from generalised tonic clonic, tonic, or atonic seizures. There was no correlation between the use of anti-epileptic drugs and the presence of antibodies. 4 patients had an atopic constitution and 1 had a co-morbid autoimmune disease. The patient profile of the patients with VGPC antibodies differs from previously described patients with limbic encephalitis-like syndrome.
Conclusion: The results of this study support the idea that auto-immune antibodies to VGPC and to GAD could play a distinct role in epilepsy, but it is possible that they arise secondarily to the primary pathology.

p316
Gender Differences in the Development of Hippocampal Atrophy in Epilepsy.
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Purpose: Recently it has been suggested that men may be more vulnerable to the damaging effect of seizures than women. We wished to examine whether hippocampal atrophy develops faster in male than in female epilepsy patients.
Methods: 180 persons aged 15-50 years (mean age women (n=107) 31.6 ± 9.8 years, men (n=73) 31.5 ± 10.8 years) with a diagnosis of epilepsy had MR scans of the brain including volumetry of the hippocampus. Clinical information was obtained from the Epibase database at the outpatient clinic, Aarhus University Hospital, Denmark, where our epilepsy patients have been systematically registered since 1999. Linear regression analysis was used to examine the relation between hippocampal volume and the duration of epilepsy in men and women.
Results: Mean duration of epilepsy was 14.0 ± 11.7 years in men and 14.4 ± 12.6 years in women. The left and right hippocampal volumes correlated with the duration of epilepsy in men ($p=0.001$ and $p<0.001$) and women ($p=0.02$ and $p=0.05$). The linear reduction in left hippocampal volume as a function of epilepsy duration was larger in men than in women (-0.04 and -0.01 cm3/year, $p<0.05$). The linear reduction in right hippocampal volume also tended to be larger in men than in women (-0.02 and -0.01 cm3/year), but this difference was not statistically significant. Seizure freedom was equally frequent in men and women (26.0% and 34.6%, NS).
Conclusion: Our male epilepsy patients developed left hippocampal atrophy faster than women. This suggests that the male hippocampus is more vulnerable to the damaging effect of seizures.

p317
Is Multidrug-Resistance (MDR)-1 Gene Polymorphism the Genetic Susceptibility to Cryptogenic Partial Epilepsy?
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Purpose: Multidrug-resistance (MDR)-1 gene encoding an integral membrane protein, P-glycoprotein (PGP), is known to export substances from the inside of cells. A few studies have showed that over-expressed PGPs have been found in the epileptogenic lesions. To know whether MDR-1 gene polymorphism is the genetic susceptibility to cryptogenic partial epilepsy (CPE), we performed this study.
Methods: Genomic DNA was extracted from peripheral blood leukocyte of 171 consecutive epilepsy patients and 166 normal controls. A single base pair polymorphisms at position 3435 in the exon 26 (C3435T) and 2677 in the exon 21 (G2677T) of the MDR-1 gene were analysed by the polymerase chain reaction-restriction fragment length polymorphism. To keep the study group homogeneity, we included CPE only.
Results: 37% (64/171) had CPE. There were significantly less presentations of C3435T and G2677T heterozygotes in CPE compared to normal controls [47% (30/64) in CPE vs 64% (107/166) in controls, OR=0.4 (95% CI 0.2-0.7, p=0.02) for C3435T, and 33% (21/64) in CPE vs 48% (80/166) in controls, OR=0.5 (95% CI 0.28-0.99, p=0.04) for G2677T]. Also, the frequency of linkage of MDR-1 haplotype (2677T, 3435T/2677T, 3435T) was significantly higher in CPE than

in controls [11% (7/64) in CPE vs 4% (6/166) in controls, OR=3.3 (95% CI 1.05-10.15, p =0.03)].
Conclusion: Not only heterozygotes of MDR-1 gene polymorphism (C3435T or G2677T) but also linkage of MDR-1 haplotype (2677T, 3435T/2677T, 3435T) may be have a genetic susceptibility to CPE.

p318
Partners in Epilepsy (PIE): International Epilepsy Management Package and Electronic Records Registry System: Data Analysis in Adults
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Purpose: To analyse epilepsy characteristics, outcome and antiepileptic drug (AED) use in a large international adult patient cohort.
Methods: Electronic record management in daily clinical practice (demographics, aetiology, syndrome and treatment) in epilepsy centres in Belgium, France, Portugal, Spain, Switzerland, United Kingdom: 4312 patients (47%F) were analysed.
Results: Mean age at first attack (range) was 24.5 (0-102) years. Follow-up lasted on average 678 days (1 day-52.6 years). Among 1883 records of aetiology, trauma (13%), benign cerebral tumour (6%) and cortical malformations/developmental disorders (5%) were most commonly identified. Epilepsy was classified in only 39% of patients: 23.5% localisation-related, 7.4% generalised and 8.1% undetermined. 52.6% were seizure-free at the last follow-up visit after at least 6 months. Among those still experiencing seizures, 31.8% had predominantly focal seizures, 20.4% generalised seizures. Monthly seizure rate averaged 10 (0-600) for partial seizures, 13 (0–900) for generalised seizures. AEDs were prescribed in 84% of patients (most common: valproate (37.7%), carbamazepine (34%), lamotrigine (23.4%), topiramate (14%), phenytoin (12.2%), levetiracetam (11.5%)). 73% were on monotherapy, 18.4% on two, and 8.4% on three or more AEDs. The most common AED combinations were carbamazepine/valproate, lamotrigine/valproate, carbamazepine/lamotrigine and carbamazepine/topiramate (6.5%-3.2%). The most common side effects were somnolence and drowsiness (7.6%), weight gain (3.1%), tremor (3%) and impaired concentration (2.6%).
Conclusion: Registry analysis provided valuable information on epilepsy characteristics, outcome and AEDs. Epilepsy was classified in 39% of adult patients only (predominantly localisation-related). About half were seizure-free. The majority was on monotherapy. (PIE is supported by Janssen-Cilag.)

p319
Imprisonment and Epilepsy
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Purpose: The aim of this study is to determine the characteristic of epilepsy in imprisoned patients, the relationships between misdemeanour and epilepsy and the course of epilepsy in imprisoned patients.
Methods: We present a study including 62 epilepsy patients collected from Tunisian prisons. All patients have had a neurological examination.
Results: The mean age of patients was about 31.7 years with a sex ratio of 30. The mean age of onset was 17.5 years. Idiopathic epilepsy was noted in 30.7% of cases and symptomatic in 69% of cases. Status epilepticus was observed in 32.2% of cases. The more frequent cause of epilepsy was cranial trauma. Drug addiction was observed in 30.6% of cases, 42% of whom have had a foreign stay. The more frequent cause of imprisonment was violence. The interval between seizure and misdemeanour was from one day to weeks. There were no seizures during unlawful acts. Seizure frequency was decreased in 25.6%, stable in 43.5 % and increased in 30.7% of cases. There was no correlation between the nature of seizure and the nature of misdemeanour.
Conclusion: Epilepsy associated to cranial trauma and drug addiction is frequent in imprisoned patients. There was no misdemeanour due to epilepsy. Imprisonment had no effect on the course of epilepsy.

p320
Status of Free Radicals and Oxidative Stress in Platelets in Cases of Epilepsy and Epilepsy with Psychiatric Comorbidity
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Purpose: To assess the free radical status and oxidative stress in cases of epilepsy, and epilepsy with psychiatric co-morbidity, by measuring the levels of Malonal-aldehyde (MDA) and super-oxide dismutase (SOD) in platelets of cases and controls.
Methods: A sample of 157 patients was assessed in detail for epilepsy, depression and psychosis by DSM-IV criteria. MDA and SOD levels were estimated in platelets of cases and controls by spectrophotometry. Clinically, cases were subgrouped into 6 groups viz. Group-I (n=30) Epilepsy, Group-II (n=27) Epilepsy with Depression, Group-III (n=25) Epilepsy with Psychosis, Group-IV (n=25) Depression, Group-V (n=25), Psychosis, Group-VI(n=25) Control.
Results: MDA levels in patients with epilepsy (group I) was 2.49±0.347, significantly higher ($p< 0.01$) in comparison to the control group (1.54±0.438). MDA levels in cases of epilepsy with depression and epilepsy with psychosis and in cases of simple depression and psychosis were respectively 3.12±0.42, 3.09±0.486, 2.31±0.35, 2.18± 0.28 and significantly higher ($p<0.01$) than control group. Values of SOD in Group I, Group II, Group III, Group IV, Group V and Group VI were respectively 3.42±0.304, 3.12±0.257, 3.36±0.437, 3.78±0.238, 3.87±0.38, 4.39± .236 and all groups showed significantly lower values ($p<0.01$) in comparison to the control group.
Conclusion: Oxidative stress is found to increase in the cases groups in comparison to the control group, as shown by increased MDA levels and decreased SOD levels in cases groups. Associated depression and psychosis with epilepsy associated with more oxidative stress in comparison with epilepsy alone.

p321
Auditing Epilepsy in General Practice: A Collaborative Approach
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Purpose: Collaboration between primary and secondary care to audit the epilepsy patients of a General Practice. Patients were invited to attend a consultation with their GP and an Epilepsy Specialist nurse, to review their epilepsy. Aims: to discover the care and management currently received by epilepsy patients, encourage patients to express their needs and concerns, recognition of patients who require referral to a neurologist, provision of information and advice as appropriate.
Methods: 64 epilepsy patients ≥16yrs old were initially identified. 28 female and 17 male, with an age range of 19-77yrs (mean age 41.6yrs). Issues covered using a patient review checklist included: details of diagnosis and seizure classification, seizure frequency, investigations performed, last neurological review, medication regimes and duration of treatment, side effects of treatment, women's issues, driving, employment and general information and advice previously received.
Results: 51% of patients had seizures in the past year. The majority of diagnoses (69%) were made within a year of the first seizure.

Unemployment was high (27%). 73% of patients had been on anti-epileptic drugs for longer than 5 years. 90% (9) post-menopausal women had been on enzyme-inducing drugs for over 10 years; potentially increased risk of osteoporosis. 93% of patients were on medications first produced >15yrs ago, some were on more than one. 15.5% of patients were on the newer generation of medications. Investigations were often not recorded or easily accessible in GP records.
Conclusion: Patients concerns were identified. Advice and information was offered. 11 (24%) patients were referred for neurological review. This audit was sponsored by UCB.

p322
Senile Myoclonic Epilepsy in Middle-aged Down Syndrome Patients: A video Presentation
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Purpose: The authors present 5 observations of late-onset myoclonic epilepsy in Down syndrome (LOMEDS), with 3 patients examined by video-EEG.
Methods: All patients were recorded by means of a 10-20 International System Video EEG with polygraphy.
Results: In all cases they showed a typical EEG, with massive myoclonus linked to short generalised spike and wave discharges
Conclusion: In the late clinical stages of the 21st chromosome trisomy a significant massive or parcellar myoclonus and tonic-clonic seizure appears after the installation of a progressive cognitive deterioration of Alzheimer-type. The evolution is progressive, together with cognitive decline. Nevertheless, the therapy is satisfactory (valproate, piracetam, levetiracetam, benzodiazepines). This type of epilepsy is not yet completely understood; it derives probably from a lack of inhibitory mechanisms, as the other forms of epilepsy in Down Syndrome (DS), especially those present in early childhood (infantile spasms, reflex epileptic seizures). Late-onset myoclonic epilepsy can be considered a very specific kind of epilepsy in the late stages of DS, but it also occurs late in the evolution of Alzheimer disease.

p323
How to Improve the Prevention and Treatment of Epilepsy in Latin America
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1) I.L.A.E. Commission on Latin American Affairs

Purpose: The aims of this presentation are to describe the crucial factors determining the gap in epilepsy treatment between Latin American and more developed countries, as well as to promote solutions and practical actions through a series of proposals.
Methods: A review of the literature, mainly on epidemiological aspects, was performed. Reports of ILAE chapters, particularly those defining the profile of epilepsy in Latin America were also taken into account. Additionally, the experience of, and discussion within the Commission on Latin American Affairs, was integrated.
Results: The 'scenario' is not the same in every Latin American country. Thus, specific measures must be considered for each case. In those countries where cysticercosis or other preventable causes of epilepsy are highly prevalent, several simple, cost-effective measures should be introduced on a national and a regional scale. On the other hand, in those areas with relatively advanced medical training and technological access, further local development and interrelation with neighbouring centres should be encouraged. For all settings, education, both for medical personnel and the general population, seems to be relevant. In this sense, structured, regionally-tailored educational programmes, are to be coordinated.
Conclusion: A series of practical measures can significantly improve the prevention and treatment of epilepsy in Latin America, provided there is a collective action to solve the identified problems. This Commission has several proposals and wishes to encourage potentially involved medical individuals and institutions to put those proposals into practice through well-defined concerted activities in order to modify the situation in this region of the world.

p324
Long Term Follow-up in Juvenile Myoclonic Epilepsy Patients
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Purpose: The outcome of juvenile myoclonic epilepsy in adults is not well known. The purpose of this study is to report long term follow-up of patients with juvenile myoclonic epilepsy.
Methods: 106 adult patients for whom clinical electroencephalography recording (EEG and/or video EEG) and imaging findings were consistent with the diagnosis of JME were included in the study, with a follow-up of 10 to 20 years in the University Hospital.
Results: The onset of the condition in the majority was in childhood and adolescence. The long term follow-up of our patients reveals good control of generalised attacks (grand mal) in most patients (more than 90%) with low antiepileptic doses a few years after onset in the majority. In about 30% of cases treatment was successfully discontinued. A small percentage needed a high dose of antiepileptic treatment. More details will be reported in the meeting.
Conclusion: Our long term follow-up in juvenile myoclonic epilepsy patients revealed successful discontinuation of treatment in more than 30% of cases after less than 20 years of treatment, and the majority of patients were well controlled with small doses of antiepileptic treatment.

p325
Seizure Occurrences on a Video-EEG Unit
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Purpose: It is generally agreed that one needs to record 4-5 technically correct and clinically 'typical' seizures in order to make a pre-surgical decision. How to best illicit these is not known. Hospital stays are costly and inconvenient for the patients. We opened a new Epilepsy Center 1.5 years ago. We have analysed our data on the presurgical video-EEG subjects for this presentation.
Methods: Over 100 subjects have been recorded. We eliminated those admitted merely for diagnosis (some NES, some PGE, etc.) and reviewed the time of the first seizure occurrence in the remaining 61 subjects. Our drug withdrawal policy is as follows: If patients are on 1 AED only and have a high seizure frequency (>2 per week), no withdrawal occurs. If they are on one drug with a low seizure frequency, it is discontinued on the day of admission (short half life drugs) or 48 hours prior (long half life drugs). If subject is on two AED's, the longest half-life drug is stopped 48 hours prior to admission and the remaining one follows the rules for 1 drug. On >2 drugs, the longest half-life drug is stopped 48 hours prior to admission, the second is stopped and the third is cut in half on the day of admission. Although sleep deprivation has not been shown to reliably induce seizures we sleep deprive the subjects (3 hours of sleep) every other night beginning with the first night. Daily stimulants include exercycle and increased caffeine consumption. If the subjects have not had an adequate number of seizures by the 4th day of recording we encourage alcohol in the evening, and give 10 mg amitryptaline, hs. We have plotted the number of seizures per shift (8 hours), the number of subjects remaining, the time to occurrence of the first seizure, and the cumulative seizure count. We excluded subjects who had had 6 or more seizures in one 8 hr shift (status or pre-status).
Results: By day 5, 59% of the subjects had completed their stays (range 1-10 days). The average stay was 4.9 days. The seizures began the second shift of the first admittance day and peaked by the second

day, remaining elevated until the second shift of the 4th day when they steadily declined. No more 'first seizures' occurred by the 6th day of admission. There was no abrupt peak on day 5 following the extra perturbations on the evening of day 4.
Conclusion: For presurgical evaluation an average stay of 5 days on a Video-EEG unit was found, with little benefit gained by continuing up to 10 days. Between now and Sept 2005, we will discontinue sleep deprivation and look at the difference in curves with and without it. We will examine the outliers (subjects requiring >5 days to complete) to determine factors that might have helped to shorten their stays.

p326
Breast Cancer Resistant Protein (BCRP) in Cortical Dysplasia with Refractory Epilepsy and Failure to Produce Pharmacological Coma
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Purpose: Malformations of cerebral cortical development have been described associated with refractory epilepsy (RE). Several multidrug resistance proteins (P-gp; MRP-1 and MVP) have been related with RE phenotype. The breast cancer resistance protein (BCRP) has been poorly investigated in RE. We describe an infant with severe cortical dysplasia with RE and BCRP high expression, not only in the vascular endothelial cells, but also in abnormal neurons at the malformation level.
Methods: An 18 month old boy with cortical dysplasia demonstrated by MRI and RE since 5 months of age, with persistent low plasmatic levels of several AEDs, developed status epilepticus. Treatment with nimodipine (2 mg/kg/d) and six consecutive high doses of phenobarbital (PhB) (total doses: 80 mg/kg), failed to produce a pharmacologic coma. However, seizures were partially controlled. The plasmatic levels of AEDs increased and PhB reached 120 ug/ml (toxic range). The patient remained awake without toxic symptoms, but finally died after a pulmonary infection. Brain anatomopathologic examination showed a severe right frontoparietal malformation with pachygyria, non-laminar polymicrogiria and focal cortical dysplasia with 'balloon' cells (Taylor's type). Using monoclonal antibodies, the brain expression of P-gp, MVP and BCRP were investigated by immunohistochemistry techniques. MRP-1 was not studied.
Results: BCRP was positive in both vascular endothelial cells and several abnormal neurons. P-gp and MVP were not detected.
Conclusion: We don't know if AEDs are substrates of BCRP, but our results suggest that RE phenotype and acute drug tolerance can share similar mechanisms where BCRP could play a role not yet described.

p327
Temporal Lobe Epilepsy (TLE): Analysis of 50 Patients from a Private Neurological Clinic
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Purpose: To analyse the clinical outcome of patients with temporal lobe epilepsy from a private neurological clinic.
Methods: A total of 50 patients with temporal lobe epilepsy were analysed.
Results: 50 patients, 31 females, 19 males. The mean age of patients was 24.2 years (range: 7 to 57 years), the mean duration of epilepsy was 13.9 years (range: 6 months to 52 years). 9 patients had a history of febrile convulsions. 26 patients had refractory epilepsy and 24 had well-controlled seizures. The aetiology was indeterminate in 21 patients, 17 had mesial temporal sclerosis, and 2 had dual pathology. 11 patients underwent surgery (5 temporal anterior lobectomy, and 6 surgery for brain tumour and cavernous angioma). 4 patients were in pre-surgical evaluation. All patients were using carbamazepine and we did not identify adverse medication side effects.
Conclusion: For many patients who do not respond to initial trials of antiepileptic medications, epilepsy surgery is a treatment alternative that offers the possibility of complete control of seizures and improved quality of life. Adequate education of patients and physicians regarding relative risks of recurrent seizures compared to surgery, screening for adverse medication effects should offer substantial improvement in the overall health of persons with epilepsy.

p328
Epilepsy in the Elderly: Aetiology and the Challenge of Therapy
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Purpose: To give an overview of the epidemiological data and pharmacological management of epilepsy in elderly patients.
Methods: We retrospectively analysed data of 1449 patients with epilepsy admitted at Department of Neurology «Sestre milosrdnice» University Hospital from January 2003 until December 2004.
Results: 312 patients were older than 65 (21.5%). 281 patients (19.4%), 164 males (52.6%) and 117 females (37.5%) had a newly diagnosed epilepsy. Aetiology of the seizures included cerebrovascular diseases in 152 (54.1%), trauma in 24 (8.5%), primary tumours in 14 (4.98%), metastases in 13 (4.6%), alcoholism in 38 (13.5%) and meningoencephalitis in 4 patients (1.4%). The initial antiepileptic drug (AED) was methylphenobarbital in 86 (30.6%), carbamazepine in 97 (34.5%), carbamazepine plus methylphenobarbital in 9 (3.2%), valproic acid in 8 (2.8%), diazepam in 11 (3.9%) and oxazepam in 7 patients (2.5%). Lamotrigine was introduced in 9 patients as a monotherapy (3.2%) and in 9 patients (3.2%) as an add-on therapy. Topiramate was introduced in 7 (2.5%) patients as a monotherapy and in 4 patients (1.4%) as an add-on therapy. Gabapentin was introduced in 4 patients (1.4%) as a monotherapy and in 2 patients (0.7%) as an add-on therapy. In 29 patients no AED has been introduced.
Conclusion: Cerebrovascular disease is the most common cause of new-onset seizures in the elderly. Methyl Phenobarbital and valproic acid are the first choice agents for generalised tonic-clonic seizures, with carbamazepine preferred for partial seizures. The newer AEDs, such as gabapentin and lamotrigine also warrant some consideration as first-line agents because of their efficacy and favourable effect profile.

p329
A Trans-Mediterranean Internet Transfer of EEG Video Files: Help for the Care of Patients with Refractory Epilepsy
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Purpose: We tested the ability to transfer EEG video files between the University Hospital of Rouen in France and the University Hospital of Tunis. It may be useful to exchange by network the clinical, MRI, neuropsychological and EEG video data of patients with refractory epilepsy to discuss classification, medical or eventually surgical treatment.
Methods: The 2 hospitals have the same EEG video recording systems connected by high speed internet to a server in Rouen Hospital. The data have been secured for medical transfer files. The main difficulty is to send EEG video files. The size of these files, which usually include video seizure recording, wake and sleep EEG recording samples, is about 400 MO. The server is connected to a dedicated network for research, administration and hospital use (RENATER in France, GEANT in Europe and EUMEDCONNECT between Europe and other Mediterranean countries).
Results: A file of 400 MO takes nearly 1 hour (just below the 'time out' of the Tunisian internet agency) to send via the international network from the hospital in Tunis. Both hospitals have the same

software with which to analyse the data. So, it is very easy to discuss cases of patient's with refractory epilepsy.
Conclusion: It is possible to exchange EEG video files between very distant sites via high speed internet. It may be useful to be connected to dedicated networks. We plan to initiate epilepsy surgery (without deep electrodes) in Tunis after discussion, via a medical network, on the seizure recording of each patient.

p330
When French Epilepsy Patients Speak English!
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Purpose: In complex partial seizures (CPS), speech automatisms are common but rarely in a second language. Have they a value for seizure localisation ?
Methods: We selected 4 patients with intractable epilepsy in presurgical evaluation in the Epilepsy Unit at the Hospital of La Pitié-Salpêtrière, Paris, from 1997 to 2005, because of their English speech production during or after their seizures. They are right-handed and speak French as a mother tongue and English as a second language (learned at secondary school). All patients had video-EEG with scalp electrodes and one with intracranial electrodes.
Results: 2 men (34 and 45 years) had English speech automatisms during their CPS. The EEG localisation was on the right hemisphere. Imaging evaluation (MRI, PET-scan, ictal SPECT) showed that the right temporal lobe (hippocampus and lateral cortex) was involved. 2 women (37 and 54 years) answered in English after a CPS even if the question was in French. They have left-sided epileptogenic zone. The MRI was normal for 1 patient and showed a left mesio-temporal sclerosis for the other one.
Conclusion: Speech automatisms in a second language, occurring during a seizure, involve the non-dominant temporal lobe, like speech automatisms in the mother tongue. When they occur postictally, they involve the dominant hemisphere, like aphasia in the mother tongue. In the latter case, they may result from the compensatory implication of the non-dominant hemisphere. These results are in agreement with previous functional imaging studies showing differences between the first and the second language brain representation.

p331
Progressive Myoclonic Epilepsy: Experience in a Tertiary Care Centre in India
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Purpose: To delineate the features which distinguish progressive myoclonic epilepsies from cases of non-progressive benign epilepsies.
Methods: Approximately 5-10% of epilepsies in young individuals are myoclonic in nature. There are some clinical and electrophysiological clues that help in prognosis from the onset of the syndrome; the EEG being an important guideline. Among the causes of progressive myoclonic epilepsies we have encountered cases of neuronal ceroid lipofuscinoses, hereditary dentatorubral-pallidoluysian atrophy, myoclonic epilepsy with ragged red fibres (MERRF) and Lafora body disease. A case of Lafora body disease is presented in detail as a representative case.
Results: Out of 1000 consecutive cases of epilepsy, 70 cases were myoclonic. There were 5 cases of neuronal ceroid lipofuscinoses, 2 cases of hereditary dentato rubropallidoluysian atrophy, 2 cases of myoclonic epilepsy with ragged red fibres (MERRF) and a case of Lafora body disease. A 16 year old boy, born of consanguineous parentage presented with recurrent myoclonic seizures with generalisation since 2 years of age. His birth and developmental milestones were normal and he remained asymptomatic until age 14. There was no family history of seizures. The boy was moderately built and nourished. There were no neurocutaneous markers. He had visual hallucinations and mental regression. Multifocal asymmetric myoclonii with bilateral appendicular and axial ataxia was evident on examination. There were no other neurological deficits and eyes were normal. EEG showed repeated polyspike discharges with a slow background. A cerebrospinal fluid study including antimeasles antibody was normal. Axillary skin biopsy stained with PAS revealed lafora bodies. Seizures were controlled with valproate and clonazepam.
Conclusion: A clinician should be careful when giving a prognosis on a young individual presenting with myoclonic epilepsy.

p332
Pure Sleep Epilepsy with Tonic clonic Seizures
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P Purpose: Pure sleep epilepsy is characterised by the occurrence of seizures exclusively during sleep. Simple, complex partial seizures with or without secondary generalisation, or generalised tonic clonic seizures are the prominent seizures.
Methods: In a prospective study we present the clinical EEG and neuroimaging characteristics, as well the prognostic factors of patients with pure sleep epilepsy with tonic clonic seizures and without obvious focal onset. The age of onset of seizures varies between 12 and 30 years.
Results: 34 patients (14 male and 20 female) have been prospectively examined for more than 5 years. The frequency of seizures varied from 1 every month to 1 every year. The EEG showed variable abnormalities and the MRI was normal for all patients. All patients had good response to carbamazepine or oxcarbazepine. However, withdraw of treatment in 15 patients free of seizures for 3 to 5 years and normal EEG and MRI examination provoked recurrence of seizures.
Conclusion: Pure sleep epilepsy with tonic clonic seizures, without neuroimaging findings, has a good prognosis. However, it is probably a life long epilepsy. The nature of this epileptic syndrome as idiopathic or partial cryptogenic have to be elucidated and the role of sleep microstructure has to be defined.

p333
Neuro-rehabilitation of Patients with Gray Matter Ectopy
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Purpose: Ectopy of the brain grey matter is a malformation of cortical development usually associated with epilepsy and delayed developmental milestones. Disorders of cortical development may occur in isolated patients, as cases have been reported, or as part of familial disorder.
Methods: We studied a randomly chosen group of 5 patients with refractory epilepsy whose substrate was diagnosed by MRI as grey matter ectopy. Among other diagnostic procedures we used EEG, EMIT, psychological evaluation, and in some cases peri-metry and all-night recording.
Results: 4 of our patients had epilepsy and the fifth is suffering from pulsating headaches, but irritative changes recorded with all-night polygraphy are opening the possibility of convulsive events during the night. All of our patients (5), had a neuropsychological disorder.
Conclusion: Although there is a possibility of treating those patients surgically after an extensive pre-operative work-up, we treated them conservatively. Neither operative nor preoperative procedures were available in Croatia. The effect of our treatment was: a) reduction or elimination of seizures; b) psychological support and counselling of patients and their families; c) patients were allowed to use alternative therapies (acupuncture, music therapy, aromatherapy, homeopathy.)

p334
Triphasic Wave Activity in Drug-related Encephalopathies Mimicking other Neurological Disorders
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Purpose: Toxic and metabolic encephalopathies are typically characterised by the presence of a triphasic wave activity (TWA) on the electroencephalogram (EEG). TWA can occur in a sporadic but sometimes also in a periodic, pseudoperiodic or rhythmic manner. In the latter cases, EEG might suggest other neurological disorders.
Methods: We analysed all EEGs recorded in our unit in the past two years in patients who were suspected of having a drug-related encephalopathy. EEGs that are characterised by periodic, pseudoperiodic or rhythmic activity of triphasic waves that disappeared after the discontinuation of the incriminated drug, were collected and compared to the initial diagnostic hypothesis.
Results: During the past two years we found eight cases of cefepime-related encephalopathy and one case of a combined intoxication of mirtazapine and olanzapine, all of which mimicked a non-convulsive status epilepticus. One case of carbamazepine toxicity was suggestive of Creutzfeldt-Jakob disease and one case of lithium intoxication resembled frontal epileptic activity.
Conclusion: Drug related encephalopathies are quite common and are usually characterised by typical electroencephalographic findings. In rare cases, however, the EEG alone might be misleading if historical and clinical data are not examined. Drug intoxication should always be considered in the presence of rhythmic or periodic TWA on EEG.

p335
The EEG Abnormailties in Cerebral Venous Thrombosis. The Electro-clinical and Electro-Imaging Correlation
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Purpose: To assess the correlation between clinical, electrophysiological (EEG) and imaging findings (CT, MRI) in 42 subjects with cerebral venous thrombosis. Methods: Scalp EEGs were evaluated by two independent observers. The EEG abnormalities were divided into focal/diffused, non-specific/specific and were compared with clinical and imaging findings.
Methods: Scalp EEGs were evaluated by two independent observers. The EEG abnormalities were divided into focal/diffused, non-specific/specific and were compared with clinical and imaging findings.
Results: Twenty-four patients (57.1%) had neurological deficit, 18 (41.3%) suffered from acute symptomatic seizures, in 6 (14.3%) the seizure was the inaugural sign, 4 (9.5%) developed consecutive epilepsy (n=42). Three of all patients with CT or MRI negative had seizures. CT or MRI showed brain lesion in 26 subjects (61.9%), with a predominance of haemorrhage. In the 15 patients with abnormal imaging who had seizures (57.7%), 13 had haemorrhage (86.7%). All the performed EEGs were abnormal (n=32 patients). Specific EEG findings in acute phase were observed in 7 subjects, one of whom had only subclinical seizures. Focal deficit was found in 20 patients (62.5%). In 10 patients (31.3%) CT and/or MRI were normal. In strictly unilateral thrombosis (n=15) the EEG abnormalities were found ipsilateral in 40%, contralateral in 13.3% and diffused in 26.7%. In deep vein and/or sagittal sinus and/or bilateral sinus thrombosis (n=17), the EEG abnormalities were bilateral in 64.7% and unilateral in 35.3%.
Conclusion: EEG is a useful method in clinical diagnosis or evaluation of cerebral venous thrombosis. First, haemorrhagic lesions are highly epileptogenic and the diagnosis of subclinical seizures can be established. Second, in patients with normal neurological examination and/or imaging, focal abnormalities on EEG should conduct to further investigations.

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Small Spikes in EEG Only Recorded After Seizure: Possible Consequence of Oxidative Stress
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Purpose: To demonstrate the important value of small spikes (SS) during long term simultaneous video and EEG (EV) among some patients with epilepsy.
Methods: More than 320 patients have been submitted to EV in the last 3 years. The duration of EV was up to 4 days. If taking antiepileptic drugs, patients were ordered to halve their therapy during the investigation. One third of patients in the sample had only epilepsy.
Results: A total of 3 patients with small spikes (SS) in EEG were found. The first patient was subjected to EV 3 times to EV after each of his three seizures. SS were recorded 1 to 11 days after a seizure and especially over posterior regions during the first minutes after the onset of sleep. The second patient recorded clearly visible spikes in the right temporal during non-REM sleep especially during S3. SS in the third patient have been recorded on the first night after his secondary generalised tonic clonic seizures.
Conclusion: SS are usually overlooked and missed if the EEG has not been analysed very carefully. SS in our group were discovered a day or two after a seizure, had little or no localised value, had been seen during sleep recording only, and visible during the period of one day to several weeks after generalised convulsive epileptic seizures. The occurrence of SS might be the late consequence of oxidative stress. Our data justify the EV and biochemical investigation of oxidative stress factors after hypermotor epileptic events.

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Real Time Computer Detection of Epileptic Events during 24 Hours EEG-Video Monitoring
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Purpose: Continuous EEG-Video monitoring is very useful for diagnosis, both of epileptic seizures (type of seizure, topography, focal or or multifocal onset) and of non-epileptic paroxysmal manifestations. The interest in the method leads to a huge increase in the demand. The analysis requires continuous EEG monitoring over several days and requires the attention of a neurophysiologist for a very long time. This time can be reduced by the use of computer analysis software, thus allowing the neurophysiologist to focus his interest on the actual events. Nevertheless, the rate of error of the various types of software remain significant (false positive or false negative, specifically for single and/or short seizures and spikes). The authors are presenting the result of evaluative use of the SMART software by Micromed in detecting on-line events within EEG-video monitoring non stop over several days.
Methods: EEG recordings were taken for10 patients, according to the standard protocol with 23 electrodes disposed according to the international 10-20 system and were analysed in real time by SMART software that uses neuronal networks with artificial intelligence. The data supplied by this real time analysis used a very precise methodology, taking into account direct and non direct criteria well known as leading to event detection.
Results: The study proves that SMART software is efficient for the detection of most critical events. It nevertheless appears to be less useful for accurately defining the type of epileptic events and detecting short events.
Conclusion: SMART software is an efficient computer aided tool for EEG monitoring and may save up to 90% of the time of interpretation of EEG-video long records.

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Nonconvulsive Status Epilepticus: Clinic and EEG Features, Risk Factors and Therapeutical Outcome
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Purpose: To present clinical and EEG features, risk factors and therapeutic outcomes in our patients with nonconvulsive status epilepticus (NCSE).
Methods: We analysed the data of 14 patients (6 male, 8 female, mean age 67 years) admitted at two Neurology Departments in Prague with NCSE diagnosis.
Results: The patients were hospitalised because of an acute or waxing and waning pleomorphic clinical symptoms: namely confusional state associated with bizarre behaviour, agitation, staring, mutism or subtle myoclonus. Because of present psychiatric symptoms, the correct diagnosis of NCSE was initially unrecognised and therefore delayed in 9 patients. In these patients EEG was not initially recorded. In all of these patients EEG and therapeutical trial with antiepileptic drugs allowed the best diagnostic measures. All EEGs were recorded during present confusional state. EEG abnormalities were pleomorphic: epileptiform and slow, generalised and localised. Shortly after initialisation of parenteral antiepileptic drug treatment, both the clinical state and EEG showed marked improvement in all patients. Potential risk factors were: age over 60, epilepsy in medical history, stroke, diffuse encephalopathy, hypertension, neuroleptic medication.
Conclusion: NCSE is an emergent condition. NCSE may not initially be considered a manifestation of epilepsy. Establishing a correct diagnosis is generally more difficult than in the case of convulsive status. The symptoms of NCSE are pleomorphic and often diagnosed as a psychiatric condition (mostly delirium or dementia). EEG and a therapeutic trial with antiepileptic drugs are essential diagnostic tools for patients presenting with an unexplained confusional state.

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Electroencephalographic Findings During Sleep Among Severely Handicapped Persons with Intractable Epilepsy
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Purpose: Epilepsies of handicapped persons are intractable, and the duration of seizures often exceeds 20 years. We performed this study to identify the electroencephalographic findings during sleep among these intractable epilepsies.
Methods: We examined 105 severely mentally and physically handicapped epilepsy patients (male: female = 48: 57). Head CT or MRI and EEG were performed in all cases. 35 (33.3%) still had seizures and 21 out of 35 had suffered from seizures for over 20 years. We noticed the characteristics of these 21 persons' EEGs during sleep. Age-, gender- and spike foci- matched but seizure-restrained handicapped persons were selected as controls. Gender- and spike foci- matched handicapped persons who have had seizures for less than 20 years were also selected as a comparison.
Results: Sleep disturbance (late to fall asleep, sleep interruption and daytime sleepiness) was seen in 20 (95.2%) out of 21 persons. 12 (57.1%), 4 (19.0%) and 2 (9.5%) had frontal, temporal, occipital spikes, respectively. Sleep architecture was abnormal in confirmed cases. The group showing frontal spikes had many more discharges compared to controls but propagation varied. All in the temporal spike group had contralateral mirror foci and propagated markedly during sleep. The occipital spike group propagated during light sleep only.
Conclusion: EEG findings during sleep were highly characteristic among 21 cases. Most are thought to be the effects from the intractable epilepsy, but some may be the causes of epilepsy. Adjustment of sleep architecture of severely handicapped persons may provide new aspects to improve their quality of life.

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Video Home System: High Incidence of Psychogenic Seizures
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Purpose: To assess final diagnosis in a subgroup of adult patients in whom a first hospital-based video-EEG failed to document characteristic episodes. As diagnosis was not established, patients where asked to document paroxysmal attacks at home using their own video equipment. A repeated video-EEG exploration led to diagnosis confirmation.
Methods: Over a total of 250 video-EEG examinations, we retrospectively identified in a 5-year period, six patients who fulfilled the above inclusion criteria.
Results: A single patient had nocturnal frontal lobe epilepsy. 4 patients had non epileptic, psychogenic seizures. The last patient had both nocturnal tonic seizures and daily psychogenic seizures. In 4 patients, there was a marked contrast between a high number of home-recorded spontaneous episodes and final hospital-based video-EEG confirmation.
Conclusion: Home video documentation of paroxysmal events is a valuable alternative to hospital-based video-EEG, especially when non epileptic, psychogenic seizures are suspected.

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Women with Epilepsy: Changes of Alpha Rhythm and Paroxysmal Activity during Menstrual Cycle and Pregnancy
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Purpose: Hormonal fluctuations related to menstrual cycle and pregnancy modulate electrical cerebral activity, and in particular in women with epilepsy, may influence paroxysmal activity (PA). The aim of this study was to evaluate the modifications of PA and of absolute power of alpha rhythm (APAR) during the menstrual cycle and pregnancy in 3 women with idiopathic generalised epilepsy (IGE).
Methods: None of the 3 women with IGE were treated with antiepileptic drugs. All were studied during a menstrual cycle, and patient 3 was also evaluated during the course of pregnancy and puerperium. Serial determinations of sex hormones were carried out during menstrual cycles/pregnancy/puerperium, with EEG recordings performed on the same days as the hormonal study. During menstrual cycles the study was performed daily (only a few days were missed for each patient), during pregnancy it was carried out every month and during puerperium every week.
Results: All menstrual cycles studied were ovulatory and showed a significant increase of PA in the periovulatory and/or perimenstrual period; no significant correlations were observed between PA and reproductive hormones, apart from FSH in 1 patient. In all patients APAR showed a significant increase on ovulation day, coinciding with the LH surge. During pregnancy PA was poorly represented, showing a dramatic increase near delivery, while APAR showed a gradual and significant increase and withdrawal on the day of delivery.
Conclusion: Sex hormone fluctuations, particularly when peak-shaped and short lasting, exert a more evident influence on APAR than on AP. Gradual changes of hormonal levels have minor repercussions on neurophysiological parameters.

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Shared Participation of the Temporal Lobes in Medial Temporal Lobe Epilepsy
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Purpose: To collect evidence about the role of the temporal lobe contralateral to seizure onset and/or lesion in MTLE.
Methods: 1) Analysis of contralateral propagation types of MTLE seizures. 2) Collecting patients with MTLE contralateral to a temporal lesion. 3) 18 yrs video-EEG follow up of a patient with late contralateral epileptogenesis. 4) 2-10 yrs postoperative outcome study of 19 MTL patients with bilateral spiking before surgery.
Results: We found three types of contralateral propagation pattern of unilateral temporal seizures: 1) Seizure is triggered from the lesional side and rapidly propagates to the contralateral side. Symptomatogenic area is situated in the contralateral side. 2) Seizure starts and continues on the lesional side and after delay propagates to the contralateral side. 3) When seizure from the lesional side ends, a contralateral seizure starts. Case 1) and 3) shows that the contralateral side is involved more than being merely a passive receiver of the seizure propagation. Case histories will be enumerated with epileptogenesis contralateral to the lesioned temporal lobe. Evidence for late contralateral epileptogenesis will be demonstrated in a patient followed by video-EEG monitoring along a 18 yr time span. Seizure outcome correlates negatively with the presence of postoperative bilateral spiking in patients with bilateral spike activity before surgery.
Conclusion: All this evidence supports the possibility that interplay between temporal lobes has a role in unilateral seizure genesis of MTLE.

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Electroclinical Features of Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis Versus Mesial Temporal Lobe Epilepsy Defined by Specific Aetiology
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Purpose: To evaluate whether mesial temporal lobe epilepsy (MTLE) with hippocampal sclerosis (HS) and MTLE defined by specific aetiology can be distinguished on electroclinical grounds and whether MTLE with HS is an homogeneous condition.
Methods: We reviewed clinical records of outpatients with focal epilepsy referred to our Epilepsy Centre who had a clear lesion within the mesial temporal lobe structures detected with MRI.
Results: 74 patients were included in this retrospective study. 50 showed an hippocampal sclerosis and 24 had other lesions within the mesial temporal lobe structures (7 malformation of cortical development, 5 DNET, 3 hamartomas, 2 gangliogliomas, 3 neuroepithelial cysts, 2 gliosis and 2 atrophy of the temporal lobe). Febrile convulsions were present in 42% of patients with HS and in 12.5% of the second group, whereas familial history for epilepsy was positive in 10% and in 4.1% respectively. Mean age at onset of seizures was 15 years for patients with HS and 16.1 years for the other group; 6 and 3 patients respectively showed a silent period. AED resistance was established in 66% of patients with HS and in 58.3% of other. Interictal epileptiform discharges were present in routine EEG recordings in 44% of HS and in 46% of other (bilaterally in 18% and 16.6%). No differences were found in critical clinical features with EEG-video monitoring (performed in 20 and in 8 patients). We further divided patients with HS in 4 groups: 'typical' MTLE (when febrile convulsions were present); 'atypical' MTLE (no history of febrile convulsion); bilateral HS; dual pathology. No significant clinical difference among these groups was found.
Conclusion: Two groups of MTLE are not clearly distinguishable only on the basis of commonly available electroclinical features. We confirm that MTLE with HS is an heterogeneous condition.

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Clinical and EEG Findings of Non-convulsive Status Epilepticus: Two Case Report
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Purpose: The diagnosis of non-convulsive status epilepticus (NCSE) is often difficult and no clear and widely recognised clinical and EEG definition for NCSE has been established. In this report, we present two unusual cases of NCSE in patients with focal epilepsy.
Methods: Case 1: A 76 year-old, right handed woman was admitted to our department with episodes of loss of consciousness and unresponsiveness lasting approximately 1 to 1.5 minutes, every 5 to 10 minutes for the last 2 days. She had right hemiparesis due to 2 previous ischemic strokes (the first was in 1997 and the second in 2003). Before these events she was independent and was able to walk and communicate with her relatives with simple words. During the 40 minutes ictal video-EEG monitoring we recorded 14 seizures. Clinically she was unresponsive during the seizure period and couldn't follow commands. Ictal EEG showed 10-12 Hz rhythmic alpha waves maximum over the left FP1-F3-C3-P3 localisation lasting 40 seconds to 1.40 minutes. Immediately after the EEG activity ceased she became responsive and followed commands. These episodes were diagnosed as NCSE with altered consciousness only and successfully treated with IV phenytoin. We couldn't give her IV diazepam because she had lung disease.
Results: Case 2: A 35 year-old, right handed woman was admitted to the emergency department with a series of approximately 30 episodes characterised by an epigastric rising sensation followed by oral and manual automatisms with preserved consciousness lasting 30-40 seconds. During these attacks she asked to drink water. She had been having these attacks for 15 years, especially during menstruation, but hadn't been diagnosed with epilepsy. Ictal EEG showed 8-10 Hz rhythmic alpha activities over the F8 localisation which spread to the T4-T6 electrodes position then to the entire right hemisphere. During the seizure she followed commands but post ictally had amnesia for key words. These episodes were diagnosed as NCSE characterised by automotor seizures with preserved consciousness; another lateralising sign for the non-dominant hemisphere was peri-ictal water drinking. The MRI showed a large heterotopic grey matter in the right temporal lobe. She was treated with phenytoin and put on antiepileptic drug therapy.
Conclusion: The clinical representation of these two cases of NCSE were unusual and delayed diagnosis, especially in the older patient population, affects the prognosis.

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Optimal Surgical Outcome in One Patient with Temporal Lobe and Idiopathic Generalised Epilepsy
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Purpose: The coexistence of idiopathic generalised epilepsy (IGE) and partial epilepsy (PE) has been previously recognised. We report the surgical outcome in one patient with mesial temporal lobe epilepsy secondary to mesial temporal sclerosis and adult onset absence epilepsy.
Methods: We reviewed the charts of 412 patients who underwent presurgical evaluation and found one patient with both generalised and temporal lobe epilepsy who underwent epilepsy surgery.
Results: The patient is a 49 year old, right-handed woman. She had an uncomplicated febrile convulsion at 3 years of age. She does not have a family history of epilepsy. She started to present afebrile seizures when she was 7, beginning with an ascending abdominal aura followed by complex partial seizures with automatisms and rare secondary generalisation. Seizures have been pharmacoresistant, and occurred around 10-12 times a month in spite of multiple antiepileptic

drug combinations. Four years ago, she developed a new seizure type that she describes as brief loss of consciousness (lasting seconds) without automatisms. The interictal EEG showed two types of epileptiform abnormalities: sharp waves located over the right temporal region and 3-4 Hz spike and wave generalised discharges, which occurred in long runs lasting up to 20 seconds. During some of these runs of SW discharges the patient had a blank spell. The video EEG showed two types of seizures: 4 complex partial seizures with automatisms originating in the right temporal region and 2 generalised tonic-clonic seizures with a generalised EEG onset. The MRI showed right mesial temporal sclerosis associated to blurring of the grey-white matter interface in the temporal pole. She underwent an anatomic right temporal lobectomy two years ago. She has had no complex partial seizures since surgery. However, she still has absences which do not interfere significantly with her daily life and she had 4 generalised tonic-clonic seizures when her carbamazepine dose was reduced. She is currently on carbamazepine, topiramate and clobazam and has not had any convulsions in the last six months.
Conclusion: Epilepsy surgery may be considered in selected cases which present both a generalised and a focal epilepsy. Partial onset seizures may disappear and generalised seizures may be controlled with adequate antiepileptic drugs.

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Efficacy and Safety of Long-term Zonisamide Monotherapy and Adjunctive Therapy
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Purpose: This retrospective chart review study was conducted to investigate the efficacy and safety of zonisamide as monotherapy or adjunctive therapy.
Methods: Charts of male and female neurology clinic patients with various seizure types were reviewed; patients treated with zonisamide for ³3 months were identified. Zonisamide efficacy was assessed via seizure frequency reduction, and safety was assessed via reports of adverse events (AEs).
Results: 112 zonisamide-treated patients were identified. 90 patients were taking zonisamide therapy for > 3 months and were included in the efficacy analysis (n=45 monotherapy, n=45 adjunctive therapy); all 112 patients were evaluated for safety. Mean patient age was 54 years (range, 14-97 years). Mean duration of zonisamide therapy was 24.3 months (range 3-46 months), and mean zonisamide dosage was 324 mg/d (range 100-1000 mg/d). The most common seizure types were complex partial and partial with secondary generalisation. Overall, 38 of 90 patients (42%; n=25 monotherapy, n=13 adjunctive therapy) achieved seizure freedom on zonisamide. An additional 26 patients (29%; n=9 monotherapy, n=17 adjunctive therapy) had ³50% seizure frequency reduction. In 15 patients (17%; n=8 monotherapy, n=7 adjunctive therapy) zonisamide had either no effect or unreported effect on seizure frequency. AEs were reported in 30 of 112 patients (27%) and included weight/appetite loss (5.4%), fatigue (4.5%), sedation (2.7%), and gastrointestinal distress (2.7%). A total of 22 patients (20%) discontinued zonisamide therapy, including 13 patients (12%) due to AEs.
Conclusion: Zonisamide as long-term monotherapy or adjunctive therapy in patients with various seizure types was safe, effective, and well tolerated.

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Onset of Action of Levetiracetam: A Randomised, Double-blind, Placebo-controlled Study with Therapeutic Intensive Seizure Analysis (TISA)
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Purpose: To evaluate the time to onset of levetiracetam's (LEV. Keppra®) clinical effects and correlate this with LEV daily serum concentrations, using therapeutic intensive seizure analysis (TISA), in pharmacoresistant focal epilepsies with LEV used as add-on therapy.
Methods: Adult patients (age >16 yrs) with pharmacoresistant focal epilepsy entering presurgical evaluation at the Epilepsy Centre, Erlangen were enrolled. Eligible patients taking no more than 1 AED, with ≥2 seizures during a 48-hour baseline phase, were randomised to 7 days treatment with either LEV or placebo. LEV was initiated as add-on therapy at 1000 mg on Day 1, titrating to 2000 mg from Day 2; serum concentrations were monitored daily 1 hour after dosing. Continuous 24 hour video-EEG recording was used to monitor seizure number (N/24h) and duration (D/24h) per 24 hours.
Results: 23 patients completed the study (LEV, n=11; placebo, n=12). 7 patients taking LEV and 2 taking placebo achieved seizure freedom during the treatment phase. Intergroup comparison of the N/24h and D/24h reductions from baseline to treatment phases favoured LEV ($p<0.05$). LEV significantly inhibited D/24h from Day 2 ($p=0.013$) with a more marked effect from Day 3 ($p=0.009$). There was a linear relationship between daily LEV dose and serum concentration; steady state concentration being reached 72 hours after drug initiation.
Conclusion: The present study quantified the antiepileptic effect of LEV in focal epilepsies relative to its serum concentration. For the first time, direct measurement has proven the onset of action of LEV to be 2 days after drug initiation.

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Attitudes Towards Generic Drug Substitution Differ for Anti-epileptic Drugs and other Medications: Results from a European Multinational Survey
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Purpose: Generic substitution laws differ across countries and the practice is mandatory in some. To date, assessment of reactions to this practice has been predominantly confined to the United States. Here, views of patients and physicians toward generic substitution of anti-epileptic drugs (AEDs) are reported from 4 European countries.
Methods: Telephone-based surveys were carried out with 847 adult patients diagnosed with epilepsy and 387 physicians treating epilepsy from France, Germany, United Kingdom and Spain.
Results: A third (32%) of patients and 77% of physicians are aware that pharmacists may substitute a branded AED for a generic without physician consent. 30% of physicians would be uncomfortable prescribing a generic medication to treat their patients' epilepsy. The efficacy of generic AEDs is a concern to 44% of physicians and 70% of patients. Fewer physicians (27%) and patients (47%) are concerned about the efficacy of generic medications for acute care. Concerns about the safety of generic AEDs exist amongst 45% physicians, compared with 27% for generic acute care medications. Nearly a quarter (23%) of patients feel they do not receive adequate information about their epilepsy medication.
Conclusion: Both patients and physicians are concerned about the efficacy and safety of unrestricted generic AED substitution, yet generic substitution practices are not well-understood by patients, and

not completely understood by physicians. Doctors have a role to play in helping inform their patients about the risks and benefits of generic AED substitution. Study supported by GlaxoSmithKline Research and Development.

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Prevalence and Profile of Users Adults of 45-65 Age Group with Epilepsy in Mexico
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Purpose: In Mexico epilepsy has been identified as a mayor public health problem; its prevalence in the general population is 15/1000 but remains unknown elderly population. The aging of our population has also become an increasing problem since patients in the 45-65 age group require health services four times more than the rest of the population. The purpose of this study was to identify and describe the use of a telephone epilepsy information line by users with epilepsy.
Methods: We performed a cross-sectional study, sampling the calls of 5000 users of a telephone information line provided by the Priority Program of Epilepsy. 87 users were neither patients nor relatives; the remaining 4913 users were either patients (1671) or relatives (3242). We obtained variables such as age, gender, region of residence, reasons for the call, nature of medical, treatment or general information on epilepsy requested.
Results: The prevalence was 632 of 4913 users who were 40-65 years old, representing 12.86% of the total sample. The rest was distributed by age, as follows: 0-9 (720), 10-19 (1011), 20-29 (1595) and 30-39 (1042), with the following percentages 14.65, 20.57, 32.46 and 21.20 respectively. The users came mainly from the Federal District, State of Mexico and Veracruz. The most frequent requests were information on places to seek medical attention, general information on epilepsy and doubts regarding persistence of seizures despite medical treatment.
Conclusion: This survey used the opinions of the users with epilepsy in perspective of their quality of life being better.

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Occipital Epilepsy versus Charles Bonnet syndrome: Successful Treatment of Charles-Bonnet Syndrome with Valproate and Gabapentine
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Purpose: To provide a differential diagnosis of idiopathic occipital epilepsy with visual hallucinations against Charles Bonnet Syndrome (CBS).
Methods: Case report, literature review.
Results: CBS is characterised by vivid, complex and recurrent visual hallucinations associated with eye pathology in cognitively intact persons. Hallucinatory episodes vary in duration from seconds to hours. Formed visual hallucinations are also experienced fairly often in epilepsy. Pictures of people, animals or scenes may be perceived, either static or moving. Visual illusions also occur as a seizure phenomenon. A case of Charles Bonnet syndrome in an elderly patient with macular degeneration and iatrogenic hyperthyroidism is described. The hallucinations stopped after a natrium valproate administration and appeared if its administration had ceased. When the treatment was started again the hallucinations disappeared. Later, valproate was replaced, due to alopecia, by gabapentine with good effect.
Conclusion: Both CBS and occipital epilepsy can present with illusions and hallucinations and then difficulties with diagnosis can occur. Therapeutic response to antiepileptic drugs in both conditions may be good. Occipital epilepsy is defined by its symptoms, the EEG and other evidence of its site of origin. CBS appears only in visually impaired persons.

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Patient Perceived Cognitive Side Effects of Anti-Epileptic Drug Treatment: An International Perspective
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Purpose: To provide a patients' perspective on the cognitive side effects of anti-epileptic drug (AED) treatment and the consequences for quality of life.
Methods: A nine-item questionnaire comprising a combination of forced-choice and open-ended questions was distributed to 4,500 members of nine chapters of the International Bureau for Epilepsy (Austria, Belgium, Denmark, France, Ireland, Israel, Norway and Scotland).
Results: Data analysis was performed on 837 completed questionnaires. The average age of respondents was 40 years, 54% were female and 95% were taking medication for their seizures (60% polytherapy vs 39% monotherapy). Average length of time on treatment was 18.07 years (± 18.07). Indicators of cognitive impairment considered to be affected 'very much' or 'moderately' included sleepiness/tiredness (57%), slowness of thought (42%) and difficulties learning something new (41%). Two thirds stated that cognitive impairment was related to their condition or AED therapy, with 41% attributing impairment to their AED therapy alone. More than half (59%) stated that cognitive impairment had prevented them from achieving a goal and approximately 50% reported that their quality of life had been affected including: work (48%), education (46%), relationships (48%) and leisure pursuits (44%). When asked what side effects they would most like to avoid, respondents reported indicators of cognitive impairment most frequently, including sleepiness/tiredness (35%), memory problems (19%), lethargy/sluggishness (9%) and difficulty paying attention (8%).
Conclusion: Insights gained from this survey highlight the debilitating effect of cognitive impairment on individuals with epilepsy and the importance ascribed to minimising cognitive side effects of AEDs.

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Recurrent Prolonged Impairment of Consciousness and Hypothermia due to Valproate Treatment in a Female Patient with Severe Mental Retardation
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Purpose: Differential diagnosis of recurrent impairment of consciousness in mentally handicapped patients may be difficult.
Methods: A 36 year old mentally handicapped woman suffering from a focal epilepsy with complex partial and secondary generalised tonic-clonic seizures of unknown aetiology was admitted with the diagnosis of non-convulsive status epilepticus (NCSE) lasting for more than 40 hours. Treatment was valproate 1800mg/day, topiramate 400mg/day and phenobarbital 125mg/day. Control of epilepsy was reported to be bad over the last months with recurrent prolonged complex partial seizures. Clinically relevant side effects were not reported. Vital signs were normal except for a persistent hypothermia of 33.3 degrees centigrade. Routine biochemistry showed pathological results for CRP (2.8mg/dl), GGT (59U/l) and mild anaemia (HB 11.2g/dl, HKT 33%). EEG showed diffuse rhythmic slowing. Ammonia was determined because of the unknown aetiology of the epilepsy and was found to be excessively elevated (up to maximum of 560ug/dl). Hints for an error of metabolism of urea cycle were not found in laboratory tests.

Treatment with dietary and reduction of enteral production of ammonia was initiated and valproate discontinued under protection of benzodiazepines.
Results: General condition and EEG improved rapidly, ammonia and body temperature normalised within a few days.
Conclusion: In this patient, prolonged recurrent impairment of consciousness in the past was probably due to metabolic decompensation with cephalic and diencephalic encephalopathy and not a result of repeated NCSE as suspected. Reason for misinterpretation of clinical data was the mental retardation of the patient with limited communicative skills in combination with a therapy-resistant epilepsy.

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Reversible Cytotoxic Edema in the Splenium of the Corpus Callosum Related to Antiepileptic Treatment: Report of 2 Cases and Literature Review
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Purpose: Clinically silent lesions localised in the splenium of the corpus callosum (SCC) are a rare finding in the MRIs of patients receiving antiepileptic drugs. They are usually of benign character, but may induce unnecessary complementary exams if their nature is unrecognised. So far 22 cases were described in the literature and different aetiologies were proposed. We describe two further cases and discuss the probable lesion aetiology.
Methods: We report 2 cases of a 25 year old male patient and a 12 year old female patient with a transient SCC lesion, discovered in the context of a presurgical epilepsy evaluation.
Results: Comprehensive MR imaging, including MR-spectroscopy and diffusion tensor imaging-based fibre tracking of the lesion suggested the presence of a cytotoxic edema not affecting neuronal fibres. Serum arginine vasopressin (AVP) measurements revealed an altered secretion during the acute phase.
Conclusion: On the basis of our results, we hypothesise that the lesion consists of a cytotoxic edema, related to alterations of AVP secretion which may be a result of abrupt antiepileptic drug concentration changes in the brain.

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Sleep Pattern in Patients with Epilepsy during Topiramate Monotherapy
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Purpose: As many antiepileptic drugs (AEDs) act via GABA-ergic or other mechanisms that affect brain function, they may potentially affect sleep patterns. We explored the effect of topiramate on sleep.
Methods: In an open study, patients with diagnosed epilepsy and without AEDs for the last 3 months, were weekly escalated with topiramate 25 mg/day to 100 mg/day. At baseline and after 4 weeks, seizures were evaluated, sleepiness was rated on the Epworth Sleepiness Scale (EES) during daytime and ambulatory full-night polysomnography was performed.
Results: 13 patients (5M/8F, 19-72 years), mostly with recent-onset epilepsy (6 focal, 7 non-focal) were studied. Median monthly seizure frequency decreased during topiramate ($p<0.001$). Sleepiness scores improved from 5.2±2.5 to 3.9±2.8 (NS). Sleep period, wake time, total sleep time (TST), sleep efficiency, latency to NREM1,3 and 4 and REM sleep remained unchanged. The number of awakenings and movements, and sleep latency to NREM2 decreased (NS). NREM1 and its % of TST decreased from 37.6 min (9.9%) to 23.5 min (6.3%) ($p<0.005$). Other NREM phases did not alter significantly. REM latency decreased significantly from 113.8 min to 81.5 min ($p<0.05$). There were no changes in wake time and number of awakenings. There were no associations between changes in EES and changes in sleep variables. The most frequent adverse event was paraesthesia (n=8).
Conclusion: Except for a decrease in NREM1 and shorter REM latency, we found minimal influence on sleep structure during topiramate monotherapy in patients with epilepsy. There was no evidence of increased sleepiness (Funded by Janssen-Cilag).

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Paraesthesia During Topiramate Monotherapy for Epilepsy: Characterization of its Onset and Disappearance
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Purpose: Paraesthesias is a well known side effect of topiramate treatment. We prospectively studied time course and severity of paraesthesias with topiramate monotherapy in an open naturalistic study in patients with untreated new onset epilepsy, or failing a first antiepileptic drug.
Methods: Topiramate treatment consisted of 4 weeks titration to 100 mg/day (weekly +25 mg/day; any other AED tapered off simultaneously), subsequent individual dose adjustment and continued treatment for at least 6 months. To study time course and features relevant to recovery of paraesthesia, patients completing the 7-month study were selected (n=554).
Results: Paraesthesia was noted in 15.6% of patients (more frequently among female (25.6%) than male patients (12.4%; $p<0.05$)). Paraesthesia started during the first 4 weeks (titration) in 73.3% of cases, within the first 8 weeks in 90.7%. By month 7, paraesthesia was no longer present in 58.1%, while it persisted in 41.9%. Onset of paraesthesia was somewhat later in persistent than in transient cases. Daily incidence of transient paraesthesia was the highest at the end of titration (week 4), followed by its progressive decrease. Peak incidence of persistent paraesthesia was reached by week 8, whereafter it remained stable over time. Severity was mild in 86.0% and moderate in 14.0%. There was no difference in severity between transient and persistent paraesthesia.
Conclusion: Paraesthesia during topiramate started in the first 1-2 months of treatment and resolved during treatment in more than half the patients. (Funded by Janssen-Cilag EMEA.)

p356
Autonomic Dysfunction and Phantom Absences
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Purpose: Partial and generalised seizures often affect the autonomic nervous system function during ictal, interictal and postictal periods. Activation and inhibition of areas of the central autonomic network can cause cardiovascular, gastrointestinal, respiratory, cutaneous, pupillary, urinary and genital manifestations. Autonomic dysfunction when representing a sole seizure manifestation may be a problem for differential diagnosis of non-epileptic conditions. Phantom absences are often clinically overlooked unless they appear as absence status epilepticus (SE) or in conjunction with GTCS, when EEG evaluation shows generalised spike-wave complexes (S-WC) or poly S-WC greater then 2.5 Hz. The aim is to present a case of idiopathic generalised epilepsy (IGE) with the EEG signs of phantom absences and the main clinical manifestations of autonomic dysfunction.
Methods: A male patient aged 24 years was sent to neurology from cardiology because of manifesting paroxysmal events with palpitation, nausea, vomiting, with ECG signs of tachycardia, occasional arrhythmia, high blood pressure (BP), lasting for hours repeating once or twice per year in the last 7 years, responsive to Diazepam administration.
Results: These events unrecognized as seizures happened usually on awakening, after partial sleep deprivation. The patient himself reports mild cognitive impairment and the feeling of fear during these

seizures: 'being slow, seeing things not so clear as usual', but alert, responsive, not amnesic for these periods. In his family history: his father had epilepsy with GTCS during sleep, assumed to be secondary GTCS because of head trauma in childhood, when after head surgery started on Hydanphen by his neurosurgeon, in the last years on his own stopped the AED, no reports of seizures, no risk factors except smoking, died unexplained in sleep at the age of 55, SUDEP may be considered. Patient's somatoneurological status normal without nausea, vomiting, palpitation, tachycardia and high BP after administration of diazepam. Psychological functioning, clinically evaluated, with slowness as mild cognitive impairment during seizures. Laboratory findings normal. EEG showed generalised 2.5 – 4 Hz S-WC and poly S-WC in a series each lasting a few seconds, fragmented with a few seconds of normal background activity, representing EEG signs of phantom absences. Brain imaging normal. Diazepam and valproate (VPA) were administered, VPA as regular treatment of 900 mg per os. Repeated EEG normal.
Conclusion: Phantom absences are often overlooked. Autonomic dysfunction as a sole seizure manifestation is often overlooked as an epileptic phenomenon. EEG may help in diagnosing the epileptic nature of both conditions. Both of these conditions may affect a patient's morbidity and mortality. Having in mind the possible connection of SUDEP and paroxysmal autonomic dysfunction, the autonomic dysfunction of the patient and the possible SUDEP in his father, the AED VPA, effective in IGE has started to affect the patient's morbidity and mortality.

p357
Premonitory Symptoms in Epilepsy: Are They Infrequent?
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Purpose: Epilepsy and its consequences: refractoriness, impact on cognitive function and life quality, have stimulated an investigation on the early detection of seizures (SE). "Bergey, G. Early seizure detection: Theoretical and Applied. In: Epilepsy. Scientific Foundation of Clinical Practice. 2004 p. 467-482. Hughes, J Seizure 1993 Sep; 2(3): 201-3" Our objectives were: 1) To determine frequency of premonitory symptoms (PS) in our population. 2) To know the variety SP that precedes to the EC. 3) To determine the time that these symptoms precede to the EC.
Methods: A prospective investigation; an ad hoc format was applied during 1 month, in order to register the phenomenon in the population with epilepsy who presented for consultation at one of two hospitals.
Results: 104 patients were included in the epilepsy consultation, of which 19 them showed SE (18.27%). The PS more frequent were: 12 headache (41.3%), 5 irritability (17.24%), 8 anxiety (27.,59%), 2 depression (6.89%), 2 others (6.89%). The time average in which these symptoms preceded to the SE was: 2-4 days (36.84%), 1 day (26.32%), 4-6 hours (15.79%) and 1-2 hours (15.79%).
Conclusion: We have observed that SP are not infrequent in our population, allowing the continuity of the investigation, being able to make EEG during the SP and restoring intermittent prophylactic therapy; avoiding the consequences of chronic therapy and in that way, improving the quality of life of our patients.

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Ictal and Postictal Coughing: Incidence, Semiologic Features and Correlation with the Epileptogenic and Symptomatogenic Zone in Focal Epilepsy
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Purpose: To study the incidence of ictal/postictal coughing, semiologic features and correlation with the epileptogenic/symptomatogenic zone in focal epilepsy.
Methods: We retrospectively reviewed 232 consecutive children/adult patients with focal epilepsy, studied with prolonged video-EEG monitoring in the Universidad Católica de Chile Epilepsy Program, between January 1998 and December 2004. All patients with at least one documented electroclinical seizure with ictal/postictal coughing were selected. Video recordings were exhaustively analysed for studying other ictal/postictal clinical signs. The relationship between coughing and the epileptogenic zone (according to non-invasive/invasive EEG and structural/functional neuroimaging findings) was evaluated. Ictal coughing occurrence was correlated with the evolution of EEG pattern.
Results: 7 patients had ictal and 2 postictal coughing (11-44, mean 27 y.o.; 5 men), in all cases not established by clinical history. 52 seizures were registered (2 to 14 per patient). 6 patients with ictal coughing had also head version and tachycardia. The presumed epileptogenic zone was temporal/frontotemporal, being left lateralisation more frequent in ictal coughing (71%). In TLE, at ictal coughing occurrence, the epileptiform discharge was never confined to one temporal lobe.
Conclusion: Ictal and postictal coughing are uncommon phenomena in focal epilepsy. In our study it occurred preferentially in adults, it was usually ictal, and it was related to temporal and frontotemporal epilepsy, more frequently affecting the left side. Ictal coughing is probably due to epileptic activation of not well-defined cortical centres that subserve autonomic function, given its correlation with epileptiform activity propagated from temporal to ipsilateral frontal lobe or to the other hemisphere.

p359
Frontal Lobe Epilepsy: Clinical Seizure Lateralisation due to Clinical Seizure Semiology
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Purpose: Only a few studies have examined the lateralising value of clinical seizure semiology in patients with frontal lobe epilepsy (FLE). We systematically analysed the lateralising value of clinical seizure semiology in FLE.
Methods: We studied 228 seizures (s) in 31 consecutive patients with medically refractory FLE who underwent prolonged video-EEG-monitoring. Several clinical symptoms were assessed for their incidence and positive predictive value (PPV) correctly lateralising the seizure onset.
Results: Unilateral clonic movements (32/228 s (=14%)/ PPV: 81%), unilateral dystonia (46/228 s (=20%)/ PPV: 80%), version (47/228 s (=21%)/ PPV: 75%) and asymmetric tonic posturing (20/228 s (=9%)/ PPV: 100%) were reliable lateralising signs pointing to a contralateral seizure onset zone. Figure 4 sign (18/228 s (=8%)/ PPV: 67%) and asymmetric ending (9/228 s (=4%)/ PPV: 89%) were also of important lateralising value. Unilateral grimacing (19/228 s (=8%)/ PPV: 32%), unilateral automatisms (28/228 s (=12%)/ PPV: 39%) and early head-turning (21/228s (=9%)/ PPV: 67%) demonstrated discordant results in lateralising the epileptogenic focus. Unilateral eye-blinking (3/228 s (=1%)/ PPV: 100%), postictal automatisms (2/228 s (=1%)/ PPV: 100%) and postictal nosewiping (4/228 s (=2%/ PPV: 100%) were only rarely observed, their lateralising value therefore could not be assessed reliably. Vocalization appeared in 63/228 s (=28%), especially in seizures of right hemispheric origin (46/63 s =73%).
Conclusion: The results of clinical seizure lateralisation corresponded with the final lateralisation of the epileptogenic focus in 81% of our patients.

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Adult Phenotype of Severe Myoclonic Epilepsy in Infancy
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Purpose: Severe myoclonic epilepsy in infancy (SMEI), Dravet syndrome, is an epileptic encephalopathy with a characteristic presentation in early childhood. Adults with SMEI may be under-recognised as their early history is often not obtained. The aim of this study was to delineate the adult phenotype of SMEI.
Methods: 15 adults with SMEI were identified. Each patient was personally examined and a detailed seizure, developmental and intellectual history was obtained.
Results: The mean age at study was 25 years (median 23, range 18-47). Seizures began at a median age of 5 months and were associated with fever in 10/15 patients. All patients had multiple seizure types in childhood. In adult life, all have GTCS, 7 partial seizures, 2 myoclonic seizures and 3 absence seizures. Seizure frequency decreased in all compared with childhood, but none are seizure free. Psychomotor development slowed after the first year of life in 14 patients. 1 adult is of normal intellect; intellectual disability is mild in 3, moderate in 4, and severe in 6. 3 patients regressed in adulthood. Mild pyramidal signs are present in 6, extrapyramidal signs in 4, and cerebellar signs in 5 patients. Microcephaly did not occur.
Conclusion: Clues to the recognition of SMEI adults are the heterogeneous seizure types with nocturnal GTCS predominating, intellectual disability, motor signs and the lack of microcephaly. The key to diagnosis remains, however, the characteristic features in the first years of life.

p361
MELAS Syndrome Presenting with Status Epilepticus
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Purpose: MELAS syndrome, a rare mitochondrial disorder, is characterised by mitochondrial encephalopathy, lactic acidosis, and recurrent stroke-like episodes. Various degrees of cognitive dysfunction, dementia, seizures, migraine, stroke, and transient ischemic attack can be seen due to cerebral involvement. Although MELAS is a well-known syndrome, various clinical presentations of the disease, like age of onset, can obstruct or delay the diagnosis.
Methods: In this paper, we present data on a 31 year old female patient presenting with status epilepticus diagnosed as MELAS syndrome.
Results: We present a 31 year old female patient presenting with seizures and aphasia. At first, she was diagnosed with encephalitis and treated with antiviral and antiepileptic agents. Two months later, the patient presented with status epilepticus. Based on history, physical and neurological examinations, neuroimaging and histopathological studies she was diagnosed with MELAS syndrome. The patient was treated with coenzyme Q and antiepileptic agents. In spite of appropriate therapy, she presented with status epilepticus 5 times more in the following three months. The disease progressed, and cognitive functions declined.
Conclusion: We presented this case to emphasise MELAS syndrome can rarely occur with status epilepticus.

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Two HIV (-) Patients with Neurosyphilis Presenting Convulsive and Nonconvulsive Status Epilepticus in Different Stages of their Disease
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Purpose: A previous study showed that the incidence of seizures in patients with neurosyphilis ranged from 14 to 60%. Status epilepticus (SE) is very rare in neurosyphilis literature in which eight cases have been published until now. Jarisch-Herxheimer reaction, which may occur in about 30% of patients with neurosyphilis after taking penicillin, is a serious complication. The 2 patients admitted to our clinic who were presenting two different types of SE complained about forgetfulness, and their EEG showed periodic lateralised epileptiform discharges (PLED). In both patients, CSF and serum VDRL and TPHA were all positive but HIV serology was negative.
Methods: Case 1: 42 year-old man presented progressive memory impairment and speech difficulty for one year. During his ambulatory investigation for dementia, he had focal motor status epilepticus. On the 8th day of penicillin treatment, his EEG findings which were seen to have PLED on the right side of hemisphere, disappeared. His cranial MRI showed cerebral atrophy and hyperintensity on bilateral mesial temporal regions.
Results: Case 2: A 71 year-old woman was brought to the hospital with memory complaints and gait disturbance. Cranial MR revealed moderate global atrophy and white matter abnormalities. In the 12th hour of penicillin treatment she developed non-convulsive status epilepticus resulting from Jarisch-Herxheimer. On her EEG, PLED was seen.
Conclusion: The two patients had no history of primary syphilis and epilepsy. They both mentioned no illness that required antibiotics treatment for long. Neurosyphilis is a disease that should be considered when investigating the aetiology of SE.

p363
Benign Non-epileptic Myoclonic Status in Two Elderly Patients
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Purpose: Myoclonic status epilepticus is a rare complication in idiopathic generalised epilepsies, and generally occurs in a dramatic context of chronic or acute encephalopathy. We wish to report two recent benign cases of apparently non-epileptic myoclonic status (MS) observed (with EEG-video documents) in elderly patients.
Methods: We recently evaluated two patients who presented with MS: a 77 yr old man without a prior neurological history, and an 89 yr old woman with diabetes and a history of myocardial infarction. In both cases, MS started abruptly without any apparent triggering factor. The face was initially involved, and the myoclonias spread quickly, first to the upper limbs before becoming generalised. Consciousness was preserved.
Results: MS was assessed using video-EEG. Patient 1 had a normal MRI, patient 2 a normal CT scan. No biological abnormality was present. The EEG failed to show any paroxysmal activity. IV clonazepam quickly stopped the MS in both cases, and there was no recurrence during a 1 yr follow-up.
Conclusion: Such uncommon clinical presentations are not well understood or explained. They appear to be benign and easily accessible to treatment. In elderly patients, non-epileptic MS may occur as a single, treatable event.

p364
Refractory Status Epilepticus in a Pregnant Woman
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Purpose: Status epilepticus is a possible complication in pregnant women with epilepsy. This situation requires strict monitoring of risk and benefits of therapy.
Methods: We describe the case of a 33 year old pregnant woman, affected by epilepsy with simple partial motor seizures in a cortical malformation. She was treated with PB, with good control of seizures. At the 24th week of pregnancy she developed a partial motor epileptic status, 'refractory', with a risk of premature delivery.
Results: We initially treated the patient with BDZ, PHT, VPA ev, without efficacy. A sedation with propofol for 12 hours, with assisted ventilation and quite continuous monitoring of EEG and of foetal activity, stopped the status.
Conclusion: The patient's pregnancy progressed to full term, without other problems.

p365
Post-stroke Status Epilepticus in the Elderly
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Purpose: The purpose of this study was to analyse the onset and risk factors of post-stroke status epilepticus.
Methods: In a retrospective study we analysed the data of 95 patients (aged 60-92 years) with a history of stroke who developed status epilepticus (55 focal, 37 generalised, three unclassifiable status) in the last six years. In 35 patients (37%) status was the first manifestation of epilepsy.
Results: Ischemic stroke of large artery territories were diagnosed in 52 (54.7%) (12/52 acute ischemic stroke), hemorrhagic stroke in 11 (11.6%) (5/11 acute) and small vessels disease with lacunar infarction in 30 (31.6%) patients. In the group with late-onset status, the rate of status within the first six month after ischemic stroke was twice as high compared to the rate of status within the next year. Atrial fibrillation was seen in 29.5%. Systemic infections, chronic obstructive pulmonary disease taking theophylline and metabolic disorders were diagnosed in 31% of the patients.
Conclusion: Cardioembolic ischemic and hemorrhagic stroke had the highest risk of post-stroke status epilepticus. The mechanisms of post-stroke epilepsy are still not clear. In the group of patients with late-onset status the time of onset suggested that post-stroke epilepsy developed within the first six months after the stroke. After that time associated risk factors such as a history of cardiac arrhythmia, pulmonary infections and metabolic disorders played an important role for developing post-stroke status epilepticus in the elderly.

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Complex Partial Status Epilepticus as Presenting Features of MELAS: Case Report and Review of Literature
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Purpose: Complex partial status epilepticus (CPSE) presenting features of mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS) is rarely reported. We studied a 38 year old woman with late-onset MELAS syndrome presenting with CPSE on occasion of her first stroke-like episode.
Methods: Serial clinical, EEG and CT findings of the patient were analysed. The other case reports of CPSE as presenting features of MELAS were reviewed.
Results: The patient presented with vomiting, confusion, behavioural disturbances, dysarthria and auditory hallucinations lasting from a week. A CT scan documented a right temporoparietooccipital stroke-like lesion. EEG showed the coexistence, on the right hemisphere, of prolonged temporooccipital seizure discharges and frontotemporal periodic lateralised epileptiform discharges (PLEDs). On carbamazepine and idebenone therapy, for a period of 25 days, serial EEGs documented the disappearance of the seizure and PLEDs activity. Over a period of 3 months, CT scans showed the gradual regression of the stroke-like lesion. Analysis of mtDNA from peripheral lymphocytes evidenced a A3243G point mutation. In the literature four other MELAS patients presenting with CPSE have been reported. In these cases, EEG during the CPSE showed prolonged focal seizure discharges in three, and focal seizure discharges alternated with PLEDs in the same cerebral region in one patient.
Conclusion: CPSE may be a rare presenting feature of MELAS. In our case the spatial independence of PLEDs and seizure discharges on EEG is a peculiar finding that documents the multifocality of neuronal hyperexcitability in the context of the cerebral stroke-like lesion in this syndrome.

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Monitoring of Pregnancy in Epilepsy Patients
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Purpose: To analyse the course of pregnancy and its outcomes in 114 patients with epilepsy on antiepileptic drug (AED) therapy. The scheme of pregnancy monitoring in epilepsy patients was elaborated.
Methods: In case of remission of epileptic seizures the frequency of clinical, EEG and laboratory examinations was performed every two months. In case of actual epilepsy the frequency of those examinations was performed every month and after each epileptic seizure. The diary of epileptic seizures, neurological status and usual scalp EEG-research were analysed during every clinical examination. Laboratory analysis included: clinical and biochemical analysis; serum concentrations of AEDs, evaluations of foeto-placental status (alpha-foetoprotein, oestriol, progesterone, placental lactogen and cortisol). Foeto-placental status was evaluated at the end of the first trimester of pregnancy and further monthly. We are in process of accumulating data of concentrations of neurospecific antibodies in the blood of pregnant patients. Dynamic ultrasound examinations will be carried out at statement of the pregnant woman on the account, at 19-21 weeks (with the exception of malformations) and further once every four weeks. Possible specific teratogenic influence of each AED has been taken into consideration.
Results: The majority of epilepsy patients (68.4%) have been consulted by a neurologist and obstetrician before/during pregnancy and (31.6%) have been consulted only during pregnancy. Dynamic evaluations of serum concentrations of AEDs revealed relatively stable concentrations of carbamazepine and valproic acid. Serum concentrations of phenobarbital and phenytoin decreased from one third to one half of all patients during the second and the third trimester of pregnancy. Ultrasound examinations allowed us to determine one malformation – teratoma of sacral localization at 18 weeks gestation. Amniocentesis and determination of concentration of alpha-fetoprotein in amniotic liquid was done only in one case. Chorion biopsy has not been performed.
Conclusion: The technique of observing pregnant epilepsy patients is recommended in Russia in methodological recommendations from Department of Health of Russian Federation № 2001/130. This scheme monitoring pregnancy allows us to determine small deviations and to install correct therapy.

p368
Densitometric Assessment of Bone Tissue of Epilepsy Patients
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Purpose: Long-term therapy using an anticonvulsant may influence bone and mineral metabolism called 'anticonvulsant osteomalacia'. The study is an attempt to assess the usefulness of quantitative ultrasound (QUS) to describe bone status in epilepsy patients.
Methods: The study was done on 93 epilepsy patients in comparison with a control group consisting of 25 age-matched individuals. Evaluation of the skeletal status was based on QUS measurements at the heel. The speed of sound – SOS (m/s), broadband ultrasound attenuation – BUA (dB/MHz) and stiffness index (%) were measured with the Achilles system (Lunar, Madison, WI, USA).
Results: QUS assessment (SOS, BUA, stiffness index) showed significantly lower values in patients in comparison to the control group.
Conclusion: The method proved to be useful tool in the assessment of skeletal status and shows that prevention ought be applied in early stages of the therapy.

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Women with Epilepsy, Mothers with Epilepsy: The Infant Desire
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Purpose: The medical risks of epilepsy and its treatment during pregnancy have been the subject of many studies. In contrast, no research has been interested in women with epilepsy, and their wishes when they consider maternity. What about the desire of women with epilepsy to have a child?
Methods: This research approaches a set of themes on the infant desire of 15 women with epilepsy, 22 to 40 years old. Half of these women do not have a child yet. Realized on an interview guide, the recorded and transcribed interviews were subjected to a thematic analysis and a computerised analysis of speech (software Tropes).
Results: Preliminary results: The unconscious infant desire is in conflict with anxieties concerning the risks of epilepsy and its treatment. This conflict amplifies parental pressures and distresses. The pregnancy is marked by the fear of a hereditary transmission of the epilepsy to the foetus, culpability about the possible risks, the wish of an IVG in the event of foetus malformations. The childbirth is sometimes experienced as traumatic due to lack of sufficient support. The fantasy infant in the women without a child and the real child among women already mothers are paradoxically invested of a protective role: it is able to bolster and reassure the mother after a seizure (inversion of the maternal role).
Conclusion: The interest of this research is to emphasise the importance of subjectivity on the infant desire of women with epilepsy, pregnancy investment and the attachment bond to the child. These women sometimes express a request for psychotherapy.

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13:15 – 14:15
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Unilateral Temporal Lobe Epilepsy in Children: A Developmental Study of some Socio-cognitive Competencies of the Temporal Cortex
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Purpose: Socio-cognitive competencies integrate and attribute meaning to non verbal cues delivered by the human environment. In adults, cerebral functional imaging studies have shown that the temporal cortex is involved in this type of information processing (face identity, gaze direction, emotional expression, voice identity and emotional prosody). Autistic children, who exhibit several deficits in socio-cognitive competencies, show a bi-temporal cortex hypometabolism. Children with epilepsy, in whom the epileptic focus is bi-temporal, are more likely to show autistic features than children with a unilateral focus. These data suggest that temporal cortex damage is likely to be associated with abnormal socio-cognitive development. To uncover the relationships between the temporal cortex and visual and auditory social competencies during abnormal and normal development and to study possible differences between visual and auditory post-lesional plasticity we prospectively studied children with unilateral temporal lobe epilepsy, using tasks that allow evaluation of auditory and visual perceptual processing of cues delivered by faces and voices.
Methods: We analysed cognitive deficits taking into account the localisation of ictal and interictal EEG activity, the age of onset and the duration of the epilepsy and the data provided by cerebral neuroimaging techniques (MRI, PET H2O15 and FDG).
Results: We report on methodology and preliminary results (15 children studied on submission). Our first results suggest that in children with a unilateral hippocampal sclerosis and temporal hypometabolism, several deficits are found in auditory and visual social tasks while memory tasks and IQ performances are not affected. In the absence of a detectable anatomical abnormality or lesion we did not observe a cognitive deficit. In children with multifocal or extra-temporal abnormalities the observed deficits are much less specific and also involve memory and IQ performances. Surprisingly, contrarily to what is observed in adults with epilepsy, the deficits were not exclusively associated to right hemisphere damage.
Conclusion: This is the first time that socio-perceptive deficits were demonstrated in children with unilateral temporal lobe epilepsy.

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Cognitive Effects of Antiepileptic Drugs on School Aged Offspring who were Exposed in Utero
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Purpose: To establish the cognitive effects of antiepileptic drugs on school aged offspring of women with epilepsy whose children were exposed in utero.
Methods: As part of an ongoing prospective study on outcome of pregnancy in women with epilepsy, 52 mothers and their children (93) were studied. They were compared to a matched group of children (93) and mothers (54) and fathers (35 and 41) were studied in both

groups. The tests included intelligence, memory, language, attention, and motor and somatosensory measures.
Results: No significant differences on any cognitive measure was demonstrated between the fathers in the experimental and the control groups. Experimental mothers were significantly different from the control mothers on many cognitive measures and their children differed on object assembly, in performance IQ, in full scale IQ, in perceptual organisation, and in freedom from distraction regardless of whether the mother had or had not had seizures during the pregnancy.
Conclusion: No difference in fathers' cognitive ability likely demonstrates adequate group matching. Findings for the mothers with epilepsy are probably related to their epilepsy and/or medication; and the findings for the children demonstrate that thee are specific negative cognitive consequences of in utero exposure to AEDs.

p372
Neuropsychological Profile in Children with Partial Epilepsy
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Purpose: Early studies of the influence of epilepsy on cognitive functions mainly evaluated global deficit as dependent on epilepsy and its causes. More recently, some authors have described specific neuropsychological deficits in epilepsy patients with a normal IQ, also showing relations between different forms of epilepsy and the nature of the deficits. We investigated neuropsychological functions in children with partial epilepsy.
Methods: We studied 40 subjects, 23 boys and 17 girls, aged between 8 and 11 years, with frontal lobe epilepsy (10 subjects), parietal lobe epilepsy (10 subjects), temporal lobe epilepsy (10 subjects) and occipital lobe epilepsy (10 subjects). We selected subjects with no neurological, cognitive, visual or auditory deficits, and normal imaging MRI. Seizures were classified according to the 1989 ILAE. The battery of tests included: WISC-R, Raven's progressive matrices, Zazzo's "deux barrages" test, Benton's D-form of visual retention test, Rey's complex figure test (B-form). We performed the same tests on a control group without epilepsy, matched for sex, age and economic situation.
Results: Student's, and Mann-WhitneyU test showed no significant differences between the performance of both groups. The static comparison of the scores attained by subjects with epilepsy is not meaningful, in relation to the variable partial epilepsy vs control group without epilepsy.
Conclusion: Our study showed no significant difference in performance of the two groups of subjects with focal epilepsy and the control group without epilepsy. This can be due to the selection criteria; we excluded patients with evident focal injuries, and those with intractable and early-onset epilepsy.

p373
Inhibitory Processes in Children with Idiopathic Epilepsy
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Purpose: Evaluation of inhibitory processes in children with idiopathic epilepsy.
Methods: 22 children with generalised (n=11) or focal (centro-temporal spikes epilepsy, n=11) idiopathic epilepsy aged 7-12 without intellectual deficiency were included. 15 children was treated with valproic acid (n=11) or oxcarbazepine (n=4) and 7 children had stopped medication at least six months earlier. Evaluation included standardised tests (WISC-III, Stroop, Wisconsin) and 3 experimental tasks: attentional capture task which evaluated distracter resistance capacities, two-choice task which evaluated frequent response inhibition and peripheral cueing task which evaluated the validity effect of cueing. Experimental tasks have been performed in a control group aged 7-12.
Results: 20 out of 22 children with epilepsy scored below the normal range in, at least, one subtest, especially in 'code' (m=6.6, sd=2.8) and 'arithmetic' subtests (m=7.2, sd=2.6) known to be sensitive to attentional impairments. On the experimental tasks, children with epilepsy were significantly slower (by 180ms, $p<0.001$) and the number of omissions was larger (by 1.5 omissions, $p<0.003$) than that of controls. The magnitude of interference from distracters was significantly larger in children with focal epilepsy (53ms) than those with generalised epilepsy (17ms, $p<0.01$) and than controls (17ms, $p<0.008$). The response probability effect was significant only in children with focal epilepsy (220ms, $p<0.01$). The validity effect was not significantly different between the 3 groups.
Conclusion: Epilepsy per se may have a deleterious effect on sustained attention and information processing speed. The results suggest the implication of different mechanisms regarding epilepsy type and a specific impairment of inhibitory processes in centro-temporal spikes epilepsy.

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Methylphenidate Therapy and its Effects on Epilepsy and EEG
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Purpose: Attention deficit disorder with or without hyperactivity causes social problems, especially in children with epilepsy who show manifold severe problems anyhow. Treatment with methylphenidate is often inevitable, but are there influences on EEG or even generation of seizures?
Methods: After baseline examination 38 children (33 boys, 5 girls; age 5½ to 12¾) were treated with methylphenidate (2x5 versus 2x10 mg/die, double blind, placebo controlled). Side effects were rare and could be reduced by dose reduction. Conners scales, Steinhausen questionnaire and other tests were done weekly, as well as EEG and seizure protocols. After 4 weeks and evaluation of the psychological testing it was confirmed in which week the child received methylphenidate or placebo and what dosage.
Results: 9 children with cryptogenic, 8 with symptomatic, 4 with idiopathic focal epilepsy, 10 with idiopathic generalised epilepsy (8 with absence seizures), 1 with unclassified epilepsy, 2 with pathologic EEGs but no epilepsy and 4 with normal EEG and no epilepsy were treated with methylphenidate. Except for 1 child, none had an increase of seizures; this 1 child was given alternative antiepileptic drugs without any increase of fits. The EEGs showed no significant changes; in 2 cases they were improved. A positive effect on behaviour and attention was seen in 27 children (71%), 11 showed no effect.
Conclusion: In our children with different types of epilepsy methylphenidate has no adverse side effects on EEG and seizure frequency, when epilepsy is well treated. There is no reason against methylphenidate therapy for children with epilepsy.

p375
Multi-disciplinary Coverage of ADHD (Attentional Deficit Hyperactivity Disorder) in an Institution for Children with Epilepsy
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Purpose: Often wrongly used, the term 'hyperactivity' goes back to a social condition which affects 3 to 5% of the school population of normal age. According to the criteria of DSM IV, the diagnosis of ADHD can be laid down when a child presents a motor unrest, a deficit of attentional components and an important impulsiveness. TAC attends to, in an educative boarding school, children with epilepsy who often have some social integration difficulties and more especially some school difficulties.
Methods: Between September 2003 and January 2005, 23 children out of 104 came to TAC with an epilepsy and concomitant ADHD. Children's problems were estimated on Conners' scale and through various cognitive tests (neuropsychological, language and

psychomotor developmental). 7 to 23 children are receiving methylphenidate therapy. 10 receive psychotherapy help and 18 are followed in rehabilitation. The rehabilitation includes some oral and written language rehabilitation and\or some relaxation, psychomotor therapy, work on the structuralization of tasks.
Results: We arrived at a new evaluation for 15 young people. The remaining 7 will be evaluated in 4 months. There is a reduction of observed symptoms in 14 children. Only one girl has no positive evolution.
Conclusion: The multi-disciplinary coverage improves ADHA symptoms. Young people are able to attend an adapted school and have a more normal social life. To continue the study, it would be interesting to investigate interactions between ADHA and epilepsy evolution.

p376
Electrical Status Epilepticus during Slow Sleep (ESES): An Important Cause of Childhood Dementia
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Purpose: The cognitive and behavioural outcomes of 22 children presenting with ESES were studied longitudinally within the Neuropsychology service at a tertiary paediatric neurosciences unit.
Methods: Participants were assessed using the WISC-III and WPPSI-R. Diagnoses reflected a broad spectrum of epileptic aetiologies including symptomatic as well as cryptogenic, focal, and idiopathic epilepsies of childhood. The majority showed a spike wave index over 85% of slow sleep. All children presented with significant clinical deterioration, including variants of motor, behavioural and cognitive regression.
Results: A statistically significant deterioration in full-scale IQ (Z=-2.037, p=0.042) and in performance IQ (Z=-2.155, p=0.031) was found over time (mean latency period=3.6 years). 7 children (32%) showed a decline of ≥1 standard deviation in full-scale IQ (mean IQ T1=86 (sd 15); mean IQ T2= 67 (sd 15)), therefore displaying a clinically and statistically significant decline in cognitive function (mean age T1= 5.6 years, sd=1.3 years; mean age T2=9.1 years, sd=2.9 years). From these 7, five had normal MRI findings. A further 14 children showed no clinically significant change in IQ, but demonstrated a range of developmental disturbances. 9 children (41%) had a learning disability and of these, 4 had an IQ within the severely disabled range.
Conclusion: Treatment response was found to be very poor in terms of preventing cognitive deterioration in middle to late childhood, an important developmental period. Around a third of the sample showed a significant and irreversible dementia over a relatively short time period. ESES is an important cause of childhood dementia with thus far, disappointing responses to treatment.

p377
Risk Factors of Neuropsychological Deterioration in Temporal Lobe Epilepsy
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Purpose: Epilepsy affects 1-2% of the whole population. Temporal lobe epilepsy (TE) represents one of the most frequent types of focal epilepsy. Neuropsychological disorders in TE are frequent and have a multifactor origin. This research was aimed at identifying some risk factors related to neuropsychological deterioration in patients suffering from TE.
Methods: A prospective and descriptive study was carried out on 207 patients with TE having a follow-up treatment at Abel Santamaría University Hospital during January 2000 - January 2005. A structured form to record information was applied which included demographic, clinical and paraclinical data as well as a complete neuropsychological assessment. Recorded information was stored in a data-base for further statistical analysis.
Results: Manifestations of neuropsychological deterioration were observed in 61.7% of patients. Temporal mesial sclerosis and disorders of cortical development were the most frequent aetiologies. Multivariate analysis of the age of epilepsy onset, high frequency of seizures, structural lesion presence, poor response to pharmacological treatment, necessity of polytherapy, atrophy of the hippocampus measured by means of IMR and the presence of low focal activity in electroencephalogram were associated with a worse neuropsychological deficiency. Disorders of verbal memory were most frequent when the origin of seizures were located in the left temporal lobe ($p<0.01$) and disorders of visual-space memory when the origin was the right temporal lobe ($p< 0.01$).
Conclusion: Definition of some risk factors related to neuropsychological deterioration in TE can play a very important role in selecting the candidates for a pre-surgical evaluation for surgery in epilepsy.

p378
Haptic Search: Sensitive to Subtle Parietal-lobe Lesions in Epilepsy?
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Purpose: High-resolution MRI has revealed previously unsuspected cortical lesions, often in parietal regions, in patients with epilepsy. Existing neuropsychological tests of parietal lobe function detect only gross lesions. We devised a haptic search task similar to stereognosis tests but designed to be more sensitive. It requires tactile discrimination among objects identical except for size. Past research suggests that this skill depends on the integrity of parietal cortex; thus our test should be a valuable diagnostic tool.
Methods: 120 healthy volunteers and 16 patients completed control tasks of manual dexterity, two point discrimination, and handedness. They were subsequently administered two tasks using wooden balls that increased or decreased in increments of 1/32 inches from the diameter of a reference ball (1¼ inches). The first task determined size discrimination thresholds. In the second, subjects located one target (odd ball) among other balls, all identical in size. Both tasks had bimanual and unimanual conditions.
Results: A hand-efficiency index for the bimanual search task produced a normal curve, with most healthy subjects showing no hand advantage, whereas the right hand showed a moderate advantage on the unimanual task. Patients tested thus far showed impairments on the contralateral hand, but with no primary sensory deficit, when focal lesions were in the parietal cortex.
Conclusion: Results from the healthy population indicate that this haptic search task has a viable design, and initial results with patients suggest that it is sensitive to damage in parietal regions. Large asymmetries on the bimanual search condition were rare in healthy subjects; therefore hand differences in patients should be meaningful.

p379
Tracking Cognitive Side Effects of Antiepileptic Drugs: EpiTrack
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Purpose: Achievement of maximum seizure control while preservation or even improvement of patient's cognitive capabilities is the major aim of epilepsy therapy. With EpiTrack, we introduce a screening tool for reliable detection and tracking of cognitive AED side effects. This screening tool comprises functions of attention and executive control.

Methods: The 15-minutes test comprises the TMT-A/TMT-B, a test of response inhibition, digit span backwards, word fluency, and a maze test. EpiTrack was standardised and validated in 220 healthy subjects (100 of them were tested twice) and in 184 patients with epilepsy.
Results: A scoring scheme was developed assigning subtest scores to a seven-point scale. Principal component analysis with Varimax rotation yields a two-factor solution (verbal/visuo-spatial) accounting for 63.8% of the total variance in controls, and a one-factor solution (54.7%) in patients. Criterion validity is indicated by significant correlations to global scores of attention (r=.85) and language (r=.67) in healthy subjects and patients. Correlation to a vocabulary intelligence score was .62. According to standardisation, only 2.7% of the controls in contrast to 48.4% were impaired. EpiTrack is sensitive with regard to actual seizure frequency (mainly CPS) and to the number of AED. It shows negative cognitive effects of VPA and TPM, but not of LEV, CBZ, or LTG in mono-/polytherapy.
Conclusion: EpiTrack is a promising 15-minutes screening tool for the detection and tracking of cognitive side effects of AED and seizures in patients with epilepsy. Future application will show its value in prospective studies on AED side effects.

p380
Comparative Clinical and Neuropsychological Analysis of Post-traumatic Epilepsy Patients Complicated and Non-complicated by Alcoholism
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Purpose: The main target of the study is evaluation of clinical features and higher psychic functions (HPF) in patients with post-traumatic epilepsy complicated and non-complicated by alcoholism.
Methods: The patients of two basic investigated groups; post-traumatic epilepsy (PTE) and post-traumatic epilepsy complicated by alcoholism (PTE-A) (each group included 65 patients) were compared to each other and to the control group, consisting of 85 patients with non-traumatic epilepsy (NE). We evaluated clinical features and the results of the study of HPF, using a standard set of diagnostic neuropsychological methods developed by St. Petersburg Bekhterev Psychoneurological Institute.
Results: Paroxysmal symptomatology did not have substantial differences in patients of two basic and control groups, with the exception of paroxysms of twilight conditions, registered in patients of PTE-A (40%), PTE (29%) and control group (17.6%) ($p<0.05$), as well as transient post-paroxysmal impairments of consciousness, fixed in 95.6% patients of PTE-A, 53.2% - PTE, 48.2% - NE ($p<0.001$). Neuropsychological methods revealed the prevalence of impairment of short-term memory of different modalities (visual, acoustic-vocal, sensor-motor and topographic). They had a primary character. Results obtained include the sign of underlying disease of mediabasal and medium cerebral structures. The disorders of HPF were less evident in cases of PTE, and the most evident in cases of PTE-A ($p<0.001$). The last group revealed a wider spectrum of neuropsychological impairments of HPF: dynamic and constructive praxis, visual and topographic gnosis, account operations and body-scheme, expressive and impressive speech. There is evidence of diffused impairment of cortical and under cortical structures of both cerebral hemispheres, with more involving the left one. Patients of NE occupied intermediate position by clinical features and heaviness of impairments of HPF.
Conclusion: Comparative neuropsychological investigation of the patients with PTE-A and PTE testifies to more significant impairment of mediabasal, medium cerebral and cortical structures in PTE-A patients. It means an unfavourable current of pathological process in these patients with greater frequency of twilight conditions and transient post-paroxysmal impairments of consciousness.

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Impact of Newly Diagnosed and Untreated Symptomatic/Cryptogenic Epilepsy on Cognition
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Purpose: Recent research indicates that the initial damage associated with chronic epilepsy might have a greater impact on cognition than a history of uncontrolled seizures. Therefore, cognitive impairment in newly diagnosed symptomatic/cryptogenic epilepsies was evaluated.
Methods: N=31 adolescent or adult patients (mean age 37 +/- 15 yrs, 42% female) with symptomatic/cryptogenic epilepsies were consecutively enrolled in this ongoing study. All patients underwent standardised neuropsychological testing of IQ, attention, language, and memory functions.
Results: MRI in 25 patients revealed 15 symptomatic and 10 cryptogenic epilepsies. Accordingly, 7 patients had temporal lobe and 8 patients extratemporal lobe lesions. Mean duration of seizure history was 2.5 yrs (0-11 yrs, median 15 months). 17% of the patients showed an IQ below 85; attention, language, verbal and numeracy memory was impaired in 36-48%. Only 26% of the patients were unimpaired. ANOVA showed a trend of poorer verbal memory in temporal lobe epilepsy. Relating performance to age, onset, and duration of epilepsy, poorer performance in psychomotor speed, mental flexibility, working memory, and verbal learning and memory was correlated with a later onset, older age, and a shorter duration of epilepsy.
Conclusion: 74% impaired patients confirm frequent cognitive impairment in untreated epilepsy. Except for IQ, a broad range of domains is affected. This pattern of impairment and the relation of worse performance to older age and a shorter interval since the first seizure indicate a minor role of the time of uncontrolled seizures for impairment. Follow-up evaluation will reveal the impact of seizure control and medication on cognition. This study was supported by Novartis Deutschland GmbH.

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Executive Functions in Patients with Temporal Lobe Epilepsy and Juvenile Myoclonic Epilepsy
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Purpose: Patients with temporal lobe epilepsy (TLE) due to mesial temporal sclerosis (MTS) frequently present memory alterations, while juvenile myoclonic epilepsy could interfere with executive functions. The aim of this study was to analyse executive functions and correlate the findings with the level of schooling.
Methods: Patients were evaluated through digit subtests (WMS-R) digits forward (DF) and digits backward (DB), Stroop I, II and III, and Trail Making A and B, in order to investigate immediate recall, working memory, attention, control of inhibition and mental flexibility.
Results: 24 patients had TLE related to right MTS and 22 to left MTS; 28 patients presented JME. Patients with JME had a greater level of schooling than those with TLE (32.1% and 17.3% with university level, respectively). Patients with right MTS benefited more from schooling than those with left MTS in the working memory performance (Digits DB: $p<0.01$), attention (Stroop I: $p<0.05$) and control of inhibition (Stroop II and III: $p<0.01$). Patients with JME showed better performance in immediate recall (7 digits DF) and working memory (5 digits DB) than patients with MTS (5 digits DF and 4 digits DB, respectively). Patients with university level in both groups performed better in all tests, mainly in Trail B, in which they took half the time of that taken by those with primary educational level to conclude the task.
Conclusion: Level of schooling plays an important role in executive functions. Patients with JME present better executive performance than those with TLE related to MTS.

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Selective Dysexecutive Impairment in a Case of Ring Chromosome 20
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Purpose: Ring chromosome 20 has been associated with epilepsy and mental retardation. However, this global cognitive impairment has been established on the basis of only IQ performances. Recent neurophysiological and functional neuroimaging studies have proposed a relevant role of fronto-subcortical circuits in this sort of epilepsy, so it might be possible to find a more focal neuropsychological profile similar to frontal lobe epilepsy.
Methods: In order to clarify these questions, we analysed the cognitive profile of a 21 year old woman with ring chromosome 20 (35% of lymphocytes studied) and epilepsy using a broad neuropsychological battery consisting of 30 different measures. Moreover, her results were also compared to a frontal lobe epilepsy group (n=10). The impairment cut-off for all the measures was 1.5 sd under the normal group's performance.
Results: The patient performed in the normal range at most of the neuropsychological tasks, but for the motor inhibition task (Go/Nogo) and the perseveration percentage on the Wisconsin Card Sorting Test, she was more than 4 sd under the normals. Compared with the frontal lobe group, the dysexecutive impairment was not so broad as in this group but it was more marked in the motor inhibition processes.
Conclusion: Ring chromosome 20 is not always associated to a general cognitive impairment, but to a more selective frontal-dysexecutive syndrome, with special dysfunction of motor inhibition processes. This result is in accordance to recent neurophysiological and PET studies showing the special involvement of the prefrontal cortex and basal ganglia circuits in this sort of epilepsy.

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Cognitive Functioning in Epilepsy Patients on Monotherapy
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Purpose: To analyse the pharmacological variable with epilepsy patients (EP) on monotherapy with different antiepileptic drugs (AED), comparing their cognitive functioning.
Methods: Cognitive functioning of EP can be altered by many factors such as aetiology, age of onset, duration of epilepsy, frequency of seizures, type of seizures and pharmacological treatment. Methodological difficulties in studying these variables altogether prevents revealing the real impact of each cognitive function factor. Our aim is to study if EP on monotherapy show cognitive problems, if there are differences in cognitive function depending on different AEDs and if cognitive output improves in relation to the therapeutic effect of AEDs. Patients in treatment with lamotrigine (7), oxcarbamazepine (4), topiramate (7) and sodium valproate (7), were assessed with a comprehensive neuropsychological battery that includes executive function skills, memory, attention and language, and were compared to a control group of patients (5) with a recent diagnosis of epilepsy and without pharmacological treatment.
Results: At this preliminary phase of the study we did not find statistically significant differences between groups. In a descriptive way, the most common cognitive problems observed in our sample are those concerning attention, verbal working memory, denomination, categorisation and planning. However, our aim is to increase the sample as well as repeat the neuropsychological assessment in six months in order to define different cognitive patterns more accurately.
Conclusion: Our study shows that epilepsy patients on monotherapy do not show cognitive dysfunction due to different AEDs.

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Neuropsychological Functioning During Non Convulsive Status Epilepticus in Ring Chromosome 20: Selective Impact on Cognitive Measures
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Purpose: Ring chromosome 20 (r20) epilepsy syndrome is a rare syndrome which manifests itself in childhood with slowing of previous unremarkable cognitive development after epilepsy onset. It is accompanied by prolonged, daily periods of non convulsive status epilepticus (NCSE). Purpose of the study was to detect the areas of impact of these periods of NCSE on neuropsychological measures and assess the assumed cognitive decline over years.
Methods: 2 young adults (both female, age 21 and 20) underwent serial neuropsychological evaluation during several days with concomitant EEG-video monitoring. Testing focused on executive measures (Card sorting test; Tower of London, Stroop interference), verbal measures (naming (BNT), Verbal Fluency), memory (auditory verbal learning test (AVLT)) and auditory and visual simple and complex reaction times (RT). Comparison of test results between NCSE and NCSE-free periods was accomplished by intraindividual profile analysis. Additional Wechsler intelligence test data were collected for long term follow- up.
Results: We found evidence for consistent, selective, transient impairment of cognitive functions during NCSE. Apart from a general slowing down, the most affected functions were verbal fluency, naming, list learning and dealing with novelty, whilst non-verbal executive measures and complex visual RT were preserved. NCSE initiating after normal list learning lead to impaired recall but not impaired recognition. Patient 1 shows significant fluctuations of IQ over a 10-year period but no evidence of mental deterioration, whereas patient 2 shows stagnation in cognitive functioning after epilepsy onset 12 years earlier.
Conclusion: EEG monitoring appears crucial in neuropsychological testing of patients with r20 and NCSE to detect spared and affected areas of functioning. The results are consistent with the left frontal lobe onset of the epileptic activity. Results find application in school and job counselling.

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Lexical Ambiguity in Epilepsy
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Purpose: Performance in tasks measuring lexical and syntactic ambiguity is impaired in surgically treated patients with temporal lobe epilepsy. It is currently unknown whether this deficit is observed in other groups of epilepsy patients. Our objective was to investigate whether interpretation of lexical ambiguity is impaired in patients with partial and generalised epilepsies.
Methods: 23 patients with generalised (7) and partial (16) epilepsies and 22 matched controls entered the study. The partial epilepsy group was further subdivided into temporal (13) and frontal (3) lobe subgroups. All subjects were given the ambiguous-Words-Test (AWT), a 45-item questionnaire measuring various linguistic aspects of lexical ambiguity, developed by the authors. It consists of a set of incomplete sentences. Subjects were asked to select the meaning of a target word, among three options, in order to form a meaningful sentence. One of the words had the correct meaning, according to the contextual information, the second one was semantically irrelevant (semantic error), and the third one was phonologically similar to the target word (phonological error).
Results: Patients with partial epilepsies produced a higher total number of phonological errors (2.64 ± 2.05) compared to patients with generalised epilepsy and the control group (0.8 ± 1.3 and 0.39 ± 0.58

respectively, p<0.05, ANOVA and Tukey post-test). In addition, patients with partial epilepsies produced fewer correct responses (11.7 out of 15) compared to controls and the generalised epilepsy group (13.7 and 13.2, respectively, p<0.05, ANOVA and Tukey post-test) when nouns were used as target words.
Conclusion: Interpretation of lexical ambiguity is impaired in partial epilepsy.

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Language Brain Dominance in Patients with Refractory Temporal Lobe Epilepsy: A Comparative Study Between Functional Magnetic Resonance Imaging and Dichotic Listening Test
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Purpose: Functional MRI (fMRI) has shown promise for demonstrating lateralisation of language in pre-surgical epilepsy patients. Previous studies found a strong correlation between Wada language scores and fMRI brain activation generated by verbal tasks. Also the dichotic listening test (DLT) has been employed to find lateralisation of language dominance. The purpose of this study was to identify brain dominance for language functions with the DLT and correlate these results with those obtained from fMRI in patients suffering from intractable temporal lobe epilepsy.
Methods: This study reports on 13 patients who underwent pre-surgical epileptic evaluation between April and October 2004 at the Epilepsy Surgery Program, Hospital Sao Lucas, PUCRS (PCE-HSL-PUCRS). In the DLT, dominance was assessed through a consonant-vowel task, whereas in fMRI they performed a verb generation task.
Results: Our results identified a correlation between the fMRI lateralisation index and the DLT ear predominance index and reply difference index (r=0.6, p=0.02; Pearson Correlation Coefficient), showing a positive correlation between results obtained from fMRI and DLT.
Conclusion: The DLT was found to significantly correlate with fMRI. These findings indicate that DLT (a non-invasive procedure) could be a useful tool to evaluate language brain dominance in pre-surgical epilepsy patients; cheaper and easier to perform than fMRI.

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Wada Test Items Useful for Determining Epileptogenic Focus in Japanese Patients with Temporal Lobe Epilepsy
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Purpose: To evaluate which test items in the Wada test (intra-carotid amytal test; IAP) are useful to determine the epileptogenic focus in temporal lobe epilepsy.
Methods: 18 medically intractable epilepsy patients with mesial temporal lobe epilepsy who are seizure free after a temporal lobectomy were included in the study. The epileptogenic focus was in the left in 8 patients and right in 10 patients. All the patients were native Japanese-speaking people. The Wada tests were performed as a part of the comprehensive pre-surgical evaluation including history, long-term video/EEG monitoring, MRI, SPECT, PET, and neuropsychological tests. The Wada test was performed with injecting the sodium amytal of 125mg in the internal carotid artery. Immediately after the injection, 16 test items were presented to the patients. The Wada test 16 items consists of four pictures, four kana nouns, four kana adjectives, two kanji and two designs. After the patients recovered from the anaesthesia, the recall test was conducted. One point was given when they recall the item correctly. The epileptogenic focus determining index (EFDI) was calculated as follows: points obtained during seizure side anaesthesia were divided by points obtained during contralateral anaesthesia. Thus, the higher score of the SFI indicates better sensitivity to determine the epileptogenic focus.
Results: The EFDI was 1.85 for design, 1.43 for kanji, 1.40 for picture, 1.39 for kana adjective and 1.15 for kana noun.
Conclusion: In the Japanese Wada test, test items of kanji-letters, designs and pictures have better sensitivity in determining the epileptogenic focus compared to the kana.

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Wada Test as an Indicator of the Prognosis of Memory Dysfunction after Anterior Temporal Lobectomy in Unilateral Temporal Lobe Epilepsy
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Purpose: The Wada test (WT) is based on the assumption that through temporarily inactivating one of the brain hemispheres, the post-surgery memory and deficit risks could be much better predicted. For this reason the WT has been used as part of the epilepsy pre-surgical assessment but its predictive value is still debated. The aim of this study was to review WT results compared to pre and post-surgery memory tests.
Methods: The study analysed the ability of the WT to predict memory deficits verifying which criteria best predicts post surgery memory deficits. 34 patients with unilateral temporal lobe epilepsy submitted to anterior temporal lobectomy (10 right and 24 left) were studied pre surgery and 6 month post surgery. The WT results for contralateral reserve, ipsilateral capacity and asymmetry were compared with pre and post surgery scores on Rey Auditory Verbal Learning Test and Rey Complex Figure Test.
Results: The WT results analysed through contralateral reserve, ipsilateral capacity, asymmetry and combined criteria were neither sensitive nor specific to predict the memory deficits in temporal lobe epilepsy patients.
Conclusion: The WT criteria for reserve and capacity were not able to predict memory decline after ATL of unilateral temporal lobe epilepsy.

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Short Term Memory Deficits are Accountable for Modality-specific Cognitive Impairments Following Hippocampal Asymmetry in Epilepsy Patients
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Purpose: To test whether the memory deficits often reported following temporal lobe epilepsy and hippocampal asymmetry are related to an encoding or a consolidation deficit.
Methods: 8 patients, aged between 9 and 19 years, who presented hippocampal atrophy (left 6, right 2) and seizure onset during childhood or adolescence (age at onset 2-18) were submitted to a battery of neuropsychological tests. These included IQ (WISC-IV or WAIS-III scales) and memory (CMS or WMS-III, CVLT and Rey complex figure) assessments. The IQ measurements were subdivided into their verbal, non-verbal, auditory and visual attention factors. The memory batteries were also divided in terms of their visual or verbal components.
Results: With relationship to their respective IQ, all children who presented a left hippocampal atrophy showed a significantly lower (p<0.05) working memory factor (assessing auditory attention). This auditory attention deficit was accompanied by lower scores in verbal comprehension (n=3) and verbal memory (n=2) in some patients. By contrast, patients who had a unilateral right hippocampal atrophy showed deficits in tasks assessing speed of visual processing and hence, visual attention. This deficit co-occurred with visual memory impairments in all patients.
Conclusion: The verbal or visual memory and cognitive deficits encountered in cases of unilateral hippocampal atrophy may be

tributary of the corresponding modality-specific attention (verbal or visual) limitations that prevent adequate encoding and processing of information.

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Utility of Visual Memory Tests in Assessing Epilepsy Patients
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Purpose: The assessment of verbal vs visual memory is a critical part of neuropsychological testing for epilepsy surgery candidates. The utility of visual memory tests has been questioned by some investigators because of the possibility that they may be verbally mediated by patients and not reflective of visual memory functioning. The current study compared performance on traditional neuropsychological measures of visual memory to results of memory assessment during the Wada procedure.
Methods: Neuropsychological tests and Wada results of 22 epilepsy surgery candidates were reviewed retrospectively. Performance on visual memory subtests from the Wechsler Memory Scale, 3rd edn (WMS-III) were compared to recognition scores from the Wada.
Results: WMS-III visual memory subtests were found to be significantly correlated with right hemisphere recognition scores from the Wada test. This was found for summary scores (visual immediate index score: $r=+.700$, $p<0.0001$) as well as for specific subtests (family pictures scaled score: $r=+.771$, $p<0.0001$; faces scaled score: $r=+.546$, $p<0.009$). Analysis of specific scores within the family pictures subtest indicated that the character scores ($r=+.566$, $p<0.006$) and activity scores ($r=+.625$, $p<0.002$) were also significantly correlated with Wada performance.
Conclusion: These results indicate that the WMS-III is a reliable measure of non-dominant memory. Concerns regarding the efficacy of nonverbal memory tests in the epilepsy population are not supported by the current results.

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Remote Memory in Temporal Lobe Epilepsy
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Purpose: Although anterograde memory deficits have been well documented in temporal lobe epilepsy patients, few studies have explored the effects of this pathology on memory for the past. This study aims at characterising remote memory in patients with temporal lobe epilepsy (TLE) and it considers the impact of some variables such as lateralisation of the lesion, duration of epilepsy, age of onset and seizure frequency on remote memory.
Methods: We examined the performance of 40 patients with unilateral TLE (14 right TLE and 25 left TLE) on eight remote memory tasks. Memory for personal events was assessed using the Autobiographical Memory Interview and the Modified Crovitz Test. Memory for public events was evaluated by means of the Dead/Alive Test, questions about famous events and photographs of famous faces and famous scenes.
Results: Both groups had impaired memory for personal and public events, regardless of the lateralisation of the epileptic focus. However, personal semantic memory was preserved relative to normal subjects. Duration of epilepsy, age of onset and seizure frequency influenced performance on the Modified Crovitz Test and the Dead/Alive Test.
Conclusion: The comprehensive neuropsychological study of 40 TLE patients showed that this neurological condition affects differently remote memory systems. We discuss the different factors that could account for this pattern of performance on the bases of the functional brain organisation of different memory systems.

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Mesial Temporal Sclerosis and Modality Specific Memory Deficits: Relevance for the Functional Organization of Memory Networks
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Purpose: Theoretically, a left hippocampal epileptic focus is associated with verbal memory deficit, while a right mesial focus is likely to disrupt visual memory. This lateralised model of episodic memory lacks confirmation by clinical studies as well as by recent data with fMRI. The aim of this study was to investigate whether memory deficits are dissociated in left (L) and right (R) mesial temporal sclerosis (MTS), using the Montreal Memory Test (MMT).
Methods: We carried out a prospective study including 23 patients with L-MTS, 24 with R-MTS and 33 matched controls. Assessment procedures included the MMT with evaluations of delayed-recall of abstract verbal and visual material at 24 and 48 hours.
Results: Mean and standard deviation (SD) of the verbal score at 24 h for L-MTS, R-MTS and controls were 3.4 (sd=2.3), 6.3 (sd=3.3) and 8 (sd=2.5) ($p<0.01$). For the same groups and time the scores for visual material were 5.4 (sd=2.5), 7.5 (sd=3.7) and 9.5 (sd=2.8) ($p<0.01$). Comparisons between controls and patients at 48 h revealed that the performance of left and right temporal patients was significantly poorer for both modalities ($p<0.001$), but both groups of patients were indistinguishable on the same measures.
Conclusion: This study indicates that there is no dissociation of memory deficits in MTS. According to our results, the left hippocampus is dominant for verbal and visual memory, while the right hippocampus seems to be important for consolidation of both memory modalities.

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On the Definition/Perception of Health in Focal Epilepsy
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Purpose: The aim of the present study was to clarify the relationship between health perception and some sociodemographic, clinical and neuropsychological variables in individuals with focal epilepsy.
Methods: A sample of n=75 Portuguese individuals (n=40 female), with mean age of 37.59 years (SD=12.32, 16-70) and focal epilepsy of mild severity, was assessed. The instruments used were: a sociodemographic and clinical questionnaire, the SF-36 (question 1 – current health perception), the Hospital Anxiety and Depression Scale (HADS) and a neuropsychological battery.
Results: 37 individuals considered their health 'fair'. Health perception was correlated with age ($r(75)=-.27$, $p=0.01$), education ($r(75)=.28$, $p=0.01$); memory (logical memory II: $r(69)=.24$, $p=0.03$, digit span: $r(71)=.27$, $p=0.01$), attention (attentive matrices: $r(71)=.43$, $p=0.000$), perception (Rey complex figure - type I: $r(61)=-.29$, $p=0.02$, - points I: $r(65)=.34$, $p=0.005$, - type II: $r(59)=-.28$, $p=0.03$, - points II: $r(64)=.38$, $p=0.002$), language (semantic fluency: $r(71)=.37$, $p=0.001$, token test: $r(67)=.28$, $p=0.01$), 'executive functions' (Wisconsin Card Sorting Test (WCST) - categories: $r(71)=.36$, $p=0.002$, - errors: $r(71)=-.34$, $p=0.004$, - Perseverative errors: $r(71)=-.30$, $p=0.01$); anxiety ($r(75)=-.50$, $p=0.000$), and depression ($r(75)=-.49$, $p=0.000$). There was no statistically significant correlation between health perception and disease onset, age at disease onset, Logical Memory I,

Corsi span, WCST non perseverative errors and percentage of perseverative errors.
Conclusion: These results suggest cognitive abilities, anxiety, and depression may have a central place in the personal definition of health. Consequently, individuals with mild focal epilepsy may consider themselves 'fairly' healthy essentially because some psychological aspects need to be improved. If replicated with samples balanced in clinical terms, these results can guide health promotion interventions.

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Role of Spirituality in Quality of Life of Patients with Partial Epilepsy
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Purpose: Recent scientific literature has shown an evolution of the concept of quality of life (QOL) towards a multidimensional, subjective, and dynamic perspective. In this framework, the complexity of unique personal qualities giving direction and meaning to human experiences, i.e. personal spirituality, deserves special attention. This study was thought to learn more about the role played by spirituality in QOL of people with partial epilepsy.
Methods: 30 adult patients with partial epilepsy of temporal lobe origin were evaluated after informed consent. All patients compiled self-evaluation inventories for QOL (WHO-QOL100), spirituality (WHO-Spiritual, Religious, and Personal Beliefs, SRPB), mood (Beck Depression Inventory, BDI; Stait-Trait Anxiety Inventory, STAI) and cognitive efficiency (Multiple Ability Self-Report Questionnaire, MASQ) and underwent neuropsychological testing.
Results: All patients willingly collaborated to the investigation. The total score of the WHO-QOL100 scale significantly correlated with the scores derived from mood scales (BDI and STAI: $p<0.001$), MASQ ($p=0.003$), and SRPB factors (hope and optimism: $p<0.001$; acceptance of life events: $p=0.001$; inner independence: $p=0.001$; peace: $p=0.002$; life meaning: $p=0.003$). Subsequent regression analysis revealed that the WHO-QOL100 total score was significantly predicted by trait anxiety ($p<0.001$) and acceptance of life ($p<0.001$).
Conclusion: These preliminary results suggest that spirituality plays an important role in QOL of epilepsy patients, interacting with cognitive self-efficacy and mood. Personal spirituality could contribute to enhance positive attitudes in coping with sudden and unforeseeable disturbances affecting epilepsy patients. The data support a reappraisal of QOL definition and encourage further studies on the subject.

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Cognitive Function and Quality of Life after Six Months Treatment with Levetiracetam (LEV)
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Purpose: Antiepileptic drugs (AED) have been shown to be one of the factors responsible for cognitive function impairment in epilepsy patients. The aim of this paper was to perform a follow-up study on patients treated with levetiracetam to evaluate possible changes in cognitive functions and quality of life after six months of treatment.
Methods: From a wide group of epilepsy patients, 28 (13 women, 15 male) participated in a prospective and open study. Patients were assessed with a complete neuropsychological battery which included measures of attention, memory, motor and frontal functions and a quality of life inventory. The first evaluation was performed before treatment was begun and three subsequent evaluations were made at one, three and six months of treatment. Patients received doses of 500 mg/day the first week, and reached 2000 mg/day by the end of the first month. This dosage then remained stable throughout the study period.
Results: A significant improvement was observed in prospective memory ($p<0.001$), working memory ($p=0.029$), motor function ($p=0.021$), verbal fluency ($p<0.001$), cognitive flexibility ($p=0.043$) and quality of life ($p=0.005$). The other cognitive functions showed no significant changes. After 6 months of treatment, 78% of patients showed a reduction in the number of crisis of over 50%, with a confidence interval of 95% between 59% and 92%.
Conclusion: Levetiracetam is a new AED that has an adequate crisis control, shows improvement in memory, attentional, motor and frontal functions and in quality of life. This study was partially financed by UCB Pharma.

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Behavioural Effects of Lamotrigine in Patients with Epilepsy
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Purpose: This study was conducted to assess emotional status, dominant personality changes and quality of life effects of lamotrigine (LTG) in patients with epilepsy.
Methods: Our series consisted of 33 patients, 15 male, 18 female, who were on monotherapy with LTG, mean age 31.84, mean educational level 12.44 (11 patients were previously eliminated because of speech language difficulties). In order to follow the topics we used Quality of Life in Epilepsy Inventory-89 (QUOLIE-89) and Profile Index of Emotion (PIE). The patients were tested before using LTG, and retested after 8 and after 16 weeks (LTG in regular therapeutic dosage). T-test was used to compare baseline performance with mean scores on first and second testing. Values of $p<0.05$ were considered statistically significant.
Results: Statistically significant improvements were found on all subscales on QUOLIE-89, except for physical function, pain, language and medication effects, on both controls. PIE show increased frequency degree > 25% on the following personality characteristics: sociability, open-hearted and precautious, 8 weeks after using LTG. Also, after 8 weeks, the following emotional states become more frequent (>25%): happiness, increased expectations, increased ability to adapt, higher self-confidence and willing to be socially accepted. At 16 weeks patients show no changes on PIE compared with 8 weeks.
Conclusion: The results suggested that LTG contributes towards improvement of quality of everyday living through higher frequency and intensity of positive emotions. The dilemma still remains whether these achievements are the result of improvement in seizure control, or direct results of the influence of LTG.

Monday 29th and Tuesday 30th August 2005
13:15 – 14:15
Poster Session
Epilepsy Surgery

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Characteristics of Initial Precipitating Injury in Pathologically Proven Mesial Temporal Sclerosis
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Purpose: Initial precipitating injuries (IPI) were studied retrospectively in 32 mesial temporal lobe epilepsy patients with pathologically proven hippocampal sclerosis.
Methods: 22 were left-sided MTS, 10 were right-sided. In 94% of the 32 patients there was an IPI history. IPI was febrile convulsion (FC) in 60% and non-FC in 40%. The non-FC group included birth trauma, head trauma, CNS infection and severe systemic infection.

Results: In the FC group left and right-sided MTS numbers were equal (50%). In non-FC group 83% of patients were left sided, whereas 17% were right-sided. Latent period (LP) was longer than 5 years in 83% of the FC group, and shorter than 5 years in 11%. In the non-FC group these values were 58% and 42%, respectively. IPI age was under 4 in 89% of the FC group and 83% in the non-FC group. In the FC group when IPI age was under 4, LP was more than 5 years in 81%, and less than 5 years in 19%. In the non-FC group when IPI age was under 4, LP was more than 5 years in 60%, and less than 5 years in 40%.
Conclusion: It is noteworthy that 94% of the MTS patients had an IPI history, mostly FC. Left hippocampus seemed to be involved more easily than right side. IPI age was mostly under 4 in both groups. In the FC group, the percentage of patients with longer LP was greater compared to the non-FC group. Finally when IPI age was under 4, LP was more than 5 years in both groups.

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Quantified Analysis of Wrist and Trunk Movements Differentiates between Hypermotor and Automotor Seizures
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Purpose: To evaluate the movement characteristics of hypermotor and automotor seizures based on an observer independent objective method.
Methods: We included video recorded automotor (n=10) and hypermotor seizures (n=10) of 17 patients, in whom the camera position was perpendicular to the trunk facing the camera in an upright position and wrist and trunk movements were continuously visible on the video recordings. The movements were quantified from the videos by analysing all video frames during the entire seizure (25/s). Seizure duration, relative wrist-trunk (absolute maximum and mean) speed, movement extent and predominant frequencies (power spectral analysis) of the movements were analysed (Wilcoxon rank sum test).
Results: Maximum relative wrist-trunk speed (median 902 vs. 223 pixel/s, $p<0.001$) and extent (median 45597 vs. 2304 pixel², $p<0.001$) of wrist movements were significantly faster and greater in hypermotor than in automotor seizures. Wrist movement extent separated all automotor from hypermotor seizures. Extent of trunk movement (median 4459 vs. 413pixel², $p<0.001$) and mean relative trunk-wrist speed (median 70 vs. 34 pixel/s, $p<0.2$) were significantly greater in hypermotor than in automotor seizures. The maximum relative wrist-trunk speed of wrist movements was above the lowest value in hypermotor seizures (553 pixel/s) in only one automotor seizure (585 pixel/s). Predominant repetition rate of automatisms in automotor seizures was at 1-2/s, but not present in hypermotor seizures. The duration of automotor seizures (median 81s) was longer than that of hypermotor seizures (median 34s) ($p<0.04$).
Conclusion: The quantitative analysis of wrist and trunk movements provides objective measures for the differentiation of hypermotor and automotor seizures.

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Quantitative Movement Analysis of Extent of Wrist Movements Identifies Hypermotor Seizures in a Non-selected Sample of Focal Epileptic Motor Seizures
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Purpose: To evaluate the sensitivity and specificity of a novel quantitative analysis of movements during epileptic seizures for the identification of different motor seizures.
Methods: We included 100 randomly selected videos of epileptic motor seizures of 60 patients, recorded in the epilepsy monitoring unit. Only videos were included where the camera position was perpendicular to the trunk facing the camera in an upright position and wrist and trunk movements were continuously visible on the video recordings. The movements were quantified from the videos by analysing all video frames during the entire seizure (25/s). Extent of trunk and wrist movement, speed (absolute maximum speed and mean speed) of relative wrist-trunk movements, and predominant frequencies (power spectral analysis) of the movements were analysed. Sensitivity and specificity of the quantitative parameters in the identification of hypermotor and automotor seizures were calculated.
Results: Minimum extent of wrist movement as defined by an earlier study on hypermotor seizures was used and identified objectively all hypermotor seizures (sensitivity 100%, specificity 70%). Extent of trunk movement misclassified only one hypermotor seizure (sensitivity 95%, specificity 80%). Absolute maximum speed of relative wrist-trunk movements identified 9 out of 14 hypermotor seizures (sensitivity 65%, specificity 94%). Mean relative wrist-trunk speed misclassified only one hypermotor seizure (sensitivity 95%, specificity 80%). Analysis of repetition rate had a low sensitivity (16%), but high specificity (100%) in detecting automotor seizures.
Conclusion: The observer independent quantitative analysis of ictal movements helps to objectively identify hypermotor seizures, a seizure type more likely to be generated outside the temporal lobes.

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Prognostic Value of Seizure Recurrence During the First Year After Anterior Temporal Lobectomy
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Purpose: Very little information is available regarding the long-term prognostic significance of seizure recurrence in the first-year after anterior temporal lobectomy (ATL). We set out to evaluate the significance of seizure recurrence during the first year after ATL in predicting long-term seizure outcome.
Methods: 243 patients who underwent ATL for refractory temporal lobe epilepsy and had a follow-up of >2 years were studied. In patients who had a seizure recurrence, we ascertained the timing of recurrence, provoked versus unprovoked, type of seizure(s), and number of seizures. We assessed the influence of these variables on seizure outcome at terminal follow-up.
Results: 98 patients (40%) had seizure recurrence in the first post-operative year. Patients with seizure recurrence during the first year had a less favourable long-term seizure outcome compared to those without seizure recurrence (29.6% vs 81.4%; P = <0001). Prognosis was better when the initial recurrent seizure was an aura compared to those with complex partial or generalised seizures (P = 0.034). The timing of the seizure recurrence and the presence of a precipitating factor did not influence the outcome. The terminal seizure outcome was no different between patients with more than and less than three seizures during the first year (excellent in 22.4% vs 38.5%; P = 0.07). Age at surgery, side of surgery and the histopathological findings did not predict the outcome.
Conclusion: Seizure recurrence during the first postoperative year irrespective of the timing, type, number and presence of precipitating factors predicts poor long-term seizure outcome.

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Clinical Characteristics of MTLE/HS Associated with Microscopic Malformation of Cortical Development in Temporal Pole
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Purpose: The purpose of the study was to correlate clinical characteristics with temporal pole histopathology findings in patients with mesiotemporal lobe epilepsy associated with hippocampal sclerosis (MTLE/HS).
Methods: Series of 38 patients, aged 9-51 years, with histopathological diagnosis of HS were included in the study. Patients with other MRI pathologies in the temporal lobe were excluded. Thorough medical history with special concern for initial precipitating injury (complicated febrile seizures, meningitis, encephalitis, perinatal hypoxia, trauma) was obtained. Semiology of seizures, results of non-invasive video-EEG monitoring and histopathological data were analysed retrospectively.
Results: Mean age of onset was 9 years, mean age at surgery 27 years. One half (19 patients) had histologically proven isolated HS (HS group), the other half had HS associated with malformation of cortical development (MCD) in temporopolar region (HS+ group). At least one of the risk factors was present in the history of 18/19 patients of HS group and in 10/19 of HS+ group only. Complicated febrile seizures were found in both groups with similar frequency, CNS infections significantly prevailed in HS group. Absence of aura and initial rhythmical theta in ictal EEG recording were found more often in HS group. Lateralisation of epileptogenic zone and side of subsequent surgery was in the left hemisphere in 16/19 patients of HS+ group while symmetrically distributed between both sides in HS group.
Conclusion: Dual pathology is common in patients with MTLE/HS. Absence of initial precipitating insult in a patient's history should point to possible MCD. Presence of such insult does not exclude the possibility of associated MCD.

p402
Clinico-Pathological Study of a Series of Patients with Intractable Epilepsy and Circumscribed Calcified Lesion in Amygdala
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Purpose: To identify clinical and pathological characteristics of patients with intractable temporal lobe epilepsy and circumscribed calcified lesion in amygdala on CT scan.
Methods: 14 patients with intractable partial epilepsy who had a circumscribed CT lesion in amygdala and underwent epilepsy surgery were investigated with respect to clinical course, EEG, seizure manifestation, MRI, pathological finding of surgically resected specimen and postoperative outcome.
Results: Onset age was under 5 years in 11 patients, and 10 had mental retardation. In addition to interictal focal EEG spikes, 8 had bilateral synchronised spikes and 4 had diffuse bilateral synchronised spikes. 9 patients showed seizure manifestations of temporal lobe origin and 5 had those mimicking frontal lobe origin. Surgically resected specimens showed microscopic features of tumorous lesion consisting of neuronal and glial cells. Mitoses were rarely encountered. Numerous calcospherites were observed in increased capillary vessels or in glial lesions consisting of fibrillary astrocyte. None had a specific glioneuronal element, which is a principal component of dysembryoplastic neutroepithelial tumour (DNT). In addition, 10 specimens showed hippocampal abnormalities such as dispersion of granule cells and abnormal laminar structure of CA1. 13 patients became completely free from seizures after temporal lobectomy.
Conclusion: We presented an unique group of patients who had a circumscribed calcified lesion in amygdala, which was similar but different from DNT, and severe partial epilepsy as well as cognitive disturbance.

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Astrogliosis and Apoptosis in Temporal Cortex, Hippocampus and Amygdala of Surgically Treated Temporal Lobe Patients
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Purpose: Cellular injury in temporal lobe epilepsy patients has been reported in sectors CA1 and CA4 of hippocampal pyramidal cells, dentate gyrus cells, temporal cortex and layer III of the entorhinal cortex. In the present study we evaluated cellular apoptosis, expression of caspase-activated DNA (CAD) and of heat shock protein 27 HSP27 as well as the astrocytic response in the temporal cortex, hippocampus and amygdala of 7 patients with mesial temporal lobe epilepsy (MTLE) and 7 non-epileptic control patients.
Methods: All patients were subjected to temporal lobectomy with amygdalohippocampectomy at the National Institute of Neurology and Neurosurgery.
Results: In MTLE patients our postoperative analysis of the temporal cortex showed apoptosis in 50% of cells, CAD expression in 55% of pyramidal cells and HSP27 expression in 60% of microglia cells compared to controls. In the hippocampus we found a reduced number of apoptotic cells (20%) as well as low CAD expression (18%). HSP27 immunoreactivity was registered in 10% of cells compared to the control group. In the amygdala we found apoptotic cells in only one specimen, and no CAD expression. However, we found HSP27 immunoreactivity in 80% of microglial cells. We observed dense fibrillar astrogliosis in cells of the cortex and hippocampus, but diminished astrocytic reaction in amygdala when compared to the control group specimens.
Conclusion: Our results suggest that apoptosis in the temporal cortex and hippocampus is a result of frequent electrographically determined seizures, whereas DNA fragmentation and HSP27 expression are markers for secondary damage and seizure induced stress.

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Oxidative Status as Predictors in the Outcome of Epilepsy Surgery
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Purpose: Oxidative stress has been recognised in the pathogenesis of epilepsy. Blood antioxidant status was also improved after treatment in epilepsy patients (Suhda k et al Clinica Chimica Acta 2001;303:19-24). Therefore, the purpose of this study was to investigate the role of oxidative stress in the prediction of the outcome of epilepsy surgery.
Methods: Brain specimens were obtained from 15 patients undergoing epilepsy surgery, including 5 males and 10 females, aged 8~65 year-old. Oxidative stress (ROS, reactive oxygen species; MDA malondialdehyde; Hcy, homo cysteine) and anti-oxidative enzymes (SOD, superoxide dismutase; GPX, glutathione) were determined in these specimens. Post-operative seizure frequency was documented for comparison with the antioxidative stress.
Results: Among these 15 patients, 9 patients had become seizure free after surgery. We found that the brain specimen of these seizure free patients had a lower ROS (7829±6017 vs. 9506±8473 RLU/mg tissue), MDA (6020±4269 vs. 12657±4212 μM/g tissue) and higher SOD (47286±21008 vs. 30954±18969 unit/mg protein), as compared to the non-seizure free patients.
Conclusion: Lower oxidative stress (ROS & MDA) and higher anti-oxidative stress (SOD) are the predictors for a better outcome of epilepsy surgery. We also suggest that the improvement of

antioxidative status may provide a better control for medically intractable seizures.

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Correlation Between Histopathological Findings and Post-operative Surgical Outcomes of Patients with Mesial Temporal Lobe Epilepsy
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Purpose: The aim of this study is to reveal any correlation between the histopathological findings and clinical outcomes in patients who had surgery for intractable mesial temporal lobe epilepsy (MTLE).
Methods: 18 patients (12 females and 6 males) aged between 15 to 45 years with clinically, electrophysiologically and radiologically proven MTLE have been included in the study. Age at seizure onset was 8 months to 18 years, the time passed until operation was 3 to 29 years.
Results: Hippocampal pathology was present in 13 patients with left and 5 patients in right. The histopathological examination results were mesial temporal sclerosis (MTS) in 7 patients, Ammon's horn sclerosis (AHS) in 5 patients, microdysgenesis in 2 patients, focal glioneuronal hamartia (GNH) in 1 patient, focal cortical dysplasia (FCD) ± C2 AHS in 2 patients, FCD+ diffuse GNH +Ammon's Horn Hypoplasia in 1 patient. Among them 2 patients' operations were ineffective and hippocampal tissue was not completely resected. The postoperative follow up period was 1 to 5 years. 10 patients were assessed as class I, 6 patients as class II, and 2 patients as class III according to the Engel Classification.
Conclusion: Seven patients' histopathological findings correlated with MTS and 5 patients with AHS had excellent outcomes; 9 patients among them were Engel class I, the other 3 patients were class II. Histopathologic findings related to FCD and GNH and ineffective surgical procedures showed a poor prognosis. There was no correlation between the patients' ages, the time passed until operation and post-operative outcomes.

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Prognostic Factors of Long-term Surgical Outcome for Mesial Temporal Lobe Epilepsy with Unilateral Hippocampal Atrophy on MRI
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Purpose: To identify the clinical and electroencephalographic factors which are independently predictive of a postoperative long-term outcome in mesial temporal lobe epilepsy with unilateral hippocampal atrophy on MRI.
Methods: We studied 51 consecutive operated patients who had more than 4 years of follow-up and had mesial temporal lobe epilepsy with unilateral hippocampal atrophy on MRI. The surgical outcome was classified as either seizure-free or not seizure-free in the first postoperative 2 years and the subsequent 2 years. Several clinical and scalp EEG variables were included. Variable factors were subjected to univariate analysis.
Results: Overall, 36 patients (71%) became seizure-free during the postoperative 4 years. On univariate analysis, only one factor was significantly associated with poor outcome ($p<0.05$): ictal scalp EEG propagation pattern such as bitemporal asynchrony or switch of lateralization. The seizure-free outcome was seen in 88.9% of patients without bitemporal asynchrony, or switch of lateralization, while only 54.5% of patients displayed those patterns ($p=0.007$) during the postoperative third and fourth year. However, those propagation patterns did not show the prognostic value during the first 2 years ($p=0.449$). Other variable factors were found not to be predictive of prognosis on early or late recurrence.
Conclusion: Bitemporal asynchrony or a switch of lateralization in the ictal scalp EEG might be a highly predictive factor for an undesirable surgical outcome, late recurrence of seizure during a follow-up period after anterior temporal lobectomy, and probably an index of bitemporal epileptogenicity in mesial temporal lobe epilepsy.

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Prognostic Factors for the Surgery of Neocortical Epilepsy: Multivariate Analysis
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Purpose: Determining prognostic factors of surgery for neocortical epilepsy is important for identifying ideal candidates and predicting the prognosis of individual patients. We tried to identify the prognostic factors of neocortical resection for neocortical epilepsy with univariate and multivariate analysis.
Methods: 193 neocortical epilepsy patients including 91 non-lesional cases were included in this study. There were 61 frontal lobe epilepsy (FLE), 80 neocortical temporal lobe epilepsy (nTLE), 21 parietal lobe epilepsy (PLE), and 22 occipital lobe epilepsy (OLE) patients. The primary outcome variable was patient status two years after surgery: seizure free or not. Clinical characteristics and recent diagnostic modalities were considered as prognostic factors. Univariate and standard multiple logistic regression analysis for outcome at two years after surgery were used.
Results: The seizure-free rate was 57.5% at two years after surgery. By the univariate analysis, concordant focal lesion on MRI, localised ictal EEG, other epilepsies than FLE, correct localised hypometabolism on FDG-PET, and other pathology findings than cortical dysplasia were significant for the postsurgical outcome. However, the multivariate analysis revealed that the presence of focal lesion on MRI ($p=0.003$), correct localised hypometabolism on FDG-PET ($p=0.007$), and localised ictal rhythms on EEG ($p=0.01$) were independent significant predictors of a good surgical outcome.
Conclusion: The presence of focal lesion on MRI, correct localised hypometabolism on FDG-PET, and localised ictal rhythms on EEG were good predictors for surgical outcome. These findings are helpful in selecting better candidates for neocortical epilepsy surgery.

p408
Outcome Subsequent to Initial Seizure Recurrence after Temporal Lobectomy
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Purpose: Outcome after temporal lobectomy often focuses on the initial seizure recurrence or period of remission. However, we know little about the relevance of these episodes to outcome in the following years. We aimed to examine outcome after a) the initial post-operative seizure recurrence or b) a period of post-operative remission.
Methods: Seizures < 28 days after surgery were discounted. Rather than individual seizures, we measured the months in which seizures occurred. Survival analysis was used.
Results: There were 190/325 patients who experienced a seizure. Mean follow-up was 9.8 years (±4.4). Amongst these patients there was a 76% (95% CI 59-82) probability of a further seizure 'month' within two years. Also at this time, there was a 65% (95% CI 58-72) probability of persistent epilepsy (a further two seizure months after recurrence) and 42% of patients had frequent seizures (>=3 in 12 months). At least one 2 year seizure remission occurred in 61 patients. Two years after remission, the probability of remaining in remission was 58% (95% CI 41-72). Some patients experienced lengthy periods between recurrences. The median remission time was 2.8 years (IR

2.25-3.8; range 2 to 8.7) for those who had a remission followed by seizures.
Conclusion: Patients who experience one seizure after surgery are very likely to experience another, and most will develop persistent epilepsy. Of those who attain seizure remission, 40% will relapse within 2 years. The lengthy but limited remissions have implications for classification of seizure outcome.

p409
Long-term Follow-up After Surgical Treatment for Refractory Temporal Lobe Epilepsy
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Purpose: To evaluate the long-term efficacy of surgical therapy in patients affected by drug-resistant lesional temporal lobe epilepsy.
Methods: 10 patients (age 1-32, mean 18) were evaluated; epilepsy onset was 6 months to18 years; disease duration was 1 to 20 years; drug insensitivity was formally stated. Presurgical study consisted of epileptological evaluation, video-EEG, MR imaging, CBF-SPECT and neuropsychology. Fits were: 7CPS, 1 infantile spasms and CPS, 1 psycho-affective, 1 polymorphic. Satisfactory anatomo-electro-clinical correlation was shown in all cases. Pathologies were: 5 dysplasia, 3 MTS, 1 DNET, 1 cavernous angioma. The delay between onset of epilepsy and surgery was 1 -15 years (mean 9). Intraoperative ECoG was performed to plan the cortectomy; depth electrode recordings were carried on into the amygdala and hippocampus. Surgery consisted of extended lesionectomy.
Results: None had surgical complications. 2 patients suffered from isolated seizures immediately after surgery. At follow-up (3-8 years), 8 patients were seizure free and drug free, 1 patient was seizure free but continued medical therapy, 1 patient had only sporadic fits (1B).
Conclusion: Surgical therapy should be indicated early in case of refractory lesional epilepsy. The time span before surgery is again too long and is determined by a prejudice towards this approach. Our data agree with the Guide Line from the Quality Standard Subcommittee of the American Academy of Neurology, that affirms: "Studies indicated that the benefits of anteromesial temporal lobe resection for disabling complex partial seizures are greater than continued treatment with antiepileptic drugs, and the risks are at least comparable."

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Drug Resistant Epilepsy and Focal Cortical Dysplasia: Long Term Outcome after Surgical Treatment
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Purpose: Studies of long term outcomes after epilepsy surgery of focal cortical dysplasia (FCD) are rare. In this retrospective study the authors report their experience with long term outcome after surgical treatment.
Methods: We retrospectively analysed the records of 49 patients (26 female, 23 male, mean age 25 ± 11 years) with FCD according to the new classification (Palimini) and clinical follow up after surgical treatment according to the International League Against Epilepsy (ILAE) Classification.
Results: A structural lesion was detected on presurgical MRI in 98% of cases and 57% had presurgical invasive EEG evaluation. The resected tissue was classified as FCD type IIb in 41 cases and FCD type IIa in 8 cases. Overall 78% were seizure free (ILAE 1A or 1) after a mean follow up of 7 ± 4 years. A year to year follow up was available in 40 cases. The rate of patients with successful outcome (ILAE 1A or 1) decreased from 73% to 60% during the first eight years of follow up. Demographic data, FCD localisation and surgical procedure had no influence on the year to year follow up. In cases with presurgical invasive EEG evaluation or FCD type IIa the rate of successful outcome decreased under 50% after six years of follow up.
Conclusion: Surgical treatment of epilepsy with focal cortical dysplasia has not only a successful short term result but also a satisfying long term outcome. Palmini A, et al. Terminology and classification of the cortical dysplasias. Neurology 2004; 62:2-8.

p411
Institutional Experience in One Hundred Surgically Treated Temporal Lobe Epilepsy Patients with a Follow-up of Over 2 years
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Purpose: It has been recognised that to lessen the medical, economical, and social burden for thousands of patients with intractable epilepsy, of which mesial temporal lobe epilepsy (MTLE) is the most refractory, surgical programs must be developed, regulated and institutionalised within comprehensive epilepsy programs. In Mexico, the Epilepsy Priority Program has recognised the need for regulatory measures and objective descriptions of actual practices. The aim of this study is to describe the results obtained during a two year follow up of the temporal epilepsy surgery program at the National Institute of Neurology and Neurosurgery.
Methods: All patients were subjected to standardised presurgical evaluation, including review of previous studies and medical history, neurophysiological studies, neuroimaging including interictal SPECT, neuropsychological and psychiatric evaluation, and amytal test in special cases. None of these cases required invasive evaluation. Electrocorticography and acute depth electrode implantation were carried out systematically to tailor surgical resections.
Results: The principal cause of MTLE was mesial sclerosis in 60% of patients; the most frequent surgical procedure was amygdalo-hippocampectomy and temporal lobectomy in 69.6% of cases. The mean time interval between onset of refractory epilepsy and surgery was 8 years. Among 100 patients, 84% are seizure free, 10% are classified as Engel II, and 6% did not improve. The mortality and morbidity rates were 0% and 2%, respectively.
Conclusion: Our results, comparable to internationally published series, show that surgical success is dependant on adequate candidate selection and complete resection of epileptogenic area. Temporal lobe surgery is a feasible, safe and effective approach to intractable MTLE, and should be thoroughly integrated within comprehensive epilepsy centres.

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Epilepsy Surgery in the Czech Republic
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Purpose: Epilepsy surgery has been introduced in three centres in the Czech Republic, each independent of the other. An analysis of the results in 248 adult patients (post-surgical follow up > two years) did not differ from the results achieved in countries with a longer tradition.
Methods: In this study, the results from two centres: Epilepsy Centre Brno and Epilepsy Centre Homolka, Prague, were compared. Homolka's team had been educated primarily in English-speaking countries; the Brno Centre was based on the model of a French school.
Results: Subdural recordings were dominant in Homolka (62%), while depth electrodes dominated in Brno (92%). Extratemporal epilepsies

were operated more frequently in Brno (36% vs 25%). The surgical results (Brno, n= 111, Homolka, n= 106 [Brno is listed first in each]): Engel I, II in 74.5 vs 77.3, Engel IV,V in 14.5 vs 8.6%. Complications: 5.8% vs 11% In temporal epilepsy, Engel I and II: 84% vs 90%, in extratemporal epilepsy: 58% vs 41%. Vagus nerve stimulation (Brno n=45, Homolka n=21): 50% seizure reduction in 63% vs 76%, complications in 0 vs 4.5%.
Conclusion: Two epilepsy surgery centres with different traditions and with different methodological approaches displayed similar surgical outcomes. The probable explanation is that each surgery centre has developed its own optimal strategy, including the selection of surgery candidates and the choice of technique. Despite several methodological differences, the surgical outcome in both centres is comparable with the long term outcome in large centres with long traditions of epilepsy surgery across the world.

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Epilepsy Surgery Programme at the University Hospital, Innsbruck: Procedures and Outcome
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Purpose: Surgery has become a valuable treatment option for the treatment of refractory focal epilepsies. We present the procedures and outcome of the Epilepsy Surgery Programme, Innsbruck, 1999-2004, from the Departments of Neurology and Neurosurgery at the University Hospital Innsbruck, Austria.
Methods: Patients (pt) were admitted to the intensive video-monitoring unit (1-13d). 21 pt had an invasive EEG recording (13 subdural depth electrodes, 9 foramen ovale electrodes). All patients had high-resolution MRT, F18-FDG-PET, interictal and ictal HMPAO-SPECT respectively. Patients had detailed neuropsychological testing and a WADA-test/fMRT for lateralisation of speech dominance, when feasible. Follow up was 1, 3, 6, 12 month postoperatively, then annually.
Results: 117 pt had surgery (60f, mean 40±11.4a; 98 TLE, 12 FLE, 5 PLE, 2 OLE). 63 pt had a selective amygdalohippocampectomy, 12 anterior temporal standard resection, 5 modified standard resection, 32 lesionectomy and 5 other resections. Histopathology showed in 44% hippocampus sclerosis, 15% vascular malformations, 17% gliosis, 9% dysplasias, 12% tumours (3% others). After a mean follow up of 2 years (N=91 FU>1a) 77% were seizure free during the previous year (=Wieser Class 1; 2% Cl. 2, 3% Cl. 3, 16% Cl. 4 and 1% Cl. 5). Complications resulted in an NIII/NIV paresis in 5 cases, a hemiparesis, aphasia, intracranial bleeding, and iatrogenic pneumothorax in 2 cases, postoperative psychosis, status epilepticus, pulmonal embolism in 1 case each.
Conclusion: Our results confirm that epilepsy surgery can achieve a favourable outcome in refractory epilepsy patients, holding little risk of complications. An interdisciplinary approach is the basis of a successful epilepsy program.

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Epilepsy Surgery with Non-invasive Recording
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Purpose: Temporal lobe epilepsy is the most common type of medically intractable epilepsy. It is reasonable and feasible to perform temporal lobectomy in patients with intractable epilepsy without invasive recording when strictly diagnostic criteria are used in presurgical evaluation.
Methods: Between October 1997 and October 2004, a total of 96 patients underwent resective surgery (temporal n=88 extratemporal 8) for medically intractable epilepsy at the Department of Neurosurgery, University of Damascus. There were 60 male and 36 female patients, ranging in age from 2 to 42 years (mean 19 years). All patients had medically intractable epilepsy lasting for a minimum of 1 year. For all patients, incomplete seizure control at maximal tolerable serum levels of at least two first-line anticonvulsant agents, had to be proven before they were referred for presurgical evaluation. Confirmation of epileptogenicity was done in all patients with interictal and/or ictal scalp EEG. MRI imaging studies revealed mesial temporal lesion (hippocampal sclerosis) with or without extrahippocampal structural lesion (neocortical lesion). The following surgical procedures were performed In the temporal lobe (n=88): anterior temporal lobectomy with hippocampectomy (n=82), anterior temporal lobectomy without hippocampectomy (n=6). Extratemporal resection (n=8) included frontal lobectomy, occipital lobectomy, functional hemispherectomy and parietal lesionectomy. In 58 patients (66%) histological examination of the resected tissue showed hippocampal sclerosis; in 38 patients different pathological patterns were found.
Results: At a mean follow up interval of 28.4 months, 83 patients (86%) have been seizure free since the operation (Engel`s classification I), 8 patients (8%) had no more than two seizures per year (Engel II), and 5 patients (5 %) showed a reduction in seizure frequency of at least 75% (Engel III). There was no operative and postoperative mortality. We noticed significant differences in seizure outcome with respect to the site of resection, e.g., temporal versus extratemporal. The most positive results were observed in patients with temporal resection: 94% were seizure free after resection.
Conclusion: In the majority of cases, the underlying pathology is mesial temporal sclerosis. Since the introduction of high-resolution MRI, which uncovers structural lesions in a high percentage of cases, no invasive recordings are required to perform temporal lobectomy in patients with intractable epilepsy who have structural imaging, suggesting unilateral temporal sclerosis, and concordant interictal and ictal surface EEG recordings and clinical findings .

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Temporal Lobe Surgery for Medically Intractable Complex Partial Seizures
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Purpose: The results and complications of the anterior temporal lobectomy/amygdalohippocampectomy (ATL/AH) and of the anterior temporal lobectomy/lesionectomy in patients with medically intractable complex partial seizures are presented.
Methods: 12 patients (7 male, 5 female) underwent noninvasive (video/scalp EEG, brain MRI, neuropsychological testing) evaluation. Mesial temporal sclerosis was diagnosed in 8 patients. 2 patients had an hippocampal-amygdala tumour (oligodendroglioma: n=1, astrocytoma grade II: n=1), 1 patient had a fusiform/parahippocampal gyrus ganglioglioma and 1 patient had a lateral temporal astrocytoma grade II. The patients' ages at operation ranged from 20-58 (mean 33) years. 11 patients underwent an ATL/AH with or without intraoperative electrocorticography. The patient with the lateral temporal astrocytoma underwent a tailored anterior temporal lobectomy/lesionectomy with intraoperative electrocorticography. The follow-up ranged from 1 to 36 (mean 17 months).
Results: At the latest follow-up visit of the ATL/AH patients, 5 are seizure-free (45%), 4 are significantly improved (>90% seizure frequency reduction) (36%), 1 has simple improvement (50-90% seizure frequency reduction) (9%), and 1 patient is unchanged (9%). According to the ILAE criteria, 5 patients are Engel class I (45%), 2 are Engel class II (18%), 2 are Engel class III (18%) and 2 patients are Engel class IV (18%). The patient with the lateral temporal astrocytoma is seizure-free. One patient (8%) developed postoperatively a contralateral distal foot pain compatible with a complex regional pain syndrome which resolved in 3 months.
Conclusion: The beneficial seizure outcome (seizure-free and significant improvement) is highly dependent on the accuracy of methods available for patient selection.

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Surgical Treatment of Multifocal Epilepsy Involving Eloquent Cortex
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Purpose: In 1989 Frank Morrell and co-workers published in Journal of Neurosurgery a new approach to the surgical treatment of focal epilepsy in patients who cannot be treated by resection, because their epileptogenic lesions were located in cortical territories controlling speech, movement, primary sensation, or memory. He called this technique 'multiple subpial transection' (MST). This report describes our initial follow-up for combined resective surgery and multiple subpial transection (MST) in patients with refractory, drug resistant epilepsy involving eloquent cortex areas.
Methods: Beside preoperative EEG with activation, CT, MR scanning and SPECT, a somatosensory evoked potentials test was performed to distinguish motor and sensory cortex in 26 cases. Intraoperative ECoG indicated in 22 cases one large epileptic focus which extended to motor, sensory or speech areas. In 7 cases there coexisted two or more independent foci, usually not connected with principal focal changes. This appearance was detected in one lobe. In the remaining 4 patients, in addition to resection procedure MST was performed in adjacent lobe (temporal+frontal in 2, temporal+parietal, occipital+parietal). MST alone was used in 6 cases and combined with classical resective surgery in 20 cases. MST was performed in 2 to 18 places in each patient.
Results: 2 patients were rejected from outcome assessment due to short period of observation. In the remaining, the follow-up ranged from 6 to 32 months. We report no mortality with minimal temporary morbidity; 3 patients had transient and mild motor or sensory deficit, and 2 patients suffered from moderate speech disturbances which disappeared within a few days. Outcome was assessed using a modified Engel's scale: Class I – 11, Class II – 7, Class III – 3, Class IV – 3 patients respectively.
Conclusion: Taking these results under consideration we stated that MST as a sole method or combined with cortical resection is helpful and promising in this specific and difficult group of epilepsy patients.

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Seizure Reoccurrence Originating in the Contralateral Cerebral Hemisphere after Hemispherectomy in Cases of Hemimegalencephaly
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Purpose: The purpose of this paper is to evaluate seizure outcome after a hemispherectomy, in special reference to seizures originating at the contralateral side of the operation.
Methods: The seizure outcome of the hemispherectomy was discussed in a case of our experience and in the literature.
Results: The case was a boy who had intractable seizures from the first day of life. Brain MRI revealed left sided hemimegalencephaly. The brain SPECT and the ictal EEG demonstrated that the seizures originated from the side of hemimegalencephaly. No seizure activity was found on the contralateral side. Seizures disappeared transiently after the operation but reoccurred from the contralateral side of the hemispherectomy a few months later. Even though there were no signs of epileptic focus in preoperative evaluation, there are some cases where epileptic activity becomes overt on the contralateral side after hemispherectomy, as found in our experience. A literature search identified 8 reports on 72 cases of hemimegalencephaly that received hemispherectomy. Among the 72 patients, 29 became seizure free, 32 achieved seizure reduction over 50%, but 11 showed no reduction of seizures. In some cases the patient had another cortical dysplasia in the hemisphere contralateral to the operated side, though some of them achieved seizure reduction by varying degrees.
Conclusion: It should be noted that there is a possibility of seizure recurrence from the cerebral hemisphere contralateral to the side of hemispherectomy. In addition, the presence of another cortical dysplasia on the contralateral side of hemimegalencephaly is not thought to be a contraindication of the operation.

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Hemispherectomies and Multilobar Resections: Data from the Swedish National Epilepsy Surgery Register 1990-1999
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Purpose: Hemispherectomy is a surgical procedure in children with intractable epilepsy and widespread unilateral aetiology. The seizure outcome is, in general, good. Subtotal hemispherectomy or extensive multilobar resection is sometimes an alternative, in order to preserve function. This is a comparison of the outcomes of these different approaches on a national basis.
Methods: The Swedish National Epilepsy Surgery Register includes data on all epilepsy surgery procedures in Sweden since 1990. All cases of hemispherectomies and multilobar resections 1990–1999 were analysed, as was seizure outcome at two years follow-up.
Results: Hemispherectomies or multilobar resections were performed in 52 patients: 19 hemispherectomies, 5 subtotal hemispherectomies and 28 multilobar resections. 37 were children or adolescents under 19 years, 15 were 19 years or older at operation. 63% in the hemispherectomy group were seizure-free at follow-up, and 16% had >75% reduction of seizures. Out of the 5 who had undergone subtotal hemispherectomies none were seizure free, 3 (60 %) had >75% reduction of seizures, 2 (40%) had no benefit. In the multilobar resection group 21% were seizure free and 14% had >75% reduction of seizures.
Conclusion: In the Swedish series 79% of the patients had a good seizure outcome after hemispherectomy. Subtotal hemispherectomy was a much less successful procedure and should be proceeded by a careful risk/benefit analysis whether hemispherectomy might not be considered a better alternative in selected cases. Multilobar resections in general resulted in poor seizure outcome, but may be the only possibility in some cases.

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Standardising Seizure and Developmental Outcome Measures Following Paediatric Epilepsy Surgery for a Prospective Patient Survey
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Purpose: The goals of epilepsy surgery in children are seizure control and optimisation of cognitive and psychiatric development. With the support of the ILAE Executive Committee and the Commissions on Neurosurgery and Paediatrics, the Paediatric Sub-commission for paediatric epilepsy surgery undertook the process to develop common outcome measures that have been validated in children, suitable for serial measurements, and can be applied at multiple centres for collaborative studies.
Methods: Members of an international working party met with collected data on existing measures of seizure outcome, cognitive outcome and quality of life. Discussion was undertaken and a consensus view reached.

Results: A revised Engel scale for documentation of seizure outcome that can be applied to resective and functional procedures has been proposed. With the wide age and developmental range, it was concluded that screening cognitive, behaviour and quality of life scales could only be used; it is proposed that prospective data collection use the Vineland, Child Behaviour Check list, Developmental Behaviour Checklist and Family Stress Index. A continuing working group has been identified to further evaluate standardising scores of cognitive outcome.
Conclusion: In order to move forward in determining the possible benefits of early surgery for epilepsy it will be important to collect standardised data from multiple centres. This can only be done effectively with a consensus view on measures to be used. A multicentre prospective study is planned using measures proposed here.

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Fibre Tracking of Optic Radiation in Vivo: Relation to the Temporal Horn of the Lateral Ventricle
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Purpose: To investigate optic radiation in the temporal lobe and its relation to the temporal horn of the lateral ventricle in vivo.
Methods: Diffusion-tensor MR imaging data was acquired using a Philips Intera 1.5T MR system (singleshot EPI, TE 76 ms, nearly isotropic 2mm voxels, 15 diffusion-sensitising gradient directions, b-factor 900 s/mm2, The Netherlands) from two healthy volunteers. Fibre tracking was performed using the DTI tool in PRIDE research software (Philips, the Netherlands). Regions of interest were set lateral to the lateral geniculate body. Distance between tip of the temporal horn of the lateral ventricle were calculated and compared with results from fibre dissection studies.
Results: Four temporal lobes were studied. The distances from the temporal pole to the tip of the temporal horn were 30, 34, 34 and 36 mm respectively (mean 33.5mm, SD 2.5mm). The distance between the tip of the temporal horn and the most anterior extent of the optic radiation was 34, 34, 34, and 40 mm respectively (mean 35.5mm, SD 3mm). In no case was the optic radiation anterior to the tip of the temporal horn of the lateral ventricle.
Conclusion: Fibre tracking can visualise fibres in optic radiation in the temporal lobe. Results are consistent with previous data from dissection studies. The most anterior point of the optic radiation is in close relation to the temporal horn of the lateral ventricle which is entered when performing a lateral temporal lobe resection or a selective amygdalohippocampectomy.

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Continuous Intraoperative Monitoring of Corticospinal Pathways in Drug-resistant Non-tumoural Frontal Epilepsy
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Purpose: To demonstrate the feasibility and safety of intraoperative continuous monitoring of corticospinal pathways during frontal resections for drug-resistant non-tumoural epilepsy under general anaesthesia. The possibility to define the central sulcus is of great help in the identification of the motor cortex, but injuries to the motor pathways may occur subcortically; therefore continuous monitoring of motor evoked responses is advisable.
Methods: 3 cases of frontal epilepsy were submitted to the resection of the epileptic focus with the assistance of intraoperative neurophysiological monitoring. The central sulcus was identified using the somatosensory phase reversal technique (stimulation of the contralateral median nerve and recording directly from the cortex through a strip multicontact electrode placed perpendicular to the expected central sulcus). The motor cortex was mapped and the corticospinal tracts continuously monitored. Motor potentials were evoked by direct cortical stimulation using trains of 3-5 stimuli, 0.5ms, ISI 4 ms, up to 20mA. Muscle responses were recorded from muscles of upper and lower extremities
Results: In all cases, central sulcus identification was possible through the N20-P20 phase reversal. Continuous motor monitoring was performed in all the patients; no change in muscle responses was detected throughout the operation. No motor deficit was present postoperatively. No complications were observed, particularly intra or post-operative seizures. The 3 patients are seizure free at a mean follow up of 2 years.
Conclusion: Our data confirm the importance of motor cortex mapping and corticospinal pathways continuous monitoring. Our technique is feasible under general anaesthesia, is reliable and safe for epilepsy patients

p422
Does Electrical Brain Stimulation during Stereoelectroencephalography Aid in Defining the Epileptogenic Zone?
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Purpose: To access the value of seizures triggered by direct electrical brain stimulation for defining the epileptogenic zone to be resected during epilepsy surgery in patients presenting with temporal lobe seizures (TLs) or frontal lobe seizures (FLs).
Methods: We reviewed data collected during stereoelectroencephalography (SEEG) in 49 patients with TLs and 22 patients with FLs considered as surgical candidates. For each patient electrically induced seizures (EIs) using biphasic and bipolar stimuli (single pulse or pulse trains) were compared to spontaneous seizures (Ss) recorded during SEEG sessions.
Results: Both fast electrical discharges or propagated after-discharges were considered as positive responses if associated with clinical signs. EIs were obtained in all patients with TLs (100%) but only 12 of 22 patients with FLs (55%). In TL epilepsy, rhinencephalic structures appeared more prone to generate EIs than the lateral temporal cortex. In FL epilepsy, stimulation proved more effective when applied to neurodevelopmental abnormalities (cortical dysplasia, DNET). The degree of concordance between EIs and Ss was globally similar in TLs (90%) and FLs (86%). However, the clinical pattern of EIs reproduced the whole sequence of spontaneous FLs in all except one patient whereas only one third of the EIs reproduced the complete semiology of spontaneous TLs.
Conclusion: These data confirm that electrical brain stimulation can reliably reproduce the patients' habitual seizures. It is therefore a valuable aid to identifying the epileptogenic zone (or network) involved in epileptogenesis and can improve the definition of the limits of the planned cortical resection.

p423
Electrocorticography in Tumour Surgery
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Purpose: Epilepsy is often the main symptom in tumour patients. Has electrocorticography (ECoG) during tumour surgery on these patients any impact on patient outcome regarding seizure frequency?
Methods: 106 patients aged 1 to 65 years (mean 31.9) were operated through 1993-2004 on the Hospital of Hvidovre and Rigshospitalet in Copenhagen, Denmark. Most patients had epilepsy for more than 6 months with seizure frequencies of more than 10 per month. Preresective ECoG revealed spike activity in approximately half the registrations. Complete resection of the lesion including the epileptogenic area (determined by ECoG) was intended. Postoperative follow-up at 3 months (vascular) and 1 year (tumour) after surgery.

The group where resection of the spike focus was possible was compared with the group without spikes or where the spike area was not resectable.
Results: The majority of the lesions were tumours mainly low-grade gliomas and vascular malformations most frequently involving the temporal lobe. There was no operative or postoperative mortality. Surgical intervention resulted in considerable improvement of seizure control. Two-thirds of patients were seizure-free or experienced reduction in seizure frequency. If resection of the epileptogenic area was possible a significantly better Engel score was obtained at follow-up ($p<0.05$).
Conclusion: This study shows that removal of the spike active zone leaves tumour patients with a better chance of reduction in seizure frequency in comparison with the group where spike resection was impossible or where no spikes were found. ECoG in tumour patients with epilepsy is worthwhile, removing the main symptom experienced by the patient.

p424
Proposal of an EEG Time Index Variation of Spikes (ETIVS) during Endoscopic Disconnection in Intractable Epilepsy Associated with Hypothalamic Hamartoma (HH).
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Purpose: Interest of EEG Neuromonitoring during endoscopic surgery for HH has not been documented. We propose an 'original' method to analyse the variation of EEG during time and discuss the opportunity to give an online 'EEG predictive value' (EPV) of post operative outcome.
Methods: One patient, 2 years old, suffering from intractable epilepsy with Gelastic crisis and a bad psychomotor deficit. Endoscopic surgery was proposed by a right approach for the disconnection of the left side of HH. On-line EEG recording was performed during surgery (Micromed ® (Italy) 32 channels, 512 Hz, HFF128 Hz -LFF1 Hz). EEG was visualised and analysed using monopolar, bipolar and averaged reference. Off line analysis was performed using linear and temporal techniques (wavelet and FFT) with EEmagine ® /ASA software (Germany) to calculate the number of discharges. EEG-time index variation of spikes was calculated and compared between hemispheres.
Results: 1791 spikes on the right Fp2 and 3177 spikes on the Fp1 during recording time (148 min) were observed. A statistical significance decrease of spikes (56% $p> 0.05$) during disconnection and a change of the EEG in term of reduction of spikes with an increase of small multi spike discharges during the disconnection. At 128 min (end of disconnection) we observed an increase of the total spikes number ($p> 0.05$).
Conclusion: We propose a neuromonitoring method during endoscopic surgery to analyse the on line variation EEG and discuss the opportunity to give an online 'EEG Predictive Value'. We expect that this approach may be a help in the comprehension of mechanisms in epilepsy network.

p425
Benefit and Risk of Invasive Presurgical EEG Monitoring with Multiple and Complex Intracranial Electrode Arrays
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Purpose: To evaluate the benefit and risk of complex invasive EEG monitoring with implanted electrodes in patients with refractory epilepsy.
Methods: 651 consecutive patients, who underwent electrode implantation for invasive EEG monitoring between 1990 and 2003 were reviewed. 120 complex electrode implantations were defined as: 1) 66 combinations of multiple subdural strip and grid electrodes; 2) 28 additional depth electrodes; 3) 7 combinations of grid and depth electrodes; 4) 16 multiple interhemispheric strip electrodes with or without other electrodes. 531 procedures with standard combinations of temporal depth- and strip electrodes, and implantation of single electrode types were excluded.
Results: Procedures were completely uneventful for 71 patients (59%). 15 patients (13%) had significant blood loss and anaemia. 23 patients (19%) showed minor morbidity, e.g. a small subdural haematoma on a grid electrode. 9 patients (7.5%) had temporary major morbidity after electrode implantation; most of them due to larger subdural grid haematomas, which required surgical intervention. 2 patients (1.7%) had persisting neurological deficits: one mild hemiparesis and one hemianopia. There were no deaths. In 13 patients no further epilepsy surgery was recommended: 3 patients (23%) improved gradually with new medication or vagus nerve stimulation. 107 of 120 patients (89%) were considered candidates for epilepsy surgery: 51 procedures (48%) were done in the frontal or fronto-central area: 23 patients had frontal lesionectomies only, 22 patients had lesionectomies plus multiple subpial transections (MST), while 6 had MST only. 34 procedures (32%) were mainly temporal: 24 lesionectomies, 8 lesionectomies plus MST and 2 MST only. 22 patients (20%) were operated in various other areas. 60 patients became seizure free (56% Engel I). 7 patients had rare seizures only (7% Engel II). 15 patients had a more than 75% improvement (14% Engel III), and 24 patients did not improve (22% Engel IV). Mean follow up was 35 months.
Conclusion: Complex invasive monitoring enabled or supported epilepsy surgery in 89% of patients in this series and 63% of those attained satisfactory seizure control. The risks of these diagnostic tools should be noticed, especially a significant rate of temporary morbidity. However, the rate of permanent morbidity was only 1.7%.

p426
Correlation of Simultaneously Recorded Scalp EEG And Magnetoencephalography (MEG) With Invasive EEG In Neurosurgical Candidates
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Purpose: Since an invasive pre-surgical evaluation increases the inherent risks of epilepsy surgery, an optimising non-invasive method has great importance. We evaluated the contribution of MEG and EEG individually and in combination with the pre-surgical localisation of epileptogenic zones, and compared it to the invasive method.
Methods: A 30-minute artefact-free segment of MEG data was analysed, using established methods, by blinded investigators. The MEG-EEG data were subsequently compared with the data obtained during the patient's standard pre-surgical evaluation, and with the invasive data obtained during invasive monitoring, and/or intra-operative electrocorticography.

Results: We have so far studied 6 of 30 planned patients: 3 with normal EEG, 1 suggestive of a left- and 2 of a right-sided focus. Video-EEG suggested a left temporal lobe (LTL) focus in 1 patient, left hemisphere (LH) vs. LTL in 1, LH in 1, right TL (RTL) in 2, and 'probable' RTL in 1. MEG and EEG were comparable in terms of localisation in 3 patients, and EEG alone better localised in 1 patient. Invasive data revealed seizure foci in the left superior temporal gyrus (1), right anterior TL (3), left mesial TL (1), and left neocortical temporal area (1). To date, 4 patients are seizure-free, 1 has only auras and 1 has fewer seizures.
Conclusion: MEG identified the ultimate focus in 1 of 3 patients with normal routine EEG. In the remaining 3 cases, MEG and EEG were similar in terms of final localisation. More data and further studies, including new conceptual and analytic approaches, are needed.

p427
Usefulness of Magnetoencephalography for Surgical Treatment of Patients with Neocortical Epilepsy
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Purpose: To clarify the utility of magnetoencephalography (MEG) for surgical treatment of patients with neocortical epilepsy (NE).
Methods: We investigated 39 patients (26 males and 13 females, aged 2 to 52 years, mean 24.2 years) who underwent cortical resection for medically intractable NE. Magnetic resonance (MR) images were abnormal in 28 (Group A) and normal in 11 (Group B). We evaluated the distribution and location of the equivalent current dipole (ECD) sources of interictal MEG discharges for cluster formation. MEG findings were compared to postsurgical seizure outcomes during the follow-up period of 12-53 months.
Results: MEG revealed a single ECD cluster in 26 and multiple clusters in 13 patients. The patients with a single cluster were 21 of 28 (75%) in Group A and were 5 of 11 (45%) in Group B. 23 (88%) of 26 patients with a single ECD cluster, especially 20 (95%) of 21 patients in Group A, had good seizure outcomes (Class I, II) ($p < 0.001$). In contrast, 11 (85%) of 13 patients with multiple ECD clusters had poor outcomes (Class III) regardless of Group A or B ($p < 0.0001$).
Conclusion: A single ECD cluster evaluated on MEG can predict a good seizure outcome for the patients with NE, especially with lesion(s). Conversely multiple ECD clusters predict poor outcomes after surgery. Therefore, MEG analyses make a great contribution to evaluate the patients with NE for surgical candidates.

p428
Fluoro Deoxy Glucose Positron Emission Tomography (FDG-PET) and Surgery for Epilepsy in the Temporal Lobe
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Purpose: FDG-PET is useful in seizure focus lateralisation, especially in temporal lobe epilepsy. Less obvious is the ability of FDG-PET to localise the seizure focus within the temporal lobe (namely, medial versus lateral temporal lobe epilepsy).
Methods: To evaluate FDG-PET to localise a seizure focus within the temporal lobe, we evaluated all patients with intractable temporal lobe epilepsy since 2000 who had FDG-PET performed during the presurgical evaluation in addition to pre- and postoperative MRI. Inclusion criteria included: no prior epilepsy surgery, no mass lesion, temporal lobe epilepsy based on EEG, MRI and semiology, no multiple subpial transection as part of the surgical procedure, and >1 year follow-up. Each subject's FDG-PET was coregistered with the pre- and postoperative MRI, and regions of interest (ROI) were defined on the MRI for the hippocampus, amygdala, lateral neocortex, and resection using iPlan (BrainLab, Munich). Analyses were performed for each subject including: ROI volumes were determined; FDG-PET activity was quantified for each ROI using ImageJ (National Institute of Mental Health, USA); an asymmetry index was calculated for homologous structures in each hemisphere and comparison of medial and lateral temporal structures.
Results: 13 subjects were seizure free after temporal lobe surgery. 6 subjects had recurrent seizures after surgery. A comparison of asymmetry indices determined for lateral versus medial temporal structures found a difference in activations that was close to reaching significance ($p < 0.1$).
Conclusion: FDG-PET may be useful in distinguishing mesial from neocortical temporal epilepsy focus in the presurgical patient with intractable temporal lobe epilepsy.

p429
Corresponding PET and MRI: Is there any Prognostic Value for Epilepsy Surgery Outcome?
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Purpose: There are insufficient data evaluating the prognostic value of corresponding PET and MRI findings for epilepsy surgery results. This research aimed to assess the prognostic value of corresponding or non-corresponding PET and MRI for epilepsy surgery outcome in patients operated on for temporal lobe epilepsy (TLE).
Methods: Documentation of 35 patients operated on for TLE between September 1999 and September 2002 with a lesion visualised on MRI, PET or both was reviewed, their Engel score was assessed more than 2 years post-surgery and correlated to MRI/PET results. All patients had convincing seizure semiology confirmed by ictal VEEG.
Results: 31 patients had selective amygdalohippocampectomy (AHKE), 4 had anteromesial temporal resection. The average post-operative evaluation time was 31.2 months. Correspondingly localising MRI and PET resulted in 77% Engel I, 19% Engel II, and only 4% worse; the average Engel score was 1.27. Non-corresponding MRI and PET resulted in 22% Engel I, 45% Engel II, and 33% Engel III-IV scores; the average score was 2.33. The difference is highly significant.
Conclusion: Corresponding MRI and PET findings predict excellent or very good epilepsy surgery outcome of limited resections (AHKE) in TLE. Non-corresponding findings predict a much worse outcome.

p430
Ictal SPECT Value in Presurgical Evaluation
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Purpose: To determine ictal SPECT value in a presurgical workup protocol of patients with focal epilepsy.
Methods: We selected 51 patients, suffering from focal epilepsy, that were subjected to MRI, video EEG and ictal SPECT in the last three years. In data analysis we considered concordance between video EEG and ictal SPECT whenever they pointed the same foci localisation/lateralisation. Ictal SPECT was considered useful when it was responsible for a change in the diagnostic/therapeutic strategy.
Results: 51 patients with mean age of 32.82 years old (7-59 y) were examined; 22 were male (43.13%). Mesial temporal sclerosis occurred in 29 patients (56.9%) and there was complete concordance among MRI/video EEG/ictal SPECT in 86.2%. MRI was negative in 13.7% (7 patients), and concordance between video EEG and ictal SPECT occurred in 42.9% patients in this group; in 70% of the patients ictal SPECT gave us new information regarding the epileptogenic focus localisation. In the group of 15 patients (24.9%) which had MRI with a lesion (excluding mesial temporal sclerosis) there was total concordance between the 3 exams in 80% of the cases.
Conclusion: In the mesial temporal sclerosis group of patients, ictal SPECT didn't change our clinical decision. In those patients with a negative MRI, the ictal SPECT was useful because it redirected our diagnostic workup. In the group of patients with a lesional MRI, ictal

SPECT wasn't responsible for a change in the diagnostic/therapeutic fluxogram.

p431
Methohexital or Amobarbital in the Wada Test: Implications for Determining Language Lateralisation
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Purpose: To compare the occurrence of paraphasia in Wada testing using sodium methohexital or sodium amobarbital.
Methods: Records from 30 adult patients were examined to determine the presence of paraphasic errors during Wada testing. 20 consecutive patients had undergone Wada testing with amobarbital whereas 10 consecutive patients had been tested with methohexital. Because of the brief duration of action in methohexital, all patients received at least two successive injections (3+2 mg). Both hemispheres were tested. During Wada testing, language is assessed immediately upon hemiplegia and until the patient has fully recovered (fluent language and no motor weakness). Language testing includes: counting, saying one's own name, comprehension, reading short words, naming objects, repeating words and sentences. Language representation is indicated by negative symptoms (speech arrest), preferably followed by positive signs (paraphasic errors).
Results: All except one patient assessed with amobarbital demonstrated positive signs of paraphasia during recovery (i.e. 5% had no paraphasia). One patient demonstrated paraphasic speech during injections in both hemispheres, suggesting bilateral language representation. Using methohexital, paraphasia could not be evoked in 7 out of 10 patients.
Conclusion: Paraphasic errors during Wada testing can be considered the least ambiguous evidence of cerebral language representation. The rare occurrence of paraphasia following injection with methohexital, possibly due to a briefer duration of action, may interfere with determination of language lateralisation. These results suggest differences associated with the two barbiturates that have not previously been reported.

p432
Refractory Seizures in Encephalopathy with Electrical Status Epileptical during Slow Sleep (ESES syndrome) and Hemispherotomy: Contribution of EEG
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Purpose: Prospective Study in a population of children with symptomatic ESES syndrome and refractory epilepsy and who were treated by hemispherotomy between 1997 to 2003.
Methods: Pre-surgical assessment included scalp video-EEG and complete neuropsychological testing in the pre- and post-operative course. The EEG analyses are presented.
Results: 11 children (9 M, 2F) aged from 5.4 to 11.2 years (mean age 7.4 years) with a hemispheric cortical malformation (polymicrogyria: 9, hemispheric porencephalic cyst: 2) presented with infantile cerebral hemiplegia. Seizures onset was between 8 months and 4 years (mean 1 year). Pre-operative EEG's demonstrated interictal foci of subcontinuous multifocal spike-and-waves over the affected hemisphere, diffusing to the contralateral hemisphere during sleep with the aspect of ESES at an average age of 4.6 years. This EEG pattern was correlated with a severe cognitive regression. Seizure types were clonic or tonic-clonic hemibody seizures contralateral to the affected cerebral hemisphere (N=6): EEG were characterised by a generalised low-voltage fast EEG rhythm. There were atypical absences (N=11), myoclonic seizures (N=6) and atonic falls (N=6): EEG exhibited generalised bilateral, synchronous spike-and-wave pattern. Seizures increased in frequency, resulting in frequent status epilepticus and were not controlled by benzodiazepine or corticosteroid therapy. In post-operative course, all children were seizure free; antiepileptic drugs were discontinued and cognitive function improved. EEG exhibited a normalisation of background activity over the non-operated hemisphere whereas persistence of pre-operative spike over the affected hemisphere continued.
Conclusion: Despite the generalised ictal EEG pattern, children presented with a clinical hemispheric syndrome and were successfully treated by hemispherotomy.

p433
Hemispherotomy in Refractory Epilepsy Associated with Hemispheric Cortical Cerebral Dysgenesis: Earlier is Better
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Purpose: Results of a retrospective study in a population of children born with hemispheric cortical dysgenesis (HCD) associated with refractory epilepsy (RE) and treated by hemispherotomy in our department in order to determine parameters influencing long-term outcome.
Methods: From 1990 to 2000, 83 children underwent hemispherotomy (vertical approach) and 30 of them (36%) presented HCD. Cognitive and social long-term outcome were evaluated in French-speaking children (N=22) by assessment of verbal developmental quotient (VDQ) measured by standardised scale and by the Vineland Adaptative Behavioural Scale (VABS). The pre-operative delay (Pre-D) was the time duration between the age at onset of seizure and at surgery and the post-operative Delay (Post-D) was the time duration between the age at surgery and at the last evaluation.
Results: Pre-D was correlated with VDQ, VABS and also with the side of hemispherotomy. Statistical difference was found with a negative correlation between Pre-D and global score of VABS for the hole population ($r = -0.58$, $p=0.006$) and between Pre-D and communication score of VABS ($r = -0.74$ $p=0.02$) for children with right hemispherotomy (N=9). A longer pre-D equated with a lower score. We classified the children according to the result of VDQ: Group1: VDQ>50 (N=5), Group 2: VDQ: 30 to 50 (N=10) and Group 3: untestable (N=7). Statistical differences were found ($p<0.05$) between group 1, 2 and 3 and the Pre-D which was respectively 0.6 (SD=0.4), 3.0 (SD=2.5) and 5.7 (SD=7.3).
Conclusion: Hemispherotomy has to be proposed as soon as possible after the onset of seizures.

p434
Psychiatric Disorders in Patients with Drug Resistance Medial Temporal Lobe Epilepsy Associated with Dysembryoplastic Neuro-epithelial Tumours and Improvement After Surgery
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Purpose: Interictal psychiatric disorders have been described in patients with medial temporal lobe epilepsy (TLE). We decided to evaluate the prevalence of psychiatric disorders in patients with temporal dysembryoplastic neuro-epithelial tumours (DNET) before and after epilepsy surgery.
Methods: We analysed the occurrence and the kind of psychiatric disorders in 13 consecutive patients with drug-resistant medial temporal lobe epilepsy symptomatic of DNET.
Results: 7 patients presented interictal psychiatric disorders, with according to the DSM IV: undifferentiated schizophrenia (1 case), 'border-line' personality (2 cases), intermittent explosive troubles (2 cases), unspecific psychiatric disorder caused by a general medical disease (1 case) and unspecified psychiatric disorder (1 case). 10 patients were operated. Psychiatric disorders disappeared in all except the subject with schizophrenia who had a decompensation three months after surgery. However, at five years follow-up after surgery, his mental condition has improved dramatically.

Conclusion: From the literature, the presence of 'alien-tissues' might represent a risk factor for psychiatric disorders in epilepsy patients but other factors like a temporal lobe epilepsy, a long duration, a drug resistance, psychosocial factors etc appear to be critical. Classically, severe psychiatric troubles contra-indicate epilepsy surgery. In our study, the prevalence of psychiatric disorders appears to be high in epilepsy patients with a temporal lobe DNET and a medial temporal lobe epilepsy. The improvement after surgery suggests that this therapy should be performed in these patients and severe psychiatric disorders do not contra-indicate this procedure.

p435
Medical, Social and Neuropsychological Predictors for Social Outcome of Epilepsy Surgery
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Purpose: Epilepsy surgery aims to improve the patients' independence and social relations. There is, however, a dearth of data in this domain (Thorbecke in Lüders, Epilepsy Surgery 2nd ed., 2001). We tried to predict independent living, social contacts and partnership postoperatively by social and neuropsychological variables.
Methods: Patients: 54 females and 64 males older than 16 years (x=35 years) who underwent TLR in the Bethel Epilepsy Surgery Program. Outcome: 68% Engel class I at the 2 years follow up. All patients got social and neuropsychological assessment before, 6 months respectively 2 years after surgery. Pre/post differences were assessed. Logistic regression methods were used to find predictors for changes.
Results: Changes were found in all examined variables: more patients lived independently postoperatively ($p=0.002$). There was a decrease in people who stated to have only a few or no friends ($p=0.004$) and to have no partner ($p<0.05$). Also the patients' subjective judgements concerning these social domains changed positively ($p<0.01$). In logistic regression analysis changes in the living situation were found to be influenced by the patients' economic situation preoperatively ($p=0.029$). Age was a significant factor to predict the postoperative frequency of social contacts ($p=0.021$). Having a partnership postoperatively could be predicted by having a partnership before the surgery ($p<0.001$) and by the seizure outcome ($p=0.038$).
Conclusion: Our findings suggest that epilepsy surgery entails positive changes in the social domain. Objective social variables and seizure outcome predict postsurgical improvements. Neuropsychological variables were not proved as relevant predictors.

p436
Long-term Follow-up in Epilepsy Surgery: Seizure Outcome and Socio-professional Adjustment
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Purpose: To analyse long-term surgical results in patients operated for drug-resistant partial epilepsy with respect to seizure and socio-professional outcome.
Methods: Between 1992 and 2004, 326 patients (149F, 177M, 5 to 56y old, median 30y) were operated in our centre for intractable epilepsy. Age at epilepsy onset ranged from 0 to 44y (median 10y) and epilepsy duration from 1 to 53y (median 18). Presurgical evaluation included EEG-video recordings, neuropsychological and psychiatric examination, MRI, PET and Wada test; stereo-EEG was performed in 168 cases (51%, 36% after 1996). Results after at least 2 years follow-up were compared to those at 5 years or more.
Results: Surgical resection was temporal in 256 cases (79%) and extra-temporal in 70. Hippocampal sclerosis (HS) was found in 42%, dysembryoplastic neuroepithelial tumours (DNT) or ganglioglioma in 22% and cortical dysplasias in 16%. Similar seizure-free (SF) outcome was found at >2 years (n=257, SF=76%) and at >5 years (n=116, SF=77%) after surgery. The best results were observed with temporal resections (SF=79%), HS (SF=84%), DNT (SF=73%) and focal cortical dysplasias (SF=100%) whereas multilobar resections and cryptogenic cases had less favourable outcomes (SF=66% and 61% respectively). Anti-epileptic drugs were stopped in 25% and decreased in 45% of patients. Five or more years after surgery, 77% of adults were socio-professionally integrated compared to only 41% before surgery. In addition, 16% had an improvement in working conditions.
Conclusion: Surgical results not only do not decline at > 5 years follow-up but socio-professional adjustment improves in half of the patients.

p437
Discontinuation of Antiepileptic Drugs Following Non-lesional Temporal Lobe Epilepsy Surgery
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Purpose: To determine in how many patients with excellent clinical outcome (Wieser class 1, 1a) following temporal lobe epilepsy (TLE) surgery it is possible to discontinue antiepileptic drug treatment.
Methods: We retrospectively analysed 66 patients (aged between 15 and 50 years) suffering from nonlesional intractable TLE operated in our Neurosurgery Department between 1991-2002. For final analysis complete data of 62 (94%) patients were available. The postoperative period lasted from 2 to 12 years, with 47 patients followed up for more than 5 years. The patients with excellent long term outcome (Wieser's class 1a and 1) were selected to determine how many of them could discontinue drug treatment. The main reason for continuation of antiepileptic drug treatment in seizure free patients is the patient's fear of seizure recurrence.
Results: Among selected patients 36 (58%) were either seizure free or had only auras (Wieser class 1 and 2) during a postoperative period ranging from 2-12 years. 24 (66%) of them are seizure free (Wieser 1a and 1) and among those, in 14 (58.3 %) cases it was possible to discontinue pharmacological treatment and at this moment seizures have not recurred.
Conclusion: In our opinion, in the majority of seizure free patients discontinuation of pharmacological treatment following nonlesional temporal lobe epilepsy is possible even after 2 years.

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Long-term Outcome of VNS Therapy for Patients with Refractory Epilepsy
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Purpose: A retrospective study evaluating the long-term outcome of VNS therapy for patients with intractable epilepsy.
Methods: The medical records of 31 patients implanted with VNS between 1998 and 2001 were reviewed. There were 15 males and 16 females. The age range was 14-62 years. Mean duration of epilepsy 26.7 years (range 8-54). Changes in seizures frequency and adverse effects of VNS were evaluated. Follow up was assessed at 6 months and 4 years.
Results: Out of the 31 patients, 1 patient died of an unrelated cause, and 4 patients asked that their devices be removed because of lack of efficacy and adverse effects such as hoarseness of voice, cough, and vomiting. In 4 patients seizures increased in frequency and severity. 22 patients showed significant improvement in seizure frequency (>50% reduction). 20 out of 22 patients showed early improvement within 6 months and 16 patients (74.7%) continued to have sustained improvement 4 years later. 6 patients (27.2%) developed transient side effects that were tolerable, 2 patients had hoarseness, 2 developed cough, 1 had pain at the generator site and another had transient dysphagia.
Conclusion: This study demonstrates that VNS is an effective and well-tolerated therapy. VNS has early and sustained improvement in seizure reduction.

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Evaluation of Daytime Vigilance Levels and Quality of Life in Subjects with Refractory Epilepsy Treated with Vagus Nerve Stimulation
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Purpose: To determine whether vagus nerve stimulation (VNS) has any effect on daytime vigilance and perceived sense of well-being.
Methods: Multiple Sleep Latency Test (MSLT) and Visual Reaction Times (VRT) were performed on 11 epilepsy patients before and during treatment with VNS. A group of sex- and age-matched healthy subjects represented the controls. In addition, a global evaluation of patient well-being was performed during a follow-up of 6 months.
Results: As expected, patients evaluated both at baseline and during VNS showed more sleepiness than controls with MSLT scores significantly shorter, and VRT latencies significantly longer. After 6 months of VNS, MSLT latencies in patients did not change significantly with respect to baseline. However, if the single patient treated with relatively high stimulus intensities (1.75 mA) was excluded, in order to consider separately patients treated with low stimulus intensities (? 1.5 mA), a significant effect of chronic VNS on MSLT could be observed. In fact, mean sleep latency (MSL) average across these subjects significantly improved from 9.8 ± 1.9 to 10.9 ± 1.8 minutes after 6 months of VNS ($p<.05$). Conversely, the only patient treated with high stimulus intensities showed increased sleepiness with MSL decreased from 14.4 to 9.8 minutes. On the other hand, VRT latencies did not significantly change during VNS. Patients considered as a whole had significant improvements on global evaluation scores of quality of life.
Conclusion: VNS at low stimulus intensities promotes daytime vigilance in adult epilepsy patients and has a positive effect on quality of life.

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Implantation of Vagus Nerve Electrodes and Stimulator
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Purpose: The surgical technique for the exposure of the vagus nerve is usually described as being similar to the exposure of the carotid bifurcation in the neck. To avoid some pitfalls we recommend a modified technique.
Methods: The medial border of the sternocleido should be exposed over a distance of approx 5-7 cm, starting 1 cm from the sterno-clavicular junction upward. A small triangle between the sternocleido, clavicle and sternothyroid muscle is thus exposed. In this triangle, both the carotid artery (medial) and the jugular vein (lateral) are present. The vagus nerve is sometimes visible too but in most cases it runs at a lower level between the two vessels. The superior and inferior cardiac ramifications of the vagus nerve have left the vagus trunk outside-and-above the exposed operation field: the trunk itself can therefore easily be freed and prepared to accept the electrodes. The course of the vagus nerve into the thorax can visually be checked. The generator is inserted underneath the pectoral muscle in the superior left chest region paramedially in such a way that the subcutaneous electrode runs parallel and as close as possible to the body axis to minimize traction on it when the head is moved.
Results: In our series of 41 children with therapy resistant epilepsy, we did not see any persistent side effects or any infections. Lead rupture or any other mechanical failure did not occur. Manipulation of the generator was no issue: its presence was hardly noticeable and therefore well tolerated.
Conclusion: The described surgical modifications may contribute to diminish the well documented (be it low) risks: asystole and or bradycardia during and after the operation, vocal cord paresis, torticollis, deterioration of obstructive pulmonary disease, diaphragm contractions, lead fractures etc.

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Vagus Nerve Stimulation in Patients with Medically Refractory Epilepsy: The Mexican Experience
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Purpose: Since the first vagal nerve stimulator for refractory epilepsy was implanted on 15 August 2001, we have performed and completed a 12 months follow up of 35 further cases. We describe the surgical risks and effects of VNS therapy on seizure reduction and improvement in quality of life (QoL).
Methods: Patients were subjected to standard presurgical evaluation, including high density 120-channel EEG, video-EEG, polysomnography, neuropsychological tests, MRI, CT, (SPECT in some cases). Implantation of a neurocybernetic prosthesis connected to the left cervical vagus nerve was done under general anaesthesia. Time interval between implantation and start of stimulation was fifteen days. Patients were followed up regularly to adjust stimulation parameters and record seizure characteristics and frequency, on-demand use of magnet, and assessment of QoL.
Results: All 36 operations were successful; adverse effects included transitory cough and voice changes. Healing of surgical wounds was unremarkable. Temporal paralysis of vocal cords occurred in 1 patient. One patient developed left sided jaw pain and another intractable headache, requiring the stimulator to be switched off. Seizure frequency showed a mean reduction of 55.65%, was increased in 2 patients and showed no change in 2 patients. 4 patients had an improvement of over 90%, 2 of them becoming seizure free. Mean reduction in seizure intensity was 64%. The postictal recovery period was reduced by 62.8%. Mood, memory, and alertness improved 59.7, 44.8 and 56.7%, respectively, over base line assessments.
Conclusion: VNS is a safe, feasible, and effective method to reduce seizure frequency and intensity, and improve QoL. We found the greatest benefit in patients with posttraumatic seizures and patients with bitemporal syndrome.

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Epilepsy Outcome Improved Following Responsive Neurostimulation Treatment
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Purpose: The Medical College of Georgia (MCG) is participating in a multicentre study to evaluate the safety and efficacy of a responsive neurostimulator system (RNS) for subjects with medically intractable partial onset seizures.
Methods: An investigational device exemption was obtained from the FDA and approval was secured from the MCG IRB. The first 4 subjects were open-label with subsequent patients blinded. Two physicians conducted the assessment and treatment protocols. During the three-month pre-implant period, the assessment physician (AP) monitored seizure type, rate, and severity. During the four-month period after implantation of the RNS, the subject was randomised to therapy ON or OFF and the subject and AP were blinded to treatment assignment. The treatment physician managed all RNS programming. The subject and AP were un-blinded at completion of the fourth month post-implant and the subjects followed in an open-label phase for twenty months.
Results: 6 subjects have been implanted at MCG and have reached the end of their evaluation period. 2 of 6 were blinded (1 ON and 1 OFF). No serious product related adverse effects were reported. One serious health event (a respiratory infection) was reported with the patient

recovering fully. At four months, 4 of 5 patients with therapy ON experienced 50% or more total seizure reduction.
Conclusion: Although preliminary results suggest that the RNS may improve epilepsy outcome, additional data will be needed to fully determine if the RNS is an effective epilepsy therapy. Funding supported by NeuroPace, Inc. Sunnyvale, California, USA

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Deep Brain Stimulation of the Subthalamic Nucleus for the Treatment of Refractory Epilepsy
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Purpose: To evaluate the effects of deep brain stimulation of the subthalamic nucleus (STN-DBS) for the treatment of refractory epilepsy.
Methods: From March 2003 to December 2004, we implanted STN-DBS in 9 patients with refractory epilepsy. All the patients were diagnosed with refractory epilepsy by 2 neurologists after 24-hours video-EEG, brain MRI, and nuclear medicine studies were performed. The stereotactic methods used to localise STN were based on MRI with the Leksell stereotactic system and the navigation system (BrainLABTM). DBS leads (Model 3389, DBSTM, Medtronic) were implanted to the bilateral subthalamus nuclei of each patient. The electric stimulators were implanted about 10 days later. After the surgical procedures were completed, we started the STN-DBS with the bipolar mode, a frequency of 130 Hz, pulse width of 60 μs, and voltage of 1 V immediately. In the following periods, all of the STN-DBS were programmed with the continuous bipolar mode but various electric amplitudes. The outcomes for the patients were analysed using a seizure diary and were presented with the Engel's classification.
Results: 7 patients were followed up for 12 months or more. Among them, 1 (14.3%) was seizure-free (Engel's class 1), 2 (28.6%) revealed rare disabling seizures (Engel's class 2), 2 (28.6%) showed meaningful improvement in seizure frequency (Engel's class 3), and 2 (28.6%) showed no change in seizure frequency (Engel's class 4).
Conclusion: STN-DBS is an option of surgical treatment for patients with refractory epilepsy.

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Frequent Occurrence of Malformations of the Cerebral Cortex Amongst Patients at the Danish Epilepsy Centre, Dianalund
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Purpose: Malformations of the cerebral cortex (MCC) are important causes of severe epilepsy and developmental delay in human beings. Advances in neuroimaging studies and genetics have revolutionised our understanding of these malformations, which has in turn enriched our knowledge of epileptogenesis. The aim of the present study was to ascertain the spectrum of epileptogenic MCC in a specialised epilepsy centre.
Methods: Patients with epilepsy and MCC diagnosed by MRI were identified from 2256 cases in the Danish Epilepsy Centre, Dianalund. The following data was assessed: age on epilepsy onset, seizure semiology, MCC, psychomotor development, EEG, family and medical history.
Results: 102 epilepsy patients were identified to have MCC based on MRI. 7 patients were diagnosed with pachygyria, 11 with polymicrogyria, 6 with lissencephaly, 4 with subcortical band heterotopia, 42 with cortical dysplasia, 18 with heterotopia, 11 with schizencephaly and 3 with hemimegalencephaly. 27.5% of the patients had generalised seizures, 25.3% had complex partial seizures and 47.2% had secondarily generalised seizures. Mean age of seizure onset was 6±8 years. The onset of epilepsy tended to be earlier in patients with widespread changes such as lissencephaly (3±2 months), compared to focal malformations like polymicrogyria (6.5±6 years) and heterotopia (13±11 years).
Conclusion: The study shows that 4.5% of the patients at the Danish Epilepsy Centre have epileptogenic MCC. However, since only 55% of the 2256 patients have had an MRI we expect 5-10% of all the patients to have MCC.

p445
Limbic Atrophy in Malformations of Cortical Development
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Purpose: Pathological and imaging studies suggest that structural abnormalities in malformations of cortical development (MCD) extend beyond the obvious lesion. Volumetric MRI of the hippocampus has shown atrophy in up to 20% of patients, mostly with heterotopia. Our purpose was to determine the occurrence of mesial temporal atrophy in the most frequent types of MCD.
Methods: Three mesial temporal structures (hippocampus, amygdala, entorhinal cortex) were segmented on high-resolution MRI in 71 adult patients (31 focal cortical dysplasia [FCD]; 20 heterotopia [HET]; 20 polymicrogyria [PMG]) and 48 sex and age matched controls. All patients had video-EEG telemetry.
Results: Based on normal controls' cut-off score of -2 standard deviation, at least one structure was atrophic in 49/71 (70%) patients. The proportion of mesial atrophy was no different among MCDs. The entorhinal cortex was the only atrophic structure in 29% (14/49), the hippocampus in 16% (8/49), the amygdala in 8% (4/49). The most frequent combination was atrophy of the hippocampus and entorhinal cortex (27%=13/48 patients). All three structures were atrophic in 6.2% (3/48). Mesial temporal atrophy was equally found in patients with temporal and those with extra-temporal epileptic foci (58% vs 76%, p=0.2). We found no association between side of mesial temporal atrophy and MCD.
Conclusion: Mesial temporal atrophy was found in 70% of MCD patients. Isolated entorhinal atrophy was the most common finding, followed by concomitant entorhinal-hippocampal atrophy. Atrophy was distributed equally among different groups, indicating that mesial temporal pathology occurs regardless of extent and location of MCD.

p446
Temporal Pole MRI Abnormalities in Epilepsy Patients with Hippocampal Sclerosis
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Purpose: Clinical significance of temporal pole MRI abnormalities in temporal lobe epilepsy patients with hippocampal sclerosis is still unclear. The aim of study was to correlate 'mild' MRI changes in the temporal pole with histopathological findings in this region.
Methods: Series of 35 patients with histopathologically proven hippocampal sclerosis were included in the study. Patients with overt MRI dual pathology in the temporal lobe were excluded, i.e. also patients with Taylor type cortical dysplasia (type IIA and IIB). Preoperative MRI scans were independently assessed by 3 observers. The following features were assessed as present or absent by each observer for each patient: atrophy of temporal pole, diffuse increase in T2 signal and grey-white matter demarcation loss in the temporal pole. Mean of ratings was calculated with range 0 to 3. Results were correlated with histopathological findings in the temporal pole with special respect to malformations of cortical development.
Results: MRI changes in the temporal pole (mean rating ł 2) predict presence of focal cortical dysplasia type IA or IB with high specificity

(90%). Normal MRI finding of the temporal pole (mean rating < 0.5) predicts absence of malformation of cortical development with lower specificity (78%). In nearly half of patients MRI finding was rated as equivocal and had no predictive value.
Conclusion: Temporal pole MRI abnormality is significantly correlated with histopathological finding of focal cortical dysplasia in patients with hippocampal sclerosis. Normal MRI appearance of temporal pole does not exclude this finding.

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3D Morphology of Focal Cortical Dysplasia and its Spatial Relationship with the Underlying Gyral-sulcal Structure: A Clue for Surgical Planning
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Purpose: Structural abnormalities revealed by MRI in patients with focal cortical dysplasia (FCD) represent gross histologic changes of a spectrum in which the extent of subtle peripheral histologic alterations cannot be demonstrated by MRI. This study aims to characterise the morphology and spatial relationship of MRI visible FCD in relation to the gyral-sulcal structure that harbours them.
Methods: FCD lesions of 15 patients investigated for partial seizures were manually labelled by an epilepsy-trained neuroradiologist, using a software that allows for navigation through orthogonal and curvilinear reformatted MRI images. The labelled images were rendered into 3D objects and subsequently analysed regarding morphology and their spatial relationship with the gyral-sulcal structure affected.
Results: The lesions were classified into superficial (involving the gyral crown), deep (involving the gyral fundi) and whole-gyrus (affecting the entire extent of an individual gyrus). Superficial lesions presented a more widespread distribution, whereas fundi lesions were positioned near the gyral walls, following its length. Overall, our results showed that FCD lesions have a tendency to distribute along a cone shaped region with its vertex pointed towards the nearby ventricular surface.
Conclusion: The results presented suggest an underlying pattern relative to the spatial distribution of MRI visible FCD lesions. Such cone-shaped configuration is in straight agreement with the embryologic mechanisms involved in cortical formation. Better characterisation of this spatial configuration may facilitate estimation of its MRI invisible component, improving surgical planning for seizure control.

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Preoperative Visualisation of Cortical Veins by 3D Reconstruction of Magnetic Resonance Images: Correlation with Intraoperative Findings
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Purpose: The topography of superficial cortical veins shows a high interindividual variation and brain pathology may cause additional displacement. The preservation of cortical veins is crucial for many neurosurgical procedures to avoid complications. We aimed to preoperatively visualise the exact anatomical localisation of the veins with regard to the lesion and the planned neurosurgical resections.
Methods: We included 23 patients in the study, where structural MRI was acquired with a slice thickness of 1.2 mm and an in plane resolution of 1.0 mm. Additionally contrast enhanced venous MR angiography (MRA) was recorded using 64 slices with 2mm thickness. Interactive image registration of both datasets was performed prior to 3D reconstruction of the combined dataset using volume rendering techniques. Digital intraoperative photographs were acquired and semitransparent superimposition of photographs and 3D reconstructions was used to evaluate the quality of preoperative reconstructions.
Results: Preoperative 3D image processing correctly visualised 78.2% of the surgically relevant veins. Intraoperatively documented veins were missed in 11.7% by the 3D images. False positive findings in 3D images occurred in 4.5% and in 2.2% arterial vessels were mistaken as veins.
Conclusion: The preoperative visualisation of cortical veins by 3D reconstruction of MRI and MRA is an accurate and reliable method, which helps to plan and modify cortical resections. Therefore, it has become an integral part of our epilepsy surgery program.

p449
Presenting a System for Semi-automatic Segmentation (NeuroLine) for MRI Volumetric Studies
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Purpose: To develop a software to segment anatomic structures and lesions in magnetic resonance images. The system was conceived for segmentation of any anatomic region and/or lesion segmentation in images from different modalities. It was validated and is being used for MRI volumetry in patients with epilepsy.
Methods: NeuroLine segmentation is based in the Watershed transformation with markers. This method automatically obtains region contours considering for each point both grey level and its distance to the markers provided by the user. The software was developed using both C language and TclTk tools. It supports images in Dicom format. For validation studies we segmented images from 40 patients and 30 healthy volunteers and performed intra-operator and inter-operator analysis.
Results: The main NeuroLine resources comprehend tools for drawing and edition of markers, integration of manual, semi-automatic and automatic segmentation, tridimensional segmentation, visualisation tools and measurements of segmented regions (area and volume). In the validation we found a good correlation between measurements performed by the same examiner using the proposed method and a manual segmentation method. To evaluate the reproducibility, we compared the results obtained by two examiners and, in addition, a second segmentation was performed by the same operator in the same set of images.
Conclusion: The software developed in this work presented sufficient results for repeatability and reduction of human interaction for the segmentation task. It has being used in the practice for volumetry in various current studies in epilepsy. Acknowledgments: to Fapesp (The State of São Paulo Research Foundation).

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Multi-modal MRI of Epilepsy Patients with Secondarily Generalised Seizures
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Purpose: For those patients with partial epilepsy who frequently experience secondary generalised seizures (SGS), neuropsychological evaluation generally reveals a modest to severe decline in cognitive abilities. To investigate whether SGS are associated with microstructural or metabolic changes of the brain, a cross-sectional pilot study was performed, using several MRI techniques (MR spectroscopic imaging (MRSI), T2, and diffusion weighted imaging (DWI)).
Methods: 11 healthy subjects (41±15 years) and 11 epilepsy patients with SGS (ranging from <5 to >100 seizures, various primary foci, 33±13 years) were included for MRI at 1.5T. Metabolite ratios NAA/Cr and fractional cerebrospinal fluid (CSF) maps were derived

from the MRSI and T2 weighted images, respectively. Histogram analysis was performed on the diffusion maps, calculated from the DWI experiment. Statistical significance was set to $p<0.05$.
Results: The NAA/Cr ratio in the left frontal lobe, and left and right temporal lobe is significantly lower (26%) in the patient group. CSF-fractions were significantly higher (81%) for the patients in all frontal areas, as well as in the left hemisphere. The peak height of the apparent diffusion coefficient (ADC)-histogram was lower (12%, significantly in left frontal lobe) in the patient group.
Conclusion: The increase in ADC and CSF-fractions, and also the decrease in NAA/Cr ratio, particularly in the frontal lobe, may explain the potential cognitive problems occurring in these patients in terms of neuronal damage. However, the location of the primary focus might play a role and further research is needed in order to analyse the supposed relation of cognitive decline to MRI abnormalities.

p451
Identifying the Affected Hemisphere by 1H-MR Spectroscopy in Patients with Temporal Lobe Epilepsy and No Pathological Findings in High Resolution MRI
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Purpose: Up to 30% of patients with temporal lobe epilepsy (TLE) remain without remarkable changes in MR imaging (MRI). In this study we investigated the role of 1H-MR spectroscopy (1H-MRS) in lateralizing the affected hemisphere in the mentioned patient group.
Methods: 22 consecutive patients diagnosed with TLE were investigated by high resolution MRI and 1H-MRS. We examined the incidence and diagnostic accuracy of temporal metabolite alterations determined by LCModel via water reference. Metabolite values of each hemisphere of TLE patients were compared to healthy controls. Results of metabolite alterations were related to intensive Video EEG focus localisation.
Results: Reduction of tNAA in the affected hemisphere revealed the highest sensitivity (63%) at a specificity of 96%, followed by increased Cho levels (sensitivity: 60%; specificity: 98%) in intraindividual analysis. Group comparison revealed a significant reduction of tNAA (6.1±0.8)* in the involved temporal lobe compared to controls (6.67±0.4)* ($p=0.026$). Cho levels were significantly increased in the affected hemisphere (1.42±0.17)* compared to healthy controls (1.22±0.17)* ($p=0.035$). [* Concentrations in institutional units]
Conclusion: The results of our study show that 1H-MRS is able to assess the affected hemisphere of MRI negative TLE patients in terms of metabolic alterations.

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1H MR Spectroscopy in Patients with MRI-negative Extratemporal Focal Epilepsy: Correlation with Subdural Electrode Mapping and Histopathological Findings
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Purpose: Proton magnetic resonance spectroscopy (1H MRS) has proved to have a significant value in lateralisation of the epileptogenic zone in temporal lobe epilepsy. However, its role in diagnostics of extratemporal and especially MRI-negative epilepsy has not been established. In the current study we aimed to verify the hypothesis that 1H MRS could help in the localisation of epileptic focus in patients with extratemporal focal epilepsy and normal MRI findings.
Methods: 4 females and 4 males aged from 8 to 24 years with refractory focal epilepsy were studied on a 1.5-T Siemens MR magnetom-vision imager. All had repeated normal MRI studies with a protocol for patients with epilepsy. 1H MRS examination using 2D chemical shift imaging – CSI sequence in transversal plane was directed to the estimated epileptogenic zone localised by the seizure semiology, scalp video/EEG, ictal 99mTc-ECD SPECT and 18FDG-PET. 1H MRS spectra were evaluated using the program CULICH.
Results: All patients had lateralised 1H MRS abnormality and 5 of them had a clearly localised pathology. 1H MRS findings were heterogenous; the most frequent ones were decreased N-acetylaspartate concentrations. We found a good correlation of the localisation of 1H MRS abnormality and the hyperperfusion zone in ictal SPECT as well as with ictal onset zone in subdural electrodes mapping. In 7 of the 8 cases, histopathological analysis revealed MRI-undetected cortical dysplasia.
Conclusion: 1H MRS is more sensitive for discrete malformations of cortical development than conventional MRI. It can be valuable in the presurgical evaluation of epilepsy surgery candidates without apparent MRI lesion. Supported by Grant GAČR No. 309/02/D076, IGA NF 7411-3 and Research Projects No. 00000064203, 111300003 and 111300004.

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Disease Progression in Mesial Temporal Lobe Epilepsy: Evidence from 1H-Magnetic Resonance Spectroscopy
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Purpose: There is controversial discussion whether chronic pharmacoresistant temporal lobe epilepsy (TLE) is a progressive disorder accompanied by mental deterioration. Both memory performance (1) and cerebral NAA (N-acetyl-aspartate) concentrations (2) significantly decrease with age in healthy controls. It was the aim of this study to investigate differential effects of ageing on NAA concentrations in the lateral temporal lobes (TL) of patients with pharmacoresistant mesial TLE (mTLE) and healthy controls.
Methods: We cross-sectionally studied 12 patients with pharmacoresistant mTLE (7 right sided, 5 left sided) and 22 healthy controls who participated in a single voxel 1H-magnetic-resonance-spectroscopy study of TLE. Subjects were investigated on a 3 Tesla

Bruker Medspec 30/80 scanner using a STEAM-protocol (TE/TM/TR=20/30/2500ms). 2x2x2 cm3 voxels were positioned bilaterally in the lateral temporal lobes (TL). Spectra were processed with LCModel.
Results: Analyses of pooled (ipsi- + contralateral) voxels in the lateral TL: In mTLE patients the concentration of NAA was significantly (negatively) correlated with age (p=0.001, r=-0.655). In healthy controls the concentration of NAA was also negatively correlated with age but to a lesser extent (p=0.034, r=-0.327; difference between regressions: p=0.059).
Conclusion: A stronger correlation of NAA with age in mTLE patients would be consistent with accelerated ageing in mTLE patients or with disease progression with age. Although neuropsychological parameters were not analysed in this study our results somewhat contradict the study of Helmstaedter et al, who found the same age regression of memory in mTLE patients and healthy controls (2). Correlation analyses of NAA with neuropsychological measures in our patient group are under way. Longitudinal studies of NAA concentrations in mTLE patients should be performed. 1.Helmstaedter C, Lancet 1999, 354: 2133-2134. 2.Brooks JCW et al, Cerebral Cortex 2001, 11:598-605.

p454
Evaluation of Water Diffusion in Limbric White Matter Tracts in Epilepsy Patients without Mesial Temporal Sclerosis
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Purpose: Diffusion tensor magnetic resonance imaging (DTI) indirectly evaluates the axonal integrity of white matter. It also forms the basis for three-dimensional reconstruction of fibres using tractography. In a previous study we demonstrated bilateral symmetrical diffusion abnormalities (reduced fractional anisotropy, FA) in the fornix and cingulum of patients with temporal lobe epilepsy (TLE) and unilateral mesial temporal sclerosis (MTS) (Concha L, et al., 2005. Ann. Neurol. 57;188-96). Our present objective was to determine if these abnormalities exist in other forms of epilepsy.
Methods: 5 patients with primary generalised epilepsy, 5 patients with non-lesional TLE (nl-TLE), and 9 age matched controls, were scanned using a 1.5T MRI scanner. DTI was performed and the fornix and cingulum in each hemisphere were depicted using tractography. Water diffusion anisotropy was measured in these two limbic white matter tracts.
Results: The control group had a mean FA value of 0.53±0.02 for the fornix and 0.50±0.03 for the cingulum. The primary generalised epilepsy group showed no statistically significant difference from the control group for the fornix (mean FA: 0.50±0.03, p=0.08) and cingulum (mean FA: 0.49±0.03, p=0.33). For the nl-TLE group, no significant difference was observed from controls for either structure (mean FA fornix: 0.51±0.02, p=0.08; mean FA cingulum: 0.47±0.04, p=0.09).
Conclusion: Our data suggests that bilateral diffusion abnormalities seen in patients with TLE associated with unilateral MTS are not present in other forms of epilepsy.

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Negative BOLD Responses to Interictal Epileptic Spikes
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Purpose: EEG-fMRI of interictal spikes can result in positive (activation) and negative (deactivation) changes in BOLD signal. Our purpose was to evaluate the pattern of deactivations related to epileptiform discharges in patients with epilepsy.
Methods: We identified 60 studies with robust responses (p=0.01: ≥ 5 contiguous voxels with a t≥ ±3.1, at least 1 voxel at t≥ ±5.0), dividing them into three groups: activation only (A=8), deactivation only (D=9) and both responses (AD=43). We correlated the pattern of the responses with discharge type and examined the spatial relationship between the two types of responses.
Results: Deactivations were seen in 52 studies: 26 related to focal discharges, 12 bilateral and 14 generalised. Bilateral and generalised discharges, especially occurring in bursts, were associated with AD, while D and A were associated with isolated spikes. Deactivations tended to be bilateral, but more focal in D than AD. In AD studies, responses were ipsilateral in 97.5% and in the same lobe in 76.5%. Deactivation involving bilateral parietal, frontal and posterior cingulate regions were seen in 10/43 AD studies, mostly associated with bursts of generalised discharges.
Conclusion: Deactivations were identified in a surprisingly high percentage of studies (86%), regardless of discharge morphology or distribution. They appear to sometimes represent the epileptic discharge origin and sometimes a distant effect. Deactivations with a pattern consistent with that described as the 'default' state of brain activity for bursts of generalised discharges give evidence for a subclinical effect of the discharges, suspending temporarily the normal brain functioning at rest.

p456
Epileptic Focus Estimation by Using Functional MRI and Dipole Tracing Method
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Purpose: EEG-triggered fMRI (fMRI) is a promising technique for detecting focal epileptic brain activity by measuring hemodynamics arising from spike discharges. To reveal the relationship between the hemodynamics and the EEG spikes, we conducted both fMRI and the dipole tracing method (DT) on two partial epilepsy patients whose informed consent was obtained.
Methods: Spike localisation was produced in several scalp EEG recordings, in which foal spikes of all subjects were consistently found in the fixed channel. Focus of patient 1 was detected on T5, and that of patient 2 on F4. The fMRI scans were recorded after the discharges and scans without spikes, and were analysed using SPM99. On DT, one-dipole analysis were performed on the peaks of the spikes with a realistic three-layer head model.
Results: In the analysis of patient 1, both fMRI and DT showed activated areas in the left hippocampus. The focus detected by fMRI was found a little posterior from that of DT. In the analysis of patient 2, both fMRI and DT showed activated areas in the right dorsolateral prefrontal cortex. The focus by fMRI is about 5 mm below and a little medial from that of DT.
Conclusion: The estimated foci using fMRI and DT were located very closely in two cases. The reason why foci were not located in the same coordinate was unclear, but it may be suggested that the areas regarding to hemodynamics are around the area of epileptic discharge.

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FMRI/EEG Studies Showing Brainstem Involvement in Multifocal Epilepsy
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Purpose: We use simultaneous fMRI/EEG to explore the patterns of neural activation associated with epileptiform events in 2 refractory epilepsy patients with multifocal discharges.
Methods: Patient 1 had Lennox-Gastaut syndrome, and showed frequent slow-spike waves (SSW) and intermittent bursts of fast activity. She had multiple seizure types, including drop attacks associated with bursts. Patient 2 had MR-negative partial epilepsy, with a very active left posterior EEG focus, and an independent right-temporal EEG focus. FMRI/EEG was acquired for 45 minutes. Event-

related analysis was performed in SPM2 (Wellcome Department of Cognitive Neurology, London, UK). In each subject, two types of inter-ictal EEG events were identified, and included as different event types in the event-related analysis. All results presented were significant at $p<0.05$, corrected for multiple comparisons.
Results: Patient 1 had 97 SSW and 26 bursts. The SSW were associated with thalamic activation, and the bursts with clinical drop attacks and brainstem activation. Both events also showed pre-frontal cortex activation. Patient 2 had 17 left posterior, and 29 right temporal discharges. Right-sided discharges activated the bilateral parieto-occipital areas and the left temporal lobe and mesencephalon. Left-sided discharges activated similar areas, but to a lesser extent.
Conclusion: The role of the brainstem appears to be important in the semiology of seizures (patient 1) and in the pattern of cortical activity (patient 2). The drop attacks show brainstem involvement. Activation from all discharges in patient 2 activated cortex receiving brainstem reticular projections, with no involvement of cortex with direct thalamocortical projections.

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Memory Function Assessed by Functional MRI in Normal Subjects and Patients with Epilepsy
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Purpose: To investigate cerebral regions concerning a memory function and presence of memory lateralisation, activated areas and the difference between the right and left hemisphere in f-MRI during verbal and visual memory tasks.
Methods: We measured brain activation using f-MRI in 39 healthy subjects and 10 adult patients. Following three types of memory tasks we designed verbal memory tasks consisting of 10 words given auditorily and a visual memory task of 6 figures given visually.
Results: Most of the 30 right-handed normal subjects activated in the left hemisphere specifically on the anterior cingulate, superior, middle and inferior frontal gyri during the verbal tasks. 4 of the 9 left-handed normal subjects showed left side dominant activation. However, 3 of the 9 left-handed normal subjects had right hemisphere dominant activation during the verbal tasks. Further, the bilateral occipital lobes were activated during visual tasks. Also, in the epilepsy patients, most of the 9 right-handed cases showed left-side dominant activation during the verbal memory tasks, regardless of the laterality of epileptic foci, while 1 case with an epileptic focus in the left frontal lobe had right-side dominant activation.
Conclusion: These results suggest that the medial frontal lobe including the anterior cingulate and superior frontal gyri, middle and inferior frontal gyri is probably related to memory function via complicated circuits among these structures and that a memory lateralisation may have a relation to a handedness.

p459
Limbic Network Activation in Temporal Lobe Seizures: Ictal MRI Evidence
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Purpose: Diffusion-weighted MRI (DWI) can provide information in the peri-ictal phase in patients with epilepsy. Both transient reductions of brain water diffusion, namely a low apparent diffusion coefficient (ADC), and signs of hyperperfusion have been reported in experimental and human epilepsy case studies.
Methods: A young woman with Hashimoto encephalitis complicated by refractory temporal lobe epilepsy was admitted for clustering seizures.
Results: Video-EEG showed frequent left temporal lobe seizures (8 seizures during a 20 minute recording). They were characterised by speech arrest, pure anomia and staring. No automatism occurred. EEG showed a left anterior temporal lobe rhythmic activity during seizure. Brain MRI was performed during the peri-ictal period. T2 weighted-MRI (T2, FLAIR, DWI) disclosed a hypersignal involving the following structures: left hippocampus, amygdala, and posterior cingulate gyrus. Antiepileptic drugs adjustment provided a dramatic reduction of the seizure frequency in the following hours.
Conclusion: Clinical course and EEG results indicate that the tissue changes disclosed by MRI are related to prolonged epileptic activity. Hippocampus, amygdala and posterior cingulated gyrus are the highlighted structures in this patient. Although imaging procedures didn't allow a precise epileptogenic focus localisation because of their low temporal resolution, these methods could contribute to an understanding and characterising of epileptic activation patterns. They may also help to appreciate the role of acute tissue changes in post-ictal clinical syndromes.

p460
Remote Functional Abnormalities in Mesial Temporal Lobe Epilepsy: A Multitracer PET Study
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Purpose: To determine the utility of multi-tracer positron emission tomography (PET) imaging with 2-Deoxy-2[18F]flouro-deoxyglucose (18F-FDG) and carbon-11-labelled flumazenil (11C-FMZ), in the detection and evaluation of remote metabolic and benzodiazepine receptor changes outside the mesial temporal lobe in patients with intractable mesial temporal lobe epilepsy, before and after anterior temporal lobectomy.
Methods: 20 patients underwent a high resolution, volumetric MRI, prolonged video-EEG monitoring before 18F-FDG and FMZ PET studies. Regional cortical FDG/FMZ PET abnormalities were defined on co-registered PET images using an objective method based on definition of areas of abnormal asymmetry (asymmetry index [AI]> 10%) for FMZ uptake and visual inspection and metabolic grading for FDG uptake. The PET studies were repeated after a mean period of a one year seizure free interval following anterior temporal lobectomy in 4 patients.
Results: The mean age was 35.2 years (20-51; M:F=12:8); mean age at seizure onset, 10.3 years (birth-38 years); mean duration of epilepsy, 23.9 years (6-50). Remote areas of glucose hypometabolism seen in 15 patients were larger, multilobar and ipsilateral in 10 patients. Remote FMZ binding abnormalities occurred with early age of onset ($p= 0.008$) and long duration of epilepsy ($p=0.01$). Post surgically all remote FMZ binding abnormalities and 75% of glucose hypometabolism normalised.
Conclusion: In the absence of structural abnormalities, remote areas of glucose hypometabolism and decreased FMZ binding indicate functional disturbances consequent to long standing epilepsy and are reversible. PET imaging provides a biochemical marker of primary and secondary epileptogenicity.

p461
FDG-PET and Subtraction Ictal-interictal SPECT Correlations in Patients with Refractory Mesial Temporal Lobe Epilepsy Associated with Hippocampal Sclerosis
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Purpose: To investigate correlations between regions of interictal FDG-PET hypometabolism and ictal SPECT perfusion changes in patients with refractory mesial temporal lobe epilepsy associated with hippocampal sclerosis (mTLE-HS).
Methods: 11 patients with unilateral mTLE-HS, who had an interictal FDG-PET scan, an interictal and ictal ECD-SPECT scan were included. FDG-PET data were reconstructed using our AMAP algorithm (Baete K et al. Neuroimage 2004;23:305-17). PET images

were normalised to white matter activity and transformed to a standard space. Each patient image was voxel-wise compared with a group of 20 normal volunteers and expressed as a Z-map. Interictal and ictal SPECT images were coregistered, a Z-map of differences was calculated and transformed to the standard space. Both Z-maps for all patients were integrated into 4 new images, giving the number of patients with combinations of either negative or positive FDG-Z-values (respectively interictal hypo- or hypermetabolism) with either negative or positive SPECT-Z-values (respectively ictal hypo- or hyperperfusion).
Results: In 9 patients (82%), interictal FDG-PET hypometabolism and ictal SPECT hyperperfusion was present in the ipsilateral temporal lobe, thalamus, basal ganglia and insula. FDG-PET hypometabolism and ictal SPECT hypoperfusion were present in both frontal lobes, ipsilateral parietal lobe and cerebellum.
Conclusion: Widespread interictal hypometabolism may represent a dynamic inhibitory process comprising both the regions of ictal onset and spread, identified as ictal SPECT hyperperfusion areas, as well as regions of ictal surround inhibition, detected as ictally hypoperfused areas. This observation explains why the region of FDG-PET hypometabolism is always larger than the ictal onset zone.

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Relationship of Ictal HMPAO-Spect Studies to Surgical Outcome in Patients with Mesial Temporal Lobe Epilepsy
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Purpose: Epilepsy surgery is a widely used treatment for refractory temporal lobe epilepsy. Unfortunately, this procedure is not always successful, as up to 30% of patients fail to achieve seizure control. We therefore sought to determine whether patterns of ictal perfusion with HMPAO-SPECT are related to postsurgical seizure outcome in patients with mesial TLE.
Methods: We retrospectively studied 15 patients who underwent selective amygdalo-hippocampectomy because of refractory mesial TLE, defined as having (1) unilateral hippocampal atrophy or sclerosis on MRI scan, (2) ictal seizure onset zone and >90% of interictal spikes ipsilateral to the hemisphere of MRI pathology during prolonged video-EEG-monitoring (3) a minimum postoperative follow-up of 24 months. Ictal HMPAO-SPECT studies were obtained during complex partial seizures and studies were aligned to a normalised MRI-scan. Overall 49 regions which were drawn on a normalised MRI were then assigned to the HMPAO scan and values for each region were normalised to the cerebellum. Student t-test was used to compare values for each region between patients and a control group of 8 healthy volunteers.
Results: No statistically significant differences between patients with excellent seizure outcome (Class I, n=10) and poor seizure outcome (Class III-IV, n=5) were found except for extratemporal regions contralateral to the side of seizure onset. Whereas no patients with outcome Class I had significant contralateral extratemporal hyperperfusion, such hyperperfusion was found in 3 out of 5 patients with poor seizure control (2 patients with frontal, 1 with occipital hyperperfusion). On the contrary, contralateral temporal hyperperfusion occurred in both groups.
Conclusion: Contralateral extratemporal ictal hyperperfusion with HMPAO-SPECT might be a predictor of poor seizure control after selective amygdalo-hippocampectomy in patients with mesial TLE. However, our results await further confirmation in a larger study, also including patients with nonlesional and lesional TLE.

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Magnetoencephalographic Spike Localisation in Insular Cavernous Angioma
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Purpose: To determine whether magnetoencephalography (MEG) provides localising information on patients with insular epilepsy
Methods: Two epilepsy patients with insular cavernous angioma underwent simultaneous EEG and MEG recording. The source of the epileptiform discharge detected by MEG was estimated by an equivalent current dipole (ECD) model and superimposed on magnetic resonance images.
Results: Patient 1 had 11 spikes detected by both EEG and MEG (E/M-spikes) and five by MEG only (M-spikes). Patient 2 had 110 E/M-spikes but no M-spikes. In both patients, ECDs of the E/M-spikes were localised in the anterior temporal lobe of the lesion side. ECDs of the M-spikes of patient 1 were localised near the insular lesion.
Conclusion: MEG may detect local insular activity not seen by EEG. The E/M-spikes may represent propagated activity in the anterior temporal cortex, which is also typical of mesial temporal lobe epilepsy

p464
Comparison of MEG with Invasive EEG in Temporal Lobe Epilepsy
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Purpose: To determine the overall utility of MEG in patients with temporal lobe epilepsy (TLE) and to evaluate the equivalence of MEG compared with invasive V-EEG.
Methods: 33 patients with drug resistant TLE were evaluated at the Epilepsy Monitoring Unit in the University of Texas Comprehensive Epilepsy Program from 1999 to 2001 and underwent epilepsy surgery. The intracranial subdural electrodes or grid placement was tailored for each patient. MEG-recordings were performed with a 148-channel whole-head MEG system. Interictal epileptiform events were identified visually, while estimation of the location of their intracranial sources was performed using the single dipole model (ECD). ECD locations were superimposed on the patients' MRI. The epileptogenic region predicted by invasive V-EEG and MEG was defined in relation to the resected area (perfectly overlapping, partially overlapping, or non-overlapping). The correctness of prediction of the localisation area was defined in regard to postoperative seizure outcome.
Results: Using MEG, we were able to localise the resected region correctly in a slightly greater proportion of patients (66.7%) than with invasive V-EEG (54.5%). MEG contributed to the localisation of the resected region in 72.7% of patients for whom V-EEG only partially identified the resected zone. Overall, MEG and V-EEG results were equivalent in 54.5%. Additional localisation information was obtained using MEG in 46% of the patients.
Conclusion: MEG is a powerful tool in presurgical epilepsy evaluation of patients with TLE; it is most useful in patients with partially localising V-EEG results.

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Longterm Sequential Magnetoencephalographic Analysis for Patients with Atypical Benign Partial Epilepsy in Childhood

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Purpose: In order to discuss the aetiology and epileptogenicity of atypical benign partial epilepsy in childhood (ABPE), we analysed the change of magnetoencephalographic (MEG) findings in the patients with ABPE according to their clinical course.
Methods: 3 patients with ABPE (patient 1: 9 year old boy, patient 2: 7 year old boy and patient 3: 9 year old girl) underwent MEG analysis using 204ch helmet shape MEG system (Vector View System, Elekta Inc, Finland) with simultaneous EEG recording by international 10-20 system. Their seizures were described as unilateral facial focal motor seizures and hemi convulsive seizures in patient 1 and 2, and astatic seizures and secondary generalised tonic-clonic seizures in all patients. Furthermore, they had symptoms of pseudo-bulbar palsy: salivation or difficulty in speech, eating and drinking.
Results: Their EEG findings were continuous spike and wave complex especially in the sleeping stage during the worst seizure condition and changed to focal spiking at unilateral central and middle temporal region in regard to their seizure reduction by anti-epileptic drugs: especially ethosuximide (ESM) and asetazoramide (AZA). MEG showed unilateral epileptic activities widely over frontal and temporal operculum and insular cortex during the worst seizure condition by equivalent current dipoles (ECDs) and dynamic statistical parametric mapping. The MEG findings changed with their seizure reduction to a localised clustering of ECDs at unilateral temporal and frontal operculum in the vicinity of the primary motor area.
Conclusion: Localised findings of ECDs during seizure remission in our case definitely resembled those of Benign Rolandic Epilepsy. In clinical course, ESM and AZA were co-operatively effective for the treatment of this epileptic syndrome.

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MRI Investigation of the Thalamus in Patients with Absence Epilepsy

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Purpose: Animal models show that thalamocortical circuitry plays a key role in the elaboration and maintenance of generalised spike and wave discharges (GSWD) in absence epilepsy (AE). Imaging studies suggest more functional than structural thalamic abnormalities in the physiopathology of AE. The objective of this study was to investigate the thalamic volumes of patients with AE.
Methods: Images were acquired in a 2.0T scanner and a 3D sequence was used for volumetry. After processing to reduce interindividual variation, the thalamus was manually segmented (Display, Montreal Neurological Institute). The thalamic volumes (TV) obtained by the average between the right and left thalamus were compared with 45 controls (16 women, mean±SD age, 32±13 years, range 20 to 60) using Student's t-test. The thalamus was divided into anterior and posterior based on the number of slices segmented and compared to the controls.
Results: 26 patients were scanned (17 women, 27±12 years, range 10 to 62). All patients had AE (23 juvenile absence epilepsy and 3 childhood absence epilepsy) diagnosis (ILAE, 1989). TV of patients with AE (mean±SD mm3, 9720±550) were increased compared to controls (9312±615, p=0.007). Anterior TV (9178±834) were also larger than controls (8628±846, p=0.01). However, the posterior TV of the patients (10281±944) were not statistically different from the controls (9998±852, p=0.2).
Conclusion: The major part of the anterior thalamus in mammals is the thalamic reticular nucleus. Animal studies indicate that it is the main nucleus involved in GSWD generation. Our results support 'in vivo' anterior thalamic abnormality in patients with AE.

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Brain Atrophies in Patients with Primarily Generalised Tonic Clonic Epilepsy

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Purpose: The purpose of this study was to identify the spatial distribution of possible anatomical changes in patients with primarily generalised tonic clonic seizures (GTCS).
Methods: MR volumetry and voxel-based morphometry (VBM) was performed in 20 patients with GTCS only, and 52 control subjects. 3D-volume T1-weighted MRI scans were acquired with a 1.5T GE scanner. Proportions of white and grey matter and cerebrospinal fluid were compared between patients and controls with VBM (SPM99, corrected $p<0.05$). The specific volumes of interest were delineated manually for the putamen, thalamus, caudate, amygdala, hippocampus and cerebellum. The ratios between the respective volumes and the total brain were then compared between the two groups using repeated two-way ANOVA with Fischer's post-hoc test, ($p<0.05$).
Results: Patients with GTCS showed significantly reduced cortical grey matter fractions bilaterally in the superior, medial, and inferior frontal gyri, in the precentral gyrus, the anterior cerebellum, and in the thalamus. They also had increased CSF fractions bilaterally in the frontal, parietal lobes and anterior cerebellum, and increased white matter fractions in anterior cerebellum and in the cuneus. The structural volumes (cm3) were smaller than in controls ($p<0.001$) in caudate (4.1±0.5 vs 4.9±0.5), putamen (5.1±0.4 vs 6.0±0.5), cerebellum (56.6±6.9 vs 67.8±6.9) and thalamus (6.5 ±0.6 vs 7.2 ± 0.6). No differences were observed for the volumes of amygdala and hippocampus. The mean brain volume was reduced in patients (1166 ±113 vs 1250 ± 102; p=0.004)
Conclusion: The present data show regional changes in patients with GTCS, which primarily involve the motor system, suggesting a relationship with seizure semiology.

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Thalamic Atrophy in Childhood Absence Epilepsy

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Purpose: Patients with childhood absence epilepsy (CAE) typically show no obvious MR lesions. Functional involvement of the thalamus in seizure generation has been suggested. We assessed cortical and subcortical brain structure in CAE using optimised voxel-based morphometry (VBM).
Methods: We recruited 13 patients with clinical and EEG diagnosis of CAE (mean age 17±8 years), and compared them to a consecutive series of 109 controls (mean age 25±8 years). 3Tesla MRI included a 3D T1-weighted sequence, which was analysed with an optimised VBM protocol (Good CD, et al. NeuroImage 2001; 14: 21-36) using iBrainTM and SPM2 (Wellcome Department of Cognitive Neurology, London).
Results: Compared to controls, CAE patients showed areas of grey matter decrease prominently in both thalami and also in the area of the subcallosal gyrus (threshold $p < 0.05$, corrected for multiple comparisons). Grey matter increase was found in small areas of the bilateral frontal and parietal cortex, as well as in the globus pallidus ($p < 0.05$, corrected).
Conclusion: There is evidence for grey matter volume reduction in the thalamus of CAE patients. Additionally, we found indications for

cortical grey matter increase. The latter confirms previous morphometry studies on patients with idiopathic generalised epilepsies (IGE) (eg Woermann et al. Neuroimage 1999; 10: 373-384). Thalamic atrophy has not been described in these studies, which were using earlier VBM methodology, and assessed different IGE subsyndromes. The thalamic atrophy may be associated with the postulated thalamo-cortical circuit involved in the generation of absence seizures.

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Magnetic Resonance Spectroscopy of the Thalamus in Patients with Typical Absence Epilepsy

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Purpose: To investigate neuronal dysfunction of the thalamus in patients suffering from typical absence epilepsy (TAE) using magnetic resonance spectroscopy (MRS). Special attention was paid to N-acetylaspartate (NAA), creatine (Cr) and to their ratio (NAA/Cr). Detection of neuronal dysfunction in the thalamic region might contribute to the clarification of the participation of thalamic nuclei on the pathogenesis of epileptic activity in the epileptic syndrome being investigated.
Methods: Magnetic resonance spectroscopy was performed over the right and left thalamus in 9 patients suffering from TAE and in 9 sex and age matched healthy controls. All patients and controls were examined using the MRS-CSI (chemical shift imaging) technique.
Results: Statistical analysis of compared data in both groups demonstrated that the thalamic concentration of NAA and NAA/Cr ratio were significantly decreased in patients with TAE as compared to healthy controls. Comparison of right and left thalami between patients and healthy controls also showed a statistically significant reduction of NAA and NAA/Cr ratio. Our data showed abnormal asymmetry of NAA concentration in the right and left thalamus in the patient group, while the group of healthy controls was without asymmetry. A negative correlation between patients thalamic NAA/Cr and duration of epilepsy was revealed. A negative correlation between the level of NAA and seizure frequency was observed as well.
Conclusion: The present MRS data indicate neuronal dysfunction in the thalami of patients with typical absences. Consonantly with the recent MRS findings in different idiopathic generalised epilepsy syndromes our results confirm a role of the thalamus as an important structure in the pathogenesis of typical absences.

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A Proton Magnetic Resonance Spectroscopy Study of Metabolites with Short TE in the Thalami in Juvenile Myoclonic Epilepsy

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Purpose: The neuroanatomical basis and the neurochemical abnormalities that underlay juvenile myoclonic epilepsy (JME) are not fully defined. We aim to investigate the chemical integrity of the thalami of patients with JME using proton magnetic resonance spectroscopy (1H-MRS) with a short time of echo (TE).
Methods: We performed multi-voxel 1H-MRS with TE of 30 ms (PRESS sequence) at 1.5 Tesla scanner over the thalami of 10 consecutive right-handed patients with JME (mean age = 28.4 years and mean time of disease = 16.9 years) and 10 age and sex matched healthy right-handed subjects. All patients had a typical history of JME, normal neurological examination, EEG findings consistent with JME, and normal high-resolution magnetic resonance neuroimaging. We determined ratios for peak values of N-acetylaspartate (NAA), choline (Cho), glutamine-glutamate (Glx) and inositol (Ins) over creatine-phosphocreatine (Cr). Group differences for metabolites between patients and healthy controls were evaluated using the Student's t-test.
Results: Group analysis showed that thalamic Glx/Cr ratios were increased in JME patients (right side = 0.437 ± 0.105; left side = 0.494 ± 0.159) compared with normal controls (right side = 0.330 ± 0.159; left side = 0.339 ± 0.136) with p values of 0.09 and 0.03, respectively. We did not find significant differences of the other metabolites between patients and controls.
Conclusion: There is evidence of thalamic neuronal metabolic dysfunction in patients with JME, supporting the notion of abnormal thalamo-cortical circuitry as a substrate of seizure generation in this form of epilepsy.

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Long-term Reproducibility of fMRI Activation in Epilepsy Patients with Fixation Off Sensitivity

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Purpose: Recently EEG/fMRI investigation has been used to study interictal and ictal activity in patients with epilepsy. By contrast, there are is little data about the reproducibility of fMRI results in epilepsy studies. In this work, we used EEG/fMRI investigation to verify long-term reproducibility of this technique, by confirming our previously published data about haemodynamic correlates of epileptiform discharges elicited by the elimination of central vision and fixation (so-called Fixation Off Sensitivity (FOS).
Methods: In the same patients, we repeated, 3 years later, an EEG/fMRI study using the same experimental setting and paradigm. From an epileptological point of view, the patients' clinical condition was unchanged; the EEG showed an unchanged FOS phenomenon in 2 cases, whereas in 1 patient this pattern had disappeared 6 months previously following a modification in therapy. fMRI images were acquired using a clinical 1.5 T magnet (Philips Gyroscan). The EEG signal was recorded using an MR-compatible system (Micromed, Italy). fMRI data were analyzed using SPM99 (http://www.fil.ion.ucl.ac.uk/spm).
Results: The analysis of the fMRI data showed a main activation cluster in the temporo-occipital regions (bilateral in case 1, monolateral on the right side in case 2) related to epileptiform abnormalities in the closed-eyes condition; in case 3, in whom the FOS phenomenon had disappeared, no fMRI changes were observed.
Conclusion: This results are highly concordant with previously published data showing a good long-term reproducibility of this technique in the study of epileptiform activities

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Functional MRI of Generalised Spike Wave Activity

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Purpose: To establish the nature and spatial localisation of haemodynamic correlates of generalised spike wave activity (GSW) in a large series of patients with idiopathic generalised epilepsy (IGE) and secondary generalised epilepsy (SGE) using simultaneous EEG and functional-MRI (EEG-fMRI).
Methods: EEG-fMRI was undertaken in 30 patients with IGE and 16 patients with SGE. SPM2 was used for all image pre-processing and statistical analyses. GSW epochs were visually identified and used to derive a boxcar model, to test for GSW-related fMRI changes. An F-contrast was used to test for the variance explained by GSW. A second level multi-subject random effects group analyses was used to identify population specific fMRI changes.

Results: No GSW occurred in 10 patients during scanning; a further 3 were excluded due to motion. GSW-related fMRI changes were seen in 25 patients, with thalamic signal change (15 patients), predominantly activations; and cortical signal change, involving symmetrical frontal (20 patients), posterior parietal (23 patients) and posterior cingulate (19 patients) cortices, predominantly deactivations. fMRI changes were not syndrome specific in individual analyses. Random effects group analysis revealed thalamic activation and frontal, parietal and posterior cingulate deactivation in the IGE group and thalamic and frontal changes in the SGE group.
Conclusion: fMRI changes were in keeping with current hypotheses based on neurophysiological findings, with involvement of thalamocortical networks during GSW. The distribution of cortical fMRI change resembled those found in studies of vigilance and resting state brain rhythms (Laufs et al. PNAS. 2003;11053-8) suggesting a link, showing similar cortical networks involved in normal consciousness and in GSW.

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The Hippocampus and Mood Disturbance after Epilepsy Surgery
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Purpose: Despite improvement in seizure frequency following temporal lobectomy, some patients develop mood disorders. Neurobiological correlates of post-operative depression and anxiety largely remain unknown. This study examined mood disturbance after temporal and extra-temporal epilepsy surgery and its relationship to hippocampal volume.
Methods: 31 patients undergoing epilepsy surgery (22 temporal lobe, 9 extra-temporal) in the Comprehensive Epilepsy Program, Austin Hospital, were prospectively assessed pre-operatively, and at discharge, one, three, six and twelve months post-operatively. Assessment included a clinical interview (Austin CEP Interview), Beck Depression Inventory (BDI-II) and State-Trait Anxiety Inventory (STAI). Hippocampal volumetry was conducted on patients' preoperative T(1)-weighted MRI's and on those of 31 neurologically normal controls following stereotactic normalisation of the images.
Results: 30% of the sample suffered from depression and 50% suffered from anxiety at some point in the 12 months post-surgery. Pre-operative anxiety was related to smaller right hippocampal volumes in temporal patients ($t(19)= -2.102$, $p=0.049$). Post-operatively, a smaller hippocampal volume contralateral to the resection was related to clinical depression ($t(19) =-2.307$, $p=0.032$), anxiety ($t(19) =-2.424$, $p=0.026$) and BDI-II scores at the discharge, one and three month reviews in temporal patients ($r=-0.611;-0.524; -0.512$ respectively, $p<0.05$). There was no relationship between depression and post-operative seizures at each review ($p>0.05$ for all comparisons) in temporal patients. Contralateral volumes were unrelated to post-operative depression or anxiety in extra-temporal patients.
Conclusion: These findings highlight the predictive value of neurobiological factors, such as pre-operative hippocampal volumes, for patients at risk of developing mood disturbance following temporal lobe epilepsy surgery.

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Epilepsy Surgery and Psychiatric Disorders
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Purpose: Psychopathological symptoms are frequent both in pre and post epilepsy surgery patients. In order to obtain reliable data, psychiatric evaluation and psychiatric rating scales pre and post epilepsy surgery were performed.
Methods: In a 2 year survey, 121 patients who were candidates for epilepsy surgery have been evaluated by means of psychiatric interview and psychiatric rating scales pre surgery. 86 and 61 have been evaluated respectively 6 months and 1 year after surgery. Relations between the presence of a major depressive disorder and lateralisation, crisis frequency, psychiatric family history, and personal history for psychiatric disorder, was tested.
Results: 47 subjects had a DSM.IV-TR diagnosis pre surgery. 9 had an affective disorder, 38 had either axis I or axis II diagnosis. 74 did not have a psychiatric diagnosis. After 6 months, 6 patients were still depressed, 7 had a new diagnosis of depressive episode (chi square 81, $p<0.001$). After 1 year, 2 patients were still depressed, 3 had a new diagnosis of depressive episode (chi square 44, $p<0.001$). Lateralisation of focus was significantly different with 8 out of 9 depressed patients with left side focus (chi square 48, $p<0.05$). After 6 months this correlation was not significant. Personal history for depression is more frequent in patients who have a depression episode at the pre surgery evaluation (chi square 23, $p<0.001$).
Conclusion: Predicting which patients may experience depression after surgery is a challenge, but could permit better presurgical education and a more accurate identification of those needing treatment for depression.

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Psychodynamic Testing of Epilepsy Surgery Patients
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Purpose: To present our psychodynamic protocol aimed to diagnose psychotic features for preventing and treating psychiatric disorders in epilepsy surgery patients.
Methods: All epilepsy surgery candidates are submitted to the classical diagnostic protocol (clinical, imaging, neuropsychological and neurophysiological, non invasive and, if indicated, invasive procedures) together with a psychodynamic assessment: clinical interview, Rorschach, WAIS-R profile analysis, human profile drawing (HFD). Since 1997, 97 epilepsy surgery candidates have been submitted to the psychodynamic protocol. For the present study 20 patients (10 female and 10 male) have been considered, all submitted to resective surgery and experienced a good surgical outcome according with Engel classification (15 class Ia, 2 class Ib and 3 class II). Psychodynamic retesting was performed one year after surgery. We analysed the following data: Rorschach: (R, %R, %G, %G+, %D, %D+, %F, %F+, M, Ma, m, FC, CF, C, %A, %H, %Ban, Neiger); HFD (completeness, omission, distortion). A comparison between testing and retesting has been made.
Results: The psychodiagnostic data showed a high risk of developing psychotic behaviour for 8 out of the 20 patients considered. For the 8 patients psychopharmacological and or psychotherapeutic treatment was indicated. According to the psychodiagnosis 18 patients showed expected behaviour, while 2 patients presented an unexpected reaction.
Conclusion: Psychodynamic testing can help with early diagnosis and treatment of psychotic disturbances in epilepsy surgery patients.

Unexpected behaviour and the comparison between test and retest data are discussed.

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Assessment of Personality and Emotive Profile in Temporal Drug-resistant Epilepsy Patients: A Follow-up Study
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Purpose: The association of psychopathological symptoms to drug-resistant temporal lobe epilepsy (TLE) candidates for surgery is largely debated in the literature. Data seem to be controversial also due to the different instruments used to assess personality. Furthermore few post-surgical studies have taken into account the clinical outcome as a potential factor that may modulate the behavioural profile of patients. In this study we wanted to explore in the pre and post-surgical stage the personality profile of a group of drug-resistant TLE patients. We were particularly interested in investigating whether or not (1) hemispheric side of the epileptogenic area and of surgery; (2) age of onset, (3) clinical outcome according to the Engel's classification, may relate to the personality profile of patients.
Methods: 33 drug-resistant TLE patients were studied (18 F, 15 M; 18 left TLE, 15 right TLE; mean age 32.5; mean educational level 11.06 yrs). At the end of a personalised pre-surgical iter, surgical removal was tailored on the anatomical electrical clinical features of each patient. An extensive neuropsychological assessment was administered before and after surgery. In particular, patients underwent a clinical interview after which they completed the Beck Depression Inventory (BDI) and the Minnesota Multiphasic Personality Inventory (MMPI-2). A semi-structured interview was also administered. This interview aimed at exploring patients' subjective perception of epilepsy, their awareness of the degree of severity of the disease per se and their expectations about significant changes of their quality of life (QoL) after surgery. The post-surgical follow-up was staged at one year.
Results: A repeated measures univariate ANOVA was applied on the data set. Dependent variables were: subjects' performance on three measures (BDI; MMPI-2; semi-structured interview). Between-subjects independent variables were: 1) hemispheric side of the epileptogenic area and of surgery; 2) age of onset; 3) clinical outcome according to Engel's classification. Within-subjects independent variable: pre- vs post-surgical stage. No significant effects resulted from this type of analysis. Patients' scores were generally in the normal range. On the other hand, we found a significant correlation between the level of awareness of disease severity from the semi-structured interview and the level of depression from BDI (Spearman's Rho; B1-Beck, r=0.184, p=.03; B1-D, r=0.188, p=.031).
Conclusion: Clinical scale scores on MMPI-2 and BDI were within the normal range. TLE patients did not show psychopathological indices as a group. Furthermore, no significant changes between the pre- and post-surgical personality profiles were found independently of the clinical outcome. These results suggest that neurosurgery does not induce psychiatric morbidity per se. On the other hand a significant correlation emerged between the level of awareness of epilepsy severity and depressive symptoms as revealed by the BDI in the post-surgical follow-up (4) (5). We hypothesize that in the post-surgical stage patients acquire a deeper awareness of their disease, due to their significant QoL changes, whereas before surgery the perception of the disadvantages due to epilepsy may have been reduced by positive expectations. References 1. Paradiso S., Hermann P. D., Robinson M. D. J of Ment Dis, 183: 538-547, 1995. 2. Reynolds E. H., Trimble M.R. Epilepsy and Psychiatry, Edinburgh: Churchill Livingstone, 1981. 3. Engel J. In Engel J. (ed), Surgical treatment of the epilepsies, New York: Raven Press, 1987. 4. Robertson M. M., Trimble M.R. Epilepsia, 28: 364-368, 1983. 5. Kanner AM, Balabanov A. Neurology, Apr 23;58(8 Suppl 5):S27-39, 2002.

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Long-term Outcome for Individuals with Autism and Early Onset Epilepsy in a Community-based Cohort
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Purpose: From a population-based follow-up study of children with autism, we present the epilepsy characteristics in cases with epilepsy onset before age two years and describe the mortality, seizure and cognitive/behavioural outcome.
Methods: 120 individuals (84 males, 36 females) with autism diagnosed in childhood were re-evaluated concerning cognitive abilities and autistic symptomatology at ages 17-40 years. 6 had died, and 6 did not participate. Their medical records were reviewed and their caretakers were interviewed concerning epileptic seizures.
Results: 16 cases (6 boys, 10 girls) had epilepsy onset before age two years. There were 3 cases with infantile spasms and ACTH-treatment; 1 had total remission of seizures within a month, and 2 developed medically intractable complex partial seizures. 3 had gone through epilepsy surgery, with good seizure outcome in 2 cases. At follow-up, 2 had died, 12 had an autistic disorder in combination with severe mental retardation and 11 had a very low adaptive level in daily life. 5 out of 12 with active epilepsy had intractable epilepsy.
Conclusion: As adults, 1 in 10 diagnosed with autism in the 1980s has epilepsy since the first two years of life. In cases with very early onset epilepsy in autism, girls outnumber boys, in contrast to the opposite sex ratio concerning the prevalence of autism. Mortality is higher than expected. Epilepsy seldom remits. The psychosocial outcome is often very poor. The cases with a history of infantile spasms were all severely disabled as adults, in spite of different seizure outcomes.

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AD/HD in Children with Epilepsy
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Purpose: Epilepsy, as a major neurological disorder, can cause a lot of difficulties such as school problems, which may surface as psychiatric symptoms, impulsivity and disruptive behaviours. Children with epilepsy manifest a large range of mental health problems, not adequately measured by existing survey instruments. These include hyperactivity, impulsivity, aggressive behaviours and attention deficits. Child Behaviour Checklist, Conners' Scales and Nisonger Scale were developed to measure such problems of mental health of children in long-term care. This paper wants to evaluate the presence of ICD-10 ADHD criteria in children with cryptogenic, idiopathic and symptomatic epilepsy, and to evaluate if there is any relationship between a specific epileptic type (such as cryptogenic, idiopathic and symptomatic epilepsy) and ADHD, considering available neurobiological research.
Methods: A 97 children with epilepsy sample, 5-15 year old, in-patients in Child and Adolescent Psychiatry Department and Paediatric Neurology Department of 'al. Obregia' Hospital, Bucharest, Romania, was assessed, using Child Behaviour Checklist, Conners' Scales and Nisonger Scale for parents and children. Epilepsy and ADHD were assessed using ICD-10 criteria. We tried to evaluate the existence of statistically significant correlates between hyperactivity, impulsivity, aggressive behaviour and attention deficit items and specific types of epilepsy (cryptogenic, idiopathic and symptomatic). Statistical analysis was performed.
Results: Our data suggest that children with epilepsy have high severity scores for items assessing impulsivity and aggressive behaviour, compared with the scores for hyperactivity and attention deficit. The variables for impulsivity and aggressive behaviour were significantly correlated with those for cryptogenic epilepsy.

Conclusion: Children with epilepsy have high scores on scales assessing ADHD, especially children with cryptogenic epilepsy, and there is a high comorbidity between these two major disorders.

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Tolerability of OROS-MPH 18 and 36MG in Paediatric Epilepsy Plus Attention Deficit/Hyperactivity Disorder (ADHD)
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Purpose: To assess the efficacy and tolerability of 18 versus 36mg dose OROS-methylphenidate (OROS-MPH) for treatment of ADHD in children with epilepsy.
Methods: 15 patients (10.3±3.2years; 53% male) on antiepileptic drugs and one-month seizure free were prospectively randomised to OROS-MPH or placebo and then crossed-over, double blind, to the other condition. Clinical Global Impressions Scale (CGI) Scores, Adverse Events (AE) and seizures were noted at each visit. Each dose level was tested for one week starting with the 18 mg dose.
Results: There were no serious AE. One seizure occurred just after the placebo arm, before exposure to OROS-MPH. Active OROS-MPH and higher dose predict a greater decrease in CGI-Severity ($p<0.0001$). Response is defined as a CGI-Improvement score of 1 or 2, very much or much improved. 15 patients were given 18 mg, none discontinued, 8 responded to active OROS-MPH, none to placebo. 12 were given 36 mg, 6 discontinued on active, 2 due to emotional lability, 1 each due to insomnia, tics, nausea, and over-focus, versus none on placebo, 6 responded to active, 3 to placebo. 87% of patients given <1mg/kg/day of OROS-MPH tolerated it versus 20% given >1mg/kg/day ($p<0.05$). All AE disappeared within 18 hours of stopping OROS-MPH except the tics, which disappeared within 48 hours.
Conclusion: 18 and 36 mg doses of OROS-MPH daily produced no serious adverse effects and significant response rates in this sample of children with ADHD and epilepsy. The 54mg and 72 mg doses will be tested next and a larger efficacy trial undertaken. Acknowledgments: This study is supported by a Career Development Award from the National Institutes of Mental Health, USA. McNeil Consumer Healthcare is providing Active OROS-MPH [Concerta] and matching placebo for this study.

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Effectiveness of Lamotrigine for Attention-deficit Hyperactivity Disorder in Patients with Epilepsy
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Purpose: Epilepsy is associated with a number of neurologic and psychiatric disorders, including ADHD, affective disorders, migraine, etc. Comorbid conditions influence the course of epilepsy. On the other hand, epilepsy and antiepileptic drugs (AED) can affect these disorders. ADHD is a serious condition that affects about 5% of children with epilepsy and requires additional treatment. The classic AED do not significantly affect ADHD. The aim of the study is to establish the effectiveness of lamotrigine for symptoms of ADHD in patients with epilepsy.
Methods: 4 patients, aged 7-12 years, with epilepsy and ADHD were followed up for a period of 1-3 years. The diagnosis ADHD was set according to the diagnostic criteria of DSM IV. Lamotrigine in dose 4-6mg/kg was added to other AED, because of the pharmacoresistance of epilepsy. Patients were re-evaluated for symptoms of ADHD and epilepsy every 4 months after starting lamotrigine. Methods of clinical, neurophysiological and neuropsychological observation were used.
Results: Great improvement of symptoms of ADHD was found in 2 patients, moderate improvement in 1 patient and no significant change in 1 patient. The improvement of ADHD was not always correlated with the positive effect on seizures: the patient with the greatest improvement had 100% seizure reduction, in cases with moderate improvement 1 had 100% reduction, the other 1 more than 50%, and the patient with no change had more than 50% reduction.
Conclusion: Treatment with lamotrigine can be effective for both epilepsy and ADHD in patients with comorbidity of these diseases. Our observation is encouraging for future research about the role of lamotrigine as mono or add-on therapy for comorbid epilepsy and ADHD.

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Cognitive Function and Skills Performance of Children with Attention Deficit Disorder
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2) Institute for Childhood Postgraduate Studies, Ain-Shams University

Purpose: 1) To detect the actual functional skills of ADHD children. 2) To introduce a stochastic assessment combining psychometric tests including assessment of the intellectual functions and the neuropsychological profile of children with ADHD. 3) To suggest psychosocial, behavioural and educational strategies.
Methods: The 30 study participants were 16 boys and 14 girls aged between 6–12 years, who clearly met the DSM IV for ADHD diagnosis. All were newly diagnosed and had not received another stimulant medication prior to enrolment. Each target child was paired with a comparison child from the same classroom. For all: I) full medical history and clinical examination; II) psychometric study: a) Arabic version of Conners rating scale, b) a battery of tests: IQ using Stanford Binet test version 4 (Arabic version), Portage Assessment Program including total skills and cognitive, fine motor, gross motor, language (receptive and expressive), social and self dependency skills; III) visual acuity and hearing assessment; IV) thyroid function; V) EEG study.
Results: All 30 ADHD cases showed normal thyroid function. ADHD cases showed higher abnormal EEG findings (60%). Significant failure of academic achievement in ADHD pupils. 87.5% who showed poor scholastic achievement had ADHD, while only 14.3% of those who had an excellent level had ADHD. IQ level of ADHD children showed no significant difference from controls but perceptual reasoning showed a significant difference and also showed significant poor cognitive skills and significant poor social skills.
Conclusion: 1) Assessing the sub-areas of intellectual functions especially perceptual reasoning together with the functioning level of all developmental skills. These findings are essential for full assessment, management and follow up the effects of treatment strategy. 2) Implicating a four dimensional management program including medical treatment, cognitive training, behavioural and social therapy and parental guidance.

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Suicidal Behaviour and Comorbid Psychiatric Disorders in Epilepsy Patients
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Purpose: The aim of the study was to investigate psychiatric comorbidity in epilepsy patients with suicidal behaviour.
Methods: 77 adult epilepsy patients (31 males, 46 females) with suicidal behaviour (suicidal attempts, intentions, threats) in the interictal period were evaluated with clinico-psychopathological assessment and structured interview. Diagnostic criteria were based on the ICD-10.
Results: In all patients comorbid psychiatric disorders were revealed. Most common were mood disorders: 14 (18.2%) patients met the

criteria of major depression, 36 (46.7%) patients met the criteria of dysthymic disorder, 4 (5.2%) patients the criteria of bipolar affective disorder (depressive phase). Also, 9 (11.7%) patients had alcohol or substance abuse, 7 (9.1%) patients had interictal schizophrenic-like psychoses and 7 (9.1%) patients had anxiety disorder. It is important that 30/54 (55.6%) patients with diagnosed depressive disorders had also dysphoric symptoms. Among patients who did not meet ICD-10 criteria of depression, but had another psychiatric comorbidity, interictal dysphoric disorder was also common. Irritability, anger, fear, painful somatoform symptoms in many cases were 'trigger factors' of suicidal behaviour in all groups of patients.
Conclusion: All epilepsy patients with suicidal behaviour had psychiatric disorders. The comorbid diagnoses were: mood disorders, alcohol or substance abuse, interictal schizophrenic-like psychoses, anxiety disorder. Interictal dysphoric disorder in all groups of patients was an important factor of suicidogenesis. It will be necessary to give particular attention to specific affective disorders associated with epilepsy when new psychiatric classifications are worked out in future.

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Psychopathology in People with Epilepsy: A Clinical Study
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Purpose: This is a prospective clinical study aimed at the identification of prevalence rates and patterns of psychopathology in people with epilepsy compared to the general population, and the difference in rates among people with epilepsy according to a number of variables including sex, type of epilepsy, age at onset and duration of the condition, frequency of seizures, and treatment.
Methods: Two tools were applied in the study: a semistructured psychiatric interview form that included the diagnosis of eight psychiatric disorders, and the General Health Questionnaire (GHQ-30). The sample consisted of 100 outpatients with epilepsy of both sexes according to the inclusion criteria of the present study. In addition, a control group of 100 healthy individuals from the general population was included which was matched with the patients' group for age and sex.
Results: The study revealed that psychopathology prevalence rates were significantly higher among people with epilepsy compared to the general population. Yet no significant difference between the two groups was observed regarding patterns of psychopathology. The rates were higher among patients with partial epilepsy, where the condition had started in the adulthood period, who had the condition for more than ten years, and suffered from more than ten seizures per year.
Conclusion: People with epilepsy are more prone to psychopathology than the general population, although both had similar patterns. Yet they are not considered to be more liable than patients with other chronic diseases. They require global management regarding control of seizures, psychosocial support and guidance to prevent psychopathology, in addition to its proper treatment. People with epilepsy who were at higher risk of developing psychopathology were those with partial epilepsy, especially with secondary generalisation, long duration of the condition, high frequency of seizures, and for whom the condition had started when an adult.

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Psychiatric Disorders in Juvenile Myoclonic Epilepsy: A Study Comparing Patients Treated with Valproate and Topiramate
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Purpose: We evaluated the frequency of psychiatric disorders (PD) in a series of patients with juvenile myoclonic epilepsy (JME) treated with valproate (VPA) and topiramate (TPM) aiming to quantify their frequency and to verify the relationship between PD and factors related to epilepsy.
Methods: JME patients, using VPA or TPM in monotherapy, followed up in the outpatient epilepsy clinic for at least six months were selected. SCID I and II and K-SADS-PL were used to assess patients > and < than 18 years, respectively. Patients could receive more than one diagnosis in each axis (I e II). Fisher's exact test was applied to calculate the difference between the groups (VPA vs TPM) and socio demographic and epilepsy characteristic variables ($p < 0.05$ were considered significant).
Results: Out of 42 patients, 26 (62%), aged 17 to 54 (mean 28.8±11.1), duration of epilepsy 4 to 43 yr. (mean 16±11.9) were treated with VPA 500 to 1750 mg/day (mean 992) while 16 (38%), aged 14 to 38 (mean 22.1±7.3), duration of epilepsy 1 to 24 y (mean 9.8±8.1) received TPM 50 to 175 mg/day (mean 98.3). At the evaluation, 10 patients of the VPA and 6 of the TPM group were seizure free for more than one year. PD were found in 26 patients (62%). The most frequent were anxiety disorders (13 cases; 10 VPA x 3 TPM) and depressive disorders (9 cases; 5 VPA x 4 TPM). 11 patients (26.2%) performed criteria for mild to moderate PD (7 VPA x 4TPM). There was no association between any PD and type of drug either time without treatment or types of seizures. Anxiety disorders were associated with lack of seizure control ($p<0.039$) and patients with more than 20 generalised tonic–clonic seizures (GTCS) during their lifetimes ($p<0.029$).
Conclusion: There were no statistically significant differences between VPA and TPM treatment of JME in relation to frequency or types of PD. Anxiety disorders, however, were associated with lack of seizure control and more than 20 GTCS.

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Symbolic Function Explored in Paediatric Age Patients with Epilepsy and Headache
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Purpose: When the body gets sick, one of the possible effects that we can observe is the "attack to the thinking capacity". This attack typically consists in a "co-artation" of imaginative life, of symbolic and mythopoetic creativity, of the ability to remember and to narrate (i.e. stories or fables) and in a progressive impoverishment of mental activity of the subject. In order to protect the psychic health, the present investigation aims at exploring the symbolic function in paediatric age subjects with epilepsy and headache. In particular, we aimed at assessing the following areas: defensive strategies and styles, level and quality of mentalization, coping abilities.
Methods: A group of 74 subjects (47 males and 27 females, with a mean ge of 11.6+- 2.6) affected by epilepsy (53 subjects) and by headache (21 subjects), from the NPI in Palermo. Tecnica delle Storie Disegnate (G.Trombini): this instrument permits the subject to externalise affective themes and conflicts that could not be expressed in another way. The clinician can evaluate the degree of psychological suffering of the patient through the typology of the results obtained: positive or compensate result (EP/EC=elaborate psychological suffering); negative result (EN = inelaborate psychological suffering) or story absence (AE), (Trombini E, et. 2002); method of fables (L. Duss). This instrument put in evidence, in a valid way, the defensive strategies mainly used by the subject. The fables are assessed through a lecture grid that is comprehensive of the contributes of Duss (1944, 1950), Battaglia and Lis (1984), Passi Tognazzo and Zanettin Ongaro (1971), and of the contributions of the research group of Palermo (La grutta, Lo Baido, Sarno). In this case, the assessment parameters are: presence/absence of symptomatic behaviours; fable result (positive or compensate result, EPD/ECD; negative result, END; absence of result, AEND); presence/absence of feelings expressed by one character of the story; individuation of relationships among the characters of the

fable (these relationships are classified in: approach (AVV), moving away (ALL), absence of relationships (AR); coloured progressive matrices (CPM; Raven, 1981) to assess the cognitive abilities by excluding the possible influences of affective factors.
Results: The CPM scores show homogeneous results for the subjects of our group. In comparison to the normal population, our group shows a superior rate of negative results and presence of a significant inelaborated psychological suffering in "Tecnica delle Storie Disegnate" of G. Trombini. This is in accord with the literature. In the same direction go the results of the "Method of fables" of L. Duss. The present study permits us to identity some specific patterns related to the investigated pathologies. In fact, in comparison to subjects affected by headache, the ones affected by epilepsy show a significant increase of answers AE ($p<.001$), in both "Tecnica delle Storie Disegnate" and "Method of fables".
Conclusion: The results permit one to evaluate and qualify the suffering related to organic illness, and to make a discrimination within a group of specific ways of co-artation related to the mechanisms of dissociation and splitting rather than to the repression.

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Psychic Disorders of Epilepsy Patients: A Possibility for Diagnostic Mistakes
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Purpose: To show the elements in status psychicus of patients which can direct us to epileptic origin of the behaviour disorders.
Methods: Prospective clinical study.
Results: Case one: A boy with the first epilepsy attack at the age of 13. Ever since the age of 5, he has displayed occasional moments of hetero aggressive conduct towards his parents, as well as terms of occasional aggression, destructive behaviour, suicidal verbalisations, mainly in the evening hours. His behaviour is inappropriate to the situation, over which he has been found inadequately brought up. An EEG shows epileptic changes mutually front-temporal. Therapy was activated, the normalisation of the EEG and the boy's conduct took place. Case two: A patient aged 37 with grand mal attacks since the age of 30. He had a few episodes followed by confusion, dysphasia, dyspraxia and anxiety. The doctors thought that he had consumed alcohol. Once when he displayed a similar behaviour, we did an EEG and registered a continuous epileptic sharp wave-slow wave activity above the left hemisphere. With AE therapy, the EEG normalised and his status psychics were good. His mind was clear, the flow of thoughts was coherent and his affectivity was normal. Nonconvulsive status epilepticus lasted seven days.
Conclusion: Both patients had epileptic behaviour disorders, which at first were not recognised as such. Characteristics in status psychicus in those episodes were confusion, time orientation disorder, and anxiety. Behaviour of the patients was not in accordance with their types of personality and common behaviour.

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Prevalence of Mental and Behavioural Symptoms in a Rural Nigerian Epilepsy Clinic
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Purpose: To determine the level of psychopathology in epilepsy in a rural setting. To determine whether the presumed excess or cryptogenic and symptomatic epilepsy in low-income settings also leads to an excess of psychopathology. To determine to what extent particular anticonvulsants, in this case phenobarbitone, contribute to the development of mental and behavioural problems in this population. To have an insight into the specific mental and behavioural problems occurring in this population.
Methods: A retrospective case note survey of all patients attending our service in the 5 year period 1999 to 2004. Basic demographic and clinical data as well as EEG findings were collected for all patients. Data was analysed using the Epinfo 2000 package with appropriate statistical tests.
Results: The majority of the patients took several years (more than 20 in some cases) before presentation. Some of the patients did not have any mental or behavioural problems. Only 4 out of the 42 patients exhibited symptoms or behaviours severe enough to require clinical intervention. Psychopathology significantly was associated with seizures starting before the age of 5. Phenobarbitone appeared to be associated with hyperactivity in children with mental retardation. In addition, it was effective in controlling seizures in 6 out of 30 patients and significantly reducing them in another 13.
Conclusion: Epilepsy patients in rural Nigeria suffer a relatively low level of mental and behavioural problems. Phenobarbitone should remain a first line drug for reasons of cost, efficacy and safety.

p488
Psychiatric Symptoms Related to Hospitalised Epilepsy Patients
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Purpose: It is accepted that epilepsy predisposes to mental disorders, mainly psychosis, personality disturbance, depression and delirium. Most studies have analysed psychiatric syndromes. We want to know about frequencies, correlations and clinical features of psychiatric and epileptic syndromes.
Methods: We studied selected cases of epilepsy patients hospitalised in psychiatry during the 5 years 1996-2000. We analysed general aspects, whether they had mental retardation, the frequency of psychiatric syndromes in agreement with DSM IV, correlations with features of epilepsy (ILAE) and evolution. SPSS was used for statistical analysis.
Results: 120 cases, 61 female and 59 male, 73 with psychosis symptoms, 32 of these also with delirium, 22 personality disturbance, 19 depressed, 6 with other syndromes, 58 with mental retardation and 84 without seizure control.
Conclusion: Psychosis was the main psychiatric syndrome in hospitalised epilepsy patients, delirium was associated with 43%, and most cases were without seizure control. Mental retardation was present in about half of the cases.

p489
Psychiatric Co-morbidity in Patients with Difficult-to-treat epilepsy: A Study from a Tertiary Referral Centre in Eastern India
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Purpose: To study the pattern of neuropsychiatric co-morbidity among patients with difficult-to-treat epilepsy in the context of some biological and social variables.
Methods: This study was conducted over a period of one year in the weekly Epilepsy Clinic of Bangur Institute of Neurology, Kolkata, a tertiary referral centre. All patients with difficult-to-treat epilepsy (47 cases) who had a normal CT brain scan without any past history of cerebrovascular accident, head injury, alcoholism, or substance abuse, were included in the study. Each patient was examined clinically and diagnosis was based on DSM-IV criteria. Appropriate laboratory investigations and psychometric tests were done. Variables such as patient's age, sex, birth order, seizure type, age of onset, duration of illness, treatment history and socioeconomic status were registered.
Results: Most of the patients in the study population belong to the 13-18 year age-group (40%), with male predominance (63%). All the patients were receiving two or more drugs, generally at the highest tolerable doses. Mental retardation was present in 27 (57.4%) of cases. Duration of illness was much higher in patients with severe and profound mental retardation. Psychosis and mood disorders (20%) were the most common psychiatric co-morbidity. The other co-morbidities included attention-deficit hyperactivity disorders (4%),

autistic disorders (4%), and anxiety disorders (4%). Psychiatric disorders showed marked female preponderance.
Conclusion: This clinic-based study in a tertiary care centre shows significant co-morbidity, which is likely to interfere with the quality of life of patients with epilepsy.

p490
Stress During Pregnancy in Women with Epilepsy
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Purpose: Pregnancy in women with epilepsy has been characterised by some stressors and these can be seen as an overburden to personal adaptive mechanisms. In this setting we searched to identify some symptoms, stressors and adaptive strategies for women with epilepsy.
Methods: We followed 10 pregnant women with epilepsy. The mean age was 26 years (range 18-36), and the mean duration of epilepsy was 11 years (range 3-28 years). 4 had symptomatic; hippocampal sclerosis (2), temporal ganglioglioma (1), subcortical grey-matter heterotopia (1) and 6 had probable symptomatic epilepsies. 9 patients were on monotherapy with carbamazepine (4), phenytoin (1), oxcarbazepine (1), phenobarbital (2), valproate (1) and 1 on two antiepileptic drugs. 7 patients were considered as seizure free and 3 had 1 to 8 seizures/month. Seizure frequency remains unchanged during pregnancy in all patients. They were asked about Stress Inventory (Lipp, 1994), Sources of Stress protocol during pregnancy (Torrezan,1994) and Adaptive strategies protocol (Torrezan, 1994)
Results: Stress was observed in 9 women (stage of resistance - 5 and stage of exhaustion - 4). Two of 24 stressors were identified. Worry on delivering a healthy child and a child with epilepsy were the most frequent stressors with symptoms of fear, anxiety, irritation, insomnia, fatigue, and depression. Coping strategies were counselling with neurologist and obstetrician, home rest or standing alone and talking with friends or relatives when worried.
Conclusion: Changes observed during pregnancy are usually sources of stress. Epilepsy during pregnancy adds some stressing new sources. Additional adaptive efforts are required that can increase stress during pregnancy.

p491
Sleep Disturbances Reported by Partial-onset Epilepsy Patients Receiving Polytherapy
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Purpose: This study reports sleep disturbances among patients taking stable regimens of ≥2 antiepileptic medications and evaluates the impact of sleep problems on health-related quality of life (HRQOL).
Methods: A survey of 201 adult patients with partial epilepsy. Community-based US neurologists recorded demographic and clinical information. Patients completed the Medical Outcomes Study (MOS) Sleep Scale, the Quality of Life in Epilepsy-10 survey (QOLIE –10), and the EuroQoL-5D survey (EQ-5D).
Results: The mean (sd) age of patients was 44.2 (12.5). 34% of patients had diagnosed sleep disturbances; 10% had been prescribed sleep medications. Patients with sleep disturbance reported poorer mean QOLIE-10 (55.2 versus 63.7; p=0.006) and EQ-5D (0.5 versus 0.7; p<0.001) scores relative to those without sleep disturbances. The mean (sd) MOS sleep score was 36.2 (20.8), above the general population mean of 26. Women reported more sleep problems than men (42.3 versus 28.4; p<0.001). Patients with physician-reported anxiety or depression had more sleep problems (anxiety: 44.5 versus 33.1; p<0.001; depression: 41.2 versus 32.8; p=0.005). Higher MOS sleep problems scores were significantly correlated with poorer QOLIE-10 (r = -0.49; p<0.001) and EQ-5D (r = -0.56; p<0.001) scores. Patients experiencing a seizure within one week reported higher MOS sleep problem scores than those with a less recent seizure (41.5 versus 32.8; p=0.003).
Conclusion: Patients with partial-onset epilepsy receiving stable polytherapy regimens experience more sleep problems than the general population. Sleep disturbances are negatively associated with functioning. Recognition and treatment of sleep problems represents an opportunity to improve the care of epilepsy patients. Pfizer Funded.

p492
Interictal EEG Changes in Patients with Epilepsy and Comorbidity of Depression, Dementia or Interictal Psychosis
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Purpose: The purpose of the study is analysis of interictal changes in EEG in patients with epilepsy and comorbidity of depression, dementia or psychosis and comparison with patients with epilepsy free of mental illness.
Methods: Changes in interictal EEG in 203 patients with epilepsy; 117 women (57.6%) 86 men (42.4%), aged 18 to 50, with mean duration of epilepsy 33.3 years were analysed. Major depression was diagnosed in 100 patients (49.2%), dementia was diagnosed in 51 cases (25.1%) and interictal psychosis was diagnosed in 20 (9.8%). EEG patterns were analysed in all patients and compared between groups with and without mental illness using statistical methods like χ^2 test, Fisher exact test and model of regression.
Results: In the group with epilepsy and depression theta waves in both temporal areas and delta waves in both frontal areas were more often found than in the group without depression. In the group with epilepsy and dementia delta waves and ictal discharges in both frontal and temporal areas were more often found than in the group without dementia. In the group with epilepsy and psychosis sharp waves in the right temporal area were more often found than in the group without psychosis. These results are statistically significant in χ^2 test ($p<0.005$).
Conclusion: In interictal EEG in patients with epilepsy and comorbidity of mental illness, theta and delta waves and ictal discharges in frontal and temporal areas were observed.

p493
EEG Abnormalities and Seizures during Treatment with Clozapine
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Purpose: Clozapine is an 'atypical' neuroleptic that improves symptoms of many patients with schizophrenia, and does not induce extrapyramidal symptoms. However, clozapine can cause epileptiform EEG changes and causes seizures in 1-5% of patients treated with this drug in therapeutic doses. High doses, history of seizure activity, slow drug metabolism, rapid dose titration and a previous history of neurological abnormalities are factors increasing the likelihood of clozapine-related seizures.
Methods: In a retrospective study we analysed EEG recordings during clozapine treatment of 58 patients with normal pretreatment EEG evaluations. 30 women and 28 men aged 20-47 years were treated with clozapine in the dose range 100mg-300mg.
Results: Interictal EEG of 11 patients (18.96%) have shown epileptiform abnormalities: in 8 patients generalised paroxysmal epileptiform abnormalities (s-w and ps-w complexes) and in 3 patients focal paroxysmal epileptiform discharges temporo-central (2 on the left and 1 of the right side). 1 of them has taken a daily dose of 100 mg, 4 a dose of 125-200 mg and 6 of them 225-300mg clozapine per day. Only 1 patient (1.72%) had generalised myoclonic jerks and his EEG recordings both ictal and interictal have shown generalised epileptiform abnormalities. He has taken the clozapine in a daily dose

of 300 mg. The myoclonic jerks became completely controlled with valproate.
Conclusion: Clozapine like many other antipsychotic agents, lowers the seizure threshold and can cause epileptiform EEG changes. High doses of clozapine appear to increase the chances of an antipsychotic medication inducing seizure activity. Low doses (less than 300 mg) and slow titration of clozapine decrease the likelihood of clozapine-related seizures.

p494
Epilepsy and Giftedness
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Purpose: Some of the most famous people in history had epilepsy: world leaders, philosophers, composers, classical writers, and painters. They made important contributions to the life of their communities.
Methods: Dutch post impressionist Vincent van Gogh is today the most widely known and appreciated artist with epilepsy in the fine arts. He received little recognition in his lifetime. Van Gogh's unusual painting style and voluminous correspondence are fertile ground for different theories about him. He had a difficult life, which included depression, epileptic seizures, and bizarre psychiatric symptoms and was terminated with suicide. Van Gogh suffered from focal epilepsy and had seizures at irregular intervals in the last two years of his life, which was remarkably his most creative artistic faze. It was probably a symptomatic type of epilepsy.
Results: Probably a difficult, protracted birth caused cerebral damage to the temporal region. There was also a genetic tendency to epilepsy in his family (van Gogh's mother's sister, his brother and his sister suffered from epileptic seizures for a time). Obviously van Gogh's life style contributed to his illness: fasting, malnutrition, drinking absinthe, overworking, taking some toxic substances… Whether his illness or drug use might have contributed to his creativity is a persisting question.
Conclusion: People with epilepsy would not consider that their seizure disorder is something that enhances their natural abilities. We know that if in the early life one area of the brain is damaged, the corresponding area on the other side has a chance to overdevelop. This could explain the association between epilepsy and giftedness in some people.

p495
Sexual Differences in the Seizure Threshold and in the Anxiety Level of Epileptic EL Mice and their Relations to Peripheral-type Benzodiazepine Receptors (PBR)
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Purpose: In EL mice, an animal model of epilepsy, their spontaneous seizures and increased fear responses might be related to abnormalities in the PBR in the brain (i.e. Nakamoto Y et al. Brain Res. 1996;717:91-98). Lines of evidence suggest that acute stress tends to increase PBR densities while chronic stress leads to a decrease in the PBR densities in various tissues including blood platelets. We found recently that platelet PBR in humans were correlated with individual sensitivities to stress and anxiety (i.e. Nakamura K et al. Psychopharmacology 2002;162:301-303). In the present study, we have further investigated, using EL mice, whether sexual differences are present in their seizure threshold, anxiety levels and PBR densities.
Methods: Adult male and female EL and DDY (control animal) mice were used. Seizures in EL mice were induced by our standard method. An elevated plus-maze (EPM) was used to examine anxiety levels of mice. Receptor binding assay for PBR was also performed using blood platelets of EL and DDY mice.
Results: In EL mice, lowering of seizure threshold with age took place much earlier in males than in females. Compared with DDY mice, fear responses were significantly greater, particularly in males. Male animals appeared to have a higher density of platelet PBR than their female counterparts.
Conclusion: The results indicate that sexual differences in the seizure threshold and in the anxiety level are present in EL mice, which may be associated with PBR abnormalities.

p496
Backpropagation Neural Networks can Predict the Hippocampal Volume from Homocysteine, Folate, Vitamin B6 and Vitamin B12 in Alcoholic Patients with High Accuracy
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Purpose: Recently, it has been shown that alcohol-induced hyperhomocysteinaemia is a risk factor for alcohol withdrawal seizures and hippocampal atrophy in actively drinking patients suffering from chronic alcoholism. For further analysis of the relationship between homocysteine, folate, vitamin B6, vitamin B12 and hippocampal atrophy we applied backpropagation neural networks (BNN) to predict the hippocampal volume from the blood levels of these biochemical markers.
Methods: We applied a 4-layered BNN (4 input neurons, 15 neurons in layer 2 and 3, one output neuron) to the biochemical data of 48 chronic alcoholics (18 women, 30 men, age between 29-67 years, average age 47, training set 16 patients, validation set 16 Patients, test set 16 patients). Training was performed with learning rate of 0.5 and momentum of 0.1 until validation indicated an optimum adaptive result of the network. An Average of 10 different networks was calculated for average prediction error and maximum error.
Results: We were able to predict the hippocampal volume with an average error of 7.1% (+/-20%).
Conclusion: Taking into consideration the small number of subjects, very good prediction results indicate a nonlinear dependency of hippocampal volume and the biochemical markers. Further evaluation is needed to clarify the relation between withdrawal seizures and hippocampal atrophy.

Monday 29th and Tuesday 30th August 2005
13:15 – 14:15
Poster Session
Social Issues / Nursing

p497
Evaluation of the Assumption of Responsibility and the Quality of Services Offered to Epilepsy Patients in the Pikine Medical District
A.D. Sow[1], N.F. Ndoye[1], B. Sessouma[1], K. Toure[1], A.G. Diop[1], P. Ndiaye[1], F. Sene[1], M. Ndiaye[1]

1) Dakar, Senegal

Purpose: Epilepsy is widely distributed around the world. This very common brain disorder is associated with various socio-cultural misinterpretations in many developing countries. The large majority of people with epilepsy and their families usually refer to traditional healers rather than modern medical structures. These facilities are often missing in such countries.
Methods: The medical structures of the District of Pikine were investigated twice (one month at every round). The six months delay between the two investigations was utilised to set up educational and training programs for health workers and the general population.
Results: Our results demonstrate that there is a clear-cut lack of material and human resources dedicated to people with epilepsy in health structures in this suburban area of Dakar, Senegal. Progressively and due to the interventions led by the Senegalese League Against Epilepsy, we found an increasing interest in a better management of medical treatment against epilepsy. Phenobarbital

remains the most commonly used drug in connection with the percentage of generalised epilepsies (88%).
Conclusion: Because of the considerable treatment gap and for better accessibility of quality of care, it appears necessary to set up decentralised consultations and to train paramedical and medical personnel. The goal is to ameliorate their ability to take care of simple cases of epilepsy and to make antiepileptic drugs more readily available.

p498
Assessment of Quality of Life in Epilepsy Patients in Xi'an China
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Purpose: Epilepsy is a chronic condition. Because of fear of epilepsy attacks and hopelessness regarding treatment, they always feel disappointed, frustrated, anxious and depressed. As a result, the quality of life (QOL) of epilepsy patients is seriously affected. In this pilot study we aim to have a right assessment of QOL in epilepsy patients in our hospital.
Methods: A revised QOL questionnaire which contains 35 questions was used for the investigation in out-patients in Xijing Hospital. Altogether 100 patients were investigated, 87 qualified questionnaires were obtained. Patients included 60 males and 27 females, aged from 12 to 55. Ten of them had primary education, 60 had middle and 12 had higher education. 24 of them were married. 61 were from urban and 26 were from rural areas.
Results: There were about 2/3 of patients who indicated they were always frustrated, tired and disappointed. There were only about 1/3 of epilepsy patients who sometimes felt energetic. One third of patients indicated they have moderate memory impact which affected their normal life and work. There were about 2/5 of patients who said they couldn't finish appointed work because of emotional reasons. There were more than 1/3 of patients who indicated that their life and work or school were affected by epilepsy. About 3/5 of patients said they were limited in participating in social activities because of epilepsy.
Conclusion: QOL in epilepsy patients is poor and social and medical epilepsy workers should pay attention to and make good efforts to increase it. This work was supported by international clinical epidemiology network (INCLEN).

p499
Comparison of Impact between Paediatric Epilepsy and Type 1 Diabetes Mellitus on the Family
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Purpose: There are few reports about the psychosocial impact of paediatric epilepsy and type 1 diabetes mellitus (T1DM) on the child and family. We used an 11 item scale to evaluate the influence of epilepsy and T1DM in the major aspects of the family and child's life.
Methods: Parents rated their child's quality of life on a visual analogue scale (1-6) and completed the 11-item scale developed by Jacoby. We compared the quality of life and the impact on the family between the patients with epilepsy and T1DM.
Results: We matched 120 children's demographic characteristics (60 in epilepsy and 60 in T1DM) including sex, age, onset of conditions and duration of conditions. Parents of both groups rated their child's quality of life as similar (3.8+1.2 vs 3.9+0.9), and they thought the general impact of these two conditions had no significant difference (15.1+7.4 vs 14.8+6.8). Parents of children with epilepsy were more worried about the impact of acceptability of others ($p<0.05$) and the child's self-esteem ($p<0.001$) than T1DM group. Conversely, T1DM children's parents were more concerned about their child's overall health ($p<0.001$), their relationships with parents ($p<0.05$) and with siblings ($p<0.05$) than were parents of the epilepsy group.
Conclusion: Parents of both groups had similar concepts about their child's quality of life and impact of both disease to their children. But we found that parents of children with epilepsy are more concerned their child's self-esteem and social acceptance, and parents in T1DM group thought that the condition obviously affected the health of the child and family relationships to their child's life.

p500
Quality of Life and Depressive Symptoms in Temporal Lobe Epilepsy with Hippocampal Sclerosis
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Purpose: To evaluate quality of life (QOL) in an homogeneous group of patients with temporal lobe epilepsy (TLE) due to mesial temporal sclerosis (MTS) pre and post surgical treatment (corticoamygdalohippocampectomy) and to evaluate the correlation of depressive symptoms and QOL before surgery treatment.
Methods: Epilepsy Surgery Inventory (ESI-55) and Beck Depression Inventory (BDI) were used as a part of a surgical protocol that included MRI, video-EEG monitoring and neuropsychological evaluation. All patients had MTS pathologically proved. The ESI-55 was cross-culturally adapted to the Brazilian environment according to internationally recommended methods. Statistical analysis was calculated with Wilcoxon and Spearman tests.
Results: 30 subjects (60% with left MTS) answered the ESI-55 and BDI pre and six months post-surgical treatment. 63% were female. The mean age was 36 years and the mean duration of epilepsy was 27 years. Post surgically, QOL improved in 8 of 11 ESI-55 domains: health perception, overall quality of life, limitations due to physical and emotional problems, social function, energy-fatigue, emotional well-being and cognitive function ($p<0.05$). There was association between QOL and depressive symptoms in the following domains: emotional well-being, energy-fatigue and health perception.
Conclusion: In this series of patients with TLE due to MTS, surgery improved QOL. Depressive symptoms were positively correlated with QOL.

p501
Personal Perspectives of Living with Epilepsy or a Seizure Disorder
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1) Medical University of South Carolina, Charleston, USA 2) Colorado State University, Fort Collins, USA

Purpose: An exploratory qualitative study was conducted using the phenomenological tradition to answer the overarching question, 'What has it meant for people with epilepsy or a seizure disorder (E/SD) and their loved ones to live with the condition?'
Methods: 42 individuals representing 32 people with E/SD responded during focus sessions to questions developed from an earlier pilot study. Responses were recorded and analysed for recurring themes and content.
Results: Five major themes emerged: 1) Having to accept that certain difficulties and worries are lifelong, for example, employment, being a burden to others, isolation, loss of functions and life dreams, transportation, depression and emotional problems, substance abuse. 2) Deciding whether to hide their E/SD due to society's ignorance and stigma associated with having E/SD. 3) Searching continuously to find help from medications, technologies, and medical providers. 4) Experiencing discrimination due to governmental policies and society's lack of understanding E/SD. 5) Desiring to advise other people with E/SD based on personal experiences.
Conclusion: Judging from consistent responses from focus group to focus group, people with E/SD have excellent insight and can provide reliable recommendations to health care personnel, educators, and policy makers and other governmental providers on what is needed to

recognise E/SD as a disabling condition, and help improve public relations campaigns to de-stigmatize E/SD. Better education of medical, educational, and community professionals concerning the on-going and often desperate plight of people with E/SD and implementation of federal and state governmental programmes could help people with E/SD live as normal lives as possible.

p502
Self-esteem in Children with Epilepsy and Asthma
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Purpose: The purpose of this study is to examine self-esteem of children with epilepsy and asthma. Past studies have demonstrated that children with chronic illness are at a higher risk of psychological adjustment.
Methods: Forty-nine 8 to 13 year old children with epilepsy and 54 children with asthma were selected for this study. Children's self-esteem was assessed by Harter's Self-Perception Profile for Children (SPPC). This instrument contains six separate subscales: scholastic competence, social acceptance, athletic competence, physical appearance, behavioural conduct and global self-worth. Each subscale presented a separate score. Influences of age and gender were also investigated.
Results: Results showed that there were significant differences between two groups in four SPPC subscales, including scholastic competence ($p<0.005$), social acceptance ($p<0.001$), athletic competence ($p<0.05$), and global self-worth ($p<0.05$). Age was an effective predictor of the physical appearance subscale. Gender impact of self-esteem in the two groups was not to be found. Subjects in the epilepsy group have lower SPPC scores than in the asthma group for all six subscales.
Conclusion: Chronic illnesses involving the brain are more strongly associated with psychological problems. Harm in the brain might lead to problems related to academic learning and psychology. Furthermore, it may be more difficult to adjust to epilepsy than to asthma, especially due to the greater social stigma associated with epilepsy. Misunderstanding and discrimination against epilepsy cause high stress to children with epilepsy. However, discrimination seems not to be a problem to children with asthma. Besides providing regular drug therapy, offering more support to children with epilepsy is important. Public education about epilepsy is also necessary.

p503
Epilepsy and Quality of Life in Patients in the Course of Their Treatment and Rehabilitation
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1) V.M. Bekhterev Psychoneurological Research Institute, St. Petersburg, Russia

Purpose: To study the quality of life (QOL) of patients with epilepsy in the course of treatment and rehabilitation interventions.
Methods: Clinical method; QOL measurement (using the WHOQOL-100).
Results: 146 patients with epilepsy, aged from 16 to 64 years, were included in the study. Patients with epilepsy assessed their QOL in the majority of the WHOQOL-100 parameters as average. Two of the six major domains, spirituality and level of independence, were assessed as quite satisfactory. The lowest scores were found in the facets availability and quality of health and social care and financial resources. Patients over 40 years of age gave statistically significant lower scores in the physical domain, level of independence, and overall QOL than the younger patients. Patients under 19 years of age gave higher scores in the social relationships domain than the older patients. Patients with partial seizures gave lower scores to their QOL in physical domain, psychological domain, and environment than patients with generalised seizures. The integral QOL scores showed a highly significant correlation with the clinical effect attained in the course of treatment (using convulex, depakine, carbamazepine, and topamax) and rehabilitation (using psychosocial interventions). In patients with seizure control, a positive dynamics was found in QOL indices in all domains.
Conclusion: QOL studies allow obtaining important data on the subjective assessment of the physical domain, psychological domain, and social relationships by patients with epilepsy. These data can be used in the development of treatment and rehabilitation programmes and in the monitoring of a patient's state in the course of their implementation.

p504
Quality of Life of Patients with Epilepsy in Ulaanbaatar
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Purpose: To study the demographic characteristics and quality of life of patients with epilepsy in Ulaanbaatar.
Methods: The study subjects are patients diagnosed with epilepsy attending the participating hospitals. A questionnaire was developed to collect relevant data relating to the socio-demographic situation and history of seizures.
Results: There were 1,565 epilepsy patients, 896 males and 669 females, enrolled in the study. The age range was between 0-65 years. When considering the education, occupation and profession of 1,528 patients, it was found that 6.3% were primary and secondary school students, 4.8% university and college students, 13.1% employed, 4.3% unemployed and 69.1% disabled. Most epilepsy patients were from the low income group (43.7%). For marital status, the majority of them were single (56.4%), followed by married (25.1%). We have studied the duration of disease of patients involved in the study classified by age group. The duration varied from less than a year to over 10 years. About 60% of cases had suffered from the disease for more than 10 years, particularly the age group 15-34 (28.0%) and 35-64 (28.9%). There were 1,112 cases who had changed working conditions. The majority of them had reduced working capacity, with disability level of over 70% (46.7% of the cases), disability level between 50-70% (15.4% of the cases).
Conclusion: Quality of life is affected in patients with epilepsy in Ulaanbaatar, especially in relation to education, working conditions and family income.

p505
Impact of Epilepsy on the Family in a Developing Country Setting
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Purpose: Epilepsy is a chronic illness, which can have a profound impact on the family. This study tried to assess the impact of paediatric epilepsy on the family (n=132) in the Indian setting using both qualitative and quantitative techniques.
Methods: Children with normal intelligence, suffering from epilepsy, having no other physical co-morbidity were included in the study. The main out-come variable was quantified with the Impact of Paediatric Epilepsy Scale (IPES). In addition 'in-depth interviews' were conducted with selected caregivers. After factor analysis of the sub-scale scores of the IPES, a logistic regression method was used to find the predictors of higher impact.
Results: Higher impact on the 'interpersonal factor' was associated with higher seizure frequency (OR 2.76, 95% CI 1.11 – 6.8, p=0.03), while higher socio-economic group was protective against higher impact on the 'family functioning factor' (OR: 0.19, 95% CI 0.08 – 0.45, p=0.0002). Qualitative data showed interesting culturally sensitive findings. In general carers were aware about immediate measures needed during a seizure but many were unhappy with the treating doctors' ambiguity in providing clear guidance about prognosis of the illness. Many of them felt that having a child with epilepsy had a significant impact on the family's leisure activities, spiritual and financial well being.

Conclusion: Paediatric epilepsy has a considerable impact on the family even in a developing country setting. Culturally sensitive instruments to look into the impact and counselling of families having children with epilepsy, needs to be part of the treatment package.

p506
Psychosocial Status of a Child with Epilepsy in an Urban Pakistani Society: The Parental Perspective
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Purpose: To assess the parental perspective of the psychosocial status of a child with epilepsy in an urban Pakistani society.
Methods: The parents of 70 consecutive children (age <14 years) with epilepsy only who came for electroencephalography were interviewed.
Results: The parents of 70 patients presenting over a period of six months responded to the questionnaire. 50% of the interviewed parents were graduates or more and 50% had lower education. 30% of patients belonged to a high socioeconomic class and 70% belonged to lower. Univariate analysis revealed that the more educated (at least graduates) and affluent parents were more likely to take care of the interests and education of the child with epilepsy, as compared to non-graduated parents ($p = < 0.05$). In educated and affluent families the child with epilepsy was also readily accepted by siblings and parental in-laws ($p = > 0.05$). Educated and richer parents gave more importance to the child with epilepsy amongst other children without epilepsy, and viewed the degree of acceptance to society to be high ($p = < 0.05$). Less educated parents were more likely to consider a supernatural aetiology for epilepsy ($p = >0.05$). Affluent parents were more willing to discuss the child with epilepsy in front of others ($p = < 0.05$). It was also noted that richer parents considered a successful carrier for the child with epilepsy when compared to less rich parents ($p = < 0.05$).
Conclusion: Educational status and socioeconomic class of parents of a child with epilepsy greatly influence the child's education, interests and ultimately his or her future career in society.

p507
Can the Use of the Summary Score Obtained from the Epilepsy Impact Scale (EIS) be Justified?
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Purpose: Investigating the psychometric properties of the EIS using modern measurement theory.
Methods: EIS provides a summary score of the severity of the impact of epilepsy on the individual. A postal survey was undertaken to obtain EIS data from people with epilepsy registered with Epilepsy Action. Responses were analysed using the Rasch model to determine the appropriateness of summating the ten EIS items by testing for unidimensionality and differential item functioning.
Results: The EIS questionnaire was mailed to 2000 participants. There were 750 valid responses (54.8% female). Seventy questionnaire responses with floor and ceiling summary scores were excluded from further analysis. Responses from the remaining 680 questionnaires were analysed using the Rasch model. Initial analysis showed a poor fit of the 10 items to the model (item-trait interaction □□= 226.2; $p<0.000$). The poor overall fit related to disordered thresholds of the polytomous response categories for each question, poor individual item fit and differential item functioning (e.g. the response patterns differed for different seizure frequencies). A confirmatory factor analysis found two factors (construct) explaining 60% of the variance (first factor with Eigen value of 4.7 and second factor with Eigen value of 1.3) with 6 out of 10 items mapping on one construct, 2 out of 10 items on another and 2 out of 10 mapping on both constructs.
Conclusion: Both analyses demonstrated that the 10 items of the EIS did not measure one single construct. Therefore it is inappropriate to use a summary score as a measure of the impact of epilepsy.

p508
Effects of Epilepsy on Quality of Life
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Purpose: To measure the impact that this disease has on the quality of life of the person with epilepsy and to determine what aspects can be changed.
Methods: The design provided for descriptive and analytical research. Out of a group of 100 epilepsy patients, chosen at random from different specialised treatment centres, individuals between the ages of 15 and 65 were surveyed using a questionnaire designed for the purpose of stressing aspects such as: demographic information, educational level, occupation, financial stability, social and recreational activities, age of onset of seizures, types of seizure, severity, treatment, how treatment is tolerated, drinking habits, use of drugs or stimulants, smoking habits, eating habits, moods, sleeping habits, sexuality, support from family, self-esteem, social discrimination or rejection. Based on the criteria for including or excluding subjects, 92 patients were included in the study.
Results: The results were analysed on the basis of frequency and percentage. The quantitative variables were stated in terms of descriptive means. The average age was 32 years, with a deviation of 11 years. Of those interviewed, 50% were women and 50% were men, 65% were single and 72% were childless. As for education, 68% had only completed primary education. Out of this group, 29% were employed, 23% were students, and only 12% were unemployed. Financial stability was average in 51% of the cases, with little social activity in the case of 53%. As for frequency of seizures, for 42% it was monthly, with partial, simple seizures in the case of 45% and complex partial seizures for 34%. Severe seizures were only found in 17%; bi-therapy was present in 54% of the cases, with average tolerance in 57%. Alcohol consumption was found in 23%, and 19% smoked. Nutrition was good in 52% of those surveyed. 88% suffered from anxiety and 41% from depression. Of the group, 62% had no sleeping problems. Sexual activity was average for 59%. Insofar as support from the family was concerned, it was good for 57%; good self-esteem was found in 48%, and only 20% reported discrimination or social rejection.
Conclusion: The study highlighted the important role that support from the family plays in acceptance of epilepsy as a part of a person's life, in the effort to try to improve his/her situation. The fact that these people turn to specialised centres for early diagnosis, advice and therapy contributes favourably to the evolution of the individual as part of a productive society.

p509
Evaluating the Role of the Clinical Nurse Specialist in Epilepsy
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Purpose: Previous research by the authors has identified that Clinical Nurse Specialists in Epilepsy (CNSE) play a key role in the management of people with epilepsy (Goodwin et al, 2004 Seizure 13; 87-94). However, there remains a lack of quantitative and qualitative research that focuses on the clinical knowledge and skill base of individual CNSE's working at an advanced level of practice. This research study aimed to meet that void.
Methods: Nine CNSE were asked to participate in the study. Prospective data on their daily clinical and non-clinical activity over a period of 20 days using a self-completion diary was collected. Following quantitative collation of the initial data, the researchers obtained further qualitative data from the nine respondents using

semi-structured interviews. The transcribed interviews were subsequently analysed using thematic analysis.
Results: Overall the nine respondents were highly autonomous within nurse-led clinics. The percentage of time spent on clinical aspects of care, which included epilepsy assessment, ordering investigations and drug management was 40%. The time spent on non-clinical activities including teaching, education and research was 60%.
Conclusion: This study demonstrates the advanced level of practice of the CNSE. As advanced practitioners, the nine CNSE have demonstrated their ability to make independent and complex decisions of clinical judgement in and about patient care, utilising their unique and expert knowledge base.

p510
Clinical Value of Central Video Supervision of Patients with Epilepsy
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Purpose: The clinical value of a central video supervision unit (CSU) for patients with epilepsy was examined in the Danish Epilepsy Centre, Dianalund.
Methods: Epilepsy patients in bed were subjected to close supervision for the purpose of patient safety, diagnostic work up or control of antiepileptic treatment. We used video cameras connected to CSU. Patients in bed were constantly supervised by video recording. The patients carried a pulse oxymeter. The beds were equipped with epilepsy alarms. Video supervision allowed identification of epileptic seizures, and the nursing staff in CSU registered all possible events (epileptic and other events). Subsequently, trained physicians classified seizures observed during video recording.
Results: In the period from April to December 2004 there were 221 open days and nights in the CSU. 74 patients were supervised, and a total of 765 patient days were supervised by CSU. 53 patients were included in the evaluation. A total of 250 seizures were detected by the CSU, and as many as 150 (60%) were only detected by CSU and not by any other means (pulse oxymeter or bed alarms). 67 of 71 (94%) complex partial seizures, 49 of 61 (80%) tonic seizures, and 19 of 39 (49%) tonic clonic seizures were only detected due to CSU.
Conclusion: The CSU is of value in improving patient safety, diagnostic work up and control of antiepileptic treatment in a specialised epilepsy centre. A significant number of epileptic seizures of various types are only detected by using the CSU.

p511
Role of a Volunteer Befriending Project in Supporting Adults Isolated by Epilepsy
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Purpose: People with epilepsy may require support to attain confidence to participate in educational, employment, social and leisure opportunities. Epilepsy Connections' befriending project works towards the social inclusion of adults isolated by epilepsy through the provision of ongoing, one-to-one support by a team of volunteers.
Methods: The project links adults isolated by epilepsy with volunteer befrienders to support them to access social and leisure opportunities and explore community-based solutions to individual support needs. Befrienders complete 24 hours of training before being matched and are asked to commit to the project for 6 months. Befriendees are asked to indicate their preferred activities and set goals within the befriending relationship. Matched pairs meet every 2 weeks. Matches are supervised by the Volunteer Coordinator.
Results: 85 services users have requested a befriender. 38 volunteers have trained as befrienders. 43 befriending matches have been established and a range of social and leisure activities undertaken. Feedback indicates that service-users benefit from increased participation in their chosen activities and from opportunities to express thoughts, feelings and concerns in a non-judgemental, supportive relationship. Befrienders gain valuable skills and experience. The project has been independently evaluated by Befriending Network (Scotland).
Conclusion: A request for a befriender often represents a desire to integrate more fully into society. Demand for the service exceeds availability of befrienders. This model benefits befriendees and befrienders. Information fed back by befriendees and befrienders indicates the need for a variety of support options and services to address the educational and employment aspirations of epilepsy service-users.

p512
A Multidisciplinary Approach to Psychosocial Aspects of People with Epilepsy for a Better Socio-occupational Integration
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Purpose: Psychological and social disabilities in patients with severe epilepsy significantly worsen the outcome of drug therapy or surgery. Even seizure suppression does not always allow self blooming or a successful socio-occupational integration. To take into account the psychological disturbances and/or social conditions can be a useful adjunctive therapy in epilepsies. The authors report on the results of a multidisciplinary approach for psychosocial conditions in jobless patients with epilepsy.
Methods: 202 patients (118 males and 84 females) underwent medical, psychological and neuropsychological evaluations.
Results: 50% of the patients were 26-39 years old. 20% were 16-25 years and 30% 40-50 years. Most had complex partial seizures. Educational level was quiet low in these patients (level V to VI = 78%). 57% have had no occupational activity from 1 to 2 years or more. The main grounds for unemployment are in increasing frequency order: the severity of epilepsy; incorrect treatment (dosage, type of drug regarding the type of epilepsy); lack of professional qualifications; stigmatisation in occupational environment; associated handicap (mainly cognitive and psychiatric); psychological disturbances (self esteem and confidence, ambivalence in relation to work, social life,…).
Conclusion: Cognitive and psychiatric or psychological associated disturbances are much more frequent obstacles to employment than epilepsy itself. Treatments with non-reliable AE types of medication or dosage are not so rare. These results argue for better information about medical care but also social and psychological care for patients with severe chronic epilepsy.

p513
Challenge in Rehabilitation of Patients with Epilepsy
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Purpose: I want to inform you regarding the some of challenges coming across my practice with the person with the epilepsy, such as education and training, work and employment, family, marriage, groups, social, sexual, environmental and regional, coordination with other health groups and caregivers, insurance problems, medical, physical, occipital vocational, language problems mostly, and how to give opportunities with the epilepsy and co-morbid medical conditions, and many more conditions to come in future.
Methods: I kept the records for the last 8 years with me since I joined the practice after my post graduation in psychiatry, in my practice, but it is really challenging to calm down for questions with relatives and caregivers.
Results: Only 50% got jobs. It is always interesting to see the experience of other people, including self help groups, in this regard, and most challenging with near by perfect action, and the interaction required with epilepsy groups because there are some social problems.

Conclusion: There is a big challenge in these groups to rehabilitate people with epilepsy. There are multifactor involvements in these groups, dealing with early intervention, long term rehabilitation and difficulties with co-morbid medical conditions. We aim to assist people to become more productive in society in regards to work, by having more interactions among the society and with caregivers working in this field, as we have not been able to achieve rehabilitation up to 50% until now.

p514
What are the Benefits of Participating in Creative Writing Workshops for People with Epilepsy
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1) Epilepsy Connections, Glasgow, Scotland

Purpose: People with epilepsy often report high levels of stress and anxiety, low self-esteem and social isolation. Epilepsy Connections provides community-based support services to tackle these issues. The creative writing project aimed to provide a forum for adults with epilepsy to explore their creativity in an informal setting and produce a publication of work created during the project.
Methods: Participants attended weekly 2-hour workshops for 18 weeks. Workshops were facilitated by a professional writer and an epilepsy fieldworker. Participants were set tasks such as creating characters, keeping a daily journal and writing a book review and could also choose their own topics. Work produced was developed at home and shared with the group each week with participants invited to comment on each other's contributions. Participants selected pieces of their writing for inclusion in the publication and contributed to its design and layout. Feedback was collected from participants and facilitators during and after the workshop series.
Results: Facilitators observed that participants' confidence in their writing grew. Participants reported that they enjoyed the writing activity itself, benefited from opportunities to share experiences with others, found participation a helpful way of relieving stress and would attend more creative writing workshops. The group's first publication 'A Spot of Milk or a Slice of Lemon?': a collection of poems, prose and personal reflections was produced in September 2004.
Conclusion: Offering creative writing workshops is a legitimate strand of community-based service provision. Epilepsy Connections will develop and deliver further workshops based on this model.

p515
Efficacy of a Psycho-educational Programme (FAMOSES) for Children with Epilepsy and Their Parents
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Purpose: To evaluate the efficacy of the modular educational program for children with epilepsy and their parents (FAMOSES) developed by the FAMOSES Project Group. This two-day program aims to improve knowledge, coping, treatment outcome, emotional and practical adaptation to the condition and to reduce epilepsy related fears.
Methods: A prospective, controlled, multi-centre, pre-post study design was used to examine the efficacy of FAMOSES in the treatment group compared to the waiting group (control group). Questionnaires included generic instruments (quality of life, KINDL) and epilepsy specific scales regarding knowledge, restrictions in daily living (EPIDEG scale), epilepsy related fear etc. 54 parents of the FAMOSES group completed the questionnaire 3 months before the course and 3 months later; the corresponding waiting group included 50 parents. Respectively, 30 children, who participated in the FAMOSES program, completed the questionnaires immediately before the course and 3 months later; the corresponding waiting group included 16 children.
Results: First results using MANOVA indicate that knowledge of epilepsy improved significantly in parents and children who participated in the programme. Epilepsy related fear was reduced significantly in parents, but not in children. Parental practice and seizure frequency improved in the treatment group ($p<0.05$).
Conclusion: Considering the low costs of the educational program, it is an effective instrument to improve treatment outcome as well as to manage epilepsy by the children and their parents and to reduce epilepsy related fear and restrictions. Educational programmes should be part of the standard service of epilepsy centres.

p516
The German Epilepsy Museum in Kork (GEMK) Provides Information for a Wide International Public
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Purpose: The idea to open the GEMK was founded on both historical and contemporary questions and aims. Historical questions were based on curiosity for the medical and social history of epilepsy. With regard to the present, the museum was intended to provide information for a wide public and offer a scientific basis for academic studies.
Methods: In 1998, the GEMK was opened on private initiative. Its rooms have the following focus: history of epilepsy, diagnosis, treatment, epilepsy and art, famous people who suffered from epilepsy. The GEMK's library gives access to over 150 works on epileptology, dissertations and scientific articles from the 17th to the 20th century. The GEMK's web page (www.epilepsiemuseum.de) offers a virtual tour in six languages.
Results: Articles in German and French newspapers, radio and television broadcasts have presented the GEMK to a wider public. In 2001, its web page received a Health Award from the American National Health Information Resource Center. Some of the GEMK's exhibits were shown during the European Epilepsy Congress in Vienna last year. In 2004, the GEMK received over 2000 international visitors, and more than 50,000 people from all over the world have visited its web page.
Conclusion: During the last years, the GEMK has provided information about epilepsy for professionals and for the lay public all over the world. By its medical, historical and social approach, the GEMK stands on a crosspoint between patients and their families and loved ones, professionals, and the remainder of society.

p517
Women with Epilepsy Need Counselling: Results of the Study 'Women and Epilepsy'
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Purpose: To investigate the knowledge women with epilepsy have about their condition, their restrictions due to epilepsy, their need of counselling and desire for support.
Methods: Prospective, cross-sectional study using questionnaires. In total, 338 women with epilepsy aged from 16 to 75 yrs were included.
Results: About 60% to 70% of the women reported that they were well and very well informed about topics on antiepileptic drugs (AEDs), contraception, pregnancy, prophylaxis of malformation, and heredity of epilepsies. In contrast, the results of the knowledge questionnaires revealed considerable deficits in knowledge, e.g., only 54% of the women knew that folic acid can reduce the risk of malformations, whereas risks were overestimated for developing epilepsies or malformations in children. Altogether, knowledge was dependent on age and school education. 44% of the women had children. The majority reported that they had discussed the hope for a child with their doctor (65%) and had been informed about risks of AED (70%) and seizures (67%) for the unborn. Nonetheless the majority of women were worried during their pregnancy about risks

for the child. Every sixth woman stopped or reduced antiepileptic medication during pregnancy without consulting her doctor. About half of the women were worried that the child could be harmed during a seizure of the mother. Personal counselling by the physician was preferred by 60% of the women, followed by educational courses (31%) and brochures easy-to-understand (31%).
Conclusion: The study indicates that women with epilepsy have a considerable need for counselling and support.

p518
Fits in Fiction
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1) IBE/Public Education Commission

Purpose: We analysed the purpose, the course and the narrative function of malingered epileptic seizures in feature films.
Methods: 20 malingered seizures shown in as many international movies are checked to identify what they have in common. Attention is given to a) the context, b) the purpose intended by the struck person, c) epileptic characteristics, d) the narrative function.
Results: Epileptic fits in the cinema are always actually faked seizures. However, among the epileptic fits shown in over 200 feature films, there is a very particular form of seizure, played as a malingered one. The deceptive manoeuvre has to present symptoms easily recognisable by anybody as 'epileptic'. Therefore, the analysis of malingered film seizures is particularly suited to identify the expectations of the audience regarding the cause, the course and the effects of epileptic fits.
Conclusion: Malingered seizures are often found in detective films and have usually a criminal background. They create typical emergency situations meant to prevent undesired measures that authorities, especially those promoting criminal proceedings, may take. The purpose of their use is only a short-lived deceptive illusion, not long-term treatments. They occur in a way that their 'epileptic' nature is forced on the audience. The expectation of the audience (on the screen and the floor) is generally twofold: it feels that 'loss-of-control-and-emergency' may be as much part of an epileptic event as 'complete-control-and-illusion'.

p519
Psycho-Educative Programme about Epilepsy (PEPE) for People with Learning Disabilities: An English Language Version
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Purpose: The Psycho-Educative Programme about Epilepsy (PEPE) is an established German educational programme for people with learning disabilities and cognitive impairment designed to enhance their understanding of epilepsy and related issues. PEPE is a multimedia programme consisting of text, animations and video clips. The course consists of eight two-hour sessions and comprehensively covers epilepsy and lifestyle issues. We aimed to develop an English version of PEPE tailored to the needs and expectations of people with epilepsy and learning disability in the UK.
Methods: Written materials were translated and video footage remade for the English version. Client involvement in the remaking of the video clips was an important component in this process. This was done in close co-operation with the German originators.
Results: We now have an English version of a potentially useful resource for people with epilepsy and learning disability. We followed the original PEPE program in terms of content but emphasised the more participant-led aspects of the course to concord with the disability empowerment culture in the UK. English facilitators have been trained to deliver the PEPE course.
Conclusion: The German version of PEPE is an important source of support to the target group. We believe that our version will have a similarly significant impact in the English speaking countries, as there are no equivalent tools to educate and empower people with epilepsy and learning disability. Initial response from facilitators and participants involved in the making of the English version was promising. Further evaluation of the course is warranted.

p520
Monstrous Representations of Seizures in Film and Television
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Purpose: The objective was to review representations of epilepsy in film and television for negative imagery.
Methods: Consulting all known databases and websites concerning illness or disability, and many film scholars and neurologists, the authors collected 150 films and television shows depicting seizures. Using saturation techniques of grounded theory, the authors sought the names of films depicting seizures until we received no new names from any source. From this series, we developed and filled categories to analyse the representations. For purposes of this research, the general category of seizures included films in which characters have: 1) epilepsy (84), 2) another condition, drug use or have been shocked (45), 3) pseudoseizures (16), 4) or describe "having a fit" (5). Images were drawn from films released from 1906 to 2004 in seven languages (112 English, 25 French, 5 Italian, 3 Russian and 1 each Spanish, German, Hebrew, Japanese, and Swedish). We have seen and have clips or dialogue for all but two films.
Results: Negative images fall into four categories: 1) monstrous characterisations of those with epilepsy (Russian, Italian, French, English portrayals), 2) bizarre treatments or associations (Hebrew, Swedish, English, French), 3) seizures feigned to move the stories in negative ways (Russian, English, German) and 4) horrific reactions to someone having a seizure. To maximize the use of the images, the clips will run continuously as the authors discuss each category.
Conclusion: Over time, appalling images have increased in relation to characterisations of those with seizures, narratives related to feigned seizures, and responses to those with seizures.

p521
Development and Evaluation of an Epilepsy Education Program for Grade 5 Students: A Cluster Randomized Trial
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1) Epilepsy Support Centre, London, Canada 2) University of Western Ontario, London, Canada 3) Children's Health Research Institute, London, Canada

Purpose: An interactive grade 5 classroom unit was developed to increase students' knowledge of, and positive attitudes about, epilepsy. The unit was evaluated using a cluster randomised control trial. This is the first study of children's attitudes toward people with epilepsy. It advances information gained from an earlier study evaluating a children's epilepsy education program by taking into account clustering in the analyses. Increasing awareness and decreasing stigma about epilepsy are priorities of the WHO and the Canadian Epilepsy Alliance.
Methods: A stratified cluster randomised trial was conducted. Schools from two Ontario school boards (24 schools; 783 individuals) were randomised to either the intervention (education) arm or delayed intervention control arm. Analyses were conducted using linear regression adjusted for clustering.
Results: At baseline, on average, 23/57 knowledge questions were answered correctly. Attitudes were neutral (32/50 mean score, where 50/50 would be most positive attitudes). One month following the epilepsy education program there was a highly significant increase in the intervention group compared to the control group in both knowledge ($p<0.0001$) and positive attitudes ($p<0.0001$). Significant predictors of post-intervention knowledge were 'heard of epilepsy prior to program' and 'seen TV commercial about epilepsy prior to the program'. Significant predictors of post-intervention attitudes were gender, language spoken at home, knowing someone with epilepsy and having seen a seizure prior to the program.

Conclusion: The epilepsy education program evaluated was successful in improving knowledge and increasing positive attitudes about epilepsy. Future research could investigate if these changes translate into decreasing the stigma felt by people with epilepsy.

p522
Epilepsy as a Hidden Disability: Organising an In-Service Training Course for Educators in Malta
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Purpose: In Malta it is estimated that there are around 2000 people with epilepsy of which about 500 are children. Several of them are well controlled and in main stream education, yet there is still social exclusion and discrimination, due to ignorance and stigma, which adversely affects the employment and education of these people. These issues must be tackled if these children are to be socially included and lead more productive lives. Most of the time epilepsy is only seen by educators as 'the problem for the duration of the seizure' and nothing else is done regarding the 'after effects'.
Methods: The Malta Caritas Epilepsy Association (CMEA) thus saw the need to bridge the gap between parents and other stake holders in order to enhance the progress of the child, by organising an inservice training course for primary and secondary school teachers, personal social development and guidance teachers. This course was held in conjunction with the Education Division within the Ministry of Education. The course also tackled indirect problems that are not being addressed which often result in the child losing self esteem, and experiencing regression in progress in school.
Results: The three day course consisted of a number of talks by expert local speakers, as well as interactive workshops. The course content covered an explanation of epilepsy, basic understanding of treatment and psychological factors involved, what it is like to be a young person with epilepsy in Malta, how to tackle possible social exclusion being experienced by these young people, what implications there are for the educational and career achievement for these children.
Conclusion: The main outcomes were recognition of the most common types of seizures, understanding the basic principles of treatment and what to do in case of a seizure, understanding the psychological effects of the condition, knowing how to cope with a child with epilepsy in the class room, developing teaching strategies for children with epilepsy, preparing the environment for children with epilepsy, learning how to co-operate with parents of children with epilepsy, learning how to access further information and contacting support groups in Malta.

p523
Knowledge of and Attitude Towards Epilepsy Amongst Relatives of Epilepsy Patients and the Community in Qatar
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Purpose: Improving the patient's knowledge about epilepsy has been suggested to be a key factor for the improvement of quality of life. Similarly, the attitude towards people with epilepsy is influenced by the degree of knowledge about this clinical disorder.
Methods: This study was conducted among relatives of epilepsy patients (REP) as well as in the community at large (CAL) in Qatar. The age group targeted ranged from 10 - 50 yrs across all nationalities and religions. A semi-structured questionnaire was used to evaluate the knowledge and attitude of the interviewee towards epilepsy. The interview and questionnaire was administered to 28 individuals REP 35.7% and CAL 64.3%
Results: Almost all the REP and CAL had heard about epilepsy; 75% associated epilepsy with a central nervous system disturbance. Some REP and CAL still thought that epilepsy was contagious or caused by an evil spirit. Amongst REP and CAL, 53.6% thought that discrimination against people with epilepsy was justified. The interviewees knowledge about the clinical characteristics and first aid measures for a person having a seizure was unsatisfactory. Less than half believed that epilepsy could be cured. 57.1% thought epilepsy should be treated by modern medicine and 28.6% believed in traditional medicines. The majority (64.3%) of REP and CAL were interested in helping epilepsy patients. One third of people (32.1%) believed that it is safe for an epilepsy patient to drive a car.
Conclusion: In conclusion, there is an urgent need for improving the knowledge of the community, especially people surrounding an epilepsy patient. Public and governmental institutions including teachers should create awareness and provide basic information and assistance in health matters, such as epilepsy. The Ministry of Health physicians and the Ministry of Education should ensure through different sources of education that the community has sufficient knowledge of epilepsy.

p524
Knowledge, Attitudes and Practices of the Health Personnel Towards Epilepsy in Pikine
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Purpose: For The World Campaign Against Epilepsy, Senegal, with other developing countries, was chosen as a pilot site to implement a program against epilepsy. Thus, the aim of this study was to assess the knowledge, attitudes and practices of health personnel towards epilepsy.
Methods: From 23 October to 13 November 2001, a cross-sectional study was conducted with the health personnel in Pikine, a suburb of Dakar-Senegal, using the WHO questionnaire on epilepsy which was self-administered.
Results: The study population (142 health personnel) was composed of 25 medical personnel (medical doctors, pharmacists and dentists), 54 nurses and midwives, 63 community health workers. The mean age was 38.2 years (±10) with a sex ratio of 0.8 for female. 77.5% of the health personnel knew the definition of epilepsy and 32.4% the causes. For 76.7%, pyretic seizures are frequent at the age 3 months-5 years. The first drug of choice is phenobarbital (75.3%) and the treatment should be continued for at least 2 years and stopped after 5 years when the seizures are stabilized. 93.7% had never had training on epilepsy during the last 6 months. There was a statistically significant difference between the health personnel for the cause and treatment of epilepsy.
Conclusion: It is necessary to reinforce the knowledge, attitudes and practices of health personnel through continuing education on epilepsy.

p525
Knowledge and Attitude Regarding Epilepsy Among Medical Students in Khon Kaen
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Purpose: Preliminary planning to design a health education programme on epilepsy in Srinagarind hospital. We evaluated the knowledge and attitude of epilepsy.
Methods: A questionnaire on knowledge and attitude to epilepsy was distributed and completed by all participants. The percentages of correct responses were calculated.
Results: 101 fourth-year medical students responded. Percentages of correct responses to each item were as follows: 1) What is a seizure? Correct answer given by 91.8%; 2) Causes of seizure were head injury (74.5%), brain tumour (81.8%), sleep deprivation (7.3%), alcoholic withdrawal (40.0%), stroke (19.1%) and heavy alcoholic drinking (30.9%). 3). Type of seizures were generalised tonic-clonic (95.5%), simple partial (74.5%), complex partial (11.8%), atonic (43.6%) and absence (33.6%). 4) Seizures are a curable disease (71.8%). 5) Patients should take antiepileptic drugs for about 2-3 years was 48.2%. 6) Management of acute seizures would prevent aspiration

(61.8%), prevent injury (82.7%) and did not try to open mouth (49.1%).
Conclusion: Our results showed most 4th year medical students had a low level of knowledge and attitude regarding epilepsy. Improvement of knowledge and attitude is need.

p526
Knowledge about Epilepsy and its Social Repercussions Depend on People's Education Levels
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Purpose: Spanish society still has a very low level of knowledge about the epilepsy condition and its social repercussions on the patient's quality of life. This is mostly due to lack of information among the general population, plus low educational levels. AEAE, together with the Epilepsy Unit at Hospital Clínico San Carlos, have developed research among the general population with the aim of testing the degree of knowledge about epilepsy and its consequences on the patient's social environment. The research results show that the higher the level of education, the greater understanding of the condition and its social consequences.
Methods: We surveyed a sample of 237 people from the metropolitan area of Madrid. Individuals were both sexes, aged between 19 and 73. We classified the educational levels on three categories: primary education, high school level and university level. The questionnaire had 14 questions related to the condition and its consequences on the patient's environment.
Results: Most representative data extracted from the answers are shown on the graphics. The individuals from the youngest group and the highest educational level know and understand better the condition and its repercussions on different aspects of the patient's daily life.
Conclusion: People understand and accept epilepsy better due to 2 different factors: high education and youth. Following this direction, epilepsy will get rid of the stigma associated to it through of lack of information and social prejudices. Thus, all chances to give information and develop educational policies about epilepsy from childhood will be to the advantage of a promising, gratifying and better future for the general population and for the epilepsy patients and their environment in particular.

p527
Knowledge of Non-neurological Nurses on First Aid for Tonic-clonic Seizures
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Purpose: Knowledge of the range of first aid for tonic-clonic seizures is significantly insufficient among Polish people. To work out the strategy of educational procedure, it was decided to assess the knowledge of non-neurological nurses, who may be the future teachers in health promotion education.
Methods: The study material comprised inquiry data from 124 nurses, who answered 10 questions concerning first aid procedures for epileptic seizures and from 92 subjects from the control group (patients admitted in turn to the regional multispecialist hospital). The answers from the study group were compared to those from the control group and then the results were evaluated with statistical test Chi.
Results: The correct answers were significantly more frequent in the group of nurses as compared to the controls ($p<0.001$). However, the percentage of incorrect answers in the study group was high: 51% thought that a 3-minute tonic-clonic seizure may be life-threatening; 59.6% would recommend inserting a hard object into the mouth during seizures; 51.6% supposed that after each epileptic seizure the patient should be taken to hospital and 16.4% thought that such persons should be taken to hospital because their appearance shocks others. 9.7% would always recommend sending for a physician in the case of a seizure. It should be emphasised that 98.4% of the study group and 89.1% of the respondents in the control group advised to stay with the patients until they regained consciousness.
Conclusion: Knowledge amongst non-neurological nurses of first aid for tonic-clonic seizures is significantly higher than among the general public, but in the case of fulfilling educational functions they should be subjected to training in this subject.

p528
What Do You Know About Epilepsy? Results of a Public Opinion Poll
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Purpose: There are more myths and misunderstandings in epilepsy than in any other pathology. Does that image change throughout years? Nowadays what DO 'ordinary' people know about epilepsy? Are they ready to cope with it? Through a questionnaire: 'what do you know about epilepsy?' we tried to obtain this knowledge and simultaneously we had the opportunity to discuss epilepsy with people and inform them.
Methods: During 2003-2004 a public opinion poll was lead by the BFE Association during several meetings either in Paris and surroundings or in different regions, as well as during National Epilepsy Days (JNE). 15 items were selected, but the questions were simplified to obtain good participation and responses. They should reflect public opinions on epilepsy and people with epilepsy at the present time.
Results: Among questions: What is epilepsy? How many people with epilepsy are there in France? At what age does epilepsy appear? Do you know what to do if a fit occurs? What do you know of the causes of epilepsy? Is learning at school possible? Is it possible to succeed in University? Is a normal life possible? Can epilepsy be cured? What experience do you have of epilepsy?
Conclusion: About 500 persons answered the questionnaire. The answers to the different items are quantified here and commented on. The global results show a poor knowledge of epilepsy, needing information, but an improvement of its appearance with most of the time the notion of a neurological illness.

p529
Civic Knowledge and Attitude Towards Epilepsy In Croatia
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Purpose: Stigmatization is determined by socio-cultural specificities, and active effort is necessary to ease its burden. This study was aimed at assessing, for the first time, the public attitude towards epilepsy in Croatia, and represents the initial step for a public health awareness campaign.
Methods: 1,000 adults living in Croatia (□4.5 mil.) were randomly selected according to region and size of community as part of a larger omnibus survey. Trained interviewers asked participants 12 questions about epilepsy. Standard statistical methods were used for data analysis.
Results: 97.3% of respondents had either 'read' or 'heard' about epilepsy, 55% knew someone with epilepsy, and 44.6% had witnessed a seizure. Epilepsy was ranked the sixth serious among 8 common diseases. A moderate affective distance from epilepsy patients was expressed, as compared to a person with one of the other listed diseases. On average, interviewees were quite ready to accept a patient as a friend or co-worker. About 93% wouldn't object if their child played with a child with epilepsy, 76% believed that a child with epilepsy could succeed as well as a 'normal' healthy child, and 16.7%

listed social rejection as the worst aspect of epilepsy. While 52.5% would approach a seizing person and help, 33.3% would call '911'.
Conclusion: Civic awareness and attitude towards epilepsy in Croatia appears similar to that in more developed countries. The detailed social context, possible confounding factors for these results, and the value of the data as a strategic basis for a public health intervention campaign are discussed.

p530
Public Awareness Understanding and Attitudes Towards Epilepsy in Bavi, Vietnam: First Report from the EPIBAVI Study
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Purpose: Data on the epidemiology of epilepsy from developing countries are scarce. The present study represents the first step in a population-based epidemiological project in Vietnam (EPIBAVI) with the overall objective to determine the incidence and prevalence of seizures and epilepsy and the effectiveness of epilepsy care in a representative region of Vietnam. To establish a basis for these further studies, we first set out to assess public awareness, knowledge and attitudes toward epilepsy in this community.
Methods: A longitudinal epidemiological surveillance system has been established in the Bavi District in northern Vietnam building on quarterly door-to-door surveys of households representing approximately 50,000 inhabitants. A survey including 10 questions used in demonstration projects of the Global Campaign was translated to Vietnamese and was applied by specially trained interviewers to a representative sample of 2,000 adult residents of Bavi.
Results: Of the 523 interviewed to date, 68% had heard about epilepsy; 52% knew someone with epilepsy; 51% had witnessed an epileptic seizure; 86% would not agree to their son or daughter marrying someone with epilepsy; 51% did not believe that epilepsy patients could hold a normal job; 49% believed that epilepsy is an organic disorder of the brain and 25% that epilepsy is a form of dementia. Only 78% thought that epilepsy patients must consult a physician.
Conclusion: These preliminary results indicate that, although a substantial proportion of residents in this Vietnamese community know of epilepsy, negative attitudes exist toward people with epilepsy similar to those previously reported from China.

p531
Knowledge of Epilepsy Among the Auxiliary Nurse Midwifery Students
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Purpose: To identify knowledge of epilepsy among basic level nursing students.
Methods: Purposive sampling technique adopted. Descriptive design.
Results: There were 50 ANM nursing students identified for this study. 35% of respondents said that epilepsy is a disease that can be found only in villages. The remaining 65% said that this disease is found in all areas. 42% of the respondents said that epilepsy is caused by sin in the past life, 35% respondents said that it is due to a problem in the brain, the remaining 23% said that it is due to nutritional problems. 32% of them said that epilepsy is curable only by way of local traditional methods; the remaining 68% said that epilepsy can be treated by way of allopathic medications. 75% believed that epilepsy can be transmitted from parents to child; the remaining 25% said that it cannot be spread. 52% said that epilepsy will affect only adults and the remaining 48% said that it can affect all people.
Conclusion: There is a need of scientific knowledge for basic level nurses, especially ANM. More practical exposure is needed by the basic level nurses. All ANM level students should get proper training in neurological wards.

p532
Knowledge and Traditional Practices Towards Epilepsy: Patients' Relatives Survey
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2) Provincial Cell of Epidemiology, Chichaoua Health Delegation, Chichaoua, Morocco

Purpose: Assessment of patients' families knowledge about epilepsy, and identification of the sociocultural aspect and traditional practices towards epilepsy.
Methods: A survey was conducted in the Neurology Department of Marrakech; a region representative of cultural patterns in south Morocco. It included 80 people, males and females,; aged 20 years and older, who were submitted to a standard 20 item questionnaire.
Results: Answers were recorded and tabulated in SPSS (version 10.5). The average age was 40.5 years (standard deviation = 23.24). Female gender was more represented with 63.75% of sample, and 45% were illiterate. Nearly 65% of respondents had heard or read about epilepsy. More than half believed in the role of spirits (jinn), and bewitchment in the development of their relatives' illness. 3/4 asserted that the patient had received treatment from religious healers and visits to shrines. Among this population 33.5% described that treatment included readings from the Koran, written down and amulets; very few were imposed particular rites and some were chained during their grand mal seizures.
Conclusion: This first study of its kind done in Morocco and Arab countries, revealed that southern Moroccans do not know enough about epilepsy and that cultural specific characteristics of understanding epilepsy lengthen the delay of diagnosis and treatment and harm the quality of care in patients with epilepsy. This confirms the need of an awareness programme in order to improve health education in general and to ameliorate the information status about epilepsy and strengthen the use of biomedical methods of treatment.

p533
Survey Concerning Knowledge of Medical Students about Epilepsy in Marrakech Medical School
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Purpose: Epilepsy is a very frequent disorder in neurology and should be understood by medical students. In Morocco, it constitutes a real health problem and most of its causes are avoidable (its prevalence between is 0.5 and 1%). The authors try to test the basic knowledge of second year medical students about epilepsy, its origin, age of onset, treatment and prognosis.
Methods: Survey using a standard questionnaire with 126 second year medical students of Marrakech. We chose second year medical students because they still have not studied either semiology or pathology of the nervous system, in order to understand the basic knowledge acquired before any medical teaching.
Results: Age of the students varied between 19 and 23 years, 67% were female. A correct definition of epilepsy was given only by 18% of the students, 63% considered it as a neurological disease. About age of onset, 26% think that it is an affection concerning all ages. About treatment, 58% think it exists and 26% think that epilepsy is an incurable disease.
Conclusion: This study is the first one done in Africa and Arab countries and very few are reported in the literature. We found that 2/3 of medical students knew some useful basic information about epilepsy, others had incorrect information inherent to their socio cultural context. Our medical students while knowing some basic facts about epilepsy, have significant false information. These results underline the necessity to sensitise the general population about epilepsy, to consolidate the basic background and to fill the major deficiencies during medical school teaching programmes.

Monday 29th and Tuesday 30th August 2005
13:15 – 14:15
Poster Session
Alternative Therapies

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VNS-Therapy for Treatment of Medically Refractory Epilepsy: Development of a Continuous Quality Improvement System in the Netherlands
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Purpose: To develop national standards and a continuous quality improvement system for consistency in application and in the quality of outcomes of VNS-Therapy in patients with medically refractory epilepsy.
Methods: A quality system is the organizational structure, responsibilities, processes and facilities for carrying out quality care. One of the core elements of a quality system is the systematic monitoring of the process of care via the quality circle. The quality system is being developed in close collaboration with participating medical specialists from several neurosurgery and epilepsy centres. Monitoring of the VNS-quality system is performed with the use of a number of selected indicators. The indicators relevant for the patient are effects on epilepsy (e.g. reduction of epileptic seizures and changes in seizure severity), effects on functioning and well-being (e.g. EQ-5D), complications and adverse events. Indicator areas relevant for the medical specialist are site profile and the number of performed VNS-treatments.
Results: A stepwise approach was used in which the following steps were taken: selection of participating medical specialists and their centres, description of a treatment protocol, formulation of quality indicators, collection of data in a national database and organisation of feedback sessions for the participants. This information is used to adjust the process of treatment, establish procedures for future development, and make agreements with health care insurers.
Conclusion: Making reimbursements for VNS-Therapy dependent on participation in a national continuous quality improvement system creates a powerful financial incentive to continuously provide effective care in an efficient manner.

p535
Does Vagus Nerve Stimulation Remain Effective in Long-term Follow-up?
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Purpose: Vagus nerve stimulation is now a recognised treatment for refractory epilepsy when a surgical approach is not possible. Mechanisms of action remain uncertain. The aim of this study was to evaluate in a cohort of paediatric patients the long term efficacy and tolerance of VNS.
Methods: VNS was used in 18 patients, 17 children and adolescents (4 to 17 years old) and a young adult (24 years old). In every case but one, seizures occurred several times per day or per week. The last one had at least 1 seizure per month. The follow-up was 18 months to 9 years. The mean seizure frequency was evaluated during a 3 month baseline period prior to VNS implantation and every 3 months during the first 12 months, then every 6 months during the total follow-up. Treatment remained unchanged during the first 3 months in all cases and 6 months in 16/18 cases. Parameters of stimulation were initially as follows: intensity 1.5 mA, stimulation on during 30 sec and off during 5 mn. These parameters remained unchanged during the first 6 months, then were modified (intensity 1.5 to 2.,5 mA, interstimulation period 1.1 to 5 mn).
Results: More than 50% reduction of seizure frequency was observed in 72% of this group (13/18) during the 12 first months. Efficacy was similar in generalised seizures (N= 7) and partial seizures (N= 6). In 9 cases the seizure reduction rate was more than 75%. VNS was not effective in infantile spasms (2 cases). In one case the seizure frequency remained unchanged but the duration of seizures was shortened more than 50%. In 2 cases the seizure reduction was not significant (between 30 and 50%) but ceasing stimulation was followed by increase of frequency and duration of seizures. During the follow-up, more than 50% seizure reduction remained in 44.4% of patients (8/18) kept, when a lack of efficacy occurred in 5 cases, improvement was obtained temporarily in 4 cases by increasing stimulation intensity or duration (from 30 sec to 60 sec). When the generator stopped (intentionally in 3 cases) the seizure frequency increased in 6 cases, leading to changing or re-activating the generator. Quality of life including behaviour, alertness, vigilance, sleep, and communication, has been considered improved both by parents and educational staff in 11 cases. The only side effects reported in 6 children were moderate and non permanent cough and hoarseness, but systematic nocturnal polygraphic registration performed in 9 children demonstrated moderate change in breathing during stimulation.
Conclusion: VNS is effective, both on generalised and partial seizures with few and moderate side effects. The percentage of responders is higher during the first year than previously described but a partial lack of efficacy occurs in 38% of responders, indicating the need for adjustment of parameters. This may be explained by fibrosis around the vagal nerve.

p536
Short and Long Term Efficacy and Tolerability of VNS Therapy in Adults and Children with Intractable Epilepsies
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Purpose: Vagus nerve stimulation (VNS) therapy is a well-established alternative treatment for adults and children with intractable epilepsies. However, specific patient groups who might benefit from VNS treatment have not yet been identified. We aimed to study the effectiveness and tolerability of VNS therapy amongst adults and children with intractable epilepsies.
Methods: We have analysed in retrospect all children and adults with intractable epilepsies who have received VNS therapy and have been followed up by the same doctor (SG) following implantation. We studied the short and long term efficacy (% reduction of seizure frequency) and safety of VNS therapy. Comparisons were made between children and adults, as well as between epilepsy types/epilepsy syndromes.
Results: There were 27 patients with intractable epilepsies, 8 (3F, 5M) children (Group A) and 19 adults (8F, 11M) (Group B). Mean (range) age at implantation was 10.5 (7-15) years for group A and 27.7 (17-45) years for group B. Mean (range) follow-up after implantation was 36.6 (2-80) months; follow-up was >1 year for 22 patients, >3 years for 16 patients, and >5 years for 5 patients. 3 patients of group B had their implant removed at 12, 45, and 60 months because of intolerable side effects. In the children's group, 5 children suffered from Lennox-Gastaut syndrome (LGS), 2 from temporal lobe epilepsy and 1 from Rasmussen's encephalitis. In the adults' group, 7 patients had LGS, 4 multifocal catastrophic epilepsies, 3 mesial temporal lobe epilepsy, 3 severe neuronal migration disorders, and 2 frontal lobe epilepsy. Mean (range) seizure reduction was 50 (20-100)% for group A and 38.4 (0-80)% for group B. Efficacy remained almost unchanged at 3 and 5 years follow-up in both groups. All children, however, showed a positive effect of VNS treatment on their mood and awareness. This was apparent immediately after implantation and was permanent.

Similar effect was reported only from 8 adult patients. In the 12 LGS patients mean (range) seizure reduction was 34.2 (0-80)%, whereas this was 43.8 (0-100)% in the remaining 17 patients with partial epilepsies. In most of the children, cough or hoarseness was mild and resolved by the third month following implantation. On the contrary, in 4 adult patients local side effects were present up to 9 months following implantation and another 2 patients had their device removed because of intolerable side effects.
Conclusion: VNS therapy was well tolerated in both age groups studied, but children have shown better efficacy and fewer side effects. In addition, attention and mood were significantly improved in children as compared to adults, immediately following implantation. The effectiveness of VNS therapy may be related to the specific epilepsy type/epilepsy syndrome classification.

p537
Long Term Vagus Nerve Stimulation (VNS) Modifies EEG Coherences and Frequency Power Spectrum in Partial Epilepsy
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1) University of Cagliari

Purpose: Though vagus nerve stimulation (VNS) is an important option for the treatment of drug-resistant epilepsy, the ample range of effects by which VNS reduces seizures in humans remain unclear. This study describes EEG modifications in coherence and frequency power spectrum in subjects affected by severe partial epilepsy after long term VNS.
Methods: The power spectrum and the synchronisation of EEG were processed with a freeware software tool for MATLAB (www.sccn.ucsd.edu/EEGLAB) with 11 subjects affected by partial epilepsy. The digital tracings recorded one year before VNS surgery were compared with the EEG obtained one year after VNS as well, with these obtained 1 month and 1 year after VNS activation in order to assess early modifications. Similar recordings were obtained from two control groups represented by epilepsy subjects treated with AEDs and by a group of non epilepsy patients.
Results: VNS failed to modify the EEG power spectrum in the range of delta (0.5-3 Hz), alpha (8-12 Hz) and beta (13-20 Hz) frequencies, while theta band (4-7.5 Hz) showed only a decreased synchronisation. Moreover, VNS increases gamma frequencies (20-50 Hz) and enhances their inter and intra-hemispheric coherence in the areas involved in the epileptogenesis.
Conclusion: Our results show that VNS increases power spectrum and synchronisation of gamma frequencies (20 and 50 Hz) and decreases intra- or inter-hemispheric synchronisation of the other bands. These results suggest that modulation of brain rhythmic activities can be involved in seizure control and, perhaps independently, might play a role in other VNS-mediated effects.

p538
Double-blind Placebo-controlled Parallel-group Trial of Omega-3 Fatty Acid Supplementation in Patients with Chronic Epilepsy
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Purpose: Nutritional studies suggest the Western diet is deficient in omega-3 fatty acids (FA). Animal studies suggest that the FA, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are effective in raising seizure thresholds. Other studies show that EPA can reduce pro-inflammatory mediators which are elevated in models of epilepsy. An open study in 5 patients suggests FA supplementation may be beneficial in patients with epilepsy. This study examined FA supplementation in a controlled trial.
Methods: Patients with chronic epilepsy were randomised and received capsules of EPA (1g) and DHA (0.7g) daily or placebo (mixed vegetable oils) in a 12-week double blind study. All patients were then given the supplements in a 12-week open phase. Seizure counts, adverse events, antiepileptic drug (AED) and red blood cell (RBC) FA concentrations were assessed.
Results: Of the 58 patients randomised, 30 received supplements and 27 a placebo. A significantly greater proportion on supplements showed at least a 50% seizure reduction in the first 6 weeks of treatment (17%, CI 1.5% to 36% [$p<0.05$]) but not in the second 6 weeks. In RBC and plasma, there was a significant rise in EPA and DHA, and a reciprocal fall in arachidonic acid and linoleic acid in the supplement group. Mean AED concentrations were unaffected.
Conclusion: In this study, seizure reduction was seen in the first 6 weeks of treatment. However, this effect was not sustained. Further studies are required to assess different FA formulations, doses and longer treatment periods. Acknowledgement: Seven Seas Ltd. UK provided study medication.

p539
Bone Mineral Density and the Ketogenic Diet
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Purpose: To report the effects of the ketogenic diet (KD) on bone metabolism and calcium homeostasis.
Methods: 19 children were prospectively commenced on the classical KD from 2002-2004. Lumbar bone mineral densitometry (BMD), serum calcium, alkaline phosphatase (ALP), 25 hydroxy-Vitamin D (25OHD), parathyroid hormone (PTH), urine calcium-creatinine ratio and renal ultrasound were performed at baseline and 6-monthly intervals thereafter.
Results: Mean age at initiation of the KD was 6.1 years (range 1.3-16.9 years). 10 children (53%) had low baseline bone mass (corrected BMD Z score <-2.5). Bone density was lower in non-ambulant children (mean Z score -3.3) compared to ambulant children (mean Z score -1.0) ($p=0.003$). 1 child had high PTH and 9 had low 25OHD levels. Serum ALP and calcium were normal in all children but 1 had hypercalcuria. There was no significant change in the mean corrected BMD Z score for the 10 children who remained on the diet for >6 months. None developed hyperparathyroidism or high ALP levels but 2 with persistently low 25OHD levels required supplementation. All children developed hypercalcuria, (transient 3, and persistent 7) but only 1 had nephrolithiasis on renal ultrasound.
Conclusion: More than half the children had low baseline bone density, reflecting the increased risk of osteopenia in non-ambulant children treated with antiepileptic drugs but the KD does not usually cause further loss of bone mass. This suggests that increased bone turnover is not the only cause of hypercalcuria and that management may need to include a reduction in calcium supplements.

p540
Using the Ketogenic Diet to Treat Intractable Epilepsy: Early Drop-out Rate and Family Acceptance
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Purpose: To record the early drop out rate from ketogenic diet treatment, and to assess parental opinion of dietary acceptance, ease of use, and effect on quality of life.
Methods: Preliminary data is presented on 74 children started on the ketogenic diet as part of a comparative trial between the classical and medium chain triglyceride protocols. The drop-out rate before 3 months was assessed, and parents were asked to complete a questionnaire after the first 3 months.
Results: 18 children (24%) stopped the diet before 3 months as they found it too difficult to follow. Parental questionnaire data at 3 months was available on 53 children (28 classical and 25 MCT diets). 35 parents (66%) found the diet easier to use than expected, with only 3 reporting it to be harder than expected. 37 parents (70%) felt their

child's quality of life had improved on the diet, with 11 reporting no change and 5 reporting a deterioration. 32 (50%) felt quality of life as a family had improved, with 14 reporting no change, and 7 reporting a deterioration. Of the 46 orally fed children, 36 (78%) reported no problems with the taste of the food. There were no significant differences in either drop-outs or questionnaire results between the two diet protocols.
Conclusion: These results do not support the suggestion of the ketogenic diet being unpalatable or difficult to use. Although some families will find this treatment too difficult to sustain, the majority report it to be acceptable and beneficial.

p541
Ketogenic Diet in Refractory Epilepsies in Childhood Efficacy and Tolerability According to Epileptic Syndrome
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Purpose: A long-term prospective study to evaluate efficacy and tolerability of the ketogenic diet (KD) in the treatment of 63 children, with refractory epilepsies according to epileptic syndrome, who remained on the diet for at least 1 year.
Methods: We used the classic KD following the criteria of the John Hopkins Pediatric Epilepsy Center. Baseline neurological and physical examination, EEG and blood chemistry including lipid profile were obtained prior to initiation and while on the KD. KD efficacy was measured as the percentage reduction of baseline seizure frequency, considering positive results as reduction of 50% or over. Acceptance of the diet and quality of life were specially considered. 38 patients were males.
Results: According to the ILAE classification (2001) the epileptic syndromes and quantity of children who responded well (more than 50% reduction in seizure frequency) were: symptomatic focal epilepsies, 4/13; cryptogenic focal epilepsies, 2/7; West syndrome, 2/5; Lennox-Gastaut syndrome, 3/7; Dravet syndrome,13/21; myoclonic-astatic epilepsy, 6/10. Adverse effects occurred mainly in the first weeks of treatment in 21 patients (33.3%), but were generally mild and transient. In 12 patients (25.3%) it was possible to withdraw one to two AEDs after 12-13 months on the KD. Its efficacy dropped significantly by 12-24 months and after the diet was interrupted.
Conclusion: After 1 year on the diet, in 30/63 children the KD was well tolerated with good seizure control. This study shows that the best results are obtained in Dravet syndrome and myoclonic-astatic epilepsy.

p542
Long-term Results of Vagus Nerve Stimulation: The Ghent Experience
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Purpose: This study evaluates the long-term efficacy and safety of patients treated with vagus nerve stimulation (VNS) at Ghent University Hospital, with a follow-up of 1 to 9 years post-implantation.
Methods: At Ghent University Hospital 96 patients have been implanted with a vagus nerve stimulator since March 1995. Patients with a follow-up of at least one year were included. We prospectively assessed changes in monthly seizure frequency and occurrence of side effects.
Results: 72 patients (37M/35F) with, at time of implantation, a mean age of 30 years and a mean duration of epilepsy of 20 years, had a post-implantation follow-up with an average of 45 months (range 12-113). The mean number of antiepileptic drugs (AEDs) taken before implantation was 3 (range 1-5). 67/72 patients had complex partial epilepsy (CPE). 5 patients had generalised epilepsy. At maximum follow-up, mean stimulation output was 2 mA (range 0.25-3.25). Mean number of AEDs remained unchanged compared with preoperatively. Mean seizure frequency changed from 39/month (range 2-300) before implantation to 15/month at maximum follow-up. 48 patients (67%) had a > 50% reduction in seizure frequency. Shortness of breath, unpleasant sensation in the throat or hoarseness during stimulation were the most frequent side-effects.
Conclusion: Our long-term experience with VNS shows that it is an efficacious and safe adjunctive antiepileptic treatment for patients with refractory epilepsy. Acknowledgments: V. De Herdt is supported by an 'Aspirant' Grant from FWO Flanders. P. Boon is a Senior Clinical Investigator (FWO Flanders).

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A Pilot Study on the Effects of Nigella Sativa Seeds Aqueous Extract on Paediatric Intractable Seizures
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Purpose: Despite administration of numerous antiepileptic drugs (AEDs) nearly 15% of childhood epilepsies are resistant to treatment. Nigella sativa (black seed) and its major component Thymoquinone recently showed an antiepileptic effect.
Methods: This pilot study was performed between Sep 2003 and Nov 2004. We prepared extracted N sativa as syrup (100 mg/ml of purified extract), then prepared a placebo with the same specifications. In this cross over double blind clinical trial we administered aqueous extract of N sativa to children with refractory epilepsy as an adjunct therapy and compared it with the placebo. 20 children were entered in the study (13 months to 13 years of age, 10 boys and 10 girls). All had been under constant treatment for at least one month before the study. They received either the extract or the placebo for a period of four weeks and between these periods two weeks they received only their pre-existing AEDs.
Results: The mean frequency of seizures before initiating the study was 5.78 ± 7.2 seizures/day. At the end of the study the mean frequency of seizures at extract period decreased to 4.21±5.77 seizures/day and in placebo period reached to 5.68 ± 6.86 seizures/day. The mean frequency of seizures significantly decreased during treatment with extract ($p < 0.01$). At the fourth week of the N sativa period, 3 of the children became seizure free and 2 had myoclonic seizures.
Conclusion: We concluded that water extract of nigella sativa has an antiepileptic effect and further studies in different types of seizures is recommended. The authors are thankful to the Vice Chancellor of Research, Mashhad University of Medical Sciences, for financial support.

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Stereotactic Radiotherapy in Temporal Lobe Epilepsy: Safety Seven Years after Treatment
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Purpose: Stereotactic radiation of an epileptogenic focus may be a therapy for patients with contraindications against surgical treatment (e.g. neuropsychological or surgical risks). Some studies show the outcome in the first years after radiation, but there is little knowledge about long term safety, e.g. carcinogenetic or encephalopathic effects.

Methods: From 1996-1998 8 patients suffering from pharmacoresistant temporal lobe epilepsy were treated with fractionated stereotactically guided radiotherapy. The dose of radiation in the focus ranged from 21 Gy (7 times 3 Gy) to 30 Gy (15 times 2 Gy). If possible the medication had to be at a stable dose in the first two years. An intensive follow up visit was performed two and seven years after treatment including neurological examination, EEG and MRI.
Results: The patients showed a mean seizure reduction of 46% (range 0 – 100%, SD 32%) after two years. As a modification of antiepileptic drugs was allowed in the following years, further effects could not be clearly assigned to radiotherapy. The MRI performed after two and seven years presented no alterations in brain structure, the neurological examinations and EEGs were also unchanged.
Conclusion: A fractionated stereotactically guided radiotherapy can be an effective and safe therapy in patients with pharmacoresistant temporal lobe epilepsy, if surgical treatment is contraindicated. A further follow-up will be done for long term safety reasons.

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Evaluation of Short Term ACT Psychotherapy and Yoga in a RCT Trial for Refractory Seizures in India
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Purpose: The purpose of this study is to develop and evaluate a non-drug treatment alternative in the form of a behavioural psychotherapy ACT and a specially designed yoga package for patients with refractory epileptic seizures.
Methods: N=30. The design was a randomised controlled group study with two conditions: acceptance and commitment therapy and a specially designed yoga therapy. Both treatment conditions were done in individual and group form lasting initially 4 weeks and then follow-ups and boosters at 6 and 12 months. The ACT therapy aimed at 1) acceptance of the seizure predisposition, 2) empowerment to pursue valued life directions and 3) seizure control skills. The yoga condition aimed at 1) stimulating the vagus nerve and 2) creating a buffer of stress control.
Results: Results after the 6 and 12 month follow-ups showed significant reduction in seizure frequency and duration. In addition, there was a significant increase in life quality for all participants in the treatment groups.
Conclusion: There is a great need to develop and evaluate drug free alternatives for 1) those who prefer not to use drugs, 2) those who suffer from side effects of drugs and 3) those who do not have access to modern epileptic drugs. This study is part of the IBE commission for development of non-drug alternative treatments. This study shows that non-drug 'free' alternatives are possible and effective to use as a compliment to drugs for refractory seizures.

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Palliative Epilepsy Surgery: Role of Callosotomy and Vagus Nerve Stimulation
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Purpose: To compare callosotomy and vagus nerve stimulation (VNS); two 'alternative' surgical procedures in drug-resistant epilepsy patients.
Methods: 52 drug-resistant epilepsy patients were submitted to palliative surgery. 1985-1998 23 patients underwent callosotomy; indication was mainly based on high frequency of generalised tonic-atonic falling seizures together with counterindication or failure of ablative surgery. 1995-2004 29 patients were submitted to VNS (7 of them have less than 1 year follow-up), main indication was again drug-resistance and counterindication or failure of ablative surgery. 'Good' outcome was defined as at least 50% seizure reduction, 'unchanged' when reduction was less than 50%. We considered the total number of the residual/persistent seizures as well as different seizure types. The outcome was evaluated after 1 and 5 years.
Results: Callosotomy patients: 'good' results were obtained in 15 patients (68.2%), 4 of them are seizure free; 6 (27.3%) were 'unchanged' and 1 worsened. The best results were obtained with generalised seizures (disappeared in 11 patients) while partial seizures had a worse outcome. VNS patients: 'good' results were obtained in 5 (22.7%) out of the 22 considered patients; 2 of them are seizure free, no patient worsened. Many authors suggest evaluating VNS results also on the basis of the incidence of cluster and status and quality of life. According to this kind of evaluation 'good' results were obtained in 12 patients (54%), the remaining 10 were unchanged; we didn't observe worsening or adverse effects.
Conclusion: Callosotomy compared with VNS shows better efficacy in seizure frequency reduction. However, it is an invasive surgical procedure. We suggest that palliative procedures in drug-resistant epilepsy surgery should be proposed in different steps. First VNS, while callosotomy could be suggested as a second approach in patients affected with falling generalised seizures.

Monday 29th and Tuesday 30th August 2005
13:15 – 14:15
Poster Session
Basic Science

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Hippocampal Pathology and Inhibitory Neurotransmitter GABA Immunoreactivity in Patients with Medically Intractable Temporal Lobe Epilepsy
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Purpose: To study pathological features of medically intractable temporal lobe epilepsy (MITE) with hippocampus sclerosis (HS), and to explore the role of reforming GABAergic system in MITE.
Methods: All 15 patients of HS group and NO-HS group are fit for the criterion of MIE. The patients have been given a definite diagnosis according to the criterion including clinical manifestation, EEG, Video-EEG, EcoG, deep electrode EEG, and MRI. 8 of the patients fit in the HS group, and 7 patients in the NO-HS group. Anteriomedial temporal lobectomy and selective amygdalohippocampectomy were selected. Cerebral lesionectomy was done on those with temporal lobe lesions. Cell counts of pyramidal cells in hippocampus CA1, CA3 pyramidal cells, granule cells and hilus cells in fascia dentate have been analysed via HE stain and immunohistochemical processing with hippocampus tissue, meanwhile GAD-IR neuron count in stratum oriens, hilus, stratum pyramidalis and stratum granule which include basket cell have also been investigated. Gray value in fascia dentate inner-/outer, molecular layer and hippocampal stratum radiatum have been tested via analysis software from NIHimage version 1.31.
Results: CA1, CA3 pyramidal cells, granule cells number were significantly different between the HS group and NO-HS group ($p<0.001$). The number of hilar neurons in the HS group was less than in NO-HS group ($p<0.001$). GAD positive neuron numbers in hippocampal stratum orient, stratum pyramidal, granule cells and hilus cells in fascia dentate were not significantly different in the two groups, but GAD grey value in hippocampal stratum radiatum and in FD inner- /outer- molecular layer in HS group was higher than in NO-HS group ($p<0.001$). GAD grey value difference in inner-molecular layer and outer-molecular layer in HS group was lower than in NO-HS group ($p<0.001$). A positive correlation was found in GAD grey value difference between FD inner- and outer-molecular and granule cell, CA3 pyramidal cell and hilus neurons. A negative correlation was found in GAD grey value and all the cells.
Conclusion: The main feature of hippocampus sclerosis is loss of FD hilus neuron, hippocampus CA3 pyramidal cell and granule cell, which may be the primary pathological feature and cause of MITE. Loss of FD hilus neurons, especially in HS, may be the major factor involved in MITE. GAD interneuron were intact with axon sprouting.

It suggests that inhibitory neurotransmitter GABA increased, especially focused on area with exiting projecting fibre.

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Aspartoacylase/Attractin Double-mutant Mice Exhibit Epileptic Seizures

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Purpose: Aspartoacylase (Aspa) gene, the mutation of which causes Canavan disease, encodes an enzyme that cleaves N-acetyl-L-aspartate (NAA) into acetate and aspartate. Aspa knockout mice showed vacuolation in the central nerve system (CNS). Attractin (Atrn) gene encodes a transmembrane protein related to pigmentation and myelination in CNS, and its mutant (Atrnmg-3J/mg-3J) mice showed tremor, vacuoles, and hypomyelination. Spontaneously epileptic rat (SER) carrying mutation at both tm (>200-kb deletion containing at least three genes including Aspa) and zi (Atrn) locus exhibited absence-like seizures and tonic convulsions, and have been used for evaluation of antiepileptic drugs. In this study, to reconstruct epileptic phenotype and produce mouse model, we developed novel Aspa/Atrn double-mutant mice and examined their phenotypes.
Methods: Aspa knockout and C3H-Atrnmg-3J/mg-3J mice were used to produce the Aspa/Atrn double-mutant mice. Three genotypes of mice, Aspa/Atrn double-mutant, Aspa-/- and Atrn mg-3J/mg3J mice, were selected from F2 progeny. Cortical electroencephalograms (EEGs) were recorded and histopathological analysis were conducted.
Results: The Aspa/Atrn double-mutant mice exhibited spontaneous absence-like seizures characterised with sudden appearance of 5-7 Hz spike-wave-like complex and tonic convulsions with concurrent low-voltage fast waves. However, no abnormal EEGs nor behavioural changes were noted in Aspa-/- and Atrn mg-3J/mg-3J mice. In histopathological analysis, the Aspa/Atrn double-mutant mice showed more severe vacuolation in the CNS than the other two mutant mice.
Conclusion: The Aspa/Atrn double-mutant mice developed in this study can be used for epilepsy research.

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Hippocampal [3H]-Flumazenil Binding in Rat Models of Temporal Lobe Epilepsy

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Purpose: Changes in hippocampal central benzodiazepine (cBZP)/GABAA receptor expression and function are thought to contribute to epileptogenesis in temporal lobe epilepsy (TLE). Flumazenil (FMZ) is a cBZP/GABAA receptor complex antagonist that is utilized clinically to image changes in cBZP/GABA in patients with TLE with positron emission tomography (PET). The purpose of this study is to perform preliminary autoradiography studies to validate the use of FMZ for PET studies in rat models of TLE.
Methods: Bipolar stimulating/recording electrodes were surgically inserted into the left amygdala of 12 rats. 4 rats underwent amygdala kindling, 4 post-kainic acid status epilepticus and 4 were used as controls. Animals were sacrificed and their brains snap frozen. Whole brain slices (20 micron) were incubated with 7 concentrations (0.5-32nM) of [3H]-FMZ and NSB assessed using 200μM flunitrazepam. Using phosphorimager (Fuji-BAS5000) autoradiography, left and right hippocampal (HC) regions were analysed using MCID software to quantify [3H]-FMZ binding. Specific binding affinity (Kd) and receptor density (Bmax) were determined by Scatchard analysis.
Results: Studies of the whole HC showed that animals in combined epilepsy group exhibited no change in Kd for left or right HC (n=6) compared to controls (n=4). The Bmax increased in HC of epilepsy animals compared to controls (954±181 to 1677±204 Bq/mg; $p<0.05$) with no difference between the left or right HC results. Analysis of HC subregions (CA1, CA3, DG) 10 weeks post-kindling showed increased flumazenil binding as well as an increase in Bmax.
Conclusion: cBZP/GABAA binding in rat models of epilepsy can be assessed using FMZ with discernible changes in key structures of the HC. We hypothesize that HC cBZP/GABAA receptor expression increases in the early stages of TLE and that progressive changes during epileptogenesis can be studied using FMZ in future PET studies.

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Spike and Wave Discharges Develop from Corticothalamic 5-9 Hz Oscillations that are Distinct from Sleep Spindles in Genetic Absence Epilepsy Rats from Strasbourg

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Purpose: Absence-related spike-and-wave discharges (SWD) occur in the thalamocortical system during quiet wakefulness or drowsiness. In feline generalised penicillin epilepsy, SWD develop from sleep spindles. In contrast, in Genetic Absence Epilepsy Rats from Strasbourg (GAERS), SWD develop from wake-related 5-9 Hz oscillations, which appear distinct from spindle oscillations (8-15Hz). The cellular mechanisms of these two physiological oscillations were compared.
Methods: EEG recordings and intracellular recordings in thalamic, relay and reticular neurons were performed in neuroleptanalgesied GAERS and control non-epileptic rats.
Results: 5-9 Hz and 8-15Hz oscillations were recorded in both strains. 5-9 Hz oscillations could last up to 20 s whereas 8-15Hz oscillations never exceeded 2 s. Intracellular recordings revealed that, in relay and reticular neurons, 5-9Hz oscillations could begin from a relatively depolarised membrane potential (>-65 mV) whereas 8-15Hz oscillations came up from an even more polarised level. In reticular cells, 5-9 Hz oscillations occurred in the trough of a hyperpolarising envelope whereas 8-15 Hz oscillations occurred during a slow depolarising envelope. In relay neurons, 5-9 Hz oscillations were characterised by a rhythmic depolarisation whereas 8-15 Hz oscillations were characterised by a rhythmic hyperpolarisation. Subanaesthetic doses of barbiturate abolished SWD and 5-9 Hz oscillations and increased the frequency of occurrence of 8-15 Hz oscillations. Our data suggest that the cortex most likely drove 5-9 Hz oscillations whereas the pacemaker of 8-15 Hz oscillations is located in the thalamus.
Conclusion: Although both the corticothalamic 5-9 Hz and the thalamocortical 8-15 Hz rhythms can give rise to absence-related SWD, they have well-distinguishable thalamic cellular mechanisms.
INSERM, FFRE, EDF.

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Large-scale CDNA Microarray Analysis of Gene Expression in Epilepsy
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Purpose: DNA microarrays are now popular tools for large-scale analysis of gene expression in the brain in both physiologic and pathologic conditions. In combination with laser capture microdissection and quantitative real-time reverse transcription-polymerase chain reaction technologies, such large-scale expression analysis can be successfully addressed in well-defined tissue specimens.
Methods: We analysed gene expression patterns in a seizure and a control brain samples obtained from the operation by dye-swapping method using CGU cDNA microarray. Using cDNA microarrays, the differential expression of approximately 4,192 cDNAs was examined.
Results: Data after normalisation, 18 genes that showed strongest up regulation and 16 genes showed down regulation in the microarray screen (5 folds). We examined the cytoband locations of those genes, and there were some hot spots at 4q21, 17p23, 22q12. Based on geneontology (http://www.geneontology.org/) classification, those genes were major on the nucleic acid binding activity, receptor activity and transmembrane receptor activity in the molecular function classification, organogenesis, protein metabolism and signal transduction in the biological process.
Conclusion: Review of the data indicates that products of genes regulated during people with epilepsy being processed belong to a variety of functional classes. These data are potentially excellent tools for creating new hypotheses about events occurring during circuit reorganisation in the brain that results in a lowered seizure threshold and epilepsy.`

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Serotonergic Projection from Dorsal Raphe into the Hippocampus: Role in Seizures and Regulation by Galanin Type 1 (GalR1) and Type 2 (GalR2) Receptors
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Purpose: Neuropeptide galanin modulates classical neurotransmission through activation of GalR1 and GalR2 receptors. We examined whether galanin in dorsal raphe (DR) - hippocampal serotonergic pathway regulates experimental seizures.
Methods: Status epilepticus (SE) was induced in Wistar rats by electrical perforant path stimulation. Electrographic seizures were analysed off-line. Serotonin depletion, as verified by immunofluorescence, was achieved by intraperitoneal parachloroamphetamine, 20 (PCA20), or 60 (PCA60) mg/kg, 10 days prior to SE. A mixed GalR1/GalR2 agonist galanin (1-29), or a selective GalR2 agonist galanin (2-11), were injected into DR at 5 nmole, 20 min before stimulation. GalR1 and GalR2 distribution in DR was studied using binding assay.
Results: PCA20 depleted serotonin by 55%, and PCA60 by 90%, in DR and hippocampus likewise. PCA20 mitigated seizures, while PCA60 had a proconvulsant effect. GalR1 constituted 80%, and GalR2 20% of DR galanin receptors. Galanin (1-29) increased SE severity; pretreatment with PCA20 enhanced proconvulsant action of the peptide. Galanin (2-11) inhibited seizures in naïve rats, but failed to affect SE in PCA60 animals.
Conclusion: Facilitation of SE after PCA60 suggested that serotonergic DR- hippocampal projection was anticonvulsant. Seizure attenuation after PCA20 may be explained by hypersensitisation of 5HT1A receptors, sufficient to override 55% transmitter deficit. Proconvulsant effect of galanin (1-29) likely depended on GalR1 (considering high DR GalR1/GalR2 ratio), and, based on the effects of galanin (1-29) in PCA20 rats, involved inhibition of serotonin release. Inhibition of seizures by galanin (2-11) in naïve, but not in PCA60 rats, suggested that DR GalR2 inhibited seizures by stimulating serotonin release. Supported by NIH grant NS43409.

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Photothrombosis as a Model for Post-stroke Epilepsy in Rodents: Results of Chronic EEG Recording
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Purpose: No animal model is widely accepted to study post stroke epilepsy. It has been reported that in the model of photothrombotic brain infarction in Sprague-Dawley (SD) rats, 50% of the animals develop focal epileptic seizures ipsilateral to the cortical infarct (Kharlamov et al, Epilepsy Research 2003; 56:185-203). We present the results of chronic EEG recordings in SD rats after photothrombotic brain infarction.
Methods: Photothrombosis was performed on 8 male SD rats. The scalp was retracted. Rose bengal (30 mg/kg) was injected intravenously. Photoactivation was performed with a 6 mm diameter cold white light focused over the left fronto-parietal cortex for 20 minutes. Six epidural screw electrodes were placed over the skull. EEG was recorded 4 hours per week for 6 months. 8 male SD control rats were also recorded.
Results: Among the 8 rats in which photothrombosis was induced, one died during status epilepticus 19 days after surgery. 5 out of 7 rats with photothrombosis showed 7 Hz generalised spike and wave discharges lasting 2 to 5-6 seconds. 5 out of 8 control rats also disclosed this pattern. Clinically, the animals stare during the seizure. No focal seizures were seen.
Conclusion: Since we did not find focal seizures attributable to the photothrombotic brain lesion, its potential use for the development of a rodent model of post-stroke epilepsy remains to be confirmed. Intraperitoneal injections of pentylenetetrazole are ongoing in order to see if the rats with photothrombotic brain infarction are more sensitive to proconvulsive agents.

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Effects of Antiepileptic Drugs on EEG Patterns in Lithium Pilocarpine-induced Status Model of Rats
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Purpose: This study was performed to investigate the effects of antiepileptic drugs according to the patterns of characteristic EEG progression in lithium-pilocarpine induced status epilepticus (SE).
Methods: Male Sprague-Dawley rats weighing 200-300grams were used as subjects. SE was induced 7 days after placement of epidural electrodes, by lithium pretreatment followed by a low dose of pilocarpine i.p.(30mg/kg). The intracranial EEG was continuously recorded from pilocarpine injection until the end of SE. The pattern of EEG were divided into 5 stages; discrete ictal discharge (d), merging stage, continuous ictal discharge stage (c), continuous ictal discharge with flat period (f), periodic epileptiform discharge stage. Phenytoin (30mg/Kg, PHT), valproate (100mg/Kg, VPA) and phenytoin with valproate (PNT+VPA) were injected during discrete (d), continuous ictal discharge (c), continuous ictal discharge with flat period stages (f), respectively.
Results: SE was induced in 78/96 (81.3%). The mortality was 20% (2/10) in control group, 14.3% (3/21) in PHT treated group, 18.2% (4/22) in VPA group and 8% (2/25) in PHT+VPA group. In control

group, duration of total EEG seizure was 1008.0□89.47 minutes. Continuous stage was shortened significantly in VPA-d group and PHT+VPA-d group compared to control group ($p<0.05$). Also, the durations of the periodic epileptiform discharge stage and total seizure were reduced in VPA-d, PHT+VPA-d and PNT+VPA-c groups ($p<0.05$).
Conclusion: These results suggest that analysis of a progressive EEG pattern in SE may predict the prognosis of SE and response to treatment. Early intervention using EEG monitoring and polytherapy are effective treatments in SE.

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Electrical Stimulation of the Anterior Nucleus of the Thalamus for Kainic Acid-induced Focal Cortical Seizure Status in Rats
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Purpose: The aim of the present study is to clarify the effect of electrical stimulation of the anterior nucleus of the thalamus (ANT) on the epileptic cortical seizure status induced by a kainic acid microinjection.
Methods: 15 male Wister rats weighing 250-300 g were anesthetised with a 3% halothane in O2. Bipolar twisted electrodes were stereotaxically inserted into the left anterior nucleus of the thalamus for electrical stimulation and a cannula was inserted into the left sensori-motor cortex. At 7 days after surgery, 2.0μg of kainic acid was injected into the left sensori-motor cortex. The seizure semiology and EEG were monitored using a video EEG monitoring system. The 5 rats (Group A) were used for a control study without any stimulation. Convulsive seizure status occurred about 90 minutes after KA injection and seizures persisted for about 6 hours. In 10 rats (Group B), after induction of convulsive seizure status, electrical stimulation (130 Hz) of ANT was performed. Stimulation was ON for 30 min. and OFF for 30 min. in every 60 minute cycle.
Results: All rats exhibited focal cortical seizure status after kainic acid injection. Unilateral electrical stimulation of ANT can significantly reduce both spike counts (□30%) and seizure frequency (□28%) and duration (□15%), specifically with respect to the severity of their seizures and the frequency of secondarily generalised tonic-clonic seizures (□50%).
Conclusion: The electrical stimulation of the anterior nucleus of the thalamus (ANT) is safe and a potential therapeutic option available for the treatment of intractable cortical seizures.

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Enriched Environment Reverses Cognitive Deficits Caused by Neonatal Isolation and Seizures
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Purpose: Neonatal seizures have rarely been induced in experimental animals with a damaged brain. The purpose of this study was to determine whether neonatal isolation (NI) increases the vulnerability of the immature brain to subsequent seizures and the potential therapeutic effects of enriched environment (EE).
Methods: Rats were randomly assigned to the following five groups: control (CONT) rats; NI rats that underwent daily separation from their dams from postnatal day 2 (P2) to P9; status epilepticus (SE) rats, induced by lithium-pilocarpine model at P10; NI plus SE (NIS) rats, and NIS rats receiving EE between P25 and P40 (NISEE). At P10, plasma CORT levels were examined at both baseline and 2 h after onset of SE. As adults, the rats underwent spatial learning and memory tests in Morris water maze between P50~55. The evaluation of hippocampal neuronal loss and mossy fibre sprouting was carried out at ~P80.
Results: Rats undergoing NI demonstrated an exaggerated increase of plasma CORT after onset of SE at P10 (NIS group) than the normally reared rats suffering SE (SE group). When studied as adults, the NIS rats exhibited significant cognitive deficits as compared to CONT, NI and SE rats. NISEE rats showed no spatial deficits. All rats were free of spontaneous seizures later in life and had no discernible neuronal loss in the hippocampus.
Conclusion: Repetitive NI causes enhanced response of plasma CORT to SE, exacerbating the neonatal SE-induced long-term spatial deficits. Enriched environment reversed the spatial deficits.

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Assessment of the Effects of Matricaria Chamomilla Extract on Chemical Epilepsy in Rats
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Purpose: Earlier work suggested that there is a decrease in seizure stages frequency by Matricaria Chamomilla (MC). In the present study we evaluate the effects of MC extract on chemical epilepsy in rats.
Methods: This experimental study was performed on 50 male rats (5 groups). In kindling procedure animals received one IP injection doses of pentylenetetrazole (PTZ) 50 mg/kg every 48 h for three times. Convulsive behaviour was observed for 20 min after PTZ injection. The seizures were classified in 0-5 stages: 0, no response, 1, ear and facial twitching; 2-3, myoclonic jerks without or with upright position; 4-5, clonic-tonic seizures alone or with loss of postural control. Besides the increase in seizure intensity, any subsequent mortalities, and frequency of stage 5 in the final 3 doses of PTZ injection were noted. Animals received vehicle or MC extract (25, 50, 100 and 200 mg/kg) 20 min before of PTZ IP injection respectively.
Results: In the PTZ group (vehicle) 25% of animals died, while in the MC–treated rats, mortality decreased by 5%. Overall, all doses of MC produced a dramatic decrease in seizure mortality rate in PTZ-treated groups ($P<0.01$). Also, 60% of animals in the PTZ group (control) showed stage 5 of seizure with the final 3 doses of PTZ injection but in MC groups (100 and 200 mg/kg) frequency of stage 5 decreased (12%) significantly ($P<0.01$).
Conclusion: Data suggest anti-seizure effect for MC. Further research is required to determine the mechanisms by which MC has a modulatory effect on seizures.

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Nitric 0xide Synthase and NMDA Receptor Expression in Cavernoma Tissue with Epileptogenesis
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Purpose: Seizures in cavernoma patients have been reported to be due to surrounding hemosiderin deposits. However, this opinion is controversial and the mechanism of inducing seizures in cavernoma remains unclear. In this study, we examined nitric oxide synthase (NOS) and NMDA receptor expression in cavernoma surrounding tissue with epileptogenesis and the relationship to hemosiderin deposits.
Methods: By using immunohistochemistry and Berlin blue stain we evaluated the distribution and density of NOS and NMDA receptor expression and hemosiderin deposits in cavernoma surrounding tissues of 5 patients and normal tissues of 4 patients on whom were performed anterior temporal lobectomy.
Results: NOS and NMDA receptor expression were strongly increased in cavernoma surrounding tissues with many hemosiderin deposits compared to normal tissues for control.
Conclusion: A previous study reported that there were high levels of glycine and serine in the peripheral zone of the cavernoma. Activated NMDA receptors by them and iron due to hemosiderin deposits may

induce excess NO production which have a potential role in mechanisms regulating seizure induction and propagation.

p559
Intracortical Activation Sequence of Spontaneous and Evoked Spike-Wave Complexes in Humans
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Purpose: To describe intracortical trans-membrane current flow during evoked and spontaneous spike-wave complexes (SW) in humans.
Methods: Intracortical multielectrodes were implanted acutely in the medial temporal gyrus (T2) of epilepsy patients (n=4) undergoing anterior temporal lobectomy. Electrical stimulation (0.2ms, 5-15mA, 0.5Hz, n=25) was delivered via strip electrodes in different locations along the T2 gyrus. Current source density (CSD) profile was computed, time locked to the stimulation. The tissue containing the multielectrode track was removed and sectioned for recording contact localisation. Informed consent was obtained from the patients under the auspices of the Hungarian Medical Research Council according to the declaration of Helsinki.
Results: Spontaneous SW complex started as a sharp surface positivity with middle layer sink accompanied by elevated multiple unit activity (MUA). The next prolonged surface negativity was generated by superficial sinks and less pronounced firing. The surface positive part of the wave was accompanied by superficial sources and strong decrease in MUA, while the final slow surface negative part was marked by middle layer sources and neuronal silence, suggesting disfacilitation or active inhibition. Low intensity electrical stimulation evoked similar CSD sequence as it was observed in the spontaneous SW, except for the initial sharp surface positivity. However, high intensities were able to evoke the whole SW sequence.
Conclusion: Intracortical CSD distribution during SW were very similar across patients, suggesting a common final pathway in epileptic manifestations. These results could help with diagnostic strategies; and aid EEG/MEG source localisation techniques by applying additional spatiotemporal constraints to the backward solution.

p560
Bone Mineral Density in Epilepsy Patients: Comparison between MD with DXA Method
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Purpose: In a previous study we showed that epilepsy patients on antiepileptic drug therapy had a reduction in bone mineral density (BMD). Our aim of this study was to clarify whether microdensitometry (MD) method was useful as a screening examination of BMD in epilepsy patients.
Methods: 61 epilepsy patients (28 men and 33 women) aged 18-64 years participated in this study. Each had received treatment with antiepileptic drugs. We examined the BMDs using both MD and Duale energy X-ray absorptiometry (DXA) and compared the two. In MD method, mean MBD ratio was used as an index. In DXA method, we used quantitative digital radiography (QDR) and measured the BMDs of their lumbar spines and femoral necks. We obtained informed consents from all patients.
Results: The mean ratio of MBDs in DM method was 2.63. In DXA method, the mean value of MBDs of the lumbar spines was 0.934 gms/cm2 and that of femoral necks 0.724 gms/cm2. In all patients there were significant correlations with the results of MD and those of both their lumbar spines and femoral necks (both $p < 0.01$). Categorised by men or women, we also obtained same significant correlations (both $p < 0.01$).
Conclusion: We showed the MD method was useful as a screening examination of bone mineral density in epilepsy patients, because there were significant correlations between the results of MD and DXA.

p561
Decrease of Serotonin Transporters in Blood Platelets After an Epileptic Seizure
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Purpose: The aim of this study was to investigate whether modifications were present in blood platelets serotonin transporter of people with epilepsy at various stages after the last seizure. Such changes may reflect alterations in the brain serotonin system related to the condition.
Methods: Platelets were prepared from epilepsy patients with generalised tonic-clonic seizures and sex and age matched controls. Platelet membranes were challenged with labelled paroxetine at various concentrations in order to determine the parameters of its binding to SERT.
Results: No difference was shown either in the binding constant K or in B-max between the control group and the patients population. However, a significant 25% reduction of B-max was found in patients having undergone a seizure less than 4 days before blood sampling.
Conclusion: If the data found in platelets can be extended to the brain, they show that the brain may react to an epileptic seizure by potentiation of the serotonin system. In turn, this is reached by a decrease of the expression of the neurotransmitter transporter.

p562
Neural Progenitor Cells are Present in the Hilus of Hippocampus in Humans with Mesial Temporal Sclerosis (MTS) and Temporal Lobe Epilepsy
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Purpose: Mesial temporal sclerosis (MTS) is the most common cause of medically refractory temporal lobe epilepsy (TLE) and is associated with marked hippocampal cell loss and synaptic reorganisation, particularly in the hilus, CA3 and CA1 regions. The normal hippocampus is also the site where, throughout life, new granule neurons are continuously generated in the dentate gyrus. In animal models of MTS, hilar ectopic granule cells (HEGCs) are found and exhibit enhanced recurrent excitatory circuitry and may play a role in the pathogenesis of epilepsy. We determined in patients with MTS whether neuroblasts might be present in the hilus of hippocampus, demonstrating a possible role of progenitor cells in human TLE.
Methods: Hippocampal samples were taken from 6 patients undergoing resective surgery for TLE. Sections were immunostained for immature neuronal markers (PSA-NCAM, Tuj1), proliferation marker (PCNA), and nuclei (DAPI). Samples were examined with confocal microscopy for co-localisation of these markers with three dimensional reconstruction of Z-series confocal images. MTS samples were compared to epilepsy control tissue; cell types were determined in the hippocampus, particularly along the GC/hilus border.
Results: Hippocampi with MTS had a moderate number of neuroblasts (marked by PSA-NCAM+PCNA+DAPI+) located in the hippocampal hilus. Other features of MTS were present in tissue, including dentate granule cell dispersion, marked cell loss in hilus and CA3 and gliosis.

Conclusion: Neural progenitor cells are present in the hilus of the adult human hippocampus affected with MTS and may be due to abnormal proliferation and migration of granule cells.

p563
Unexpected Expression of Orexin B in Basal Conditions and Increased Levels in the Hippocampus during Pilocarpine-induced Epileptogenesis in Adult Rats
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Purpose: Orexin B (OxB) is a peptide derived from a prepro-Ox precursor and was considered to be exclusively synthesised by hypothalamus neurons, which provide projections to the hippocampus. Recent evidence has shown that OxB can increase synthesis of endocannabinoids, known to inhibit GABA release in the hippocampus. We thus hypothesised that OxB presence may increase during epileptogenesis elicited by pilocarpine-induced status epilepticus (SE).
Methods: SE was induced in adult male Sprague-Dawley rats by pilocarpine injection (300 mg/kg), and stopped by diazepam (10 mg/kg). Controls received diazepam injections only. Prepro-Ox mRNA was quantified in the hypothalamus and hippocampus using real-time RT-PCR at 8h, 1, 2, 3 and 7 days post-SE. Immunohistochemical detection of OxB was assessed at 1-4 days post-SE.
Results: In the hypothalamus, prepro-Ox mRNA decreased to its minimal level at 1 day post-SE (-56%, $p<0.01$), basal level being recovered at day 3. By contrast, prepro-Ox mRNA in the hippocampus, that we are the first to evidence in this structure in basal conditions, increased massively as soon as 1 day post-SE (+125%, $p<0.001$) and maintained at a plateau until day 3 before recovering control values at day 7. Concurrently, OxB-like immunoreactivity increased in CA1-CA3 pyramidal neurons, granule cells, and numerous interneurons scattered throughout the dorsal hippocampus.
Conclusion: Specific OxB induction within hippocampal neurons around day 3 post-SE may play autocrine/paracrine functions aimed at activating locally the synthesis of endocannabinoids, which, in turn, may down-modulate GABA release in the hippocampus.

p564
Propagation of Non-Synaptic Epileptiform Activity In-vivo
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Purpose: Recent experiments show that non-synaptic epileptiform activity can be induced in-vivo in the hippocampal CA1 region when synaptic transmission is blocked. However, the ability of this type of epileptiform activity to propagate to other brain areas is unknown. This epileptiform activity generated in hippocampus pyramidal cells should propagate antidromically and project along the axons to remote brain areas.
Methods: This hypothesis was tested in an in-vivo rat preparation by inducing non-synaptic seizures in the left hippocampus and by recording spontaneous and evoked field potentials in both left and right hippocampi.
Results: The results show that one type of non-synaptic epileptiform activity, late-bursts, observed in the left exposed CA1 and CA3 regions could propagate to the contralateral intact CA1 and induce seizures with onsets of high frequency rhythm. A cut of the commissural fibres near the midline of the brain prevented this propagation. In addition, the measurement of time delays between the exposed CA3 and contralateral CA1, as well as between the two recording electrodes in the contralateral CA1, showed that the burst activity propagated through the commissural pathway. Experimental data also show that these late-bursts in the left hippocampus first appeared in the Schaffer collaterals of the CA1 region, travelled to the ipsilateral CA3 region and then propagated through the commissural fibres.
Conclusion: These results show that non-synaptic epileptiform activity can propagate along axon projections to intact brain area causing seizure activity. This non-synaptic activity propagating through axonal pathway provides a possible mechanism for the generation of high-frequency low-amplitude onset activity observed in human epileptic EEGs.

p565
Changes in Brain Glycogen Content in Different Mouse Strains Submitted to a Convulsant
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Purpose: Carbohydrate metabolism changes have been observed in man during temporal lobe epilepsy and during grand mal type of epilepsy-like seizures induced by methionine sulfoximine in rodents. Herein we look for a possible relationship between the carbohydrate glycogen changes and seizure genesis in mice submitted to methionine sulfoximine.
Methods: Mice were intraperitoneally administered with 75 mg/kg of methionine sulfoximine and brain glycogen content was measured. Astrocytes were also cultured and submitted to the convulsant.
Results: Swiss and C57BL6/J strain mice displayed typical seizures 8 h after dosing. The convulsion frequency steadily decreased 4 hours after. By contrast CBA/J mice died during the first seizures. In C57BL6/J and in Swiss mice, the brain glycogen content increased during the pre-convulsive and post-convulsive periods. During the convulsive period although the glycogen content was higher than in controls, this content was lower than during the pre-convulsive and post-convulsive periods. In CBA/J mice, the increase was observed during the convulsions but not before. In the brain, astrocytes are cells that accumulate glycogen. Glycogen content increased in cultured astrocytes derived from C57BL6/J mice while no change was observed in cultured astrocytes derived from CBA/J when methionine sulfoximine was present in the culture medium.
Conclusion: 1) Mice in which the magnitude of the glycogen increase is high displayed long duration convulsions and mice in which this increase is moderate did not. Perhaps, glycogen plays a role in sustaining the convulsions. 2) Glycogen content alterations is probably not a consequence of the convulsions.

p566
Recurrent Seizures Lead to Zinc Depletion in Mossy Fibre Terminals in the Kainate Mouse Model of Mesio-temporal Epilepsy
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Purpose: Mossy fibre sprouting is one of the characteristic morphological changes in temporal lobe epilepsy and is classically detected by Timm Staining, which reveals the zinc stored in presynaptic vesicles. In the kainate-mouse model of mesio-temporal lobe epilepsy, mossy fibre sprouting develops rapidly along with epileptogenesis. However, the intensity of the Timm staining reduces progressively after a few weeks. The present experiments were aimed to determine the mechanisms underlying this decrease of zinc in the hippocampus.
Methods: The changes of Timm staining, VgluT-1 and Synapsin-1 immunoreactivity (IR) were examined at 7, 14 and 28 days following injection of kainate (KA: 1 nmole/50 nl) in the hippocampus of mice. Suppression of seizures was obtained by continuous injection of midazolam and the consequences of such suppression on zinc storage

and glutamate release were examined by Timm staining and microdialysis, respectively.
Results: At 7 and 14 days post-KA, the labelling patterns of Timm staining, VGluT-1-IR and Synapsin-1-IR were similar. At 28 days post-KA labelling of VGluT-1-IR and Synapsin-1-IR progressed whereas Timm staining had completely disappeared. When midazolam was infused continuously for 24 hours in mouse at 28 days, a suppression of recurrent seizures was observed on the EEG as well as a reduction of glutamate release as measured by microdialysis in the hippocampus. In these animals, the intensity of Timm staining was regained.
Conclusion: This study suggests that the enhanced release of glutamate, which is associated with recurrent seizures in the KA-mouse model, leads to a decrease of zinc storage in synaptic vesicles.

p567
Modelling Molecular Cascades Involved in Temporal Epilepsy Genesis: A New Systems Biology Integrative Approach
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Purpose: We developed a large-scale model of the cascade of intracellular molecular events leading to the onset of human temporal lobe epilepsy. Our objective is to generate a new molecular hypothesis to treat this disease.
Methods: This approach consists in the systematic screen of the scientific literature to build this molecular interaction network in humans, store it in a dedicated database and represent it as an oriented graph. This network is specifically designed to be usable in mathematical models of the dynamics of the genesis of human pathology (hippocampal sclerosis).
Results: We present our intracellular molecular interaction network building strategy and describe it. The final network will aim at representing the combination of transitory hypoxia, neuronal apoptosis and death, inadequate axonal sprouting resulting from neuronal loss, changes in excitatory/inhibitory (including ionic responses) and neuromodulatory neurotransmissions. It currently includes more than 600 molecules and 2000 interactions. It is structured on interconnected, overlapping, partially redundant, convergent and divergent feedback loops linking neurotransmitters, membrane receptors/channels, intracellular signalling molecules and transcription factors. These loops influence each other leading to non linear dynamic responses of the resulting combined signal transduction network. One feature of the network is its heterogeneous structure which influences subsequent model computing.
Conclusion: The availability of an exhaustive network of intracellular signal transduction opens the way to integrative modelling of the dynamics of epileptogenesis at the molecular level.

p568
Perioral Afferentation from the Snout Included in the Mechanism of Spike-Wave Discharge Regulation in WAG/Rij Rats.
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Purpose: To research the role of peripheral afferentations from the peri-oral region in spike-wave discharges (SWD) generation.
Methods: Before surgery WAG/Rij rats were anaesthetised by phenobarbital ('Somnorol', Cambridge) in a dose of 47 mg/kg. Monopolar electrode inserts into the frontal cortex and n reticularis thalami (NRT). The duration and number of SWD were calculated. Software program 'CONAN' was used. The deafferentation of the perioral region of rats was induced by 2% Novocain on both sides of the head by deed injection of anaesthetics under the foramen infraorbitalis n. maxillaris (r.nassalis ext., r.labialis sp., n.buccalis etc.). The blockade of n.facialis was used as the control.
Results: The duration and the number (on average - 35/hour in base) of SWD in the cortex and thalamus of WAG/Rij rats were recorded in chronicle experiments. Acute deafferentation of the perioral region of the snout by Novocain induced complete inhibition of SWD in the cortex and nucleus reticularis thalami (NRT) during e 1st only h after Novocain blockade of n.trigemenis, but not - n.facialis. Control injections of saline did not induce a decrease of absences. In all cases with the n.facialis blockade by Novocain the number and duration of SWD increased when compared with the base recording. Neither the duration, nor the number of SWD in the cortex and NRT of WAG/Rij rat's brain re-established during 3 hours (number of SWD: 5±0.25) in comparison with controls (20±5).
Conclusion: Local peripheral anaesthesia of WAG/Rij rat's snout (n. trigemenis) evoked the abolition of sensory afferent bursts to the thalamus and cortex, at first to the region of perioral representatives of this part of the snout, that temporarily destroyed the mechanism of generation of SWD.

p569
Selective Inhibition of Caspase-1 Reduces interleukin-1 (IL-1) Beta Production and Release in Rodent Brain and Protects from Kainate-induced Seizures
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Purpose: We found that IL-1 beta has proconvulsant activity in experimental models of epilepsy. Here, we tested the hypothesis that seizure inhibition may be effectively achieved by impairing the brain production of the mature, biologically active form, of IL-1beta. Thus, we assessed seizure activity in rodents after selective blockade of interleukin converting enzyme (ICE/caspase-1) using pralnacasan or VX-765, and in caspase-1 knock-out (KO) mice.
Methods: We used adult Sprague-Dawley male rats or C57BL6 mice, and 2 week-old hippocampal slice cultures, derived from 7-day old C57BL6 mice. We measured cytokines in hippocampal tissue and slice medium by western blot or ELISA. Seizures were assessed by EEG recordings in freely-moving rodents.
Results: ICE/caspase-1 inhibition was achieved by brain or systemic administration of pralnacasan or VX-765 to rats. These inhibitors reduced by 50% the seizure-induced production of the mature form of IL-1beta. Exposure of organotypic slices to pralnacasan or VX-765 inhibited by >80% the release of IL-1 beta and IL-18 from hippocampal slice cultures induced by proinflammatory stimuli, with more modest effects on IL-6 and TNF-alpha release. Caspase-1 inhibition in vivo decreased by 40-70% the time spent in kainic acid-induced EEG seizures in rodents and delayed by 2 to 3-fold their onset time. Caspase-1 KO mice showed a 70% reduction in the number and total duration of seizures and ~4-fold delay in their onset time.
Conclusion: This study indicates that selective inhibition of caspase-1 in brain represents an effective, specific and novel strategy to inhibit seizures by reducing the brain availability of IL-1beta.

p570
Age Influence in Life Expectancy of Untreated Rats with Epilepsy
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Purpose: To observe the effect of epilepsy on rat life expectancy.
Methods: Male Wistar rats were submitted to the pilocarpine model of epilepsy and observed 24h/day until death or by 16 months. These rats

were submitted to electroencephalographic recordings and echo-cardiogram evaluation. The animals were submitted to histological and histopathological study.
Results: In chronic rats with epilepsy, the seizure frequency showed a great oscillation until the 11th month. After that, the animals showed 4-5 seizures per week until death. Despite the constant epileptiform activity, the frequency of behavioural seizures in aged animals was similar to that observed in young adult rats. Aged control rats did not present any EEG abnormality. Aged rats with epilepsy and controls showed the same abnormalities in the echo-cardiogram evaluation. Aged rats with epilepsy showed more exuberant histological alterations of the hippocampal formation, including cell loss, gliosis and axonal sprouting when compared to young rats with epilepsy. The life expectancy in experimental animals was shorter (11.8±5.4 months) when compared to control group (15.5±3.5 months). Finally, rats with epilepsy and control animals died in consequence of pneumonia.
Conclusion: Aged rats with epilepsy showed a discrepancy between EEG and behavioural manifestations, in addition to a progressive neuronal damage and increased reorganization of axonal sprouting. The animals with epilepsy showed a higher mortality rate that was not related to cardiac dysfunctions. We could hypothesize that epilepsy-related physiologic changes might anticipate organic conditions that propitiate the precocious death of these animals.

p571
Neuronal and Apoptotic Markers in Temporal Lobectomized Patients
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Purpose: Temporal lobe epilepsy (TLE) is one of the most frequent types of human focal epilepsy. A wealth of previous studies reported pathological alterations in extrahippocampal regions in TLE. The main goal of the present work was to examine some apoptotic markers in temporal tissue from lobectomised patients and to determine the contribution of apoptotic mechanism to epileptic process in these patients.
Methods: We studied 4 temporal cortex from TLE patients and the tissue control group (n=5) was obtained from death not-neurological patients. The immunohistochemical evaluation was carried out using the following neuronal markers: enolase, neun, synaptophysin, GABA and GAD 67/65. The apoptosis study was realised for the occurrence of terminal deoxynucleotidyl transferase-mediated UTP nick end labelling (TUNEL) and anexin-V, caspase3 and 8, p53 and Bcl2 markers. The propidium iodure was used in others to identify the total number of cells. The final evaluation of temporal cortex tissue was done by confocal microscopy and the analysis was done using LSM 5 Image Browser.
Results: The results evidence there are a decreased total number of cells and neuronal (enolase+, synaptophysin+ cells, $p<0.001$) in epileptic temporal cortex tissue when compared with control group. Only the TUNEL+ cells were statistically decreased ($p<0.01$) in epileptic tissue, the other apoptotic markers were no different from the control tissue.
Conclusion: The death observed by TUNEL marker may not be by apoptotic phenomena but could be by necrosis.

p572
Group II Metabotropic Glutamate Receptor Agonist may Reduce Behavioural Deficit Induced by Early Status Epilepticus in Adult Rats
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Purpose: To study the neuroprotective effect of group II metabotropic glutamate receptor selective agonist (2R,4R)-4-aminopyrrolidine-2,4-dicarboxylate (APDC) against long-term behavioural consequences of early life status epilepticus (SE).
Methods: SE was induced by bilateral intracerebroventricular (i.c.v.) application of homocysteic acid (HCA) (600 nmol/side) in Wistar 12-day old pups. APDC (0.05 nmol/per side) was administered i.c.v. 15 min prior to HCA injection. Age-matched rats with i.c.v. application of saline and/or APDC were used as the controls. Behavioural testing was performed on adult rats (P>60 days). Evaluation of motor activity, anxiety level, and nonassociative, emotional and working memories were performed in the open field (OF), elevated plus maze (EPM) and delayed matching to position (DMTP) tasks. The experiments were performed in agreement with the European Community Council Directives 86/609/EEC.
Results: APDC pretreatment significantly shortened the latency to leave the centre first confronting to OF, reduced the number of rats unable to habituate in OF and hypo-activity followed by hyperactivity in EPM compared to SE rats ($P<0.05$). APDC didn't modify increased time into open arms of EPM and the incidence of rats with perseverative behaviour in DMTP task compared to SE rats.
Conclusion: APDC provided a protection only on a nonassociative form of memory and reactivity to novel stimuli, whereas it was not effective against deficit in cognitive functions and increased anxiety level induced by SE at an early developmental age. This work was supported by Grant # 309/02/1238 from the Grant Agency of the Czech Republic

p573
Hippocampal Inflammation Associated with IL-1ß Superinduction Following Pilocarpine-initiated Status Epilepticus in Adult Rats may be Maintained in the Long-term due to Diazepam-induced IL-1 RA Depletion
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Purpose: Rodent models of temporal lobe epilepsy (kainic acid administration, ventral hippocampus electrical stimulation) indicate that expression of both pro-inflammatory cytokine interleukin 1ß (IL-1ß) and anti-inflammatory cytokine IL-1 receptor antagonist (IL-1 RA) is altered following status epilepticus (SE), and that manipulation of tissue level of these cytokines can modify SE-induced epileptogenesis. We characterised for the first time the accurate alteration of IL-1ß and IL-1 RA mRNA levels following pilocarpine-induced SE.
Methods: IL-1ß and IL-1 RA mRNA levels were quantified in the hippocampus of adult Sprague-Dawley rats using calibrated RT followed by real-time PCR. Quantifications were performed during the one-week period after the onset of pilocarpine (300 mg/kg)-induced SE. Diazepam (injected to stop SE) was also administered in controls to monitor its effects, by comparison to naive rats (baseline level).
Results: IL-1ß mRNA exhibited a transient peak reaching at 8h post-SE levels that had never been reported (+5 200% vs baseline; $p<0.001$), followed by a decrease reaching a plateau level observed from day 1 to 7 (+1 100% vs baseline, $p<0.01$). By contrast, IL-1 RA mRNA exhibited an increased level at day 1 only (+928% vs baseline, $p<0.01$). Interestingly, diazepam alone differently decreased mRNA levels encoding both cytokines throughout the period examined (one

week), reaching at day 7 post-administration -80% ($p<0.001$) for IL-1 RA mRNA while IL-1ß mRNA recovered baseline levels (+35%).
Conclusion: IL-1ß and IL-1 RA appear to be highly deregulated during pilocarpine-induced epileptogenesis, and diazepam may initiate long-term inflammatory processes occurring in the damaged hippocampus through IL-1 RA depletion.

p574
Effects of Repetition Seizures on the Expression of Beta-adrenoreceptors in Rat Hearts
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Purpose: Sudden unexpected deaths (SUDEP) are common among patients with epilepsy, and account for up to 20% of deaths in patients with epilepsy. Studies have shown that seizure-induced cardiovascular dysfunction may contribute to SUDEP. This study was to investigate the effects of repetitive seizures on the expression of cardiac beta-adrenoreceptor (AR) mRNA levels.
Methods: 20 Sprague-Dawley rats were randomly divided into two groups: a control group and an experimental group. Rats in the experimental group were subjected daily to maximal electroshock (MES), for a total of 4 weeks. Ventricular beta 1-, beta 2- and beta 3-ARs mRNA and protein levels were measured by the reverse transcription-polymerase chain reaction (RT-PCR) and Western blot.
Results: In comparison with the control group, beta 1-AR mRNA and protein levels decreased by 31.5 ± 6.3 and 40.6 ± 7.5%, respectively, in the experimental group rat hearts. whereas mRNA levels encoding beta 2- and beta 3-ARs increased by 68.9 ± 12.6 and 91.5 ± 20.7%, respectively.
Conclusion: Repetitive seizures may cause a decrease in beta 1- AR and an increase in beta 2- and beta 3-AR expression, which may be associated with SUDEP.

p575
Long-lasting Changes in Opiate Receptors in the Rat Brain Following Repetitive Pilocarpine-induced Status Epilepticus during Development
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Purpose: The long-term effects of status epilepticus on the development of epilepsy is age-dependent and remains poorly understood. The present study was aimed to investigate the opiate receptors in the brain of young rats subjected to one or three episodes of pilocarpine-induced status epilepticus (SE) during early life.
Methods: Rats at postnatal day 7-9 (P7-9), were used. Following pilocarpine (Pilo) or saline injections, three groups were studied: 1SE (Pilo at P9), 3SE (Pilo at P7-9) and control group (saline P7-9). All animals were studied 30 days after Pilo injection. K-opiate immunoreactivity was assessed by a polyclonal anti-k antibody (N=4/group). Changes in mu opiate receptors labelled with [3H]DAMGO were examined in 44 brain areas of rats from the three groups studied (Psychopharmacology, 128:97,1996; N=8).
Results: There was no significant difference in k-opiate immunoreactivity between 1SE and the control group. However, k-opiate was markedly reduced in the mossy fibres of the CA3 and the hilus following repetitive pilocarpine-induced SE. Densitometric image analysis of µ-opiate receptor revealed a significant decrease in the medial geniculate nucleus (-44%, $p<0.01$) following 1SE episode compared to control group. A significant decrease in [3H]DAMGO labelling was observed after three episodes of SE located in the dorsomedial thalamus at central (-31%, $p<0.05$), medial (-22%, $p<0.001$) and lateral (-23%, $p<0.01$) levels when compared to control animals.
Conclusion: The present study shows that repetitive pilocarpine-induced SE in developing rats causes long-term changes in opiate receptor density suggesting that the opioids could take part in the mechanisms involved with hyperexcitability and epileptogenesis. Supported by Fapesp, CNPq, FADA.

p576
Physical Training Induces Alterations on the Expression of Parvalbumin Positive-neurons in the Hippocampal Formation of Rats with Epilepsy
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Purpose: Intracellular calcium binding proteins (CaBP) are important in regulating free Ca2+ during normal and excessive cell activation. A previous study demonstrated a higher number of parvalbumin-positive cells and stronger fibre staining in the hilus of dentate gyrus in the voluntary and forced exercise rats. Since the staining of CaBP has been used to study physiological and pathological neuronal changes, we performed an immunocytochemical study using the CaBP (Parvalbumin-PV; Calbindin-CB) distribution as markers in the hippocampal formation in rats with epilepsy submitted to a physical exercise program.
Methods: 24 rats were divided into 6 groups of 4 animals: 1) control rats, 2) voluntary exercise rats, 3) forced exercise rats, 4) rats with epilepsy, 5) voluntary exercise rats with epilepsy and 6) forced exercise rats with epilepsy. Sustained seizures were induced by a single i.p. administration of pilocarpine (350 mg/kg). Rats were submitted to a forced (treadmill) or voluntary (voluntary wheel running) exercise programme. After the physical exercise period, animals were perfused transcardially and the brains processed for immunocytochemistry.
Results: A higher number of PV-positive cells in the hilus of control exercise groups was observed when compared to the control group. Thus, PV-positive fibres in the hilus were strongly stained in the voluntary and forced exercise animals. Trained rats with epilepsy presented PV-positive fibres in the hilus when compared to rats with epilepsy. CB immunoreactivity did not differ between all trained groups.
Conclusion: The neuroplastic responses commonly observed in trained rats may also occur in rats with epilepsy

p577
A New Mechanism of Multiple Drug Resistance in Epileptic Brain: The Non-ABC Transporter RLIP-76 and not MDR1 is the Predominant Extrusion Protein for Drug Transport at the BBB
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Purpose: We and others have shown that the drug efflux protein P-glycoprotein (P-gp or MDR1) protects the brain from xenobiotics, but other transporters that may be involved in multiple drug resistance to antiepileptic drugs may also play a role. Unlike other selective transporters, P-gp recognizes a wide range of substrates, including AED. However, there is a significant overlap between molecules transported by MDR1 and the non-ABC transporter RalA Binding Protein 1 (RLIP-76).
Methods: We used a combination of immunohistochemistry, western blot analysis, and pharmacokinetic assays to measure levels of expression of RLIP-76; co-localisation with MDR1; and relative contribution to AED extrusion. Data were obtained from 15 epilepsy patients, age ranging from 3 months to 61 years.
Results: While MDR1 immunoreactivity was observed in neurons, glia and endothelial cells, RLIP-76 was only found in endothelium and not in parenchymal cells. Experiments of drug extrusion using antibodies capable of selective inhibition of MDR1 or RLIP-76 revealed that the latter mechanism was responsible for 72+/-8 % of 14C-phenytoin extrusion by epileptic BBB endothelial cells; MDR1 contributed to only 27+/-8 % of ATP-dependent drug extrusion. These findings are in agreement with the fact that transport of P-gp

substrates in these cells is only weakly inhibited by specific MDR1 blocker XR9576.
Conclusion: Our findings suggest that RLIP-76 and not MDR1 is the main multiple drug resistance mechanism at the blood-brain barrier of drug-resistant epilepsy patients. Support Contributed By: NIH-RO1 HL 51614, NIH-RO1 NS 43284, and NIH-RO1 NS 38195.

p578
Electrophysiological and Morphological Evaluation of Two Cuff-electrodes for Vagus Nerve Stimulation in Rats
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Purpose: A better understanding of the mechanism of action of VNS could lead to stimulation parameter optimization and identification of responder groups. Animal research is therefore crucial. The aim of this study was to evaluate two types of cuff-electrodes for rats on an electrophysiological and morphological basis.
Methods: Two cuff-electrodes were evaluated: 1) a stainless steel hook electrode and 2) a self-sizing silicone electrode. Electrophysiological measurements of compound nerve potentials induced by the two cuff-electrodes were performed under deep xylazine/ketamine anaesthesia. Subsequently, several combinations of stimulation parameters (amplitude: 0-1.5 mA, pulse width: 50-500μs) were tested. For the evaluation of morphological modifications, left and right vagus nerves were dissected from non-implanted control animals (n= 6). The hook and silicone cuff-electrodes were implanted around the left vagus nerve of respectively 27 and 10 rats and vagus nerves were dissected after 34 to 377 days of implantation. Nerve tissue was fixated with formalin, embedded in paraffin and subsequently stained.
Results: Both cuff-electrodes were able to elicit A, B and C fibre compound action potentials. The silicone cuff-electrode required lower stimulus currents to trigger the different fibres. Long-term hook electrode implantation caused substantial nerve damage, which was mainly mechanical in nature in contrast to the silicone cuff-electrode, which induced significantly less morphological changes ($P< 0.05$).
Conclusion: Both cuff-electrodes were able to induce vagus nerve compound action potentials, but the silicone cuff-electrode required lower output current. For long-term implantation, the silicone cuff-electrode induces less morphological changes than the hook electrode and is therefore recommended.

p579
Effect of Curcumin against Kainic Acid Induced Seizures, Oxidative Stress and Expression of Heat Shock Proteins in Rat Brain
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Purpose: The effect of curcumin, an antioxidant compound, was studied against kainic acid (KA)-induced seizures, the effect on markers of oxidative stress and expression of heat shock protein (HSP-72) in rat brain
Methods: Rats were administered kainic acid (10mg/kg) intraperitoneally (i.p.) and observed for behavioural changes, incidence and latency of convulsions and mortality for 4 hours. The rats were thereafter sacrificed for estimation of malondialdehyde (MDA) and glutathione (GSH) and the expression of HSP-72. Curcumin was administered 30 min before KA at doses of 50, 100 and 200 mg/kg i.p.
Results: KA induced long-lasting seizures and associated symptoms. The brain level of MDA was significantly ($p<0.05$) raised after KA administration (536+ 44 nmol/g wet tissue) as compared to control (200 + 36 nmol/g wet tissue) and significantly decreased the levels of GSH. There was also an increase in expression of HSP-72 in the KA group. Pretreatment with curcumin (100 and 200 mg/kg, i.p) significantly increased the latency of seizures (120+20 min and 115+5.7 min respectively) as compared to the vehicle treated KA group. Curcumin (100 and 200 mg/kg, i.p) significantly prevented the increase in MDA levels and ameliorated the fall in glutathione. Curcumin at the dose of 50 mg/kg had no effect on any of the parameters.
Conclusion: The study reports the potential antiepileptic effect of curcumin.

p580
Haemodynamic Characteristics of Patients with Epilepsy
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Purpose: At the beginning of the research a hypothesis was set up according to which symptomatic forms of epilepsy would give rise to more significant changes in the haemodynamics than do idiopathic generalised forms. These changes can evolve from a disintegration syndrome as a result of epileptic centre activation that leads to desynchronised working of different brain systems.
Methods: 40 patients with epilepsy - idiopathic and symptomatic - (20 men and 20 women, mean age 21.6 +/- 7.4 years) were examined. We used 24 hours ambulatory blood pressure monitoring (ABPM) and parametric statistics.
Results: It was found that the most important haemodynamic characteristic of patients with epilepsy is variability increase of systolic and diastolic BP and heart rate (both when awake and when asleep). Disturbances of the haemodynamics depend rather on the time of seizures beginning during the awake-sleep cycle than on the seizure type itself; to be more precise, on the interaction of these 2 factors. It is possible that these changes aren't specific for epilepsy, as patients with panic attacks have the variability increase of ABP. These changes can be considered from the point of view of 'paroxysmal brain', when the main role is played by the paroxysmal factor, but not the concrete nosologic factor.
Conclusion: Disturbances in the circadian regulation of blood pressure in cases of epilepsy can be the reflection of the general disadaptation of patients' organism to the environment.

p581
High Frequency Stimulation of the Substantia Nigra Pars Reticulata to Suppress Seizures in the 'Genetic Absence Epilepsy Rats from Strasbourg (GAERS)': Evaluation of Optimal Protocols for Chronic Stimulation
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Purpose: Inhibition of the substantia nigra pars reticulata (SNr) has been shown to suppress seizures in different models of epilepsy. The aim of the present study was to determine the most effective protocol for chronic high frequency electrical stimulation in a genetic model of absence epilepsy in the rat (GAERS).
Methods: 46 males GAERS were stereotaxically implanted bilaterally with bipolar electrodes at the SNr and with monopolar electrodes on the cortex. Using previously determined optimal acute parameters (bilateral, bipolar, monophasic, frequency 60 Hz, pulse width 60 μs) chronic stimulations were optimised by changing the total time of stimulation (5 s ON 15 s OFF, 5 s ON 5 s OFF, continuous ON, seizure-triggered stimulation, seizure-triggered stimulation with a minimal interval off 1 min between each seizure).
Results: Only the seizure-triggered stimulation protocol with a minimal off-period of 1 min showed a significant decrease of seizure

frequency over a 40 min period. Protocols with various ON and OFF periods were ineffective.
Conclusion: These results show that a minimal off period of 1 min is necessary to induce suppression of seizure upon chronic stimulation and suggest the existence of a desensitization phenomenon. Our data emphasise the need of a closed loop stimulation procedure to chronically suppress seizures in therapeutic applications.
Acknowledgements: This work was supported by a ENS Fellowship, French Ministry of Research and Fondation pour la Recherche sur le Cerveau.

p582
Introduction and Abolition of Autonomous Seizure Transitions in Random Networks through Weight Changes
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Purpose: In this study we were interested in identifying potential mechanisms by which networks become prone to transitions from interictal to ictal states, as well as the causes that can initiate a given transition. In particular, we were interested in exploring the characteristics of weighted networks in which such transitions can take place autonomously.
Methods: To explore the question we generated computational neural network models with random connection weights and random initial conditions. Network dynamics were categorised using variants of close return and Lyapunov exponent algorithms.
Results: Patterns of network activity fell into several broad categories, including: fixed point, periodic and chaotic activity. Certain networks exhibited multi-stability with the evolution of activity depending critically on initial conditions. Most importantly, we identified a subset of networks which exhibited intermittent behaviour in which the activity autonomously switched from laminar to turbulent epochs with a characteristic statistical profile. Weight changes were not required for obtaining ictal transitions but such changes could influence the properties of the intermittent system in a continuous manner.
Conclusion: This intermittency model demonstrates that transitions to the ictal state required neither (i) a triggering input (including noise processes) nor (ii) changes to the network structure. However, these autonomous transitions are not exclusionary of other mechanisms and continuous weight modifications can result in alterations in the distribution of epochs. The model thus offers a novel way to understand the genesis and abolition of seizure susceptibly which may form the basis for new clinical studies in the diagnosis and therapy of epilepsy.

p583
Vagal Nerve Stimulation in the Amygdala Kindled Rat
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Purpose: Vagal nerve stimulation (VNS) has anticonvulsive effects in several animal models. Animal models used to study VNS are either acute models for seizures, or chemical models for epilepsy. The use of chemicals results in widespread brain damage. The amygdala kindled (AK) rat does not have this disadvantage. We describe a technique of VNS in the AK-rat.
Methods: 5 adult male rats. Under Halothane anaesthesia, a helical electrode (Medtronic Inc, Maastricht) is wrapped around both the left vagal nerve and carotid artery. The lead is tunnelled to the occiput where a new incision is made. The rat is then placed in a stereotactic frame for placement of the amygdala electrode. Both electrodes are embedded in dental acrylic. After 1 week rest, the AK procedure is initiated (twice daily, 2s, 200 μA, 80 Hz, 1 ms block pulse). When the animals display clear seizures, VNS (30s on/5min off, 1.5mA, 30Hz, 500 μs) is initiated by connecting the VNS leads to a NCP stimulator (Cyberonics, Inc., TX, USA). Animals were stimulated for one hour. AK is performed after 30 minutes during stimulation.
Results: One rat died in the postoperative period. The other 4 rats recovered well. Left VNS was tolerated well by all rats.
Conclusion: Implantation of a left VNS electrode combined with an amygdaloid electrode is safe in the rat. VNS using the human paradigms and combining it with AK, is also safe. However, for chronic VNS an implantable stimulator should be used to allow free movement throughout weeks of stimulation.

p584
Preventing Hypoglycaemic Seizures Ameliorates Hypoglycaemic Neuronal Damage Produced In Vitro
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Purpose: The focus of an ictal event is characterised by an increase in metabolism required to support repetitive neuronal fire. When severe, cerebral hypoglycaemia (or neuroglycopenia) can result in seizure activity which can lead to irreversible neurological damage. While there is some debate as to whether seizures damage the brain, seizure activity accompanied by a lack of glycolytic substrates may exacerbate the pathology of cerebral hypoglycaemia alone. Lactate, an oxidizable metabolite of anaerobic glycolytic metabolism, is often elevated in regions specific to the seizure focus in the absence of secondary generalisation.
Methods: Using a novel in vitro model of hypoglycaemic seizures produced in the isolated, intact hippocampus of the immature mouse, we studied the roles of the monocarboxylates, lactate and β-hydroxybutyrate, as well as the importance of glycogen and adenosine on seizures produced under low glucose conditions and the resulting neuronal architecture.
Results: Our results suggest that synaptic transmission specifically requires glycolytic resources. However, the presence of lactate or β-hydroxybutyrate was able to suppress hypoglycaemic seizure activity. The adenosine A1 antagonist, DPCPX, exacerbated hypoglycaemic seizures and neuronal death. The glutamatergic antagonists, APV (60μM) and CNQX (10μM), as well as the GABAergic agonist, midazolam (10nM), were effective in abolishing hypoglycaemic seizures and preserving synaptic function.
Conclusion: Our data support the hypothesis that hypoglycaemia induced seizures exacerbate neuronal damage during hypoglycaemia.

p585
Reconstruction of Perineuronal Net around Parvalbumin Neurons Correlates with Spontaneous Recurrent Seizures after Kainic Acid-induced Convulsions
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Purpose: We investigated the changes of phosphacan-containing perineuronal net (PN) and parvalbumin neurons in the hippocampus in the neonatal rat and after kainic acid-induced convulsive status (KA convulsions) in the adult rat.
Methods: Sprague-Dawley rats were used to examine the developmental changes of phosphacan-containing PN in the

developing brain. Secondly, 8 week old male Sprague-Dawley rats were given an intraperitoneal injection of KA (10 mg/kg) to study quantifying phosphacan-containing PN and parvalbumin neurons.
Results: Phosphacan-containing PN was exclusively present around parvalbumin neurons in the hippocampus, constructed coincident with the development of synaptic organisation. At one week after KA convulsions, number of phosphacan-containing PN decreased in CA1 and CA3 of Ammon's horn, and in the dentate gyrus. Moreover, phosphacan immunoreactivity was frequently lost from dendrites. However, parvalbumin neurons were preserved in the all hippocampal subregions. Number of PN recovered to the control level by 8-15 weeks after KA convulsions in 11 of 18 rats. In these animals, intense phosphacan immunoreactivity was detected around dendrites as well as cell bodies. In the remaining 7 rats, reduction of PN was still evident and phosphacan immunoreactivity was localised around cell bodies. Surprisingly, spontaneous recurrent seizures were observed in the former 11 rats, but not in the latter 7 rats.
Conclusion: Our data suggested that KA convulsions cause a destruction of phosphacan-containing PN and establishment of new synapses inputs to parvalbumin neurons may contribute to epileptogenesis.

p586
NMDA Receptor Activation Results in Ceramide Increases and in Apoptosis in Lithium Pilocarpine Status Epilepticus.
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Purpose: Ceramide is a modulator of neuronal injury and of apoptosis in many models including kainate induced status epilepticus (SE). It is not known if ceramide increases in lithium pilocarpine (LiPC) SE and if such increases and apoptosis that result from LiPC SE are dependent on NMDA receptor activation. This was the purpose of our study.
Methods: Adult Sprague-Dawley rats were injected with lithium (3meq/Kg), and 24 hours later, with pilocarpine (60mg/Kg) (LiPC group). Controls were sham manipulated. A third group (MK) was injected with MK801 (0.2mg/kg), NMDA receptor blocker, 30 minutes prior to pilocarpine and kept at room temperature and a fourth group (MKN) was kept warm to normalize the temperature. Seizure onset and duration were assessed. Ceramide levels normalised to lipid phosphate were determined and histological sections were stained for apoptosis (TUNEL method) 24 hours after completion of SE.
Results: There was no difference of total time of seizure between the LiPC and MK/MKN groups (19518±430.7; 20253.5±557 p= 0.307). Compared to controls, the LiPC group but not the MK or the MKN groups had increased ceramide/phosphate ratios (9.07±0.91, 21.4±7, 11.9±1.9; 6.5±0.92 and p=0.014, p=0.54, p=0.6 respectively). Compared to controls, the LiPC group but not the MK or the MKN groups had higher total hippocampal TUNEL scores (0.0±0.0; 3.87±0.54; 0.33 ± 0.33; 0.125 ±0.12 and p=0.000, p=0.432, p=0.746 respectively).
Conclusion: LiPC induced SE results in hippocampal neuronal apoptosis and in ceramide increases, both of which are dependent on NMDA receptor activation.

p587
Re-examination of Expression and Subcellular Localisation of Brain-Derived Neurotrophic Factor mRNA Following Pilocarpine-induced Status Epilepticus in Rats Reveals Potential Effect of Diazepam and Transient Presence in Astrocytes
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Purpose: Brain-derived neurotrophic factor (BDNF) is involved in neuronal excitability and survival, and neo-synaptogenesis. Its expression is highly enhanced in rat models of status epilepticus (SE)-induced epileptogenesis, particularly in pyramidal neurons and granule cells of the hippocampus, coupled to the dendritic targeting of BDNF-mRNA in these neurons. We re-examined BDNF-mRNA levels and subcellular localisation in the light of the potential effect of diazepam, injected to stop SE.
Methods: SE induced by pilocarpine (300 mg/kg) in adult Sprague-Dawley rats was stopped by diazepam (10 mg/kg) after 3h. BDNF-mRNA was assessed at 3h, 8h, and 1-7 days (d) post-SE using real-time RT-PCR, and colorimetric in situ hybridization (ISH).
Results: Diazepam decreased BDNF-mRNA levels specifically in the hippocampus 5h after injection (-70%, $p<0.001$), basal levels being recovered 3d later. Maximum increase in BDNF-mRNA occurred 3h post-SE when compared to baseline (+1250%; $p<0.001$), while it was greater and delayed to 8h post-SE when compared to diazepam-matched controls (+3050%, $p<0.001$). While dendritic localisation of BDNF-mRNA was maximal at 3h post-SE, presence of BDNF-mRNA was revealed at 1d post-SE in numerous neurons and astrocytes scattered in all hippocampal subfields and in the molecular layer of the neocortex. Diazepam did not change cellular and subcellular BDNF-mRNA distribution, either in rats having developed SE or in rats with decreased (-70%) BDNF-mRNA levels.
Conclusion: Thus, BDNF-mRNA can be targeted toward dendrites even at low cellular concentration. Further, identification of BDNF-mRNA presence in astrocytes warrants a profound revision of the role they may play in BDNF-mediated plasticity during SE-induced epileptogenesis.

p588
Exogenous Erythropoietin Protects Hilar Interneurons against Degenerative Process after Pilocarpine-induced Status Epilepticus in Adult Rats
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Purpose: Basal erythropoietin (EPO) expression in the brain supports neuronal protection in ischemia, and exogenous administration of recombinant human EPO (rhEPO) enhances neuroprotection. Therefore, we determined whether: 1) the expression of both EPO and its receptor (EPOR) was increased in the hippocampus during a period of neuronal vulnerability following pilocarpine-induced status epilepticus (SE), and 2) rhEPO could counteract SE development and neurodegeneration.
Methods: SE was induced at day 0 (DO) in adult Sprague-Dawley rats by pilocarpine (300-375 mg/kg). EPO and EPOR mRNA levels were measured in the hippocampus 8h, 1d, 2d, 3d and 7d post-SE by real-time RT-PCR. Neuroprotective effect of rhEPO (Eprex®, Janssen-Cilag) administered at D-1, D0, D+1 and D+3 (5000 UI/kg/day, i.p.) was evaluated 2 weeks post-SE using immunohistological detection of neuronal marker NeuN.
Results: Expression of both EPO and EPOR was transiently increased at 2 (+510%, $p<0.01$) and 3 (+458%, $p<0.001$) days post-SE respectively, following the lasting increase in transcription factor HIF-1 mRNA. rhEPO: 1) reduced by 45% the population of rats developing SE, 2) promoted faster body weight recovery and remarkably reduced hilar interneuron degeneration (but not histological damage observed in the piriform cortex) in rats having experienced SE, 3) protected against neurodegeneration in the piriform cortex when stage 4-5 seizures, but not SE, were developed.
Conclusion: We showed that the hippocampal EPOergic system is activated following SE but not sufficiently to counteract the neurodegenerative process. Neuronal protection can be achieved by increasing brain level of EPO exogenously, but appears to be specific to some neuronal populations.

p589
Ethoxyquin, A Synthetic Molecule, does not have a Neuroprotective Effect against Pilocarpine-induced Status Epilepticus
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Purpose: The aim of our study was to investigate the effects of ethoxyquin on hippocampal formation morphology after pilocarpine-induced status epilepticus (SE).
Methods: Adult male Wistar rats were divided into three groups: (A) control rats (n=05), received neither pilocarpine nor ethoxyquin; (B) rats that received just pilocarpine (n=05); (C) rats that received pilocarpine and ethoxyquin (n=05). After a single dose of pilocarpine (350mg/kg, i.p.), only rats that displayed continuous, convulsive seizure activity were included in our study. Seizure activity was monitored behaviourally and terminated with an injection of diazepam (10 mg/kg, i.p.) after 4 h of convulsive SE. A single pre-administration of ethoxyquin (150mg/kg, i.p.) 30 minutes before pilocarpine injection was evaluated. Seven days after pilocarpine-induced SE, all the animals were perfused and their brains were processed for histological analysis through Nissl and Neo-Timm methods.
Results: The cell counts in the Nissl-stained sections performed within the hippocampal formation showed a significant cell loss in rats that received pilocarpine and presented SE (CA1= 22.08 ± 5.35; CA3= 39.43 ± 3.18; hilus= 47.12 ± 1.57) when compared with control group animals (CA1= 55.12 ± 4.47; CA3= 63.26 ± 5.58; hilus= 58.2 ± 5.13) and with rats that present SE and received ethoxyquin (CA1= 50.06 ± 3.96; CA3= 59.92 ± 5.14; hilus= 56.8 ± 3.97).
Conclusion: Ethoxyquin was not able to prevent neuronal damage after pilocarpine-induced SE. Supported by FAEP, FAPESP, CNPq, CAPES.

p590
Decreased Number of Calretinin-immunoreactive Interneurons in the Epileptic Human Hippocampi
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Purpose: Calretinin (CR) is expressed in interneurons in the hippocampus. In humans CR was found in interneuron-specific, and dendritic inhibitory cells. Hippocampal CR-containing cells are particularly sensitive to ischemia and epilepsy in animal models. Therefore we aimed to reveal the fate of this cell type in human epilepsy.
Methods: We examined the surgically removed hippocampi of drug-resistant temporal lobe epilepsy patients and compared them to control samples with different post mortem delays. The samples were immunostained for CR and the changes in the distribution and density of CR immunopositive cells were analysed.
Results: Longer post mortem delay resulted in a reduced number of immunopositive cells. The number of CR positive cells in the epileptic tissue is considerably decreased in parallel with the severity of principal cell loss. The largest cell loss was found in the hilus (60.5%) and CA3 (72.4%) of the sclerotic patients. However, a moderate number of the multipolar cells in the stratum lacunosum-moleculare and radiatum of the CA1 region are still detectable, but their dendrites are segmented and shortened.
Conclusion: Our results suggest that CR-containing interneurons in the human hippocampus are also sensitive in epilepsy, thus, interneuron-specific inhibitory cell function, which may include synchronisation of dendritic inhibition, may be impaired in human epileptic hippocampi. Post mortem delays longer than 6 hours in control samples can also cause significant loss of immunostaining, therefore examination of changes of the density of CR-immunopositive cells can be carried out only in carefully selected human samples with short post mortem delays and high quality fixation.

p591
Neurogenesis is Not Necessary for Granule Cell Dispersion of the Dentate Gyrus in Kainate-mouse Model of Mesio-temporal Lobe Epilepsy
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Purpose: Granule cell dispersion (GCD) is one of the characteristic morphological changes of temporal lobe epilepsy, the aetiology of which, however, has been controversial. Previous reports suggest that the increased neurogenesis in the subgranular layer of the dentate gyrus is related to the occurrence of GCD. In this study, we investigated the expression of doublecortin (DCX), as the marker for recently generated cells, to determine the influence of neurogenesis on dispersion in kainate-mouse model of mesio-temporal lobe epilepsy.
Methods: The model was made by the injection of kainate (KA) into the right hippocampus of young adult and aged mice. The animals were sacrificed at various time points after the injection, and DCX immunoreactivity (IR) in the hippocampus was examined.
Results: In spite of the advancement of GCD after KA injection, the expression of DCX-IR decreased progressively without transient increase. The number of DCX-IR cells in the dentate gyrus of eight-month-old mice was significantly less than that of eight-week-old mice, but the dispersion was induced equally by KA injection in both ages.
Conclusion: The progressive decrease of DCX-IR cells after injection of KA suggests that the advancement of GCD is not likely the result of neurogenesis. And the induction of GCD irrespective of the age of mouse suggests that the capabilities of neurogenesis are not related to the development of GCD.

p592
In Vitro Characterisation of Seizure Prone Q54 Mice with SCN2A Mutation
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Purpose: Generalised epilepsy with febrile seizures plus (GEFS+) has been linked to mutations in several genes coding for sodium channels: Scn1a, Scn2a, Scn3a, and Scn1b. A gain-of-function mutation in Scn2a has been reported in transgenic mice in which mutated sodium channels fail to completely inactivate, increasing persistent sodium current and leading to the development of seizures. Whole-cell patch clamp recordings of CA1 pyramidal cells detected a significant increase in persistent current for sodium channels in Q54 mice [Kearney et al Neuroscience 2001;102(2):307-17.]. Here we examine spontaneous and evoked activity in the hippocampal in vitro slice model of mice expressing the Scn2a mutation.
Methods: Experiments were performed using both heterozygous transgenic Q54-SJL/J (Tg/+) (n = 5) and homozygous wild-type (WT), Q54-SJL/J (+/+) (n = 5) mice between 4 and 8 weeks of age, prior to the onset of phenotypic seizures. Evoked field potentials (0.1Hz, 150-250μA, 100μsec) as well as spontaneous activity were recorded in both CA1 & CA3.
Results: After 1hr, a significant increase in activity in Q54(Tg/+) mice was noted by power analysis, frequency, and amplitude of bursting activity (p-values < 0.001). Specifically, normalised power analysis demonstrated an increase of spontaneous activity from 102±50% to 486±440% in Q54(Tg/+), while WT showed a diminutive increase in spontaneous activity, 99±10% to 110±10%. In addition, paired-pulse inhibition studies demonstrated no significant difference between Q54(Tg/+) and WT groups.

Conclusion: These findings support the role of Scn2a mutations in seizure development, while ongoing studies continue to explore the mechanisms behind this genetic abnormality and its relationship to clinical epilepsies. Supported by NIH R01 NS40785-01, & GAANN Neural Eng Training Grant, US Dept of Education.

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Chronic Hypoxic Preconditioning Accentuates Erythropoietin Levels and Prevents Acute Hypoxic Seizure-associated Memory Impairment

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Purpose: We investigated the effects of chronic hypoxic preconditioning on erythropoietin (Epo) levels, and on the deleterious consequences associated with hypoxic seizures in the developing rat brain.
Methods: Control rats (ctrl, N=10) were sham manipulated. Acute hypoxic seizure group (ac, N=9) was subjected to 4% O2 at P10 to precipitate acute seizures. Chronic hypoxia group (ch, N=9) was subjected to 10% O2 (P1-P11), and the fourth group (ch+ac, N=7) was subjected to chronic hypoxia and then to acute hypoxic seizures. Plasma Epo was measured at P11 (ELISA). Morris water maze (MWM) test was performed after p81 on parallel groups treated similarly.
Results: All rats in the acute hypoxic seizure group developed seizures for 25-30 minutes. Controls and ac group had comparable Epo levels (118.86 pg/ml ± 6.62 for ctrl, and 209.38 pg/ml ± 13.99 for ac, p=0.8). Compared to the ch group, the ac+ch group had significantly increased Epo levels (2983.90 pg/ml ± 694.49 for ch, and 6803.02 pg/ml ± 559.97 for ac+ch, p<000001), and both were higher than ctrl and ac groups (p<0.000046). In the water maze test, ch and ch+ac groups were comparable to controls. Only the acute hypoxic seizure group had memory impairment (MWM time in seconds: 228.13 ± 25.94 for ac, 158.08 ± 16.40 for controls, p=0.027; 148.62 ± 23.37 for ch, 123.67 ± 13.68 for ac+ch).
Conclusion: Chronic hypoxic preconditioning prevented hypoxic seizure-associated memory impairment, and accentuated the Epo levels after acute hypoxic seizures. This supports a potential role for Epo in the adaptive mechanisms operating during chronic hypoxia.

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Different Activity of Septum Neurons during Hippocampal Seizures

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Purpose: The medial septum region (MSR) is the major subcortical input to the hippocampus and theta oscillation generator, but its role in temporal lobe epilepsy is not clear. Investigations in this direction may provide a better understanding of seizure genesis mechanisms.
Methods: Single unit activity in the MSR and hippocampal EEG were recorded in control and during seizure discharges provoked by perforant path stimulation in awake rabbits. Neuronal activity was recorded extracellularly and then processed using the software for calculation of mean frequency, autocorrelation and spectral functions. EEG was converted by fast Fourier transform.
Results: During the generation of afterdischarges in the hippocampus, dense neuronal bursts 200±60 ms duration and 3.5±1.5 Hz frequency separated by periods of inhibition were recorded in the MSR. In one group of neurons, the bursts of spikes coincided with discharges in the hippocampus, in the other group they occurred during inhibitory periods. In some cases, initial afterdischarges were followed by secondary seizures. The onset of secondary seizures was preceded by an increase in the frequency of theta bursts (10±1.8 versus 5.2 ±1.7 Hz in control, P<0.01). It correlated with the suppression of high-amplitude 5.2 ±1.9 Hz waves and the occurrence of low-amplitude 13 ±2 Hz waves in the hippocampal EEG. After termination of afterdischarges, the theta pattern in the septal neurons and hippocampal EEG was disrupted.
Conclusion: Results suggest that, during seizure discharges, the septohippocampal system operates as an integral circuit, and different groups of septal neurons contribute differently to the development of seizures.

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Hippocampus Pathology and Distribution of Inhibitory Neurotransmitter Gamma-aminobutyric Acid System in Patients with Medically Intractable Temporal Lobe Epilepsy

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Purpose: To investigate gamma-aminobutyric acid (GABA) distribution in the hippocampus in medically intractable temporal lobe epilepsy (MITLE).
Methods: Definite diagnosis was made according to the criterion (Wang Xuefeng, et al. In: Wang Xuefeng editor. Medically Intractable Epilepsy. Shanghai-Shanghai Science and technology press. 2002, 9-22) including clinical manifestation, MRI (Baulac M. et al, Epilepsies, 1991 3:245-255), EEG, ECoG, and deep electrode EEG. Among 15 patients, 8 contributed in hippocampus sclerosis (HS) group, 7 in NO-HS group. Controlling with normal, pathology (Babb TL, et, In Engel J Jr editor. Surgical Treatment of the Epilepsies. New York, Raven Press,1987 511-540) and GABA distribution in hippocampus (Andre V, et al. Hippocampus. 2001 11:452-468) were studied in 2 patient groups.
Results: CA1, CA3 pyramidal cells (PC), granule cells (GC) lost in No-HS (11.20±6.31, 15.74±6.93, 100.03±67.77) (P<0.001), especially in HS (6.85±2.68, 6.38±2.70, 38.35±17.93) (P<0.001). Hilus neurons lost only in HS (50.08±11.18) (P<0.001). No difference was found between the three groups on glutamate acid decarboxylase (GAD) neurons. GAD grey value (GV) difference between fascia dentate (FD) inner- and outer-molecular layer was lowest in HS (13.78±7.95) (P<0.001, P<0.001). GAD GV in hippocampus stratum radiatum (SR) was highest in HS (50.37±4.44, P<0.001, P<0.001). A positive correlation was found between GAD GV difference in FD and hilus neurons, CA3 PC and GC r/p: 0.453/<0.001, 0.428/<0.001 0.375/<0.00. A negative correlation was found between GAD GV in hippocampal SR and all above cells (r/p: -0.645/<0.001, -0.628/<0.001, -0.494/<0.001, -0.379/<0.001).
Conclusion: Hippocampus primary neuron lost but GAD interneuron was intact with axon sprouting in MITLE. It suggests that inhibitory neurotransmitter GABA increased, especially focused on area with exiting projecting fibre.

p596

Cortical Interhemispheric Responses to Rhythmic Stimulation are Influenced by Status Epilepticus in Developing Rats

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Purpose: To study cortical excitability by means of rhythmic electrical stimuli after status epilepticus induced in two age groups of immature rats.
Methods: Lithium-pilocarpine status epilepticus (SE) was elicited in 12 or 25 day old rats. Paraldehyde (0.3 ml/kg) was administered to interrupt the convulsions. Control siblings received saline instead of pilocarpine. Interhemispheric (transcallosal) responses were elicited by stimulation of right sensorimotor cortical area 3, 6, 9, 13 and 26 days after SE. All experiments started with the estimation of threshold current intensity. Series of five pulses at 100-, 125-, 160-, 200- and 300-ms intervals between pulses with two times the threshold intensity were applied; eight responses were always averaged. The amplitude of first positive and first negative waves was measured in

every response. The ratio of the 2nd, 3rd, 4th and 5th responses to the 1st one was evaluated in all series.
Results: P12 group: clear-cut frequency potentiation was observed in control animals 3 days after injections whereas it appeared only with 100-ms interval in SE group; significant diminution of responses after SE was found mostly in 200-ms interval. No systematic difference was seen 9 days after SE. P25 group: only frequency depression was found with intervals up to 160 ms 3 as well as 9 days after SE. SE and control groups did not significantly differ at these ages.
Conclusion: Outcome of SE depends on the age when status is elicited. Signs of decreased excitability were found in the younger group 3 days after SE when frequency potentiation failed to appear.

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Adenosine A1 Receptors of Amygdala have no Anticonvulsant Effects on Piriform Cortex Kindled Seizures in Rats
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Purpose: Adenosine is an endogenous anticonvulsant which exerts its anticonvulsant effects through adenosine A1 receptors. As the piriform/amygdala is a critical circuit for limbic seizure propagation, in this study the role of amygdala A1 receptors on piriform cortex kindled seizures was investigated.
Methods: Rats were kindled by daily electrical stimulation of the piriform cortex. In the first experiment fully kindled animals received intra-amygdala 2% lidocaine (for reversal neuronal inhibition) bilaterally. 5 min later, animals were stimulated and seizure parameters were measured. In the second experiment, kindled animals received intra-amygdala N6-cyclohexyladenosine (CHA; 10, 100, 500, 1000 □M), a selective adenosine A1 receptor and were stimulated 5 min later.
Results: Intra-amygdala lidocaine reduced the kindled seizures severity. There was a significant increase in stage 4 latency and a decrease in stage 5 duration. On the other hand, different doses of CHA had no effect on kindled seizure parameters.
Conclusion: The amygdala neuronal activity has a critical role in propagation of epileptic seizures from the piriform cortex. Elimination of this activity by lidocaine decreases the severity of piriform cortex kindled seizures. However, the amygdala A1 receptors have no role in this regard.

p598
Changes in Expression of Intracerebral Glutamate Transporter Glast and Regulatory Mechanism of NO in Audiogenic Seizure Rats
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Purpose: To study the dynamic changes in the expression of intracerebral glutamate transporter GLAST in audiogenic seizure rats. Meanwhile the behavioural changes and changes in expression of GLAST in L-Arg andrg and L-NNA interfered audiogenic seizure rats were also observed.
Methods: The rats were randomly grouped as the control and the experimental; the latter were grouped as the postattack 30min, 1h, 3h, 6h and 72h. Audiogenic seizure was produced with the electric bell stimulation. Methods including immunohistochemistry ABC, western blot and reversed transcript polymerase chain reaction (RT-PCR) were treated slowly by 4 days peritoneal injection of NO substrate L-arginine (L-Arg, 40mg/kg/12hrs) and NO synthase inhibitor 9A9(L-NNA, 50mg/kg/12hrs).
Results: Distribution of GLAST mainly located within the cerebellum and its expression could be observed both in neurons and gliocytes which were Bergmann cell encompassing PC in the cerebellum and astrocyte dispersedly distributed in the hippocampus and other areas. After 30 minutes of the seizure, CLAST IR in the molecular and Purkinje layer of the cerebellum began to increase and reached peak at 3 hours, which had a significant difference compared with the control group ($p<0.01$). It was also proved that GLAST mRNA expression existed in cerebral tissue. The degree of seizure behaviour was lowered with a prolonged latency when interfered with L-Arg and enhanced with a shortened latency when interfered with L-NNA.
Conclusion: Increasing intracerebral GLAST expression could be helpful in controlling seizure attacks and alleviating secondary injury to neurons, and endogenic NO might have an antiepileptic function.

p599
Sleep Disruptive Effects of Absence Seizures
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Purpose: We investigated the organisation of sleep in genetic epileptic rats of the WAG/Rij strain and an assumption of the cortico-reticular theory that anterior sleep spindles are controlled by the same mechanisms as spike-wave discharges (SWDs).
Methods: EEG recordings were made during the beginning and end of the light period in 4 and 6 months old WAG/Rij and age matched control (ACI) rats. The length of the (non-REM) sleep cycle and number of SWD and sleep spindles were determined.
Results: Large strain differences were found in the length of (non-REM) sleep cycle (WAG/Rij>ACI) and REM (ACI>WAG/Rij). Also time-of-day (longer at the beginning of the sleep period) and age-related (shorter in older rats) effects were found. The most striking outcome was that the (non-REM) sleep cycle is seriously shortened in WAG/Rij rats but only in recordings made at the end of the light period and only in older rats. SWDs and posterior sleep spindles were strain dependent, anterior spindles not.
Conclusion: Sleep cycle characteristics and phasic events are under genetic control, as are time of day and age control sleep related variables. SWDs and anterior sleep spindles are differently controlled by genotype, age and time of day and this is not compatible with the cortico-reticular theory of absence epilepsy. The sleep cycle is disrupted by absence seizures but only in fragile periods when drowsiness and light slow wave sleep dominate.

p600
Lovastatin Reduces Neuronal Cell Death in Hippocampal Ca1 Subfield after Pilocarpine-Induced Status Epilepticus
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Purpose: The aim of our study was to further characterise the capacity of lovastatin to prevent hippocampal neuronal loss after pilocarpine-induced status epilepticus (SE).
Methods: Adult male Wistar rats were divided into three groups: A) control rats (n=05), received neither pilocarpine nor lovastatin; B) rats that received just pilocarpine (n=05); C) rats that received pilocarpine and lovastatin (n=05). After a pilocarpine injection (350mg/kg, i.p.), only rats that displayed continuous, convulsive seizure activity were included in our study. Seizure activity was monitored behaviourally and terminated with an injection of diazepam (10 mg/kg, i.p.) after 4 h of convulsive SE. The rats treated with lovastatin received two doses of 20mg/kg via an oesophagiac probe 20 minutes and 24 hours after SE. Seven days after pilocarpine-induced SE, all the animals were perfused and their brains were processed for histological analysis through Nissl and Neo-Timm methods.
Results: The cell counts in the Nissl-stained sections performed within the hippocampal formation showed a significant cell loss in rats that received pilocarpine and presented SE (CA1= 27.08 ± 7.65; CA3= 38.22 ± 3.98; hilus= 46.02 ± 1.79) when compared with control group animals (CA1= 53.16 ± 5.17; CA3= 65.06 ± 6.18; hilus= 57.8 ± 5.35). The average neuronal cell number of CA1 subfield of rats that present SE and received lovastatin (52.57 ± 6.91) was statically significantly increased when compared with animals that just presented SE.

Conclusion: Lovastatin exerts a neuroprotective role in the attenuation of brain damage after SE. Supported by FAEP, FAPESP, CNPq and CAPES.

p601
Characterization of Efhc1, A Protein Mutated in Juvenile Myoclonic Epilepsy (JME), as a Mitotic Spindle Associated Protein Interacting with Tubulin
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Purpose: A novel gene, EFHC1, was recently shown to be mutated in JME (Suzuki, T. et al. Nat Genet 2004; 36: 842-849). It encodes a protein with three DM10 domains of unknown function and one EF-hand motif. To study the properties of Efhc1 and its mutant forms, we expressed Egfp-tagged proteins in HEK cells.
Methods: Tagged proteins expression and immunoprecipitation.
Results: In interphasic cells the fusion protein was present in the cytoplasm and in the nucleus. To some extent a similar distribution was observed in control cells producing Egfp alone. However, during mitosis Egfp-Efhc1, but not Egfp, clearly colocalized with the mitotic spindle microtubules, especially at spindle poles and with the midbody during cytokinesis. Transfections of other cell lines exhibited the same pattern of distribution. Efhc1 mutations did not affect the association with the mitotic apparatus. Deletion analyses of Efhc1 revealed that the N-terminus containing the first DM10 domain is crucial for association with the mitotic spindle and the midbody. To investigate the interaction of Efhc1 and tubulin we performed immunoprecipitation assay using an anti-alpha tubulin antibody. We found that Egfp-tagged protein co-precipitated with alpha-tubulin from HEK cells extracts.
Conclusion: Our results suggest that Efhc1, through its interaction with the microtubules based mitotic apparatus and the tubulin associated complex, could play an important role during cell division. The relationships with JME still have to be clarified. The mutated gene could be responsible for early abnormal cell division during brain development and could produce abnormal neuronal migration as illustrated in some cases of JME patients.

p602
Cellular Prion Protein Levels are Associated with Seizure Threshold in Null Mice and Transgenic Strains
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Purpose: Prions are infectious agents originated from conformational changes in the cellular prion protein (PrPc) that cause neurodegenerative diseases, both in humans and animals. Ablation of the PrPc gene enhances neuronal excitability of the hippocampus in vitro and mossy fibres alterations, indicating that PrPc might be related to epilepsy. In this work we evaluated the contribution of PrPc levels for the susceptibility to seizures.
Methods: We induced seizures by intraperitoneal administration of Kainic Acid (KA) in two PrPc ablated mice Prnp0/0(Zrch1) and Prnp-/-(Edbg) and their respective wild-type controls (WT), two post-natal PrPc null mice (tg37CRE and tg46CRE) and their respective controls, and transgenic mice Tg20, expressing ten times more PrPc than control animals.
Results: In null mice Prnp0/0, 100% of animals developed seizures with 7.5 mg/kg while 12.5 mg/kg were necessary to stimulate the phenotype in 85% of the WT. KA at 10mg/kg stimulates seizures in 75% (n=12) of the Prnp-/- mice, against 10% of the WT (n=10/p=0.008). In Tg37CRE, 100% of animals (n=13) developed seizures against 50% of the control (n=16/p=0.003). A trend of sensitivity to seizures was also observed in mice Tg46CRE, where 60% of the animals (n=20) developed seizures compared with 30% (n=10) of their controls (p=0.12). Tg20 mice are extremely resistant to KA, 40% of the animals (n=15) developed seizures only at 25mg/kg while 12.5 mg/kg induced the phenotype in 100% (n=9) of the controls.
Conclusion: PrPc ablated animals are not normal under injury conditions and PrPc levels are associated with the seizure threshold. Supported by FAPESP.

p603
Amino Acid Neurotransmitters and Epilepsy
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Purpose: Trying to define amino acid (aa) profile for each epilepsy type. Delineating the effect of different antiepileptics (AEDs) on aa concentration, and deducing the probable mechanism of action for each.
Methods: 54 Egyptian patients with drug naïve, newly diagnosed generalised epilepsies were studied. They were classified according to seizure type into 3 groups, 22 absence patients, 9 patients with myoclonic, and 23 patients with tonic–clonic. All patients had an unremarkable examination, normal CT and MRI, and liver functions. EEG was done for diagnosis and follow-up. Plasma and CSF samples were collected before administration of antiepileptic drug treatment (AEDs), and six months later.
Results: Ages ranged from 4.5-24 years (12+/-4). Plasma and CSF aa profiles determined before treatment showed: 1) positive correlation between CSF glycine level and duration of illness, 2) 5 parameters (CSF taurine, plasma aspartic, plasma glycine, CSF glycine and CSF GABA) constitute a distinctive profile, that differentiate between the 3 Epilepsy types studied, 3) Plasma aspartic acid level was significantly higher in males (44+/-29nmol/ml) than in females (28 +/-30nmol/ml). Valproate increased GABA and glycine concentration, and decreased glutamate, aspartic and taurine concentration. Carbamazepine had the same effects but differed in increasing taurine concentration and did not affect aspartic. Topiramate lead to a significant increase in GABA concentration and decrease of glutamate and aspartate concentration.
Conclusion: Plasma and CSF aa profile can differentiate between the different types of epilepsy studied. There are common pathways for epileptogenesis and there is a common mechanism for different AEDs, through affecting aa concentrations in the brain.

p604
Regulation of Sodium Channel Alternative Splicing in Rat Cortex
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Purpose: The importance of the sodium channel gene SCN1A in seizure disorders has become clear with the identification of dozens of mutations in people with inherited and sporadic epilepsies. We recently reported that a neonatal splice variant of SCN1A (containing exon 5N) is upregulated in human epileptic tissues, and its regulation may be correlated with sensitivity to phenytoin and carbamazepine (Tate et al. 2005, PNAS, in press). Although this neonatal form of SCN1A is dynamically controlled in the brain of people with epilepsy, we observed little evidence for expression of the neonatal form in rat.
Methods: Neocortical samples were obtained from adult male Sprague-Dawley rats (8-10 weeks old, ~250 g) and epileptic rats 3 weeks following pilocarpine-induced SE according to the Animal (Scientific Procedures) Act, 1986. Sodium channel RNAs were analysed by RT-PCR using primers flanking exon 5, and digested with Avaii.
Results: The published rat and mouse genomes contain stop codons in exon 5N (ensembl.org). In rats the amount of SCN1A containing exon 5N was at the limit of detection: 3.0±0.4% (n=4) in control animals

and 5.6±0.6% (n=5) in epileptic animals ($p<0.01$). The percentage of three sodium channel genes containing exon 5N increased significantly in experimental epilepsy in rat: SCN1A, SCN2A and SCN8A. Of these, SCN8A showed the greatest increase (14.6±4.4% in controls (n=5) and 30.0±2.4% (n=5) in epileptic tissue, $p<0.05$).
Conclusion: The presence of a non-functional exon 5N in rats and mice suggests that alternative splicing of SCN1A may play a fundamentally different role in humans and rats. Our results suggest that in rat, regulation of splicing of SCN8A may be an important result of seizure activity. Investigating the regulation of SCN8A in human tissues will be an important next step. Funded by MRC.

p605
Hippocampal Density of Dendritic Spines in Rats Submitted to Repetitive Status Epilepticus during the Early Postnatal Period
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Purpose: Repetitive seizures during development result in some maladaptive brain function, which could be related to deficient neuronal input, mediated by abnormal neural dendrites. Furthermore, the dendritic spines are altered in several neurological diseases, including epilepsy and mental retardation. Thus, the present study was designed to evaluate the density of dendritic spines in the hippocampus of rats submitted to repetitive status epilepticus (SE) during development.
Methods: SE was induced by administration of pilocarpine (380mg/kg, i.p) and the animals were divided in three groups: pups submitted to 3 consecutive episodes of pilocarpine-induced SE on P7, P8 and P9 (3SE, n=3); pups submitted to a single SE on P9 (1SE, n=3); and the control group (saline-treated, n=4). The hippocampi of them were analysed at P90, using Golgi technique.
Results: Clearly, the rats submitted to 3SE showed a marked loss of hippocampal dendritic spines in adult life, when compared with 1SE or with control group. Control and 1SE rats exhibited intense dendritic spine density, and no difference between them was found.
Conclusion: Our study shows that intense insults during early phases of development may result in severe dendritic spine loss, reinforcing previous data of our group, concerning cognitive impairment of these animals in adult life. Supported: FAPESP, CAPES, CNPq

p606
Refractory Phenotype Reversion by Nimodipine Administration in a Model of Epilepsy Resistant to Phenytoin Treatment
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Purpose: As we previously demonstrated, long term treatment with the convulsant drug 3-mercaptopropionic-acid (MP) induces high brain expression of MDR-1 gene, and develops a refractory phenotype to phenytoin treatment. The purpose of this work was to study the effect of nimodipine administration in our model of refractory epilepsy.
Methods: Lots of Wistar rats were divided into 5 groups. Groups A, B and C received a single dose i.p. of MP (45mg/kg) daily injected for 13 days. During the same period, Group D was treated daily with DPH (50 mg/kg) 30 minutes previous to MP administration. On the last treatment day, Group B was treated with DPH 30 minutes previous to MP injection, and Group C was treated with nimodipine (2 mg/kg), 30 minutes previous to DPH and 60 minutes previous to MP administration. As control group, rats were treated with saline (Group E).
Results: MP induced seizures in Groups A, B and C from the first day. DPH protected from MP-induced convulsions until the third day in Group D. However, the protective effect was completely lost at day 7. On the 13th day, Groups A, B and D developed status epilepticus (SE). Animal death was observed in Groups A, B (100%) and D (50%). Rats with nimodipine administration (Group C) did not develop SE, showed light convulsive episodes, and 100% of them remained alive.
Conclusion: Our results suggest that the nimodipine + DPH can revert the refractory phenotype in MP induced seizures and protect against SE death.

p607
Perinatal Death Among Women with Epilepsy
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Purpose: Women with epilepsy (WE) have 1.2-2.0 fold higher frequency of perinatal death of their offspring in comparison with a healthy population. The risk is also higher in women without epilepsy but with reproductive-endocrine disorders (RED). As RED is defined among 17.8-25% women with epilepsy we have a goal to study frequency of perinatal death in various groups of female patients with and without epilepsy.
Methods: For the last two years we retrospectively studied deliveries of 2236 women in four groups of patients: 1916 healthy patients (group A), 101 women with RED defined before pregnancy (group B), 171 women with epilepsy diagnosed before pregnancy (group C) and 48 women with epilepsy and RED (group D). The results were statistically analysed by c2 test.
Results: Among women with epilepsy and RED, the frequency of perinatal death is 1.2 fold higher than for women with RED only, 4 only higher than among women with epilepsy and 5 fold higher than among healthy women.
Conclusion: The risk of perinatal death is raised among women with epilepsy and RED.

p608
Behavioural and Pharmacological Characterisation of a New Model of Mesial Temporal Lobe Epilepsy in Mice
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Purpose: Both morphological and electroclinical features of human mesial temporal lobe epilepsy (MTLE) have been shown to be mimicked by a unilateral injection of kainic acid (KA) in the dorsal hippocampus of adult mice. After an initial status epilepticus and a latent period, mice develop spontaneous recurrent hippocampal focal seizures. To further validate this model, the exploratory activity and pharmacological reactivity to antiepileptic drugs of epileptic mice were assessed.
Methods: C57BL/6 mice were injected with KA (1 nmol in 50 nl) in the dorsal hippocampus and equipped for hippocampal and cortical EEG recording. Three weeks later, when recurrent seizures occurred, locomotor activity was quantified for a 30 min period in an open field. Later, the effects of 3 antiepileptic drugs on seizures (number and duration) were assessed.
Results: Epileptic mice (n=16) had a significantly higher locomotor activity than sham controls (n=8) in the 3 zones of the open field. However, during the first 5 min, they spent significantly less time in the central zone. Hippocampal seizures were suppressed following injection of diazepam (n=6) (1, 2 and 3 mg/kg) and a high dose of valproate (n=6) (400 mg/kg) whereas low doses of valproate (n=6) (100 and 200 mg/kg) and carbamazepine (n=12) (25 and 50 mg/kg) had no effects.
Conclusion: Epileptic mice display an increased locomotor activity, a higher reactivity to novelty and appear resistant to classical antiepileptic drugs. Altogether our data further validate the use of this model to study MTLE. This work was supported by Fondation pour la Recherche Medicale, by Ligue Française Contre l'Epilepsie and by Fondation Française pour la Recherche sur l'Epilepsie.

p609
Thermoregulatory Response to Hypothermia is Disturbed during Limbic Status Epilepticus
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Purpose: From experimental data it is well known that convulsive status epilepticus (SE) is associated with elevated temperature, which correlates with cerebral damage. Additionally, temperature increased in paralysed animals with convulsive SE, indicating impaired thermoregulatory response. This study investigates whether possible changes in thermoregulation also occur during experimental limbic SE, a model resembling complex partial SE in patients.
Methods: In freely moving rats self sustaining SE was induced by electrical stimulation of the perforant path. Epidural temperature was determined in animals during limbic SE (n = 6) and in nonstimulated sham controls (n = 6) for assessment of individual baseline values. Then animals were placed in a standardised cooling unit for 3 h. Animals were rewarmed until they were normothermic. Temperature changes to baseline values were compared between both groups.
Results: Temperature difference in controls was –1.52 ± 0.56 C after 1 h, -2.16 ± 0.58 C after 2 h and –2.09 ± 0.96 C after 3 h of cooling. Animals with limbic SE had a significantly higher temperature difference: -6.33 ± 1.69 C after 1 h ($p < 0.05$), -7.75 ± 1.83 C after 2 h ($p < 0.05$) und –7.94 ± 2.23 C after 3 h ($p < 0.01$). Animals in both groups became normothermic within 1 h.
Conclusion: Compared to controls, animals with limbic SE showed a significant reduction in temperature, suggesting an impaired thermoregulation. Thermosensitive neurons in the preoptic region of the anterior hypothalamus have possibly been coactivated, which could be the result of spread of epileptic activity during limbic SE.

p609
Vesicular Glutamate Transporter 1 Immunostaining in the Normal and Epileptic Human Cerebral Cortex
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Purpose: Glutamate is the main excitatory neurotransmitter in the brain where, due to the activity of specific vesicular glutamate transporters, it accumulates in synaptic vesicles. The vesicular glutamate transporter 1 (VGLUT1) is found in the majority of axon terminals that form asymmetrical (excitatory) synapses in the rat neocortex.
Methods: We used correlative light and electron microscopy to define expression and distribution of VGLUT1 in the normal human neocortex, as there is no information available. Furthermore, we analysed the distribution of VGLUT1 in the peritumoural neocortex of patients with epilepsy secondary to low-grade tumours.
Results: We found that in the normal human neocortex the distribution of VGLUT1-ir is virtually identical to that found in the rat neocortex, both at the light and electron microscope levels. In the peritumoural regions, we found alterations in the pattern of VGLUT1-ir that matched neuronal loss and gliosis, as well as a decrease in the number of asymmetrical synapses identified by electron microscopy in this tissue.
Conclusion: We assessed whether VGLUT1 immunostaining might be a useful tool to study the pathological alterations of glutamatergic transmission in the epileptic cerebral cortex. Thus, VGLUT1 immunostaining appears to be a reliable and simple tool to study glutamatergic synapses in the normal and epileptic human cerebral cortex.

p610
Dysmorphic Neurons in Patients with Temporal Lobe Epilepsy
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Purpose: Ammon's horn sclerosis has been suggested to be a maldevelopmental disturbance of the human hippocampus. We report dysmorphic neurons in 7 patients with medically intractable TLE, and compare histological, clinical, and imaging features with 10 TLE patients with classical hippocampal sclerosis without abnormal cells.
Methods: After surgery, hippocampi were fixed and histologically processed. Five-micron paraffin sections will be stained with haematoxylin-eosin for routine examination. Fifty-micron vibratome sections were processed for NeuN, neurofilament (SMI-311) and GFAP immunocytochemistry following standard protocols. Sections were then examined under light microscopy for the presence of hippocampal sclerosis and maldevelopmental features, such as tissue disorganisation and disoriented, misshapen or heterotopic neurons.
Results: Dysmorphic neurons were mainly observed in the hilus of the dentate gyrus, and were characterised by misshapen cells with abnormal orientation, size, cytoskeletal structure, and atypical dendritic processes that resembled the dysmorphic neurons from cortical dysplasias. Specimens with dysmorphic cells also contained other cytoarchitectural abnormalities including bilamination of the dentate granular cell layer (4 out 7 cases), and the presence of Cajal-Retzius cells in the dentate gyrus or Ammon's horn (5 out 7 cases). There were no statistically significant differences regarding the age at onset, duration of epilepsy, and hippocampal asymmetry ratio between the two groups of patients. Nevertheless, it is interesting to note that cases in which dysmorphic neurons were observed tended to present a relatively worst surgical outcome according to Engel's classification.
Conclusion: Our results indicate that a malformation of hippocampal development (not detectable in routine histopathological examination) may constitute an important physiopathological substrate underlying mesial TLE.

p611
Cardiac Autonomic Control in Patients with Refractory Epilepsy Before and During VNS Treatment: A One Year Follow-up Study
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Purpose: To evaluate interictal HR variability in patients with refractory epilepsy before and after one year VNS treatment.
Methods: 24 hour ECG recording was made at the baseline and after 12 months of VNS treatment in 14 patients with refractory epilepsy, and once in 28 healthy age- and sex-matched control subjects. Time and frequency domain measures, along with fractal and complexity measures of HR variability were analysed from the ECG recordings.
Results: The mean value of the RR interval ($p < 0.01$), SDNN ($p < 0.001$), the spectral components VLF ($p < 0.001$), LF ($p < 0.001$) and HF ($p < 0.001$), and the Poincaré components SD1 ($p < 0.001$) and SD2 ($p < 0.001$) of patients with refractory epilepsy were significantly lower than those of the control subjects before VNS implantation and one year after VNS implantation.
Conclusion: HR variability was reduced and the nocturnal increase in HR variability was abolished in patients with refractory epilepsy. One year treatment with VNS did not have a marked effect on HR variability.

p612
Human Hippocampal CA2 Region Generates Spontaneous Interictal Like Activity in Vitro
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Purpose: The dentate gyrus, the CA2 region and the subiculum of the hippocampal formation are known to be resistant regions in temporal lobe epilepsy. Interictal like activity is spontaneously generated in vitro in the subiculum of epilepsy patients (Cohen et al., Science 2002;298(5597):1418-21.). We asked whether the preserved CA2 region generates similar synchronous population events, and what are the electrophysiological and neuroanatomical characteristics of CA2 neurons in the human epileptic hippocampus.
Methods: Hippocampal slices (400 µm) were prepared from postoperative temporal lobe tissue derived from epilepsy patients. Field potentials and multiunit activity were recorded in vitro using multiple extracellular electrodes. Pyramidal cells were characterised in intracellular records and were filled with biocytin for subsequent anatomy.
Results: In 4 of 6 cases spontaneous, synchronous interictal like activity was found in the CA2 region of the hippocampus, independent of the subicular activity of the same slice. Five of eleven recorded CA2 pyramidal cells were spontaneously firing. All eleven fired single action potentials, burst firing could never be evoked. Spontaneous EPSPs (n=11) and IPSPs (n=2) were observed. CA2 neurons showed either depolarising (n=5) or hyperpolarising (n=3) responses to the interictal like events. Filled cells (n=2) showed the morphology of pyramidal cells with axonal projection to the CA2 and CA3 regions.
Conclusion: Our results suggest that CA2 cells show plastic changes in epilepsy, and are able to generate synchronous population events, independent of the subiculum. Inhibition and excitation are both present in the CA2 region of the sclerotic epileptic hippocampus.

p613
Cortical Spreading Depression as a Consequence of Recurrent Convulsive Seizures
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Purpose: Cortical spreading depression (CSD) has been suggested to contribute to the initiation of migraine attacks. In experimental models it has been shown that seizures induced by electrical or chemical stimulation may be associated with CSD. Hence, CSD may provide a link between seizures and migraine. The propensity to CSD was examined in a genetic animal model of generalised convulsive epilepsy (audiogenic seizures in rats).
Methods: The occurrence of CSD in the post-ictal period following a brief episode of acoustically induced generalised convulsions was established. Susceptible to audiogenic seizures, rats of Wistar and WAG/Rij strains were used. Freely moving rats implanted with bilateral electrodes were subjected to short acoustic stimulation. This induced an initial running phase of audiogenic seizures. Each rat received 20 repetitive stimulations with 3-day intervals.
Results: The first audiogenic seizures were never accompanied by CSD. But after the 5-18 seizure tests unilateral CSD was registered post-ictally. Once CSD appeared, it became a permanent component of subsequent seizures induced by repeated acoustic stimulation. The duration of the motor (running) convulsions accompanied by CSD was very short (6.8+/-0.4 s) and did not change significantly as compared to the first seizures without CSD (6.7+/-0.6 s).
Conclusion: The present findings indicate that even brief recurrent convulsive seizures can trigger CSD. It can be suggested that seizure-triggered CSD may be an underlying mechanism of post-ictal headache. Repeated seizures associated with CSD might be a useful model for studying the interaction of epilepsy with migraine.

p614
Modulation of Acupuncture on Balance of Excitatory/Inhibitory Amino Acids System during Epileptic Seizures
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Purpose: Acupuncture is commonly practiced to treat epilepsy at our clinic in China. The potential neurobiology pathway of acupuncture has been addressed in our present work, especially on the system of excitatory/inhibitory amino acids.
Methods: Experimental epileptic animals were induced either in kainic acid or penicillin model. Acupuncture was performed on either Jinsuo (Du 8) and Fengfu (Du 16) or Baihui (Du 20) and Fengfu. Acupuncture attenuated epileptiform discharge as revealed by behaviour and electroencephalogram.
Results: 1) GABA, taurine, glycine, glutamine levels increased in hippocampus perfusates using HPLC after acupuncture on Fengfu and Jinsuo acu-points, compared with penicillin-induced epileptic seizures. In another investigation, GABA and taurine were elevated after electro-acupuncture compared with kainic acid-induced epileptic models. 2) Combined with hippocampus-given AP5 or DNQX (antagonist of NMDA or non-NMDA receptor), electro-acupuncture on Jinsuo and Fengfu inhibited penicillin-induced epilepsy to a larger extent using analysis of EEG spectrum power. 3) Bicuculline, microinjected into the hippocampus, partially retarded electro-acupuncture anti-epileptic effect. 4) Acupuncture improved epilepsy in a synergistic manner to taurine, which improved epilepsy by one or two Racine grades as applied by intra-peritoneal injection at 20-80 mg/kg. Acupuncture on Baihui and Fengfu up-regulated the taurine transporter level.
Conclusion: The resulting data mentioned above suggest that the system of excitatory/inhibitory amino acid in the hippocampus, and their receptors including NMDA, non-NMDA, and GABAA or transporter like that of taurine may be involved in the epileptic activity and EA anti-epileptic effect. Financial support provided by Scientific and Technological Committee of Shanghai (Grant No. 04DZ19837).

p615
N-acetyl-L-cysteine is not Neuroprotective during Status Epilepticus
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Purpose: Levels of hippocampal reduced glutathione (GSH; an antioxidant) diminish significantly post SE (Cock et al. Epilepsy Res. 2002; 48: 157-168) co-incident with oxidative damage to mitochondrial enzymes. We hypothesise that it may be possible to reduce the mitochondrial dysfunction associated with SE by protecting the brain from GSH losses. The perforant pathway stimulation model of SE was utilised to measure hippocampal GSH and mitochondrial enzyme activity post SE, and to determine the effects of N-acetyl-L-cysteine (NAC) administration during SE.
Methods: Stimulating and recording electrodes were implanted into the perforant pathway and dentate granule cell layer, respectively, of anaesthetised rats. After a recovery period, self-sustaining chronic limbic status was induced. After 30 min, NAC (300mg/kg i.p.) or vehicle (phosphate buffered saline, 3ml/kg i.p.) was administered, then after another 2h30 diazepam (20mg/kg) to terminate seizures. Rats were sacrificed 44h later, and the hippocampi removed. Spectrophotometric assays measured mitochondrial enzyme activities in samples from sham and SE rats that received vehicle or NAC. GSH levels were measured using electrochemical HPLC.

Results: In keeping with earlier studies, vehicle treated animals exhibited reduced levels of GSH in the dentate gyrus/hilus (-19%) and CA3 (-27%) post SE (one way ANOVA and LSD, $P<0.05$). Comparable GSH reductions were measured in NAC treated animals. Activities of hippocampal alpha-ketoglutarate dehydrogenase and aconitase were significantly reduced post SE in both vehicle and NAC treated rats (one way ANOVA and LSD, $P<0.05$).
Conclusion: In conclusion, NAC administration during SE does not increase hippocampal GSH levels or have protective effects on mitochondrial function.

p616
Comparative Assessment of the Ferric Chloride Model of Epilepsy
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Purpose: Late post traumatic epilepsy (PTE) is a condition of recurrent, unprovoked seizures after head trauma. It occurs in 10-13% of head injuries for all age groups. Prophylactic antiepileptic drugs do not reduce the frequency of late seizures. The epileptogenic focus is triggered off by an irritative action of hemosiderin in the brain cortex.
Methods: Male Wistar-EPM rats, 200-300g, were divided into four groups and subjected to unilateral stereotactic surgery with an injection of ferric chloride (FeCl3,0.5mL,100mM) in the following areas: temporal cortex (n=8), amygdala (n=7), ventral hippocampus (n=8) and dorsal hippocampus (n=7). The control group was comprised of 28 animals (7 for each area), subjected to the same surgical procedure, but with saline solution injection instead of FeCl3. Incidence and frequency of seizures was evaluated for 3 months, 6 hours per week, with camera monitoring. After this period, EEG evaluation was performed. Pearl staining technique was used for histological study.
Results: The incidence of generalised spontaneous seizures in the animals submitted to FeCl3 injection was 13%. Among amygdala lesioned rats, 28% developed seizures; 13% of temporal cortex lesioned animals; 13% of ventral hippocampal lesioned animals. None of the dorsal hippocampal lesioned rats developed seizures, and none of the control group. Ferric chloride lesion at the stereotactic target was confirmed by Pearl histological study and a significant glial reaction was observed.
Conclusion: Physiopathological characterisation of PTE by hemosiderin deposition was well established by this study. We consider that ferric chloride injection in rats induced chronic spontaneous recurrent seizures and can be considered an experimental model of post traumatic epilepsy.

p617
Proteomic Analysis of Human Plasma in Epilepsy Patients
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Purpose: Epilepsy affects more than 0.5% of the world population and has a large genetic component. The definitive diagnostic serological biomarkers for epilepsy are unclear. In the present study, to identify the biomarkers for epilepsy by a more convenient method, serum proteins reflecting alterations in their proteomes were analysed.
Methods: We compared the two-dimensional electrophoresis patterns of human sera of 8 epilepsy patients with those of 8 normal subjects. The differentially expressed spots were identified by matrix-assisted laser desorption/ionization-time-of flight and electrospray ionization quadruple time of flight mass spectrometries.
Results: Twelve proteins that expressed differentially in the epilepsy group were found and six proteins among them were identified. 4 kinds of protein products and three unidentified proteins are up-regulated in sera of epilepsy whereas three unidentified proteins are down-regulated in sera of epilepsy patients. After resection of epileptic zone in epilepsy patients, MHC class I antigen, immunoglobulin heavy chain constant region gamma 2 and three unidentified proteins returned to normal range.
Conclusion: These results suggest that these proteins can be used as useful biomarkers for diagnosing and monitoring epilepsy.

p618
Possible Relation between High Serum Ghrelin Levels and Seizure Occurrence in Patients with Epilepsy
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Purpose: In patients with epilepsy, although many changes in the physiology of hormones in the neuroendocrine system can occur (especially in sex hormones, for example), the causes of these changes have not been fully elucidated. There are also relations between seizure activity and stages of sleep, for example, more frequent occurrence of seizures during the non-rapid-eye-movement (NREM) stage, and these are likewise unexplained. A possible connection between these two categories of phenomena is the peptide hormone ghrelin, which has been shown to affect both endocrine function and sleep. The purpose of this study was to evaluate serum levels of ghrelin in epilepsy patients.
Methods: To our knowledge, this is the first clinical study to evaluate serum ghrelin in epilepsy patients. A total of 35 patients currently receiving antiepileptic drug therapy were included. Of these patients, 20 had primary generalised epilepsy, 15 had partial epilepsy, 20 were female, 15 were male, and overall mean age was 30.85±10.62 years. The control group consisted of 15 healthy volunteers matched for age and gender. In all participants, serum levels of ghrelin, cholesterol and triglycerides were measured and body mass index (BMI) was determined. Patients with endocrine, immune or any other chronic diseases were excluded.
Results: In the epilepsy patients the mean serum ghrelin level was 158.81 ±55.97 pg/ml, and this was significantly higher than the control group's level of 93.43 ±21.33 pg/ml ($p<0.001$). In terms of serum cholesterol, triglycerides and BMI, no significant differences were found between the epilepsy patients and the control group ($p>0.05$).
Conclusion: The origin of higher serum ghrelin levels in epilepsy and their relation to seizures are not completely known. However, this elevation of serum ghrelin could contribute to the lengthening of NREM sleep and the shortening of REM sleep in epilepsy patients, thereby playing a role in seizure formation. From another direction, high serum ghrelin levels could cause changes and/or dysfunction in hormone secretion and physiology via its effects on growth hormone, and thereby play a facilitating role in seizure formation.

p619
Epilepsy and Neurocysticercosis in Rural Bolivia: A Population Based Survey
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Purpose: To evaluate the frequency of neurocysticercosis in a well defined prevalent cohort of epilepsy patients in the rural area of the Cordillera province.
Methods: We carried out a two phase door-to-door neuroepidemiological survey in a sample of 10,124 subjects in a rural area of the Cordillera Province, Bolivia, to detect the prevalence of the most common neurological disorders including epilepsy. (Nicoletti A.

Neurology 1999; 53: 2064-2069) A team of health workers administered a standard screening instrument for neurologic diseases; subjects found positive at the screening phase underwent a complete neurological examination. Epilepsy patients were diagnosed according to the definition proposed by the International League Against Epilepsy (ILAE 1993). Epilepsy patients identified this way underwent electroencephalographic recording, CT scan, and serological evaluation to detect antibodies against T. solium by enzyme-linked immunoelectrotransfer blot.
Results: At the end of the survey we detected 124 defined prevalent epilepsy patients. On the bases of the classification proposed by the ILAE in 1981 partial seizures were the most common type diagnosed (66 patients, 53.3%). Of the 124 patients, 105 underwent a CT scan while a serum sample was taken to detect antibodies against taenia solium in 112 patients; for 97 patients both neuroradiological and serological data were available. Considering radiological, serological and clinical features, out of these 124 patients 34 (27.4%) fulfilled the diagnostic criteria for definitive or probable NCC proposed in 2001. Out of these 34 patients 24 (70.6%) presented with partial seizures.
Conclusion: Our data confirm a high frequency of NCC among a well defined prevalent cohort of epilepsy patients.

p620
Topiramate Prevents Excitotoxic Damage in the Murine Neonatal Brain
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Purpose: Intracerebral injection of glutamate analogs (ibotenate, an NMDA and metabotropic receptor agonist or S-bromowillardiine, an AMPA/kainate agonist) to newborn mouse pups induces damage mimicking lesions observed in human pre-term and full-term neonates. The objectives of the present study were: 1) to determine the neuroprotective properties of topiramate (TPM) in the ibotenate or S-bromowillardiine mouse model of neonatal neuro-degeneration and 2) to gain insight into the mechanism of neuroprotection induced by topiramate.
Methods: Pups received ibotenate or S-bromowillardiine on P5. TPM (1-30 mg/kg) administered ip according to 3 different schedules : i) a single injection immediately after the excitotoxin; ii) one daily injection between P5-P10, starting immediately after the excitotoxin; iii) a single injection 60 min prior to the excitotoxin. Carbamazepine (CBZ: 1,5-15 mg/kg), phenytoin (PH 1,5-15 mg/kg) and diazepam (DZP: 2-20 mg/kg) were used as controls and administered according to the first schedule. To study transduction pathways underlying TPM effects, different inhibitors were administered: bisindolilmalmeimide I (PKC inhibitor); U-73122 (phospholipase C inhibitor); PD98059 (inhibitor MAPK); H89 (PKA inhibitor); Calmidazolium (calmodulin-dependent PK –inhibitor); Wortmannin (phosphatidylinositol 3-OH kinase inhibitor); Okadaic acid (protein-phosphatase 1A and 2A inhibitor). Pups were killed on P10 and P26 for lesion size determination or on P6 for cleaved caspase-3 immunohistochemistry, Tunel staining, glial fibrillary acidic protein (GFAP, a marker of astrocytes) myelin basic protein (MBP, a marker of myelin), Griffonia simplicifolia I isolectin B4 (a marker of activated microglia and macrophages), F4/80 (a marker of activated microglia and macrophages), OX42 (a marker of activated microglial cells) and O4 (a marker of pre-oligodendrocytes). To study seizure activity, P5 pups received S-bromowillardiine and one of the following i.p. antiepileptic drugs: TPM; CBZ, PH; or PBS. Seizures were recorded by video during the first 15 minutes of the 1st, 4th, 8th and 24th hours following the excitotoxic insult.
Results: In this mouse model, TPM protected the developing white matter and cortical plate in a dose-dependent and long-lasting manner against an AMPA/kainate receptor-mediated challenge. TPM had no significant effect on NMDA receptor-mediated brain lesions. TPM-induced neuroprotection potentially involved increased survival of pre-oligodendrocytes, confirming a previous study performed in newborn rats, as well as decreased neuronal apoptosis, inhibition of microglial activation and astrogliosis, and decreased seizure activity. TPM-induced neuroprotection could be blocked by inhibitors of the PLC-PKC pathway and by a protein-phosphatase inhibitor. TPM-induced neuroprotection was not mimicked by three typical antiepileptic drugs. In addition, TPM induced a moderate but significant reduction in the number of clinically detected seizures, whereas PH and CBZ had no significant effect.
Conclusion: In conclusion, the present study demonstrates that TPM is neuroprotective in a newborn mouse model of the excitotoxic white matter and cortical plate injury mimicking the brain damage observed in human neonates.

Monday 29th and Tuesday 30th August 2005
13:15 – 14:15
Poster Session
Clinical Neurophysiology

p621
Intricate Relationship between Epilepsy and Behaviour: An Illustrative Case Report
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Purpose: Psychiatric symptoms, including both depression and psychosis, in relation to epilepsy, have been described in the pre-ictal phase as a part of the ictus and in the post-ictal period as a part of the phenomenon of forced normalisation. The relationship between behaviour and epilepsy, however, continues to remain enigmatic with both agonistic and antagonistic relationships hypothesised. We discuss the clinical course of an individual with long-standing epilepsy, who during a one-month period demonstrated a complex array of epilepsy-related behavioural problems.
Methods: A 41-year old destitute woman with epilepsy of 15 years duration and a history of pre-ictal depression presented with depressive symptoms for which she was treated with anti-depressants (SSRIs). A few days later, she manifested a cluster of seizures and also demonstrated interictal and postictal psychosis. Electroencephalography revealed epileptiform activity with a left-sided focus; MRI being suggestive of left hippocampal atrophy. Treatment with antiepileptics and low-dose antipsychotics resulted in a decrease in EEG abnormality and also controlled the psychotic behaviour; however, psychotic thought processes persisted. Increase in antipsychotic doses brought about an overall marked reduction in psychotic symptoms, but resulted in clinical seizures and an increase in EEG epileptiform activity. Further management of the epilepsy resulted in amelioration of seizures as well as improvement of the EEG but coincided with the emergence of depressive symptoms and pseudo-seizures.
Results: The relationship between seizures and behaviour is complex and may hold many potential lessons about the neurobiology of these clinical states. This case underlines that the relationship is not only multi-directional and complex; it also has the potential to change rapidly within relatively short periods of time, in the same individual.
Conclusion: While several biological mechanisms underlying this relationship have been proposed, a combination of such mechanisms is likely to underlie the clinical pattern discussed herein and will be discussed in some detail.

p622
Differences between Intracerebral Activities of Patients with Idiopathic Generalised Epilepsy and Normal Controls Investigated by Low Resolution Brain Electromagnetic Tomography (LORETA)
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Purpose: EEG background activity was detected by low resolution brain electromagnetic tomography (LORETA) to test the possible differences between brain electrical activities of patients with idiopathic generalised epilepsy (IGE) and normal controls.
Methods: Resting EEG with 19 channels was investigated in 15 newly diagnosed patients with IGE compared to 16 normal controls. LORETA was computed to localise generators of EEG frequency components.
Results: Comparing patients with IGE and normal controls, LORETA showed a significant ($p<0.01$) increase of slow and medium frequency activity (up to 10 Hz) in the basal frontal and temporal areas bilaterally. A significantly ($p<0.01$) decreased fast frequency activity (from 10 to 30 Hz) was detected bilaterally on the convexity with the exception of the occipital lobes.
Conclusion: The authors conclude that basal brain areas may take a significant part in the pathomechanism of IGE. Compared to normal controls, suppressed fast frequency activity on the major part of convexity and increased slow frequency activity in the basal brain areas might be the consequence of altered thalamo-cortical regulation. These findings may be characteristic of interictal background EEG of patients suffering from IGE.

p623
Analysis of Background EEG Activity in Patients with Juvenile Myoclonic Epilepsy
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Purpose: To analyse the background EEG activity of patients with juvenile myoclonic epilepsy (JME).
Methods: We studied the background EEG activity of 12 patients with JME (mean age 21.5 + 10.7) and compared it with 211 normal subjects. The analysis was carried out with Fast Fourier Transform. The absolute power (AP), relative power (RP), mean frequency (MF) and Z-values of delta, theta, alpha and beta bands were obtained.
Results: In all EEG records polyspike and wave complexes were identified, with a mean duration of 3.5 s and frequency of 4.3 Hz. 7 patients had antiepileptic drugs and 5 did not. The mean Z-values in each band were: delta AP 0.12, theta -0.04, alpha -0.24, beta 0.43 and total AP 0.20. Delta RP 0.27, theta 0.12, alpha -0.30 and beta 0.52. Delta MF -0.43, theta -0.06, alpha 0.20, beta -0.62 and total MF -0.12. Z values of patients with and without antiepileptic drugs were compared, only significant differences in AP beta and theta were found. In beta band in C3, C4, P3 and P4 electrodes with main values in patients with antiepileptic drugs ($p= 0.009, 0.02, 0.03, 0.05$ respectively). In theta band in O2 electrode with main values in patients with antiepileptic drugs ($p=0.03$).
Conclusion: We concluded that background EEG activity in patients with JME is normal, but there are differences between patients with and without antiepileptic drugs in beta band in centroparietal regions as well as in occipital regions corresponding to theta bands.

p624
EEG Source Localisation and Multimodal Imaging
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Purpose: In the paediatric population, the number of examinations undertaken should be optimum, in order to reduce evaluation time and complexity of pre-surgical exploration. Is EEG source localisation pertinent in this context?
Methods: 51 patients who underwent surgical intervention and had a follow up of at least 6 months were included in this study. All patients had long-term video EEG monitoring, MRI, PET, ictal and interictal SPECT with subtraction analysis. In 38 patients, epileptic focus localisation has been done based on 32- to 128 channel interictal EEG recordings, using the EPIFOCUS algorithm co-registered to the patient's MRI or a standard brain.
Results: The age of the 38 patients, who had EEG source reconstruction ranged from 1 to 19 years (mean 10.2 years; mean age of onset 4.1 years). 39% of these patients had temporal epilepsy (TLE) and 61% had extra temporal or multifocal epilepsy (ETLE). EEG source reconstruction shows correct localisation in 55% of all patients. 68% of the patients had a seizure free outcome. EEG source reconstruction was correct in 71% of these patients (66% in TLE and 64% in ETLE).
Conclusion: Epileptic source localisation is a valuable tool in presurgical epilepsy evaluation for both TLE and ETLE, providing correct results in the majority of cases. It is fast and non-invasive and does not require sedation, in contrast to other techniques. This is even more crucial for paediatric patients for whom non-invasive techniques should be considered a priority.

p625
Ictal Video EEG Recording for Differentiation between Epileptic and Psychogenic Pseudoseizures
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Purpose: To assess the possibilities of ictal video-EEG recording to differentiate between epileptic and psychogenic pseudoseizures.
Methods: The study included 16 patients with seizures clinically like generalised tonic-clonic (9), simple partial (1), complex partial (1) and partial with secondary generalisation (5). Video EEG was recorded during the ictal events. In one patient the seizure occurred spontaneously and in the others, the seizures were induced: in 9 patients with suggestion, in 1 with music, and in 6 patients with injection of aqua destillata.
Results: None of the 14 patients with seizures like generalised tonic-clonic showed ictal changes in the EEG. During the 'seizure' the EEG revealed persistent alpha rhythm together with fast activity, muscle artefacts and movements. The seizures were evaluated as psychogenic pseudoseizures. In 1 patient there were presumed psychogenic nonconvulsive seizures with clinical features like complex partial (specific music provocation). The ictal EEG revealed slow activity in the right temporal region. The seizure was evaluated as epileptic (the absence of ictal changes would not exclude the epileptic origin). In 1 patient the spontaneous motor partial seizure (partial status lasting more than 24 hours) didn't show any ictal changes in the EEG and was interrupted with the injection of aqua destillata.
Conclusion: Ictal video EEG recording is an objective method for differentiation between epileptic and psychogenic pseudoseizures. Seizure induction is a valuable method for ictal recordings.

p626
Changes in Instantaneous Heart Rate during Hyperventilation: Possible Diagnostic Value in Epilepsy
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Purpose: To investigate the changes in instantaneous heart rate (IHR), as a marker of activity of the autonomous nervous system during hyperventilation in a group of refractory epilepsy patients and a group of healthy controls.
Methods: Electrocardiogram (ECG) signals were acquired in the patient group (n=6, 4 females, 2 males; focal or multi-focal epilepsy history of at least 21 years) during clinical electroencephalogram (EEG) measurements of which hyperventilation (3 minutes) was a part. The recording was continued for another 3 minutes after the activation method. The procedure was repeated with the control group (n=6, 2 females, 4 males). IHR values were computed from pre-processed ECG signals as a function of time. The percentage of normalised ratio of the average IHR within the hyperventilation and post-hyperventilation intervals is assigned as an index of changes in the IHR.
Results: None of the patients were observed to have epileptic activity in EEG during the measurements. The results of ECG analysis show that a) the increase and the decrease in the IHR have a non-linear character; b) the index assigned is lower in the epilepsy group (7.5±3.6) than in the control group (22.5±9.4).
Conclusion: In a previous study we had determined differences between patients and controls in the EEG/DC-shifts accompanying hyperventilation (Kirlangic ME et al. Epilepsia 2003;44:Suppl.8:142.). Although no epileptic discharges were observed in EEG, a difference was determined in the changes in the IHR in the current study. These differences can be utilised as possible novel features for epilepsy diagnostics and therapy evaluation.

p627
Effects of Vagus Nerve Stimulation on EEG Paroxysmal Activity in Patients with Epilepsy
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Purpose: To evaluate the effect of VNS on EEG paroxysmal activity in patients with epilepsy.
Methods: We evaluated 13 patients (8 male and 5 female, average age: 21+13 years), 9 with generalised and 4 with partial seizures. All patients received a VNS implant at least six months before the evaluation. An EEG of 120 channels was recorded, divided in three phases of 30 min each: basal state (VNS off), stimulation cycle of 30 s/5 min and 7 s/18s. The amount of paroxysmal activity per minute, the duration of it and the paroxysmal/non paroxysmal (P/NP) indices were determined.
Results: In 8 patients (61.53%) epileptiform activity decreased during both cycles. In the basal state the mean paroxysmal activity was 7.1 per minute, the duration of it 2.10 s and the P/NP index 0.60. During the 30 s/5 min cycle these values were 8.6, 1.41 and 0.39 and in the 7 s/18 s cycle 7.9, 2.08 and 0.62 respectively. A significant difference was found (by paired t test) between basal state and the 30 s/5 min cycle in the mean duration (P=0.009) and the number of paroxysms per minute (P=0.050). Differences between the two VNS cycles in the average duration of paroxysmal activity (P=0.032), the number of them (P=0.04) and the P/NP index (P=0.034) were found.
Conclusion: These findings show that VNS modifies EEG epileptiform activity recorded in patients with epilepsy and suggest that the 30 s/5 min cycle is more useful for decreased paroxysmal activity.

p628
Threshold for Intracortical Excitability in Untreated Patients with Epilepsy
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Purpose: To assess whether the recruitment of short latency intracortical inhibition (sICI) and facilitation (sICF) in untreated patients with epilepsy might be more sensitive to detect changes compared to controls. Previously, absolute changes of intracortical excitability using paired-pulsed TMS at fixed conditioning stimulus intensities have been described in patients with epilepsy, results being variable and conflicting.
Methods: 18 untreated patients with epilepsy were studied and compared to 20 age matched controls. 12 patients had generalised (GE) and 6 focal epilepsy (FE). TMS was applied with a figure-of-eight coil placed over the hot spot for the right FDI. The resting motor threshold (RMT) was obtained. In five randomly ordered blocks of 36 trials each the intensity of the conditioning stimulus was 30, 45, 60, 75, or 90% RMT. In each block, unconditioned stimuli were randomly mixed with conditioning stimuli of 2ms for sICI and 12ms for sICF. The average size of the conditioned responses was expressed as a percentage of the size of unconditioned responses.
Results: The calculated differences of sICI and sICF from 100% were significant in controls at 60%, 75% and 90% RMT concerning sICI, and for intensities of 75% and 90% RMT concerning sICF. In the whole patient group, this difference was significant for sICI with intensities of 75% and 90% RMT and at 60%, 75% and 90% concerning sICF. In FE patients, sICI differed significantly from 100% at 75% and 90%, but sICF did not. In GE patients, sICI differed significantly from 100% at 75% and 90%, and sICF at 45%, 60%, 75% and 90%.
Conclusion: Our findings of decreased sICI and increased sICF in untreated patients with epilepsy confirm the underlying disinhibition mechanisms in this patient group. Patients with generalised epilepsy predominantly caused this effect. The recruitment curves of sICI and sICF showed a higher threshold for sICI and a lower threshold for sICF in patients than in controls, especially in patients with generalised epilepsy. We therefore propose that measuring the threshold of sICI and sICF may be more sensitive than using fixed stimulus intensities to differentiate these patient groups.

p629
Kozhevnikov's Epilepsia (Epilepsia Partialis Continua)
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Purpose: Kozhevnikov's epilepsy (Epilepsia partialis continua) is one of the syndromes of Russian tick-borne encephalitis. The aim of our research was the establishment of the clinical and EEG specific parameters for the diagnosis and clinical observations of patients suffering from Kozhevnikov's epilepsy.
Methods: Clinico-neurophysiological signs of the 89 patients suffering from epilepsia partialis continua in cases of tick-borne encephalitis were studied in 20-year period of research.
Results: Using EEG, Kozhevnikov's epilepsy is shown as a combination of the registered local pathological forms of bioelectric activity with paroxysms of bilateral-synchronous slow oscillations. Criteria for determining Kozhevnikov's epilepsy were: identifying the bond between a complex of symptoms and tick-borne encephalitis; revealing the main group of clinical manifestations, taking into account electro-physiological succession of disease stages. The pathophysiologic base of the present pathology is a complex neurodynamic source, disorganising activity of all brain structures, responsible for motor acts realisation. In process of its existence, two systems (epileptic and generating extra-pyramid myoclonia) originate and actively interact between themselves. A connecting link in a complex chain of pathological phenomena becomes defect of caudal

sections of the brain stem. Asymmetric position turns it into a source of pathological influences both brain stem-subcortical-cortical and interhemispheric relations as well as spinal and brain stem intercommunications.
Conclusion: This research has shown that Kozhevnikov's epilepsy has an independent complex of symptoms arising as a result of complex changes caused by tick-borne encephalitis. The basic group of its clinical manifestations consists of the following: convulsive syndrome, spasmatic–atrophic paralysis and contractures in the extremities of the body having hyperkinesis.

p630
Characteristics and Evolution of Stimulus Induced Rhythmic EEG Discharges (SIRDs) in Three Patients with Encephalopathy
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Purpose: Background: stimulus–induced rhythmic EEG discharges (SIRDs) is a recently reported phenomenon of unknown pathophysiology in critically ill patients and little is known about their evolution.
Methods: We found SIRDs in 3 patients with encephalopathy and followed them with serial EEGs. The EEG response to different stimuli were systematically tested.
Results: One patient had acute disseminated encephalomyelitis (ADEM), had a good clinical outcome and the other 2 had hypoxic ischemic encephalopathy (HIE) and expired in the hospital. SIRDs appeared between 4-13 days after the onset of illness, were elicited by tactile or nociceptive stimuli and persisted for 2-3 days. They were detected in 2/6, 1/3 and 2/11 EEGs done between 9-32, 2-4 and 3-15 days respectively. Their morphology varied: blunt triphasic waves, rhythmic delta activity and epileptiform morphology. Only one type was seen in any given patient. Baseline EEGs in all showed a diffusely slowed or suppressed background activity. Epileptiform abnormalities were seen in the initial EEGs of both patients with HIE but not in the patient with ADEM. SIRDs were associated with clinical manifestations like jerking of limbs in one patient with HIE. This is the first report of SIRDs in ADEM.
Conclusion: SIRDs are transient phenomena occurring in patients with encephalopathy, appearing after a certain time period (hours to a few days) after the onset of illness. In this, they can be likened to triphasic waves or periodic lateralised epileptiform discharges (PLEDs). Serial EEGs and repeated testing of EEG response to tactile and nociceptive stimuli is required for their detection.

p631
Minisphenoidal Electrode Recording in Temporal Lobe Complex Partial Seizures – Utility in Comparison with Anterior Temporal Electrodes
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Purpose: Sphenoidal electrode recording has been found useful for detecting temporal lobe discharges, but it requires a painful procedure. Minisphenoidal electrodes are very small; hence, their use causes minimal inconvenience to the patient. Since, there is also literature supporting use of anterior temporal electrodes, as a convenient alternative, we conducted this study to assess if recording with minisphenoidal electrodes changes yield of epileptiform discharges.
Methods: Over a period of 18 months, we included all patients with complex partial seizures, who had undergone long-term video-EEG recording with anterior temporal electrodes, as work up for epilepsy surgery, and whose, interictal EEG, during the same, was normal. We recorded interictal EEG using minisphenoidal electrodes (10 mm long needle) in these patients, for at least 40 minutes. All these records were studied for any additional information yielded by this recording, compared with the interictal long-term video-EEG record.
Results: A total of 26 patients (11 females, 15 males) with a mean age of 23 +/- 11 years (range 10 to 65 years), were enrolled in the study. The minisphenoidal electrode study was found normal in 5 among these 26 patients (19.2%), while the rest 21 (80.8 %) had abnormal recordings. A single temporal lobe focus was identified in 17 (65.4%) patients.
Conclusion: This study demonstrates that interictal EEG recording using minisphenoidal electrodes is a useful investigation in identifying mesial temporal lobe foci in patients with uncontrolled temporal lobe CPS, improving the yield significantly, compared to recording with anterior temporal electrodes.

p632
Effects Of Prediction Horizon on Performance of Automated Seizure Prediction Algorithm in Scalp EEG Recordings
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Purpose: Seizures are preceded by transitions in spatiotemporal dynamics of the EEG. We developed an automated seizure prediction algorithm (ASPA) that can run on-line in real time. When evaluating the prediction performance, one parameter that can be varied is the prediction horizon. We tested the effect of varying the prediction horizon upon performance.
Methods: Continuous long-term (6.7 to 11.8 days) scalp EEG recordings from 8 patients with intractable partial seizures were analysed by ASPA. ASPA uses these steps: (1) calculate short-term maximum Lyapunov exponents (STLmax) every 10.24 seconds for each electrode site, (2) select critical electrode sites, (3) calculate statistical difference in STLmax among selected sites, (4) warn of an impending seizure when the difference falls below threshold. The effect of prediction horizons: 30, 60 90, 120, 150, and 180 minutes were evaluated. Warning was considered to be correct if a seizure occurred within the prediction horizon and false if it did not. Periodic and random prediction methods were also performed on the same datasets as statistical controls.
Results: For sensitivities above 80%, ASAP had false prediction rates of 0.58, 0.30, 0.21, 0.14, 0.11, and 0.09 per hour for prediction horizon 30 to 180 minutes, respectively. Performance for each of the prediction horizons was significantly better than the two control prediction methods ($p < 0.05$). However, the difference decreased with longer prediction horizons.
Conclusion: Longer prediction horizons reduce the false prediction rate, with the most reduction from 30 to 60 minutes, but also reduce the difference between ASPA and control methods.

p633
Evaluation of Health-related Quality of Life in Patients with Intractable Epilepsy
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Purpose: To evaluate health-related quality of life (QOL) in patients with intractable epilepsy .
Methods: Investigation of the following domains of QOL have been proposed by the World Health Organization using the Scale in China and Social Questionnaire.
Results: Results showed that intractable epilepsy patients not receiving free education for 9 years equalled 23%. Of 323 marriage-age patients, those who are single or divorced were 38.6% and 22.9% respectively. Serious adverse reactions were experienced 317 times (includes ataxia, skin eruption, consciousness, hepatic function damage, foetal death). There were 132 cases with depression and another 124 cases who showed postictal psychosis or delirium. 67 patients developed alternating psychosis and 48 cases showed

interictal schizophreniform psychosis. Of 400 patients, 242 depended on familial or social care.
Conclusion: In intractable epilepsy patients, health-related quality of life shows significant changes.

p634
Lateralisation of Slow Frequency Oscillations During Recognition Memory and Target Detection in Temporal Lobe Epilepsy
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Purpose: We investigated to what extent slow oscillations that have been previously described in invasive recordings from the hippocampi of patients with temporal lobe epilepsy (TLE) can also be lateralised noninvasively.
Methods: Whole-head magnetoencephalography (MEG) recordings were obtained from 24 patients (8 right TLE, 8 left TLE, 8 patients with idiopathic epilepsy) as they made an old/new-decision of newly presented and previously studied words. 8 of these patients also participated in an auditory target detection paradigm. Single trial continuous wavelet transforms were used to identify the time course of neural oscillations ranging from delta (2.7-3.1 Hz) to gamma (39.5 Hz). To identify the oscillatory patterns that covaried with the difference between correctly recognised studied (old) words and correctly rejected nonstudied (new) words, a multivariate statistical tool, partial least squares (PLS), was applied.
Results: In idiopathic epilepsy, a bilateral increase of delta amplitude dissociated old from new. In TLE patients, this difference was reliably lateralised to the contralateral (nonepileptogenic) side. A similar pattern of lateralisation was observed for delta oscillations elicited by detected targets.
Conclusion: In summary, oscillatory hippocampal responses might be lateralised non-invasively using MEG and this method might be valuable in the preoperative work-up of surgical candidates.

p635
Subiculum-temporal Cortex Interactions During Spikes and Seizure
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Purpose: To elucidate the neuronal network interactions during interictal spikes and seizures in the hippocampus and lateral temporal lobe in humans.
Methods: Microelectrodes and clinical subdural strip electrodes were implanted in epilepsy patients undergoing anterior temporal lobectomy in general anaesthesia. Two 24 channel multielectrodes, separated by 5mm were inserted into the subiculum and an 8-contact strip was placed over the temporobasal structures. Electrical stimulation of the strip contacts were used to elicit hippocampal responses.
Results: Spontaneous subicular spikes were highly synchronized across the two recording sites, and only about 5% of the events coincided with cortical spikes. Two types of CSD profiles were observed, one with initial sink in the pyramidal layer, and the second type with initial sink in the apical dendrites. Single electrical (0.2ms, 5-15mA, 0.5Hz) stimulation of the strip contacts close to the pole elicited strong response from the subiculum. Onset latencies varied between 4 and 40ms depending on the strength and location of the stimulation. Solitary afterdischarges were originated in the cortex, having comparable onset latency in the subiculum. Train (50Hz, 2sec) stimulation elicited highly synchronized self sustained afterdischarges in the subiculum and the cortex. CSD profile of self sustained activity was very similar to the evoked subicular spikes.
Conclusion: Based on our preliminary data we conclude that in the interictal state both the subiculum and cortex are able to generate spikes independently. However, self sustained seizure-like activity arises in cortico-hippocampal networks.

p636
EEG Paroxistic Activity in Children with Learning Disabilities without Epilepsy
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Purpose: To describe the paroxistic activity observed in children with learning disabilities without epilepsy.
Methods: 110 children from a public Paediatric Neurology department were included. They were learning disabled children without epilepsy or attention deficit disorder. Qualitative EEG was performed and type of paroxysms, topographical and focal or multifocal electric discharges were registered. The chi-square test was performed to compare the frequencies in the sample.
Results: 30 (30%) of the 110 children had paroxysms in the EEG. 11 (37%) were female and 19 (63%) were male. Average age was 8.75 years (SD 2.13), age range was 6 - 13 years. The most frequently observed paroxysm was sharp waves (65%) and sharp waves and slow waves (23%). Paroxistic slow waves were observed in 2 (7%) and in one of the subjects (3%) spike and slow wave complexes were observed. 70% showed focal paroxysms. Generalised paroxistic activity was observed only in 10% of the children. Significance differences were observed when the presence of paroxysm ($p=0.00$, $\alpha= 0.05$), the type of paroxysm ($p=0.00$, $\alpha= 0.05$) and focal versus multifocal paroxysm ($p=0.02$, $\alpha= 0.05$)were analysed.
Conclusion: For children with learning disabilities, it is very important to look for paroxistic activity in the EEG given the frequency of this activity observed in the disorder.

p637
Diagnosis and Prognostic Implications of Abnormal Auditory Evoked Potentials in Landau-Kleffner Syndrome
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Purpose: To describe neurophysiological and acoustic findings in 2 patients with Landau-Kleffner Syndrome (LKS) aged 19 yrs (Pt 1) and 12 yrs (Pt 2), and to correlate with language evaluation, 13 and 7 yrs, respectively, after the acute phase. LKS is characterised by normal speech acquisition followed by epileptic seizures and acquired aphasia caused by receptive and expressive language deterioration regarding verbal and non-verbal sounds, with variable long-term evolution. EEG abnormalities are seen especially during sleep in temporal areas, where verbal language and acoustic information is processed.
Methods: We performed EEG, immittance acoustic measurements, basic audiometry, transient evoked oto-acoustic emissions (TEOAE), and auditory evoked responses, with brainstem, mean and long latencies studies (ABR, MLR, cognitive potential-P300). Language was evaluated by Boston Diagnostic Aphasia Examination.
Results: EEG was normal and audiologic evaluation revealed similar results in both cases: normal ABR values, electrode effect in left hemisphere in MLR and bilateral P300 latencies, delayed at right. Language evaluation showed severe receptive and expressive impairment in patient 2, severe phonemic substitutions, with impact on social and academic levels, and the other patient evolved with normal language, school grade and interpersonal skills.
Conclusion: Although discrepant long term language outcomes between these two patients with LKS with similar neurophysiologic findings points to a failure of these tests in prognosis approach in LKS, these procedures may still be used as diagnostic tools in difficult cases. The same primary cortical dysfunction reflected by abnormal long latency evoked response probably is related to a unique pathophysiological process with different patterns of evolution.

p638

Dysgraphia of Dystonic Origin in Idiopathic Absence Epilepsies

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Purpose: Co-occurrence of age-related idiopathic absence epilepsies (IAE) and paroxysmal dyskinesia has been described in some patients suggesting a similar mechanism of origin causing a dysfunction of cortico-subcortical networks. After observing that some children with IAE have severe dysgraphia with writer's cramp characteristic, we tested the hypothesis that there may be a significant association between IAE and dysgraphia as a manifestation of focal dystonia.
Methods: We studied 80 children with IAE. Analysis of handwriting included: a) readability of the handwriting; b) speed of writing and c) shape and size of letters. Blink-reflex was also studied, using bipolar stimulation of the skin overlying the supraorbital nerves. The R2 recovery cycle was studied using paired shocks of equal intensity at various interstimuli intervals (100-1000 ms).
Results: Of the 80 patients, 12 (6 females and 6 males) had a clear-cut dysgraphia. Mean age at the time of the study was 12 years. Absence seizures began at 8 years (median 6 ± 5). 3 patients had febrile seizures preceding the onset of absences and 2 patients also had afebrile tonic-clonic seizures. Blink reflex showed a faster recovery curve in all patients than in controls.
Conclusion: The faster recovery of the R2 cycle of the blink reflex suggests hyperexcitability of brainstem interneurons, and is typically found in idiopathic dystonia. The presence of dysgraphia in 15% of patients with IAE suggests that there could be an underlying common pathophysiology. Abnormal ion channels function causing hyperexcitability in the cortico-subcortical network could underlay both absences and dysgraphia.

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High Frequency Oscillations in Epileptic Spasms of Focal Cortical Origin Confirmed by Subdural Electroencephalogram

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Purpose: There have been several reports on epileptic spasms of focal cortical origin. The objectives of this study are to identify high frequency oscillations (HFOs) during spasms by subdural electroencephalogram (SDEEG) and to examine whether HFOs localise epileptogenic zones.
Methods: We identified 2 patients with epileptic spasms of possible focal origin among 40 patients who underwent SDEEG between September 1997 and December 2004. We reviewed SDEEG (sampling rate: 1 kHz for patient 1, 200 Hz for patient 2, to find HFOs in ictal EEGs, and analysed the distribution of HFOs by multiple band frequency analysis (MBFA).
Results: In patient 1, ictal SDEEG showed HFOs at 80-150 Hz lasting 0.5-3 s. MBFA showed extensive but incontiguous distribution of HFOs over the left frontal and temporal regions. The HFO distribution was consistent among spasms of different clinical severity in patient 1. In patient 2, ictal SDEEG showed HFOs at around 50 Hz. MBFA showed HFOs in the right frontal and parietal regions. Epileptogenic zone was concordant with the area of HFOs in patient 1, but discordant in patient 2. Both patients have been seizure free after the surgery (4 months follow-up, patient 1; 7 years, patient 2).
Conclusion: We confirmed HFOs over the cerebral cortex using SDEEG in 2 patients with epileptic spasms. The HFOs higher than 80 Hz localised the epileptogenic zones in patient 1. Low sampling rate of SDEEG possibly failed to detect higher frequency activities in patient 2.

p640

Automatic Detection of Seizure Activity in Neonatal EEG Recordings: A New Approach

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Purpose: Recent insight suggests that treatment of epileptiform EEG discharges in neonates that are not accompanied by clinical features, is relevant to reduce the likelihood of developing epilepsy and learning disabilities, contrasting previous clinical strategies that were primarily only aimed at treating clinical seizure activity. This suggests a need for EEG monitoring techniques that allow reliable detection of epileptiform discharges, including those not accompanied by clinical phenomena. Our study focuses on the detection of these epileptiform discharges in neonatal EEGs, for which various detection algorithms have been proposed. The most well-known is probably the CFM, using a weighted spectrum of a single channel EEG recording. However, these, and other features, all suffer from a finite sensitivity and specificity, which may limit their clinical applicability.
Methods: We compare various features (> 20) in their ability to detect epileptiform discharges, using tools from pattern recognition. Sixteen different EEGs were used, recorded in neonates suffering from a post-anoxic encephalopathy. All epileptiform discharges were labelled by experts.
Results: Pilot results suggest that the performance of classification algorithms using several features significantly outperforms algorithms based on a single feature, in agreement with the known variability of seizure semiology. Using these combined features for classification, preliminary results suggest that sensitivities > 0.90 and specificities > 0.98 can be realised, which seems sufficient for real-time monitoring applications.
Conclusion: Using a combined features strategy, epileptiform abnormalities can be detected with sufficient sensitivity and specificity suitable for clinical applications. These techniques may assist in improving treatment of neonates suffering from (electroencephalographic) seizure activity.

p641

Evaluation of the Interictal Paroxysmal Activity Effects on Cognitive Processing in Children without Epilepsy who are Poor Readers

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Purpose: Previous studies have reported a high incidence of paroxysmal activity in the electroencephalogram (EEG) of learning disabled children without epilepsy. In this work the possible influence of paroxysmal EEG activity on cognitive processing was evaluated.
Methods: The sample was composed of 17 schoolchildren who were poor readers (DSM IV). Each child was evaluated by means of three continuous performance tasks (semantic, phonologic and colour categorization) presented as computer video games. During the performance of each task, simultaneous digital EEG in 8 derivations was recorded. To analyse the data we applied an ANOVA for repeated measures and chi-square test.
Results: In most evaluated children (16/17, 94.11%) the paroxysmal activity was associated with an intermittent disruption of cognitive processing, which was evidenced by an increased rate of errors and/or a significant modification of reaction time. This cognitive disruption was more frequent in the semantic and phonologic categorization tasks. It seems to be related with the nature of the psychological processes underlying the task and not with the difficulty of its performance
Conclusion: A disruption in cognitive processing by children without epilepsy who are poor readers, produced by paroxysmal EEG activity, similar to transient cognitive impairment (TCI) described in epilepsy patients, was confirmed. The specificity of the psychological tasks

suggests that the TCI may have a causal role in learning problems of these children. These findings suggest that in children with learning disabilities and TCI it could be a clinical form of epilepsy and could improve with anticonvulsant drugs treatment.

p642
Attention Evaluation in Children with Idiopathic Temporal Lobe Epilepsy
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Purpose: Some children with epilepsy have a direct impact over their cognitive functions and/or behaviour. Attention is one of the cognitive functions affected by epilepsy. With this research we evaluated attention in a group of children with idiopathic temporal lobe epilepsy.
Methods: 12 children (6 female and 6 male) between 8-11 years old, were studied in the Paediatric Hospital 'Juan Manuel Márquez'. A neuropsychological battery to test attention was applied. The battery was composed of eight tests for evaluating four levels of attention: sustained, selective, divided, and alternative attention. Electroencephalogram (EEG) and computerized axial tomography was applied to every child in the selected group. Mann Whitney U test was carried out in order to know the relation among different clinical variables, EEG and attention tests.
Results: A significant statistical association trend between sustained attention test and evolution time of epilepsy was found (p=0.05). 77% of pathologic EEG had a slight disturbance in the temporal region. Divided, selective and sustained attentions were the most affected levels.
Conclusion: Although the patients had idiopathic epilepsy with a slight disturbance in EEG, and the condition was clinically controlled, it was evident that cognitive dysfunctions, specifically an impairment of the attentional process were present.

p643
Influence of Levetiracetam on Ictal Propagation and Postictal EEG
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Purpose: The influence on interhemispheric propagation of seizure pattern and postictal recovery of EEG background activity during levetiracetam (LEV) treatment is investigated.
Methods: 23 adult patients with pharmacoresistant focal epilepsies (age>16 yrs) entering presurgical evaluation at the Epilepsy Centre Erlangen were enrolled for the evaluation of efficacy of LEV. Those eligible patients on a maximum of one AED were recruited into the 48 hour baseline phase and after at least two seizures were randomised into the 7 day treatment phase receiving either LEV (n=11) or placebo (n=12), all controlled by continuous day and night video EEG monitoring by the Glonner system. The daily dose of LEV was 1000mg (500mg bid.) on the first treatment day and titrated to 2000mg (1000mg bid.) from the second day on. EEG changes concerning the time delay of the interhemispheric propagation of seizure patterns and the postictal recovery of the background activity were analysed by computerised video EEG recording.
Results: The results concerning seizure severity are reported elsewhere. A prolonged latency of the contralateral propagation of seizure pattern was observed in the LEV group, whereas a more rapid propagation was observed in the placebo group (p=0.009). Postictal generalised slowing of the background activity was recorded in 21 patients during the baseline phase. A quicker postictal recovery of the EEG background activity was observed in the LEV group, but not in the placebo group (p=0.03).
Conclusion: LEV could not only cut off the propagation of seizure pattern but also helped to quickly resume the postictal background activity in EEG.

p644
Interaction between the Flash Evoked SSVEPS and the Spontaneous EEG Activity in Children and Adults
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Purpose: To evaluate the interaction between the steady-state visual evoked potentials (SSVEPs) recorded during the intermittent photic stimulation (IPS) and spontaneous EEG activities in children and adults.
Methods: EEG was recorded during the rest and under 5, 7.5, 10 and 12.5 Hz IPS in 41 children between 3 and 16 years old and 10 adults. We distinguished between the spontaneous resting EEG spectra, SSVEPs (1st harmonic) and undriven (ongoing) EEG spectra recorded during the IPS.
Results: We show that IPS influences spontaneous EEG activity by specifically suppressing individual posterior dominant resting EEG frequencies (DF) in both children and adults ($p < 0.0001$). Further, this highly significant suppressing effect positively correlates with the SSVEPs amplitude ($p < 0.001$). An inverse correlation has also been observed between the SSVEPs amplitudes and the undriven EEG spectra of the frequency band corresponding to the individual DF ($p < 0.001$).
Conclusion: Our data suggest that desynchronisation of spontaneous EEG activity under IPS and the SSVEPs are related to each other. These relationships could be interesting to study in pathological conditions where neural synchronisation and responses to IPS have been shown to be affected, such as epilepsy. In this respect, our preliminary data show more powerful visual evoked response to IPS in children with febrile seizures compared to controls. Supported by Canada Research Chair Program, CFI and CIHR.

p645
Analysis of the Relationship Between Trace Alternant in Newborns and Cyclic Alternating Patterns in Adults
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Purpose: The visual analysis of neonatal EEG implies the classification of the different phases of the sleep-wake cycle based on polygraphic features and their changes. Tracé alternant (TA), the periodic discontinuity of quiet sleep, is the newborn's equivalent of NREM sleep in adults. In the English literature, TA is known as cyclic alternating pattern (CAP). CAP is identified by repetitive stereotyped EEG patterns, lasting 10–60 s and separated by equivalent intervals of background activity. Our aim was to study if TA in babies are equivalent to the CAP of children and adults.
Methods: 32 polysomnographic studies of normal full-term newborn babies were reviewed. Polygraphic studies were performed using a 21 channel EEG machine, with internationally accepted standardised montages for the neonatal period, without sedation. We quantified the TA in normal patterns and compared them with the number of sleep phases recorded.
Results: Mean duration of the polygraphic studies was 57 minutes and the total time was 1838.4 minutes. The total number of phase changes was 424, mean 13.34 phases per exam. Quiet sleep represented 38.61% of total sleep time. The total duration of TA was 416.95 seconds, mean duration was 13 seconds per exam. Comparing TA with the number of phases showed no statistical significance.
Conclusion: The number of TA had no influence in the number of changes of sleep stages. TA cannot be taken as an equivalent to CAP.

p646
Effects of Oxcarbamazepine on the Excitability of the Human Motor Cortex: A Correlation Between Drug Serum Level and Magnetic Stimulation Study
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Purpose: The effect of different antiepileptic drugs on brain excitability have been studied using paired magnetic stimulation in normal subjects and patients. The aim of the study was to investigate motor area excitability of patients affected by chronic pain after oral administration of a progressive increasing of dose of oxcarbamazepine, starting from 150 mg to 1200 mg/day.
Methods: Motor cortex excitability was studied in 10 patients by single and paired transcranial magnetic stimulation before and after one week, 2 weeks, 3 and 4 weeks from oral administration of oxcarbamazepine. Cortical excitability was measured using different transcranial magnetic stimulation parameters: motor threshold, motor evoked potential amplitude and latency, motor recruitment, duration of cortical silent period, intracortical inhibition, and intracortical facilitation.
Results: Significant increases in motor threshold (from 60 to 65%), in silent period (from 112 ms to 130 ms) and intracortical inhibition (53% to 33%) associated with a decrease in intracortical facilitation were observed across the different recording sessions during the increased dosage of the drug, without any significant changes in motor evoked potential amplitude and latency and spinal excitability parameters. The changes of different TMS parameters were correlated to the drug serum level of oxycarbamazepine.
Conclusion: Our findings suggest that a progressive increase of dosage of oxcarbamazepine can induce significant reduction of motor cortex excitability in patients; this effect is related to the drug serum level.

p647
Nonconvulsive Status Epilepticus: Clinical and Electrographic Features in a Series of Patients in a General Hospital in Brazil
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Purpose: Different electrographic patterns may be identified in patients with nonconvulsive status epilepticus (NCSE). In this study we analysed the clinical and electrographic characteristics of a series of patients with diagnosis of NCSE in a private general hospital in São Paulo, Brazil.
Methods: We reviewed the charts of all patients who received a diagnosis of status epilepticus during a three-year period (2002-2004). SE was defined as continuous or almost continuous EEG seizure activity for over 30 minutes with unequivocal impairment of consciousness, with no overt motor signs. All EEGs were reviewed, and electrographic patterns were analysed.
Results: Twenty-two episodes of NCSE, of 18 patients, were identified. Thirty registers were analysed. 10 patients were women. Age varied from 6 months to 95 years (mean 51.6 years). The most frequent aetiologies were central nervous system (CNS) neoplasia (3 patients) and systemic infection (3 patients). The electrographic patterns were: continuous epileptiform discharges (CEDs 15 cases), PLEDs (2), merging seizures (3), recurrent seizures (1), and prolonged generalised theta ictal activity (1 case). Among the 30 exams analysed, NCSE was considered to be generalised in 18 and focal in 12. In two episodes there was a shift from localised epileptiform discharges to generalised activity.
Conclusion: In our series NCSE was most commonly due to CNS neoplasia or systemic infection. CEDs constituted the most frequent electrographic pattern. Generalised ictal discharges were more common than focal discharges, although in some cases a focal onset may have been missed, as was demonstrated in two cases. This work was supported by Instituto Israelita de Ensino e Pesquisa Albert Einstein.

p648
Continuous EEG Monitoring in Critical Patients in a Private Hospital in Brazil: A Cost Analysis
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Purpose: Continuous EEG monitoring (cEEG) is an important diagnostic tool for critical patients, particularly those with neurological illnesses. cEEG may help in the diagnosis of subclinical seizures and/or nonconvulsive status epilepticus (NCSE). However, there are several concerns regarding the cost of cEEG and its impact over the global cost of critical patients. The aim of this study is to analyse the costs of cEEG in critical patients in a large private hospital in São Paulo, Brazil.
Methods: We retrospectively analysed the charts of all patients submitted to cEEG during a 5-year period (2000-2004) in our hospital. The diagnosis in each case and the indication for cEEG were identified. Costs relative to the cEEG were calculated, and compared to global costs of each patient during the length of the hospital stay. For calculation, costs were converted from local currency to American dollars.
Results: 39 patients were submitted to cEEG during this period. The length of the hospital stay varied from 3 to 395 days (mean 68.4 days). Total duration of cEEG varied from 1 to 60 days (mean 8.5 days). Total costs varied from US$3,789.30 to US$565,866.04 (mean US$120,195.15). Costs relative to cEEG varied from US$360.78 to US$6,382.37 (mean US$1,336), which represented 1 to 10% of global costs (mean 2%).
Conclusion: In this study, costs related to cEEG represented a small fraction of the global costs in critical patients. Concerns regarding cost of cEEG should not be used against the utilisation of cEEG for critical patients. This work was supported by Instituto Israelita de Ensino e Pesquisa Albert Einstein.

p649
High Frequency Electric Cortical Stimulation Suppresses Epicortical Fast Activities in Patients with Tumour and Epilepsy
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Purpose: To delineate factors correlating with decrease of epicortical fast activities after electric cortical stimulation in patients with tumour and epilepsy.
Methods: Two patients with brain tumour and seizures who had implanted chronic subdural electrodes for presurgical evaluation were investigated after they had given written informed consent to the research protocol approved by the Ethical Committee of Kyoto University Graduate School of Medicine. Cortical functional mapping was performed for clinical purposes by using electric cortical stimulation (50 Hz, bipolar, alternating square pulse of 0.3 ms duration, 1-15 mA, within 5 sec). For 10 stimulated sites, electrocorticogram power spectra were compared in each 5 min before and after stimulation.
Results: Power spectra in 10-50 Hz at the stimulated site were significantly decreased after stimulation ($p<0.05$), and power decease in 26-34 Hz positively correlated with the total quantity of electricity (coulomb) delivered (Kendall's test, $p<0.01$, $\rho>0.5$). In 18-50 Hz band, stimulation of language areas induced a larger power decrease than that of motor cortices ($p<0.05$).
Conclusion: 50 Hz electric cortical stimulation within the safety limit suppressed fast cortical activities. The decrease of fast activities

positively correlated with the total coulomb delivered, representing the dose-dependent inhibitory effect of high frequency stimulation on cortical excitability. A more obvious decrease of fast cortical activities in language areas than in motor cortices might reflect the cortical architectonic difference. These findings may provide information to predict the effect of electric cortical stimulation when applied to seizure suppression.

p650
Emotions Induced by Intracerebral Electrical Stimulation of the Temporal Lobe
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1) University of Bologna, Bologna, Italy 2) Epilepsy Surgery Centre

Purpose: To analyse the expression of emotions obtained by intracerebral electrical stimulation in patients undergoing presurgical video-stereo-EEG monitoring for drug-resistant epilepsy.
Methods: Behavioural analysis was performed on 74 patients (mean age 25 yrs; 43 males). Stimulated brain regions were: amygdala (46 right; 31 left), hippocampus (45 right; 27 left), temporal pole (27 right; 24 left), temporal lateral neocortex (31 right; 22 left). Patients were chronically implanted with semi-rigid platinum/iridium depth electrodes (0.8 mm in diameter). Electrical stimulation was performed by delivering trains (1hz or 50hz) of electrical stimuli of alternating polarity; the intensity could vary from 0.2 to 3 mA. A total of 938 stimulation procedures (S) were performed. Data reported refer to the incidence (%) of emotional responses (ER) with respect to the total of S delivered.
Results: 79 ER (8.4%) were obtained. 67 out of 79 ER were 'fear responses'. Sad feelings were evoked 3 times, happy-pleasant feelings were obtained 9 times. Anger and disgust were never observed. The following variables had a significant effect in the determination of ER. (a) Site of stimulation: ER (always fear) were maximal at the amygdala (12%) and minimal for lateral neocortical stimulation (3%, $p < 0.01$). (b) Stimulation frequency: ER were 12% at 50hz versus 6.0% at 1hz ($p < 0.01$). (c) Stimulation intensity: ER were 12% at 1mA, 15% at 2mA and dropped to 6% at 3mA ($p < 0.01$). (d) Patient gender: in female fear responses were 16%, in male 3% ($p < 0.01$). There was no gender effect when analysing non-emotional responses. (e) After-discharges (AD): ER could be evoked even without AD, however 80% of fear responses were associated to AD spreading to the cingulate region.
Conclusion: Expression of fear is preferentially evoked by mesial temporal lobe stimulation and associated to the involvement of anterior-temporal and cingulate regions. The most effective stimulation parameters for inducing emotional responses were high frequency (50hz) stimuli with 2mA intensity. A strong gender difference in fear expression was observed and deserves further investigations.

p651
Comparison of Epileptic Focus Localisation on the Basis of EEG Mapping of Interictal and Ictal Discharges in Frontal Lobe Epilepsy
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Purpose: Reliable, electrophysiological diagnosis of epileptic seizures is based on the analysis of EEG discharges at the start of the seizure. However, as it is difficult to record epileptic seizures it is hard to perform the diagnosis. It is desirable to evaluate the diagnostic value of commonly found interictal discharges and compare the electrophysiological localisation of ictal and interictal epileptic discharges in frontal lobe epilepsy cases.
Methods: We investigated data of 99 patients with drug resistant epilepsy hospitalised in Department of Neurology and Epileptology. The routine EEG and video-EEG until the time of at least one seizure were performed for each patient. The 50 recordings were classified as frontal lobe seizures, 25 of them were digitized and included in the current study. First ictal discharges and interictal discharges were analysed by our own EEG mapping software PkNeuroTrack. The localisation and propagation of discharges were compared and their conformity was evaluated.
Results: Good conformity of localisation of interictal and ictal discharges was found in 5 (20%) cases; in an additional 17 (68%) cases the propagation of discharges was nearly the same. In 1 (4%) case the lateralisation of the lobe of discharge was confirmed only, and in 2 (8%) cases the localisation and propagation were completely different.
Conclusion: The mapping of interictal discharges may be a valuable tool used to confirm epileptic focus localisation. It must be analysed with great care as the sole electrophysiological localisation tool as it may give misleading results.

p652
Brain Electrical Tomography in Epilepsy
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Purpose: To determine the utility in epilepsy of methods in which flows of information are analysed and to define the location of the main focus.
Methods: Series of time is processed obtained by volumetric laplaciana solution and belonging to electroclinical seizures of patients suffering from complex partial epilepsy with absence seizures accompanied by oral automatisms. It was doubted, from the EEG results, whether the primary focus was frontal or temporal. An algorithm of non-lineal dynamics is applied which reflects the influence of the different regions implied in the critical event to specify the focus and its propagation. As a first step, brain electric tomography was carried out (BET) in the volumetric Loretta varying in time domain. The information of the critical period was performed by the total energy in each generator for 4.5 seconds
Results: During the test we obtained 4 generators (A, B, C, D) of which (A) was located in left frontal lobe, being that of highest intensity. The generators B, C and D were located in the right frontal lobe, left temporal and right temporal, respectively. An analysis of the influence measure showed that although the focuses B, C and D interacted among themselves, none of them affected focus A, and this one did influence the rest of them.
Conclusion: Therefore, in this combination of BET with non-lineal dynamics it is concluded that the primary focus was in the left frontal lobe (A). An activity of chaotic type was not found to be the evidence of epilepsy.

p653
Comparison of EEG Topography at Resting State Between Controls and Epilepsy Patients
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Purpose: To analyse the topographical distribution of electroencephalogram (EEG) frequency bands in a group of epilepsy patients and in a group of healthy controls at resting state.
Methods: 28-channel EEG recordings (10-20 System) were obtained from 12 patients (7 males, 5 females; age 40.25±11.18; focal, and focal secondary generalised epilepsy) and 12 healthy controls (8 males, 4 females; age 39.33±10.39) at open- and closed-eyes resting conditions. From each subject, one minute of data was taken per condition. The EEG was analysed by calculation of band power in 9 standard EEG bands after ocular artefact correction. Median values were used for reducing the impact of outliers, and the topographical distribution was statistically investigated.
Results: Not only the theta band power at fronto-central midline electrodes was higher in patients than in controls in both conditions, but also there was a generalized increase in theta power in patients after eyes-closing, whereas in controls it remains either constant or decreases. The power in the 12-15 Hz band at frontal and central areas was significantly ($p<0.05$) higher in patients in both conditions. In the

10-12 Hz range, the power ratio (closed-to-open eyes) showed significant differences at occipital areas.
Conclusion: The lower synchronisation in theta band in patients during an odd-ball task reported in our previous study (Pérez D et al. Epilepsia 2003;44(8):141.) can be explained through the increased theta power at resting state. The differences observed in other frequency bands shall be further investigated in order to determine their physiological significance.

p654
Magnetoencephalographic Characteristics of Neocortical Temporal Lobe Epilepsy with Auditory Auras
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Purpose: We report on the localising value of magnetoencephalography in children with neocortical temporal lobe epilepsy with auditory auras as the initial seizure manifestation.
Methods: We retrospectively studied 6 children; 4 males and 2 females (age range 7-14 ys). All had auditory auras as part of the initial seizure manifestations. We localised and lateralised the sources of epileptic discharges from scalp video-electroencephalography (SVEEG) and magnetoencephalography (MEG) in all 6 patients, from electrocorticography (ECoG) in 3 patients and from intracranial VEEG (IVEEG) in 1 patient. MEG auditory evoked fields field (AEF) to tones were performed in 3 patients.
Results: 2 children had only elementary auditory auras, 1 child had complex auditory auras and the other 3 had both complex and elementary auras captured on SVEEG. All patients had clustered MEG spike sources (MEGSSs) with coexisting scattered MEGSSs. Clustered MEGSSs were located in the superior temporal gyrus in 5 patients (3 left, 2 right). 1 patient had clustered MEGSSs involving the right inferior frontal gyrus with additional scattered MEGSSs in the right superior temporal gyrus. AEF was located within clustered MEGSSs in 1 patient and within the surrounding scatters in the other 2. Surgical resection was performed in 4 patients. 3 patients are seizure free at 2-3 years of follow up.
Conclusion: This study adds further evidence to the localising value of MEGSSs in neocortical temporal lobe epilepsy. In all our 6 patients with auditory auras, MEGSSs were localised in the superior temporal gyrus. These MEGSSs appeared in close proximity and at times engulfing AEF.

Monday 29th and Tuesday 30th August 2005
13:15 – 14:15
Poster Session
Paediatric Epileptology

p655
Clinical and Electrophysiological Characteristics of Photosensitive Epilepsy: Analysis of Thirteen Cases
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1) Bakirkoy Hospital for Psychiatric and Neurological Diseases

Purpose: Photosensitive epilepsy, the most common form of reflex epilepsies, occurs in about 5% of all epilepsy patients. Seizures are typically induced by intermittent light, steady bright light, patterns or television. In order to investigate the characteristics of our cases and their congruity with the literature, our data was reviewed.
Methods: Thirteen cases with photosensitivity were documented.
Results: About 2/3 of the patients were women. The mean age of onset was 10 ranging between 6-15. Our patients, although within the reported age range, seem to have a younger onset. All patients except two reported either TV affinity or precipitation of their seizures by TV. 12 patients had generalised tonic, clonic or tonic clonic seizures accompanied by myoclonic jerks in 5, complex partial in 1, and elementary visual hallucinations in 1 patient. 1 patient had only absence seizures. Only 2 of the patients' seizures were reported to be more common during sleep. In their history, 1 had perinatal hypoxia, 5 (38%) had febrile seizures and interestingly 4 (31%) had enuresis nocturna. About half of the cases (7 patients) had epilepsy history in the family, 5 of whose parents had consanguinity. The typical EEG finding of pathologic photosensitivity, a photoparoxysmal response to intermittent photic stimulation, was present in 10 cases. However, repeated EEGs in 3 cases were normal although their seizure characteristics were similar to the photosensitive epilepsies. Seizures were under control with valproate monotherapy in most of the patients; only 2 needed polypharmacy.
Conclusion: Our results were consistent with the literature.

p656
Absence Epilepsy of Early Childhood: An Under-diagnosed Syndrome?
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Purpose: "Absence epilepsy of early childhood" has been described by Doose since 1965, but it has up until now not been included in the International Classification of Epileptic Syndromes. We report on clinical and neurophysiological findings of 4 children with this syndrome.
Methods: The patients, aged between 2 to 4 years, 3 females and 1 male, had an epileptological work-up including seizure registration and neuropsychological assessment. MRI scans were accomplished in 3 patients.
Results: 2 children had a 2nd grade relative with febrile convulsions (FC). Onset of seizures was between 7 and 28 months with FC in 2 children and absences in the other 2. Absences, which were the main seizure type, showed mild impairment of consciousness, eyelid myoclonia (2/4), a retropulsion of the head (2/4), and were of short duration (3-6 sec.) with irregular epileptiform discharges. MRI scans were normal. Cognitive development was delayed (3/4), and seizures were difficult to treat.
Conclusion: Our observations underline that the absence epilepsy of early childhood is a distinct syndrome and does not belong to benign myoclonic epilepsy of infancy, Dravet syndrome, myoclonic astatic epilepsy, Lennox-Gastaut syndrome, or childhood absence epilepsy. 2 patients had seizures suggesting the syndrome "eyelid myoclonia with absences" but the FCs do not conform well to it. Genetic investigations of these patients are not available. A genetic similarity with the group of epilepsies belonging to GEFS+ is possible. Further investigations are necessary to determine the incidence of absence epilepsy of early childhood and point out its characteristic features.

p657
Childhood Absence Epilepsy
O.A. Milovanova[1]

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Purpose: To analyse the data of anamnesis, clinical-instrumental methods of investigation with the purpose of studying the dynamics and types of seizures in childhood absence epilepsy.
Methods: 12 patients with childhood absence epilepsy, aged from 4 years 1 month to 9 years old, were examined. All children were studied with a full clinical assessment including CT, MRI and EEG.
Results: Among the examined 12 patients the condition manifested from complex absence seizures, which were the leading seizure type. Absence seizures were characterised by the sudden suppression of mental functioning of brief duration (5 - 15 sec). Absence frequency was from dozens to hundreds per day. In 10 patients more than one motor component was observed during an absence attack. In 2 patients tonic-clonic seizures appeared later during the course of the condition. All children (12 patients) had a normal intelligence level before and after the beginning of seizures. EEG features of typical absence attacks consisted of generalised, symmetrical, and synchronous spike-wave complexes with a frequency of 3-3.5 Hz. Hyperventilation provoked these EEG patterns in all patients. CT and MRI

examinations did not reveal any abnormalities. Sodium valproate monotherapy showed a good final seizure response in 80% of patients.
Conclusion: Childhood absence epilepsy prevails among epileptic syndromes of childhood with typical absence seizures. It is important to follow-up patients with childhood absence epilepsy until adolescence, because sodium valproate dosage decreased at this age might result in the development of generalised tonic-clonic attacks.

p658
Deficit of Recognition Functions and Childhood Absence Epilepsy (CAE)
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1) Outpatient Clinic of Child Neurology, Kielce, Poland

Purpose: To investigate the deficit of recognition functions in patients with childhood absence epilepsy (CAE) treated with antiepileptic drugs (AED.
Methods: The cases of 114 children, aged 6-10 years, were analysed for four years (2000 to 2004). The results were assessed with a WISC-R test with the following frequency: before the beginning of the treatment, after two years of the treatment and four years after the beginning of the study. The scores were analysed in three variants: the type of seizures, the frequency of seizures, and the effectiveness of CAE treatment.
Results: This study has not found any statistically significant differences between patients' recognition functions at any time of the four years' observations.
Conclusion: The deficit of recognition function is not observed in children with CAE.

p659
Bakirkoy State Hospital for Neurological and Psychiatric Disorders
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1) Bakirkoy State Hospital for Neurological and Psychiatric Disorders

Purpose: Occipital Bening childhood epilepsy (OBCE) poses an important diagnostic problem. Clinical manifestations and EEG findings of 13 patients with OBCE were presented in this study.
Methods: Records of 13 patients diagnosed as OBCE followed in outpatient clinics of Bakirkoy State Hospital for Neurological and Psychiatric Disorders between the years 1996-2005 were reviewed and clinical manifestations and EEG findings were collected.
Results: Headache is a presenting symptom of 9 of 13 patients. 10 patients had visual hallucinations, 6 patients had vomiting and 7 patients had unilateral eye deviation. All patients had complex partial seizures. Secondary generalised tonic-clonic convulsions were described on 12 of them. 9 had also seizures during sleep. Routine EEG were abnormal on all patients and 9 had unilateral or bilateral occipital and 4 had extra-occipital localisation.
Conclusion: Diagnosis of OBCE may be difficult because presenting symptoms of headache, vomiting and autonomic symptoms may resemble other neurological and non-neurological disorders such as migraine, encephalitis, gastroenteritis etc. Routine EEG is a very sensitive and effective tool for diagnosis.

p660
Clinical Analysis of Symptomatic Parieto-occipital Lobe Epilepsy (SPOE) due to Mild Perinatal Hypoxic Ischemic Encephalopathy (HIE)
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Purpose: Perinatal HIE in term infants may cause selective brain damage over the parieto-occipital regions. We report 10 patients who grew relatively normally after perinatal HIE, then later developed SPOE.
Methods: The subjects were 8 boys and 2 girls. We retrospectively reviewed medical records, EEGs and neuroimaging findings.
Results: Eight patients were born at term, and the remaining 2 at 34 and 35 weeks gestation, respectively. 5 patients were the 1st or 2nd born of twin pregnancies, weighing from 1262g to 1970g. All patients had perinatal HIE requiring intensive care in the NICU and 4 of them had neonatal convulsions. Subsequently, 6, 5 and 1 patient demonstrated acquired mental retardation and/or behavioural problems, visual impairments and left leg monoparesis, respectively. Seizures started at ages ranging from 10 to 168 months with a mean of 72 months. These seizures consisted of complex partial seizures (CPS) preceded by visual aura in 5 cases, CPS without visual aura in 2 and focal motor seizures in the remaining 3. MRI scan demonstrated localised parieto-occipital atrophy in 9 and normal findings in the remaining 1 who showed localised hypoperfusion in the right occipital and left frontal regions on SPECT. EEG showed an occipital focus with or without other foci in 8, foci in the centro-temporal regions and normal findings in one each. Seizures were finally controlled in 5 patients.
Conclusion: SPOE in childhood caused by mild perinatal HIE tends to be pharmaco-resistant and accompanied by visuospatial cognitive and behavioural problems.

p661
Bitemporal Epilepsy and Precocious Puberty
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Purpose: To report a new form of bitemporal epilepsy associated with precocious puberty.
Methods: We studied the case of 4 unrelated children, who present this unusual bitemporal epilepsy. We also reviewed the literature regarding the mechanisms of the onset of epilepsy and the onset of puberty.
Results: Prenatal, perinatal antecedents and development were normal. They had no history of infection, trauma or febrile convulsion in infancy. At nearly six years old, they suddenly presented a prolonged status epilepticus. After this episode, the children developed a temporal lobe epilepsy. Their brain MRI show marked and isolated hippocampal atrophy and they have a cognitive impairment which more markedly affects the memory. The behaviour of these children was characterised by bursts of anger and rudeness; furthermore, all children present a precocious puberty. Previously published studies on the onset of puberty propose that the mechanisms responsible for the disinhibition and reactivation of the LHRH pulse generator can be caused by a decrease in GABAergic neurotransmission and a concomitant increase in the input of excitatory amino acid neurotransmitters (including glutamate). It is also widely recognised that epilepsy is a disorder in the balance between glutamatergic excitability and GABAergic inhibition.
Conclusion: We report a new entity, which starts by status epilepticus, then becomes a bitemporal epilepsy which associates a particular neuropsychological profile and a precocious puberty. We also try to explain the close relationship between the onset on the precocious puberty and the status epilepticus.

p662
Autonomic Seizures and Autonomic Status Epilepticus: Early Onset Benign Childhood Occipital Epilepsy (Panayiotopoulos Syndrome)
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Purpose: To study clinical and EEG features of children with ictal vomiting and no underlying brain lesions.
Methods: Subjects were 36 children (age range 2-13 years) with the following inclusion criteria: ictal emetic symptoms; normal development, neurological and mental state; normal brain imaging if performed; normal background EEG. They had the diagnosis of Panayiotopoulos syndrome.
Results: The onset of seizures occurred between 1 and 5 years of age. 14 children (38.8%) had a single seizure. Seizures were numerous in 7 cases. 14 children (38.8%) had autonomic status epilepticus. All the patients had ictal vomiting. Impairment of consciousness was reported in 30 (83.3%) children, eyes deviation in 10, and other autonomic symptoms and head deviation in 9. The seizures evolved to generalised convulsions in 3 cases and to hemiconvulsion in 8. One child reported visual symptoms. 8 children (22.2%) had seizures with speech arrest or hemifacial motor symptoms. 11 children (30.5%) had postictal symptoms. The EEG showed occipital spikes or spike-wave complexes in 27 children. Discharge blocking by eyes opening were confirmed in 7 cases. 9 patients also had rolandic spikes and 3 had only extraoccipital spikes. 6 patients had normal EEG. Somatosensory evoked spikes by foot stimulation were observed in 1 case (2.77%). No clinical differences were observed between patients having occipital or extraoccipital spikes.
Conclusion: In Panayiotopoulos syndrome the spikes are predominantly occipital but blocking by eyes opening is a less frequent feature. There is in some children the overlapping between different idiopathic syndromes.

p663
Neonatal Hypoglycaemic Syndrome
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Purpose: To study clinical, electrophysiological and neuroradiological aspects of patients with neonatal hypoglycaemic insult.
Methods: 2000 epilepsy patients from 1998–2004 visiting our epilepsy centre were studied. Those with documented neonatal hypoglycaemia on NICU discharge cards or neuroimaging suggestive of perinatal hypoglycaemic insult (parieto-occipital damage) were analysed. Detailed clinical history, perinatal risks, age of onset, type of epilepsy and thorough neurological examinations were obtained. Patients were subjected to electroencephalography (EEG), neuroimaging. Follow-UP period was 0-84 months (average 19.93).
Results: 70/2000 (3.5%) patients had neonatal hypoglycaemic brain damage. 59/70 (84.28%) showed NICU records of documented hypoglycaemia. In 11 patients perinatal hypoglycaemia was suspected on neuroimaging during epilepsy workup. 19/59 (32.75%) had neonatal hypoglycaemic seizures. Perinatal risk factors were intrauterine growth retardation in 31/70 (44.28%) and sepsis 26/70 (37.14%). 7/70 (10%) had isolated hypoglycaemia. All patients were seizure free on monotherapy at discharge from NICU. Age of onset of repeat seizures was 19.13 months (2-108). Partial seizures were 30/70 (42.85%), infantile spasms 24/70 (34.28%) and myoclonic in 7/70 (10%). Development was delayed in 54/70 (77.14%). EEG revealed focal epileptiform abnormalities in 27/70 (38.57%), multifocal in 19/70 (27.14%), hypsarrythmia in 18/70 (25.71%). 6/70 (8.57%) had normal EEG. 53/70 underwent neuroimaging studies. 20/70 (28.57%) showed isolated parieto-occipital damage suggesting neonatal hypoglycaemic insult, 18/70 (25.71%) had combinations of parieto-occipital damage and different perinatal insults. On follow up 28/70 (40%) were seizure free. 19/70 (27.14%) had poor seizure control.
Conclusion: Hypoglycaemia is a common, easily treatable condition in neonates. It is associated with significant neurological damage and epilepsy. Complex partial seizures and West syndrome were the commonest outcomes with poor prognosis in the latter.

p664
Characteristics of Epilepsy after Neonatal Seizures: A Cohort Study
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Purpose: Seizures are a frequent neurological manifestation with a variable outcome in the neonatal period. The aim of this study was to verify the outcome of newborns (NB) with seizures and evaluate characteristics of epilepsy after neonatal seizures.
Methods: A cohort study including all newborns admitted to the Neonatal Intensive Care Unit of Hospital São Lucas – PUCRS between January 1999 and December 2003.
Results: During this period 3659 newborns were admitted and 102 were recognised as having clinical seizures (Volpe's classification). In this sample 56.45 were male, with mean gestational age 36.6 ± 4 weeks, vaginal delivery in 45.5%, and 71% had birth weight adequate for gestational age. Mean Apgar score for the 1st minute was 5 ± 0.3 and for the 5th, 7.1 ± 2.5. Mean age of 1st seizure was 4.8 ± 7.2 days. From this group, 25 (25%) deceased before discharge, 9 (8.9%) deceased during the follow up period and 51% had developmental delay. 22.7% had seizures after the neonatal period and 14 developed epilepsy (West Syndrome = 4, symptomatic epilepsy = 7, undetermined epilepsy = 2, benign non familial neonatal seizures = 1), 2 had isolated single seizures and 6 had febrile seizures. Comparing NB that had neonatal seizures to the other NB from this cohort that did not have neonatal seizures the risk of developing epilepsy was10.7 times greater in the former (19.3/100 x 1.8/100) ($p<0.001$).
Conclusion: Our data suggests that neonatal seizures are a consistent risk factor for developing postneonatal epilepsy.

p665
Clinical Significance of Neonatal Status Epilepticus
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Purpose: To evaluate the neurological outcome of neonatal status epilepticus according to the underlying aetiology, seizure pattern, onset time, and duration.
Methods: We reviewed retrospectively 36 neonates (19 male, 17 female) with status epilepticus who were admitted to the neonatal intensive care unit, Inha Hospital between 1998 and 2003.
Results: The mean gestational period of the patients was 37.0±3.6 weeks and birth weight was 2.7±0.8 kilogram. 53% of the neonates were male and 67% were born at term. The most common cause of neonatal status epilepticus was hypoxic ischemic encephalopathy (36%). Intracranial haemorrhage was shown with an especially high frequency in preterm babies ($p=0.03$). Neonates with a seizure within the first 72 hours tended to be more frequent among those who developed an adverse outcome ($p=0.016$). The incidence of neurological sequelae were related to a prolonged seizure lasting more than 1 hour ($p=0.002$). Gestational age and birth weight did not show a correlation with neurological complications. Generalised tonic/tonic-clonic seizures had the worst prognosis whereas those children who have subtle seizures had better outcomes than any other types ($p<0.05$). Generalised tonic/tonic-clonic seizures were often represented on EEG by an abnormal background, whereas subtle seizure showed more significantly normal EEG than any other seizures ($p<0.05$).
Conclusion: Our results indicate that neonatal status epilepticus with early onset, prolonged duration, and generalised tonic type can predict an increased risk for neurological sequelae. So those seizures must be

perceived as medical emergencies and treated aggressively with antiepileptic drugs.

p666
Effective Treatment of Ohtahara Syndrome with ACTH in a Young Infant
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Purpose: Ohtahara syndrome (early infantile epileptic encephalopathy, EIEE) is the earliest of the age-dependent epileptic encephalopathies defined by tonic spasms and severe mental and physical impairment; the outcome is often fatal. The EEG shows a typical suppression-burst pattern. The aetiology of the disorder is unknown. Neuroimaging often reveals some malformations, but in many cases there are no pathological findings. There is no approved therapy for Ohtahara syndrome, but in some studies by Ohtahara et al, the early administered therapy with ACTH seems encouraging.
Methods: We report a male infant presenting in a routine check up at the age of 2 months with muscular rigidity and recurring tonic spasm (BNS like convulsions) which were first noticed by the mother at the age of 2 weeks and advanced in frequency and intensity. Brain imaging showed no abnormalities. There were no signs for metabolic disorders or infectious diseases. Ohtahara syndrome was confirmed by EEG and demonstrates a typical suppression-burst pattern. The patient only showed minimal clinical improvement on vigabatrin, lorazepam and topiramate.
Results: Treatment with ACTH started 4 weeks after diagnosis resulted in suspending the convulsions and normalising the findings in the EEG. The psychomotor retardation seems to be markedly depressed at the age of 8 months.
Conclusion: Ohtahara syndrome is a rare epileptic encephalopathy with bad prognosis without effective treatment but success in individual cases. Our case demonstrates ACTH therapy can be effective when administered early.

p667
Other Seizures than Spasms in Ohtahara Syndrome
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Purpose: We experienced several types of seizures except spasms in two cases of Ohtahara syndrome (OS). In general, seizures seen in OS show mainly epileptic spasms, and rarely partial seizure or myoclonic seizure and so on. Therefore, we reviewed Japanese literature and attempted to clarify the seizure type of OS.
Methods: Video-EEG monitoring was performed in 2 cases diagnosed as OS to confirm its clinical symptoms in detail. We also reviewed 41 cases with OS reported in Japanese literature to investigate seizure types besides spasms.
Results: Other than spasms, case 1 showed massive or segmental myoclonus accompanied by burst complexes on EEG, and case 2 showed eye lids myoclonus associated with burst complexes on EEG, brief tonic or atonic muscle contractions of chin, and complex partial seizure. Review of 41 Japanese cases of OS in the literature revealed as follows: tonic spasms were observed in 40/41cases (98%), partial seizures in 16/41 (39%), fragmentary or partial, or massive myoclonus in 4/41 (10%): clonic seizure in 3/41 (7%): hemiconvulsions in 2/41 (5%): tonic seizure in 1/41 (2%). Totally, 51% of patients showed other seizures than spasms. Moreover, our study showed that patients reported before 1980 having other seizures than spasms showed 20% (4 out of 20 cases), on the other hand, showed 85% (17 out of 20 cases) after 1981.
Conclusion: Many authors state that the ictal manifestations of OS show spasms in series, but it is speculated that OS is usually accompanied by more seizure patterns besides spasms. EEG-holographic recording will contribute to clarify more detailed symptomatology of OS.

p668
Epileptic Encephalopathies with Debut in the First Year of Life: West syndrome
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Purpose: To analyse the data of anamnesis, clinical-instrumental methods of investigation with the purpose of studying the aetiology, the dynamics of psychomotor development, and the outcome and evolution of seizures in West syndrome.
Methods: 25 patients with childhood epileptic encephalopathy, aged from 3 month to 3 years, were examined. The estimation of psychomotor development was conducted using the L.T.Jurba-E.M.Mastyukova scale, the G.V.Pantyukhina-K.L.Pechora-E.L.Frukht scale, and the calendar method of V.P. Zykov et al. All children were studied with a full clinical assessment including CT, MRI and EEG.
Results: Among the examined 25 patients more often West syndrome prevails of which 90% were symptomatic. The initial positive response to synacten-depo was in 70% cases versus antiepileptic drugs alone in 10%. After cessation of the therapy of synacten-depo, relapse of seizures was observed in 5 cases, in 8 cases the frequency of seizures was reduced. In 2 cases West syndrome was transformed from Ohtahara syndrome, in 2 cases West syndrome transformed to Lennox-Gastaut syndrome and in 3 cases West syndrome transformed to symptomatic partial epilepsy. All children (22 patients) have psychomotor retardation with normal development before début of seizures in 3 cases. The retardation of psychomotor development correlates with EEG showing. The disappearance of hypsarrhythmia associates with cessation of seizures and improvement of psychomotor development in 10 patients. Among 15 patients with a relapse of seizures: 2 had regional epileptiform activity without hypsarrhytmia and 3 patients had a relapse of seizures right away after cessation of the hormone therapy.
Conclusion: West syndrome prevails among epileptic encephalopathies of early infancy. The complex therapy of synacten-depo and antiepileptic treatment versus antiepileptic drugs alone showed a good final seizure response. The existence of regional epileptic discharge in EEG after hormone therapy is unfavourable for a relapse of seizure and psychomotor development.

p669
Thirteen Years Fight Against West Syndrome
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Purpose: To evaluate our 13 year diagnostic and therapy experience with children with West syndrome, including epidemiological and clinical features of West syndrome.
Methods: This study was conducted in the Children and Youth Health Care Institute in Novi Sad, during the thirteen-year period 1992-2004. We present data from 56 children with diagnosed and threatened West syndrome (WS).
Results: WS was more frequent among boys (1.3m:1f). WS occurred with a peak age of onset of 5.5 months and the average age of diagnosis was 6.5 months. The most frequent cause of symptomatic WS (67.8%) was hypoxic-ischemic encephalopathy and perinatal intracranial haemorrhage, each 28.9%. Neonatal infections (18.5%), gene diseases (13.2%), hydrocephalus (5.3%), galactosaemia (2.6%) and microcephaly (2.6%) caused the others. Initially EEG pattern showed modified hypsarrhythmia (57.1%) and hypsarrhythmia (37.5%). Clinically observed obvious infantile spasms with nonspecific EEG pattern showed in 5.4% patients. Neurologic deficit was present in 50% children before seizures, with progression in 21.4%. Only 28.6% of children with IS didn't have a neurological deficit. Neuroimaging showed cortical atrophy in 28.9%, porencephaly in 21%, hydrocephalus in 13.2%, ventriculomegalia in 10.5% and signs of tuberous sclerosis in 5.4% of children. Initially

there was no psychomotor retardation in 28.6%, but 48.2% were mildly retarded. Severe delay in psychomotor development before seizures was present in 23.2% of children. In 16.6% of children therapy started before WS was diagnosed (phenobarbital 14.3% and valproic acid 2.3%). Initial therapy was with phenobarbital (14.3%), valproic acid (10.7%), gama vinil gaba (42.6%) and clobazam (1.9%). In 12.5% of children initial treatment started with ACTH. There was absence in controlling infantile spasms in 10.7% of children. Success in controlling infantile spasms was reported on therapy with gama vinil gaba (62.5%), ACTH (14.3%), valproic acid (3.6%), topiramate (1.8%), clobazam (1.8%) and with polytherapy (5.4%).
Conclusion: We conclude that the long term outcome of WS depends directly on the WS ethnology and period we need to achieve adequate control.

p670
Genetic Aetiology of Infantile Spasms
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Purpose: To investigate the aetiological background of infantile spasms (IS) with special reference to genetic aetiology.
Methods: Medical records of all infants diagnosed with IS before the age of 12 months in the Uusimaa province in southern Finland in 1994 through 2002 (N=76) were surveyed for aetiological investigations.
Results: 33 IS patients (43%) had a proven or probable genetic aetiology. Chromosomal disorders were found in 7 infants (6 Down syndrome), microdeletions in 1, monogenic disorders in 18 (6 tuberous sclerosis). 8 infants had unidentified syndromes with dysmorphisms or malformations. Non-genetic symptomatic aetiology was observed in 27 cases (35%), in 2 of whom contributory genetic defects were found. 16 patients (22%) had a cryptogenic aetiology; 4 of them had a positive family history.
Conclusion: Genetic aetiology is common in IS. With the improvement of cytogenetic and molecular genetic methods, a specific diagnosis for a patient with IS may often be delineated. This is important for developing optimal treatment strategies and for genetic counselling.

p671
Clinical, Electroencephalographic and Genetic Study of Four Patients with Myoclonic Astatic Epilepsy
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Purpose: In myoclonic astatic epilepsy (MAE), the existence of patients with favourable seizure outcome and the discovery of sodium channel mutations have raised nosological issues of MAE (idiopathic versus symptomatic).
Methods: We studied the electroclinical characteristics of astatic and convulsive seizures, neuroimaging findings and the mutation of sodium channel genes in 4 MAE patients with favourable seizure outcomes, as a basis for discussing nosological issues.
Results: Four patients had normal neuroimaging findings, but their ictal symptoms of convulsive seizures were limited to the upper extremities or perioral region, and the onset of ictal discharges did not synchronise with the onset of ictal symptoms. Furthermore, 1 patient developed mental retardation, even after control of epileptic seizures with appropriate medication. 4 patients examined had no mutations in the SCN1A or SCN2A genes.
Conclusion: Our data suggest the MAE patients with favourable seizure outcomes may have variable developmental outcomes.

p672
Comparison of Clinical Characteristics of Familial and Sporadic Patients with Febrile Seizure Plus
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Purpose: Febrile seizure plus (FS+) is lately recognised as an important epilepsy syndrome for its corresponding genetic abnormalities. It is defined as febrile seizures continuing beyond 6 years of age or those associated with afebrile seizures. Although it is considered as an autosomal dominant inheritance with incomplete penetrance, there are many sporadic patients. We tried to compare the clinical characteristics of sporadic and familial patients with FS+.
Methods: We reviewed 2296 clinical records in our epilepsy centre and identified 71 sporadic and 54 familial patients with FS+. Their clinical features, EEG and brain MRI findings were compared. The results were analysed by SPSS10.0 software.
Results: The most common phenotype was FS+partial seizures seen in 59% sporadic and 50% familial patients. FS+generalised seizures (usually generalised tonic-clonic) were seen in 38% sporadic and 46% familial patients. In 37% of familial patients, the total seizures were more than 20, and were 57% in sporadic patients (P=0.04). Intellect abnormalities (including minor difficulties when studying to severe impairments) were seen in 46% sporadic and 12% familial patients (P=0.007). The seizure free rate (over 2 years on the study) in familial patients was higher than that for sporadic patients (28% vs. 8%, P=0.000). There was no significant difference in mean age of seizure onset, or in the appearance rate of epileptic discharge on EEG and abnormities of brain MRI.
Conclusion: The spectrum of FS+ should include focal and generalised epilepsy. Familial patients might have a better prognosis than sporadic patients.

p673
Clinical Characteristics and Risk Factors Associated with Recurrences of Febrile Seizures of Greek Children with the First Episode of Febrile Seizures
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Purpose: The frequency and other clinical characteristics of febrile seizures depend on genetic factors and are variable in different countries in the world. The purpose of our prospective study was to evaluate the range of clinical characteristics of children of our country with the first episode of febrile seizures and particularly the recognition of factors that correlate best with their recurrences.
Methods: In this study 145 children (80 boys, 65 girls) with the first episode of febrile seizures (mean age 22.,03±7.48 months) were included. A 12-month follow-up was performed with 97 children.
Results: Recurrent febrile seizures in this period of time occurred in 33 children (34.02%). The mean age of children with recurrent febrile seizures was 21.55±7.58 months, while that of children without recurrences was 22.16±7.56 months. There were 23 boys (69.7%) in the group of children with recurrent febrile seizures and 28 children (43.75%) in the group of children with no recurrences ($p<0.05$). 30 children with recurrent febrile seizures (90.91%) and 54 children without recurrences (84.38%) had an uneventful postnatal history. Mild psychomotor delay was present in 3 children (9.09%) with recurrence of febrile seizures and in 3 children (4.69%) with only one episode of febrile seizures. Positive family history of febrile seizures was found in 12 children (36.36%) with recurrent febrile seizures and in 15 children (23.44%) with no recurrences. Regarding the characteristics of the first episode of febrile seizures, 5 children (15.15%) with recurrent febrile seizures and 15 children (23.44%)

without recurrences had complex febrile seizures. 30 children (90.91%) with recurrent febrile seizures and 57 children (89.06%) without recurrences had their first febrile seizures during the first 24 hours of febrile illness, and 22 children (66.67%) with recurrent febrile seizures and 40 children (62.50%) with a single episode of febrile seizures had their first episode with temperature < 39.1oC.
Conclusion: Our study showed that 1 out of 3 children of our country with a first episode of febrile seizures will present recurrent febrile seizures in a 12 month time period, and the male sex and probably the young age in the first episode of febrile seizure and the positive family history of febrile seizures are associated with increased risk for recurrent febrile seizures.

p674
Epileptic and Genetic Status of 42 Girls with Rett Syndrome
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Purpose: Rett syndrome is a severe neurodevelopmental disorder, almost exclusively affecting females and characterised by a wide spectrum of clinical manifestations. In a high proportion of sporadic patients it is caused by mutations in the X-linked MECP2 (methyl-CpG binding protein) gene. According to the literature, epilepsy occurs in approximately 2 of 3 patients with Rett syndrome. The goal of this study was to investigate the epileptic and genetic status of children with Rett syndrome.
Methods: All patients had the classical signs and symptoms of Rett syndrome. Two groups were created: girls with genetically proven MECP2 mutation and girls without proven mutation. A detailed history was taken, physical and neurological examinations were performed on every patient. All children had undergone at least one prolonged video-EEG examination, using the international 10-20 system, awake and during sleep without sedation. Mutation analysis of the MECP2 coding region was done by direct sequencing.
Results: 42 children were examined in 2001-2004 in our department. Age range was 3-24 years. Mutations in the MeCP2 gene were found in 33/42 patients (79%). History of clinical seizures was present in 21 (50%) girls. From them all but 3 had proven MECP2 mutation. From the 21 children, who did not have epilepsy 15 (71%) had proven MECP2 mutation. Seizures began at the age of 8 months-16 years, with the majority of patients between 2-6 years. After 10 years of age the onset of seizures was uncommon. 3 girls had their first seizures at the age of 8 months, 2 of them had MECP2 mutation. 1 of them had repeated febrile convulsions, the other 1 grand mal seizures. Abnormal EEGs were found in 33 patients (79%). All children with seizures had epileptiform activity. 12 girls with abnormal EEG (paroxysmal discharges) did not have clinical seizures. They mostly belonged to the very young age group. 8/12 girls had a positive MECP2 mutation test. 9 patients until this time remained seizure-free, and their EEGs were without any pathological activity. 6/9 of them had a positive MECP2 mutation test. Most of the children had generalised tonic-clonic seizures. We did not see a specific diagnostic EEG pattern; they were remarkably similar in all patients. The records revealed abnormal background activities and multifocal epileptiform discharges in both awake and sleep conditions.
Conclusion: Mutations in the MeCP2 gene were found in 79% of our patients. 1 of 2 girls from our patients with Rett syndrome had epilepsy (50%). Epileptic seizures, especially considering the very young age group, is not an obligatory symptom of Rett syndrome. Epilepsy is widely overdiagnosed in children with abnormal or excessive movements. Video-EEG may be of benefit in identifying patients with Rett syndrome as a complement to the clinical examination.

p675
Rett Syndrome
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Purpose: Rett syndrome is a rare cause of epilepsy. We report the case of 2 girls who fulfilled the Rett syndrome diagnosis criteria. We aimed to remind medical personnel of these criteria, as Rett syndrome patients are usually diagnosed as having autism.
Methods: The 2 cases were isolated and parents were consanguineous in one case. The revealing symptom was psychomotor regression in one case and epilepsy in the other. In both cases, patients were born after uneventful pregnancies and had no birth complication. Their development was initially normal until the age of onset of the symptoms (18 months in one case and 24 months in the other). When admitted to our ward, they presented with mental retardation, epilepsy, decreased head circumference, stereotypic hand movements and growth retardation. Episodic hyperventilation was observed in one case.
Results: CT scan was unremarkable in one case and showed cortical and subcortical atrophy in the other. In both cases, electroencephalography showed a slowing of EEG activity with paroxysmal sharp wave complex.
Conclusion: As there's no radiological or biological marker of Rett syndrome, clinical features and electroencephalography are suggestive of the condition. In the mild variants, it is actually possible to diagnose Rett Syndrome on the basis of genetic testing (which reveals mutations in MECP2 gene).

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Features of Status Epilepticus in Childhood
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Purpose: To characterise the clinical features, treatment, and course of convulsive status epilepticus (SE) in children.
Methods: The admission database and all discharge summaries in a paediatric neurology department over a 2-year period were searched for children aged between 4 months and 13 years with a diagnosis of SE. The files of SE were systematically reviewed, and clinical and demographic data were retrospectively evaluated. 25 children were evaluated (the mean age of the children with SE was 4.8±4 years, female to male ratio was 1.2:1)
Results: Children with SE were neurologically abnormal (28%), had a history of neonatal seizures (12%) and febrile seizures (28%), and a family history of epilepsy (6%). Of the 25 cases, 16 (64%) patients had previously diagnosed epilepsy. Of all cases, 20 (80%) patients had the first episode of SE. Focal features were present in 7 (28%) of cases. Infection was identified in 12 of 25 children with SE. First-line anticonvulsant drug response was 60%. Duration of SE was >60min in 8 (32%) of cases as a refractory SE and infusion of midazolam was given. In addition 2 of 8 patients needed further drug therapy. Though 4 patients showed respiratory depression, there were no deaths from SE.
Conclusion: Status epilepticus is a life-threatening condition. Any mistreatment and delayed proper medication significantly increases morbidity and mortality. Patients with epilepsy should be under regular and careful follow-up. Control of anticonvulsant drug therapy lines should be done at proper times.

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Preventable Causes of Epilepsy in Mexican Children
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Purpose: The incidence of epilepsy in the world is higher in the extremes of life. In Mexico the prevalence is 15-18 per 1,000 people, although we don't have information about principal aetiologies of epilepsy, particularly in children. The purpose of our study was to describe the identifiable and preventable causes of epilepsy in a large population of Mexican children.
Methods: We chose three governmental medical centres located in Mexico City (centre, 2,200 metres over the sea), Veracruz (east coast, 1,460 metres) and Pachuca (mountain, 2,800 metres). All the centres are involved with the Mexican Program Against Epilepsy and have a certified paediatric neurologist with experience in epilepsy. All the patients have at least one cerebral CT or MRI study and a superficial EEG.
Results: We captured prospectively 2,414 children (under 15 years) with epilepsy between February 2002 and 2004 (México city 1420, Veracruz 555 and Pachuca 439). The average age was 6 years 3 months ± 3 years. The most frequent clinical type of seizures were partial (41, 65%), and the most frequent epileptic syndromes were West (2.5, 5%) and Lennox-Gastaut (3.4, 15%). The most frequent aetiology identified in the 3 centres was perinatal asphyxia (23.5, 36 y 36.3% respectively), and the causes were CNS infections and malformations. The frequency of neurocysticercosis was only 0.5, 1.6%.
Conclusion: The identifiable causes of epilepsy in Mexican children were different from those in developed countries. An inefficient pregnancy monitoring programme, with a high frequency of home births may explain the perinatal complications and secondary epilepsy.

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Epidemiology of Epilepsy Forms in Children
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Purpose: To determine the distribution of various epilepsies and epileptic syndromes in children treated in Ukrainian Medical Rehabilitation Centre for Children with Organic Injuring of Nervous System of Ministry of Public Health of Ukraine.
Methods: Data concerning 195 children, who were examined in the Centre in 2003-2004, aged 1 month to 18 years, with epilepsy was analysed.
Results: 195 children with different forms of epilepsy participated in the study: 40 (20%) had focal symptomatic epilepsies, 24 (12%) had generalised symptomatic epilepsies, 26 (13%) generalised idiopathic forms and 30 (15%) focal idiopathic forms. Among those with identified epileptic syndromes the most frequent was Rolandic epilepsy, 29 (15%); West syndrome, 12 (6%);, childhood absence epilepsy, 6 (3%); juvenile myoclonic epilepsy, 5 (2.5%).
Conclusion: The study showed that focal symptomatic forms of epilepsies and among epileptic syndromes, Rolandic epilepsy and West syndrome, are the most frequent forms of epilepsies.

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Rolandic Epilepsy
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Purpose: To confirm that spontaneous recovery is a constant characteristic of Rolandic epilepsy.
Methods: One of our patients diagnosed as having Rolandic epilepsy in 1955, considered cured at the age of 9 years and followed up to the age of 32 years, motivated our interest on long-term follow-up of children with this diagnosis. Our cohort progressively increased from 12 patients in 1957 to 222 in 1972 and 396 in 1999. We report on long-term evolution of the 288 fully documented cases with a follow-up of 1 to 25 years (mean: 3.02).
Results: Complete recovery by the age of 14 years is part of the definition of the syndrome. However, diagnosis is not always clear-cut at onset. Knowledge of seizure semiology relies on family reports; involvement of the face, considered a typical symptom, is reported in only 20% of the cases; hemi-convulsions are well described in only 22% and frequently the seizures are reported by the family as generalised.
Typical EEG with rolandic spikes is also considered indispensable for diagnosis. However, in our cohort, it was not detectable on the first EEG in 12.8% of the cases and changes of localisation were frequent (up to 29.8%). The presence of occipital or frontal paroxysms may facilitate misdiagnosis. Furthermore, rolandic spikes may be present in individuals without epileptic seizures. The active period of the syndrome was shorter for typical cases. For the great majority of our patients personal history was rather unremarkable. Benign neonatal seizures were reported in 16 cases (5.25%). Sudden death occurred in 3 of these cases. Following recovery from Rolandic epilepsy, 15 of our cases presented with other types of seizures (in 1 case 3 years after recovery, for all others after 8 to 20 years). 11 of these cases experienced only one seizure. In all cases, these were diurnal generalised tonic-clonic seizures and EEG was normal in all.
Behaviour disturbances and learning difficulties sometimes occurred during the active period of BECRS, in cases of recurrence of several seizures and of increased EEG paroxysms. Apparently, increased anxiety of the family and psychological problems of the patients played an important role, as this was shown when we compared these patients with children followed for diabetes or asthma.
Conclusion: Our follow-up study confirms that overall prognosis of Rolandic Epilepsy is favourable. However, a diagnosis of certainty is not always possible at onset; EEG aspects are not always typical and repeat EEGs may prove to be necessary. Despite an excellent outcome, psychological support may be necessary. The fact that other types of seizures may appear after full recovery from Rolandic Epilepsy, raises interesting questions about the genetic background of this disorder.

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Verbal Functioning in Patients with Rolandic Epilepsy
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Purpose: To evaluate the verbal function in patients with Rolandic epilepsy (RE).
Methods: We studied verbal functioning in patients with RE (n=61) and in healthy controls (n=35) by using sub-tests of the neuropsychological development study (NEPSY). Additionally, we investigated 64 patients with RE by the Wechsler test, taking into account the results of the 5th sub-test.
Results: Both groups were comparable regarding age and sex. The findings of the NEPSY test in patients with RE and healthy controls were as follows, respectively: verbal fluency (number of words) 36.0 ± 15 and 55.6 ± 14.2; speeded naming: a) time of task accomplishment 96.9 ± 40.1 sec and 73.2 ± 17.1 sec, b) number of errors 2.0 ± 2.0 and 0.2 ± 0.5; comprehension of instructions: a) number of errors in the first part of the task 0.5 ± 0.8 and 0, b) number of errors in the second part of the task 6.0 ± 3.4 and 1.9 ± 1.4. Children with RE accomplished all the tasks worse than the controls ($p<0.001$). In patients with RE the evaluation of Wechsler test 5 sub-test ranged from 4 to 12 points, mean 7.3 ± 1.9 points.
Conclusion: The verbal function in patients with Rolandic epilepsy is worse when compared with a control group of healthy children.

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Coexistence of Idiopathic Rolandic Epilepsy and CSWS
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Purpose: To report 2 families associating continuous spike-waves during sleep (CSWS) and benign childhood epilepsy with centro-temporal spikes (BCECTS) in first degree relatives.
Methods: Clinical, EEG and [18F]-fluorodeoxyglucose (FDG)-PET data are described.
Results: Family 1: The proband, a 5 year old girl, was 2.5 years at epilepsy onset. First seizures were partial motor at awakening with centro-temporal spikes on EEG. Focal negative myoclonias, atypical absences, psychomotor regression, and centro-temporal CSWS occurred at the age of 3 years. PET with FDG showed bilateral parietal hypermetabolism. Her epilepsy is refractory to anti-epileptic drugs, including corticosteroids. Development quotient is now 50. Her familial history is remarkable for a typical and well-documented BCECTS in her father, and febrile convulsions in infancy in her mother. Family 2: The proband, a 6.5-year-old boy, was 3.5 years at epilepsy onset. First seizures were generalised with centro-temporal spikes on EEG. Then, partial seizures with attention and behavioural disturbances occurred. At the age of 5 years, psychomotor regression with centro-temporal CSWS was observed. FDG-PET showed left parietal hypermetabolism. Ethosuximide add-on resulted in behaviour and cognition improvement, and disappearance of CSWS. IQ is now 75. Familial history is remarkable for a typical and well-documented BCECTS in his father.
Conclusion: The severity of epileptic syndromes of both probands characterised by psychomotor regression, CSWS and focal increase of glucose metabolism, contrasts with the benign course of rolandic epilepsy in their fathers. These findings support the concept that these 2 syndromes are edges of a continuous spectrum with a common genetic basis.

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Neurocognitive Evaluation of Oxcarbazepine Monotherapy in Children with Benign Childhood Epilepsy
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Purpose: Oxcarbazepine (OXC), is a novel antiepileptic drug . The aim of this study was to further explore the impact of OXC in terms of cognitive functions and academic achievement in a large sample of patients with benign childhood epilepsy with centro-temporal spikes (BECTS).
Methods: 71 patients aged 5.6 to 11.4 years (46 males, 25 females, mean 8.5±0.7y) with typical clinical and EEG features of BECTS were assigned to OXC monotherapy. Inclusion criteria were: A) newly diagnosed epilepsy; B) 2 or more seizures during the past 6 months; C) normal MRI. All of them underwent psychometric assessment at screening and after 18 months of treatment by means of WISC-III, Illinois Test of Psychomotor Abilities, DSM-IV, and Bender-Santucci Test. Seizure types, frequency, awake and sleep EEG, and dosage ranges were documented. 45 age-matched unaffected controls were assessed by the same psychometric tests.
Results: EEG discharges disappeared or decreased in 59/71 cases at 3 to 6 months but reappeared in 11/59 beyond this period. 45/71 of patients were seizure-free from the second day of therapy until the end of the trial. Cognitive assessment revealed learning deficits in 8/71 patients and 3/45 controls at baseline. This subgroup had marked difficulties in reasoning, computational skills, phonological awareness and short-term visuospatial memory. Both patients and controls had normal IQ. No child had a persistent stagnation or a regression in cognitive abilities after treatment.
Conclusion: The identification of these learning disabilities at baseline was crucial to the parents' information and strategy development. Our findings suggest that OXC has positive effects on the EEG and a favourable cognitive profile. It may prove a key medication in the outcome of this childhood epilepsy.

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Response Types to Topiramate in Children with Electrical Status Epilepticus during Sleep (ESES): A Retrospective Case Series
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Purpose: Syndromes of continuous spike-waves during slow sleep (CSWS/ESES) require fast effective treatment so as to limit neurocognitive deterioration, but often respond poorly to conventional antiepileptic drugs or steroids. We explored the effects of topiramate.
Methods: We retrospectively analysed the evolution of cognition, seizures and CSWS in 16 children with CSWS/ESES (not carbamazepine-related), followed for at least one year after initiating topiramate (November 1998 to April 2004). Topiramate was titrated add-on to AEDs, as usual or slower over time/at lower dose increments if anorexia. If possible, co-medication was tapered-off.
Results: 81% benefited; we identified 3 types of response: 1) full responders (n=4, 25%), characterised by fast cognitive and behavioural amelioration during topiramate titration, resolution of seizures and full normalisation of sleep EEG; 2) partial responders (n=9, 56%), showing clear clinical and objective improvements in cognition and behaviour during titration, disappearance or fast reduction in seizures after topiramate introduction, and disappearance of CSWS/ESES, but persistence of non-continuous focal epileptiform discharges during slow sleep; 3) non-responders (n=3; 19%), showing persisting CSWS/ESES, stagnation or worsening of cognition, behaviour and seizures: one of them deteriorated after topiramate introduction. Overall, topiramate was well tolerated. The only adverse event was anorexia, easily resolved by dose adaptation and with hypercaloric food.
Conclusion: In our experience, a majority of children with CSWS/ESES may benefit from topiramate before using steroids, other immune treatment or neurosurgery, provided topiramate is titrated as usual or slower in the case of anorexia. Yet, vigilance during follow up remains recommended. Study of more cases is desirable to confirm these results.

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Landau-Kleffner Syndrome: Basic Language Deficit Shown by Electrophysiological, Neuropsychological and Neuroimaging Studies
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Purpose: To clarify the pathomechanisms of basic language deficit in Landau-Kleffner syndrome.
Methods: Analysing and synthesizing the results of the longitudinal clinical history of a child from age 4.5 years to 6 years; electrophysiological studies: awaking and sleep EEGs, source-localisation (BESA5.o PCA-4source), event related brain potential studies, neuropsychological assessment (NEPSY) and MR-diffusion PET study.
Results: The child's history started with benign centro-temporal epilepsy at age 4.5 years, and evolved an acquired aphasia over 4 months. The EEG showed left centro-temporal spike activity when awake, with more spikes during sleep at the beginning, later generalised SW activity also occurred during awakeness and ESES during sleep. Antiepileptic drug treatment, together with ACTH

therapy was effective at the first time, but later speech deficits and behavioural disturbances remained a problem. 18 months after his first seizure the source-localisation study showed the left superior temporal gyrus to be the primary source; the secondary, the right supamarginalis gyrus, and the tertiary the left frontal inferior gyrus. The language processing analysis assessed by event related potentials showed MMN to phoneme difference, but no MMN to stress difference. The neuropsychological tests revealed marked dissociation of visuospatial functions vs verbal, auditory-attention and verbal-memory functions. The MR diffusion PET study indicated a left temporal hyper-metabolism.
Conclusion: The left temporal spike activity in LKS, which results in hyper-metabolism of the left temporal lobe and spreads to the right temporal and left frontal region results in dissociation between auditory-verbal and spatio-visual functions, and deficit of suprasegmental language processing, but spares phenomenon discrimination processes.

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Prevalence of Discognitive Epilepsy with CSWS in a Third Level Referral Epilepsy Centre in The Netherlands
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Purpose: To determine the prevalence of the CSWS/cognitive epilepsy syndrome in children with epilepsy and learning problems and to look for a relation between EEG characteristics and clinical features.
Methods: We retrospectively assessed all children presented with learning problems to our epilepsy centre during 2000-2004. All of them underwent at least one long term EEG/video registration including a full night of natural sleep. At least one psychological examination was performed.
Results: 93 children were primarily presented with learning problems with or without associated severe epilepsy problems. 20 children were found to have CSWS or CSWS-like EEG features. At the time of referral 14 had a definite decline compared to an earlier assessment. 10 children had a right, 7 a left predominant and 3 bilateral lateralisation; predominant localisation was centro-parietal in 7, frontal in 5 or temporal in 7 patients. No specific relation could be established between clinical features and different EEG characteristics. Most of the children were treated with sodium valproate, ethosuximide, lamotrigine and steroids. When already on carbamazepine this drug was usually discontinued. Change of treatment was followed by amelioration of EEG abnormalities in 13 patients, including total disappearance of CSWS in 5. EEG improvement, however, was not always correlated with clinical improvement, speech progress or increase in IQ score.
Conclusion: Cognitive epilepsy associated with CSWS represents a relatively rare but severe epileptic syndrome. More extensive multicentre studies including large numbers of patients will be necessary to elucidate specific clinical markers and the underlying mechanisms and to develop effective treatment strategies.

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Lateralisation and Outcome of EEG Abnormalities in Benign Epilepsy with Centro-Temporal spikes
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Purpose: To analyse the distribution at onset and the further evolution of the EEG epileptic abnormalities in benign epilepsy with centro-temporal spikes (BECTS) in relation to brain maturation.
Methods: We studied the EEG evolution of 36 children with BECTS (23 males, 13 females; mean age 7.9 yrs; follow-up 1-12-yrs, mean 6.3 yrs). Serial EEGs were recorded in sleep and awake condition with standard procedure of activation (hyperventilation = HV; intermittent light stimulation = ILS). The following EEG aspects were analysed: 1) distribution of abnormalities (unilateral vs bilateral) and prevailing side of localisation; 2) occurrence of other epileptic abnormalities; 3) effect of HV and ILS. EEG changes were compared with the clinical course of disease.
Results: The first EEG at onset (mean age 7.9 yrs) showed unilateral abnormalities in 25 cases (70%), bilateral in 8 (22%), no abnormalities in 3 (8%). In further recordings, the abnormalities were more frequently bilateral (47%) than unilateral (25%). At the end of follow-up (mean age 11.9 yrs) the abnormalities were absent in 18 (50%), unilateral in 11 (31%), and bilateral in 7 (19%). Extra-rolandic spikes and sharp waves were noted in 8 patients, localised in the occipital region in all cases. An increase of centro-temporal abnormalities was noted during HV only in one case; ILS induced photoparoxysmal response in 5 patients (2 during the active phase of BECTS; 3 later). 4 of these patients had other types of seizures (1 ictus emeticus, 1 version of eyes with eyelid myoclonias, 2 visual hallucinations) besides those typical of BECTS.
Conclusion: Some changes of EEG abnormalities observed during the course of disease seem to be age-related. Moreover, genetic factors with different age dependent expression might explain the association between the electro-clinical feature of BECTS and other types of idiopathic (occipital) epilepsies.

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Ictal and Interictal Abnormalities in All-night Sleep Recordings of ADHD Children
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Purpose: Sleep abnormalities have often been reported in children affected by ADHD. They range from restless legs syndrome (RLS) and periodic leg movement (PLMs), to obstructive sleep apnea syndrome (OSAS) to ictal and interictal epileptiform paroxysms activated by sleep.
Methods: In collaboration with paediatric neurology and psychiatry in our hospital, we recorded all night polysomnography of 11 ADHD children, all males, mean age 9.3, range 4-13, diagnosed according to DSM IV international criteria. Sleep EEG recording included a minimum of 8 to a maximum of 16 leads (in children who had previously displayed epileptic abnormalities on day-time EEG) with 21 electrodes (10-20 system).
Results: We found epileptic IEDs in 8/11 children, of these only 4 had positive EEGs during daytime and/or afternoon naps. In terms of localisation, IEDs were centro-temporal bilaterally (rolandic) in 4 patients, bifrontal with left predominance in 2, left anterior temporal in 1, right occipital in 1. 2 patients (1 with rolandic spikes and 1 with right occipital IEDs) had respectively 2 and 8 ictal episodes during all night recording. In neither of them the parents had been aware of previous seizures although they could recognise the motor pattern of seizures once they witnessed them. Disorders of arousal were reported and confirmed in 4 patients, enuresis in 2, bruxism in 2 and snoring with SDB (sleep disorder breathing) in 2. 7 patients had high indexes of periodic leg movements during sleep (PLMs) and 4 qualified for RLS syndrome. All 7 were started on levetiracetam 250 to 1000 mg, depending on body weight, either at night-time (in the absence of seizures or IEDs) or with divided dosing. Follow up so far ranges between 3 and 8 months; parents in all cases reported cessation of seizures and clinical improvement of nocturnal sleep with decreased motor activity and sleep discontinuity. We are currently in the process of obtaining control PSGs in all our sample to compare clinical to objective instrumental data.
Conclusion: Our results show so far a high prevalence of sleep disorders and epileptic abnormalities in ADHD children with a positive trend for sleep disorders and seizure improvement with levetiracetam treatment.

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Common Disorders of Learning or Behaviour and Epileptic Activity During Sleep
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Purpose: Epileptic activity during Sleep (EAS), predominantly during slow wave sleep, is a characterising EEG feature of the Landau-Kleffner/CSWS syndromes and is highly prevalent in the autistic spectrum disorder (ASD). Many of these patients never have seizures. EAS, indistinguishable from Rolandic epilepsy, has been found in children without seizures but with disorders of learning or behaviour. EAS has recently been reported in patients without seizures but with attention deficit hyperactivity disorder (ADHD). Neuropsychological disorders, not seizures, seem to be the common denominator of EAS. We wished to further explore this notion in children with moderate neuropsychological disorders and without a seizure history.
Methods: From our long-term EEG database for the last year, we extracted patients with moderate learning/behaviour disorders, without seizure history, showing EAS.
Results: 11 children (4 –11 years): 8 had learning disorders or ADHD, 1 had slightly retarded development and 2 had Asperger syndrome complying with DSM-4 criteria. Spike wave indexes ranged from 24 to 69% of slow wave sleep time, in up to four independent foci in one case; and only sporadic epileptic activity while awake.
Conclusion: To our knowledge EAS has not been previously reported in patients with Asperger syndrome, although some may have not been specified in ASD series. Our findings of EAS in children with ADHD and no seizures confirm recent reports. The prevalence of EAS in children with common disorders of learning or behaviour is unknown and possibly high; and must be ascertained, as well as the clinical implications. Children with disorders of learning or behaviour must undergo EEG during at least 30 minutes initial sleep or preferably 24 hr EEG, irrespective of seizure history.

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Nonlinear Analysis of Overnight Sleep EEG in Children with Neurodevelopmental Disorders
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Purpose: Our previous study documented that EEG abnormalities were not associated with symptom severity or intellectual functioning in childhood autism and other pervasive developmental disorders (PDD). The aim of the present study was to evaluate sensitivity of nonlinear analysis of sleep EEG in children with neurodevelopmental disorders.
Methods: Subjects: PDD group of 27 patients diagnosed according to ICD-10 criteria. The mean age was 7.1±3.6 years. The mean total CARS score was 36.0 pts. 14 patients were mentally retarded (53.8%), mean intellectual level was in the field of mild mental retardation. Normal EEG was found in 9 patients (33.3%), epileptiform EEG in 18 patients (66.7%). The control group was 20 mentally non-retarded deaf children with cochlear implantation with and without a mild form of developmental dysphasia. The mean age was 8.4±2.3 years. Normal EEG was found in 17 patients (85%). EEG: recording from 10 channels (F3, F4, F7, F8, C3C4, T3T4, P3, P4) of whole night sleep (inclusion of sleep stages NREM 2,3,4 in analysis). Non-linear analysis: CER: coarse-grained entropy rate (one channel). CEI: coarse-grained entropy information rate in asymmetric (information drive) and symmetric version (coupling). Analysed parameters: mean value, variation coefficient (standard derivation/mean). Statistics: multiple regression analysis, Wilcoxon test, Mann-Whitney test.
Results: CER analysis: the PDD subgroup with epileptiform EEG differed from the PDD subgroup with normal EEG in higher values of variation coefficient in frontal and central areas in NREM 3 and 4, whereas the difference in mean value was not significant. There was no association of CER analysis with the total CARS score; intellectual functioning and age was found in the entire PDD group. CEI analysis: the interhemispheric coupling was significantly weaker ($p<0.01$) in all three NREM stages (with maximum difference in NREM 3 stage) in PDD patients in comparison to matched control subjects. The PDD subgroup with epileptiform EEG showed higher variability of right intrahemispheric coupling a drive in comparison to the PDD subgroup with normal EEG. The difference between these PDD subgroups in the sense of weaker interhemispheric drive in the central region was less significant.
Conclusion: We found a significant decrease in EEG coupling and information drive in the PDD group in comparison to the age and IQ matched control group. Our results support the hypothesis of underconnectivity in autism spectrum disorders. The PDD subgroup with epileptiform EEG had more labile right hemisphere brain dynamics in EEG coupling and information drive reflected by an increase in variation coefficient. Supported by grant IGAMZ CR No 8287 and ME 701

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A New Spike-wave Detection Algorithm Showing High Sensitivity, Low False Positive Rate and Reduced Computing Time Permits Good Detection of Electrical Status Epilepticus during Slow Sleep (ESES)
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Purpose: The EEG criterion of ESES is defined as the presence of generalised or focal spike-waves occupying at least 85% of slow-wave sleep. Patients show seizures, neuropsychological or motor acquired deficits, which are related to the abundance of epileptic discharges during slow-wave sleep. Clinical and EEG follow-up are necessary. The use of an automated quantitative measure of the abundance of spike-waves is a really useful tool for an objective follow-up of these patients. Digital signal processing is often used for automatic spike-wave detection. However, some problems are commonly encountered: low sensitivity, high false positive rate, long computing time and many manually adjusted thresholds. In this study, we present a new algorithm that shows high performance in ESES detection. It needs little computing time and no parameter has to be adjusted. The algorithm is divided into two parts: pre-processing (including filtering, derivating, squaring -keeping the sign- and integrating) and a template matching that correlates the data with a reference spike-wave.
Methods: The algorithm was tested against the scoring of three experienced electroencephalography's in 30 minute EEG samples from three different subjects.
Results: The algorithm showed an average specificity of 80% and an average false positive rate of 7%. The time necessary to perform the computation on a typical PC (Pentium M) is 20 seconds per hour of EEG recording.
Conclusion: The algorithm developed shows high performance, is easy to use and is fast. It can be useful to increase the level of objectivity and to decrease the amount of diagnostic work.

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Auditory Evoked Potential Abnormalities in Infants with Infantile Spasms
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Purpose: Infantile spasms are associated with severe developmental delay possibly related to abnormal temporal lobe function. This study determined whether auditory evoked potentials (AEPs), generated in the temporal lobe, are useful in assessing cortical function in infants with infantile spasms.
Methods: 32 control infants and 30 infants with infantile spasms (IS) aged from 1-15 months were recruited. An EEG was recorded from 19

electrodes (10-20 system), referred to CPz. AEPs were recorded to pure tones (1 kHz) delivered binaurally via speakers at a distance of 30 cm and loudness of 75dB. The obligatory components P150, N250 and P350 were measured at frontal (F3,F4) and central (C3,C4) electrodes after referencing to combined mastoids and low-pass filtering at 10Hz. Recordings were made during sleep (stage II) and wakefulness.
Results: Robust and reproducible AEP components were recorded in all term infants, showing marked shortening of P150 and P350 component latencies with increasing age ($p<0.001$). In 75% of control infants, all 3 components were visible during wakefulness and sleep. However, no AEP components were identified for 50% of infants with IS. In those children with IS, in whom AEP were visible, P150 and P350 latencies were significantly prolonged compared to controls ($p<0.001$ and $p<0.0001$, during wakefulness and sleep).
Conclusion: Obligatory ERPs can be recorded reliably from 2 months of age. Abnormality of the early, obligatory AEP components suggests that IS interfere with cortical function at the level of the primary and secondary auditory cortex. This may be the cause of the encephalopathy in IS.

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Sequence of EEG Slow Wave Abnormalities and Vascular Events in Migraine with Prolonged Aura in Children: A Tool for Differential Diagnosis of Epilepsy
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Purpose: The differential diagnosis between epileptic seizures and migraines with prolonged aura (MWPA) is sometimes difficult in childhood. In partial seizures, abnormalities of EEG (rhythmic activity followed by slow waves) and cerebral blood flow (hyperperfusion followed by hypoperfusion) are well known. The sequence of EEG abnormalities in MWPA is not established. In order to compare EEG and vascular events in MWPA versus epileptic seizures, we report retrospectively on the results of investigations in a group of children with MWPA.
Methods: 11 patients were admitted in the paediatric emergency unit for MPWA. We performed EEG, transcranial Doppler (TCD) and brain SPECT as soon as possible after their admission (D1) and the next day (D2).
Results: At D1, only two EEGs were performed very soon after the beginning of the aura (between 2 and 3 hours). They were normal. The others showed unilateral diffuse or occipito-temporal slow wave abnormalities. For all patients, on the same hemisphere, the TCD showed a unilateral decrease of mean velocities and SPECT, a diffuse or localised hypoperfusion. At D2, every EEG showed strict occipital slow waves and were associated with a light hyperperfusion.
Conclusion: The sequence of EEG and SPECT abnormalities in MWPA are clearly different from those known in partial seizures. The EEG remains normal during the first hours of MWPA (as in usual duration aura) probably because of the small electrical volume of "cortical spreading depression" (CDS). The EEG abnormalities appear after several hours with the increase of the area and electrical volume of CDS.

p693
Misinterpretation of Lambda Waves as a Sign of Epilepsy in the New Born
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Purpose: Lambda waves were first described in adults orally by C.C. Evans in 1949 and in a publication by Mme Gastaud Y. in 1951. Twenty years later they were reported in children and in the new born (Westmoreland B. F. and Sharbrough F. W. Amer. J. EEG. Technol. 1975, 15, 14-19, F. Moussalli et G. Arfel Rev. EEG Neurophysiol., 1977, 7, 3, 361-364). Here we report the EEG, video and clinical features of three infants, all girls, who presented transient occipital sharp waves.
Methods: They were hospitalised after a near miss, aged 3 to 4 weeks, and did not have any particular familial or personal antecedents. Their clinical examinations and biological tests were normal. EEG videos were recorded to eliminate epilepsy.
Results: They showed transient occipital sharp waves, during which the infants were immobile and staring fixedly, but which disappeared when the child moved or closed its eyes. The sleep EEGs were normal and all three children had a normal clinical development.
Conclusion: Such EEG features are relatively unknown and could be misinterpreted as indicating epilepsy. We discuss the differences between these EEG video patterns and those observed in infants with occipital idiopathic or symptomatic epilepsy.

p694
EEG Findings in Childhood Epilepsy
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Purpose: According to the International Classification of Epileptic Seizures, absence seizures are classified as generalised seizures, with usually a favourable outcome. However, about 20-30% of the children suffering from absence seizures in childhood continue to have absences or develop other types of generalised seizures in adolescence and adulthood. Several researchers have reported the frontal lobe onset absence which are clinically no different from primary generalised absences. EEG analysis showed interictal isolated epileptic discharges in 80% of children with frontal absences.
Methods: We retrospectively analysed clinical and EEG characteristics in 23 children aged 4-12 years (12 girls and 11 boys) who were diagnosed as suffering from absence epilepsy. We compared both the clinical characteristics and EEG findings in two groups: 1) children with classical absences whose ictal EEGs showed primary generalised spikes and waves; 2) children with frontal absences (frontal onset). The aim of the study was to determine whether focal abnormalities in patients diagnosed as having absence epilepsy predict the clinical outcome of childhood absence epilepsy.
Results: 16 children showed only simple absences, and the other 7 suffered from complex absences. The primarily generalised, symmetrical and synchronous spike and wave pattern was found in 9 children (39%). Focal frontal onset of the epileptic discharges followed by secondary generalisation occurred in 14 patients (61%). The EEG analysis in our study showed interictal isolated epileptic abnormalities in 12 (85%) of 14 children with frontal onset of absences. Absence seizures in children from all groups were well controlled by antiepileptic drugs (valproate and etosuximide, or both) and all are seizure free in spite of the focal onset of their seizures or mixed type of seizures.
Conclusion: We concluded that focal abnormalities on EEGs are not uncommon for patients with childhood absence epilepsy. Focal onset of the epileptic discharges is not a bad predictor factor for the final outcome. Based on our results we further concluded that frontal onset absences should be considered as a secondary generalised epilepsy syndrome originating in the frontal regions.

p695
Evaluation of Interictal Electroencephalogram in Children with Epilepsy
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Purpose: The modern anticonvulsants can imitate normalisation of clinical futures in children with epilepsy and change the typical

epileptiform pattern of the electroencephalogram (EEG). For this reason the correct evaluation of EEG in the interictal period gains special significance for an adequate treatment strategy. The aim of this study was to decorate the criteria for evolution of interictal EEG patterns using a computer EEG approach.
Methods: The quantitative analysis of power spectrum of all frequencies of EEG potentials was analysed by Brain Surveyor (SAICO). It was also used to perform an analysis of distribution of different types of activity on the convex surface of the brain cortex using the Brain mapping approach. It was used to examine 387 patients with different forms of epilepsy, aged 3 months to 15 years. During the observations all patients retained a different variety of anticonvulsants.
Results: Quantitative spectral analysis of interictal EEG revealed that in the total EEG spectrum the most powerful is the oscillate 3-8 Hz (freq. 4-7 Hz, amplitude 60-120 Mkv). The essential prognostic value has the morphology of theta-waves and its distribution upon the convex cortical surface: the presence of monomorphic mid and high amplitude theta-waves especially in the temporoparietal cortical regions allowed us to expect the renewing of seizures after cancelling anticonvulsants.
Conclusion: The presence in interictal EEG of children treated by anticonvulsants, of monomorphic mid and high amplitude theta-waves with temporo-occipital localisation is a negative finding despite normalisation of clinical status of patients. Computer EEG analysis of interictal EEG patterns in children with epilepsy treated by anticonvulsants allows correct evaluation of the treatment strategy.

p696
Utility of the Electroencephalogram in Neuropaediatric Experience of 1000 Cases in a Hospital of Third Level in Mexico
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Purpose: The electroencephalogram (EEG) is a non-invasive, accessible and cheap study, the usefulness of which is of great value in epilepsy, observing paroxysmal EEG 76% as is the case with epilepsies. For other pathologies this usefulness is very limited or practically void without contributing any information that could serve the clinic. Nevertheless, through lack of knowledge of the usefulness of the EEG several specialists continue requesting it causing an unnecessary expense to the institution and inconvenience to the patients and their tutors. The goal is to describe the electroencephalographic characteristics of a thousand records made in this Hospital, as well as the service that requests it and the demographic characteristics of the patients and cost of the study.
Methods: We analyse the requests and the results of the EEGs requested in the last 11 months, and calculate the expense for study and for service.
Results: Of a thousand records there is a discreet predominance in men rather that in women; the nursing went to the group that request EEG. 49% of all EEG were normal, causing an expense of 51,000 Mexican pesos, (4554 dollars); the service that more normal EEG had was psychiatry with 79%. Of this group the EEG of patients with epilepsy, the sensitivity was 47% and the specificity was 83%, with a positive accuracy of 40% and negative accuracy of 86%.
Conclusion: Demonstrating the great usefulness that EEG represents for patients with epilepsy, and the little use for other pathologies, especially psychiatrics.

p697
EEG Interpretation in Infants and Children Sedated with Chloral Hydrate
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Purpose: To determine the results of the EEG interpretation in infants and children who were induced to sleep with choral hydrate.
Methods: A retrospective review of standard, 21-channel, 30-minute EEG recording performed on infants and children aged 1 month to 6 years who received EEG recording after being sedated with choral hydrate at the Division of Neurology, Department of Paediatrics, Ramathibodi Hospital, Bangkok, Thailand, was conducted. The original result of the EEG recording and the clinical presentations of each patient were blinded to the two full-time paediatric neurologists who separately interpreted the recordings. Each patient's clinical data and the administered dosage of choral hydrate were collected separately without disclosing the original interpretation result. The final results of the interpretation were compared and analysed.
Results: 84 infants and children whose ages ranged from 1 month to 69 months (median 30 months) were included in this study. Mean dosage of choral hydrate was 45. mg/kg (range 27.8–94, median 46.6). Interpretations of 68 recordings were inline which consisted of 13 abnormal and 55 normal recordings. There were discrepancies of interpretations (absent VS present of epileptiform discharges in 9 recordings (10.7%). Five recordings contained excessive beta waves interfering the interpretation. There was no adverse effect caused by choral hydrate observed.
Conclusion: Choral hydrate, which is a safe sedative drug in induction of sleep in infants and young children, might interfere with the interpretation. Interpretation with precaution is necessary. A prolonged recording in these patients might provide more recording data for more accurate interpretation.

p698
Vagus Nerve Stimulation Related Changes of Slow Cortical Potentials Measured by Direct Current EEG in Patients with Pharmacoresistant Epilepsy
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Purpose: Vagus nerve stimulation (VNS) is effective in pharmacoresistant epilepsy, but mechanisms of action are still unknown. Negative slow cortical potentials (SCP) reflect synchronised depolarisation of neurons, positive SCP indicate reduction of cortical excitation. SCP changes during chronic VNS should be investigated.
Methods: The direct current (DC) EEGs of patients with pharmacoresistant epilepsy treated by chronic VNS were examined using a DC-coupled amplifier (eldith GmbH, Germany), DC-stable electrodes and gels. Co-registration of ECG enabled the exact correlation of VNS on- and off- time. All patients were examined under VNS standard cycle (on time 30 sec, off time three or five minutes, 30 Hz and 0.5 msec pulse width). The output current ranged between 0.5 to 2.25 mA. DC potential shifts were examined topographically over 2-13 averaged VNS duty cycles, which were considered to be free of artefacts.
Results: 12 patients with pharmacoresistant epilepsy treated with VNS (absence epilepsy N=2, complex partial seizures N=10) were evaluated. In 6 patients with more than 50% seizure reduction after VNS a repeated positive shift (+150 to 1.500μV) was found during VNS off time, lasting until the next on time period. Positive deflection was localised in regions with focal epileptic activity. 4 patients without significant seizure reduction did not show any positive shift. 2 VNS nonresponders had a negative DC shift at –600 to –1.000μV.
Conclusion: Positive DC shifts induced by VNS were found in those patients who responded to VNS therapy with at least 50% seizure reduction. These results may help to understand the VNS mechanism of action using systematic investigation of SCP.

p699
Outcome Following VNS Placement in Children in a Single Large Tertiary Care Institution
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Purpose: The goal of this retrospective study was to review the outcome of vagus nerve stimulator (VNS) implantation in a paediatric population having undergone the procedure at a large tertiary paediatric referral centre (over 1.6 million patient encounters per year). The goal was to assess if there had been measurable improvement in symptoms following the procedure.
Methods: Electronic records of patients having undergone implantation were reviewed. A total of over 170 patients had undergone this procedure since 2001. 14 criteria were selected for the study, including basic demographics, seizure type, frequency, and number of anti-epileptic drugs prior to, six months, and one year following implantation, perceived improvement ranked on a scale of 0 to 3, and complications ranked on a scale of 0 to 3. The results were analysed by standard statistical methods.
Results: Preliminary analysis shows that 34% of the patients have symptomatic generalised epilepsy (SGE), 15% symptomatic localisation related epilepsy (SLRE), 19% cryptogenic generalised epilepsy (CGE), 26% cryptogenic localisation related epilepsy (CLRE), and 6% idiopathic generalised epilepsy (IGE). Frequency of seizures following implantation was significantly decreased (9.65 per day to 2.82, p=0.02). Perceived improvement was 1.51 (on a 0-3 scale) with a p value of 0.1. Further analysis by seizure type revealed significant decreases for CGE, SGE, and SLRE. Complications were not significantly different from the null hypothesis (p=0.35).
Conclusion: This retrospective study suggests that VNS therapy may be an effective and safe option in treating refractory childhood epilepsy.

p700
Use of Ketogenic Diet in Childhood Epilepsy: An Italian Experience
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Purpose: Despite the continued development and release of new antiepileptic drugs (AEDs), 20-30% of all patients with epilepsy do not respond to conventional therapy or have related side effects that preclude their continued use. Between the alternative therapies used for drug resistant epilepsy (immunoglobulins, steroids), the nutritional approach successively defined the ketogenic diet as the more ancient and the more applied before the introduction of AEDs.
Methods: We considered in our study 45 patients: 38 of them (82.5%) present an epileptic encephalopathy of different causes (malformative, cryptogenetic), 5 subjects (11.1%) suffered from Lafora disease, 2 (0.4%) are affected by deficit of pyruvate dehydrogenase. The age range at the beginning of the ketogenic diet is 1-17 years (mean 5.8). The duration of the follow up varies from 6 months to 3 years.
Results: The number of patients with a positive response was 25%, in particular in subjects with cortical malformations. Another aspect to be underlined is that in most of our responders the effectiveness of the ketogenic diet declined after 9-12 months of treatment. 3 of our patients interrupted the KD because of side effects particularly in the early months of treatment.
Conclusion: In our experience, a field of interest is the use of the ketogenic diet in diffuse cortical malformation. In fact, we found a moderate prevalence of diffuse migrational disorders among our group of responders. These findings certainly indicate that KD, at least using our protocol, did not block the course of the disease; however, because of present data, we cannot exclude the possibility of a potential ability of KD to slow-down the disease progression.

p701
Efficacy and Tolerability of the Ketogenic Diet according to K:AK Ratios: Comparison of 3:1 with 4:1 Diet
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Purpose: Ketogenic diet (KD) has been regarded as a highly potent anti-epileptic treatment for intractable childhood epilepsy. The fat proportion in the diet can be an important factor affecting its efficacy. We studied anti-epileptic efficacies and diet tolerability between ketotic:antiketotic ratio of 3:1 and 4:1 diet.
Methods: We started KD in 71 patients with refractory childhood epilepsy and randomly appointed them into 2 groups for 3:1 and 4:1 diet. Anti-epileptic efficacy and diet tolerability was evaluated after 3 months. Patients showing seizure-free outcome with 4:1 were changed to 3:1 diet, and those without seizure-free outcome with 3:1 were also changed to 4:1 diet for 3 more months.
Results: 1) Anti-epileptic efficacy was higher in 4:1 than 3:1 diet. 14 (41.2%) out of 34 patients with 4:1 and 7 (25.9%) out of 27 with 3:1 diet became seizure free. Seizure reduction over 90% was observed in 4 (11.8%) patients in 4:1, and 4 (14.8%) in 3:1 diet. 2) Tolerability was better in 3:1 than 4:1 diet. Gastrointestinal symptoms were observed in 5 (18.5%) patients with 3:1 diet and 10 (29.4%) patients with 4:1 diet. 3) Anti-epileptic efficacy was maintained after changing to 3:1 in seizure-free patients with 4:1 diet, and only a small proportion of patients showed a greater seizure reduction after changing to 4:1 than patients who were not seizur- free with 3:1 diet.
Conclusion: KD with 4:1 diet showed higher anti-epileptic efficacy than 3:1. Seizure-free outcome was maintained even after changing the ratio to 3:1 in most cases. Dietary tolerability was better in 3:1 diet than 4:1 with less frequent gastrointestinal symptoms.

p702
Topiramate Related Hyperthermia: A Comparative Study
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Purpose: To determine the frequency of hyperthermia in patients receiving topiramate and to identify the risk factors for developing it during topiramate treatment.
Methods: Patients with epilepsy seen within a 2 year period were studied. Hyperthermia was defined as a rectal temperature of 37.5º C with flushing, hotness, obvious discomfort and irritability requiring intervention. The frequency of hyperthermia in patients on topiramate was compared to that in patients on other AEDs and the association of hyperthermia with specific risk factors was determined.
Results: Hyperthermia occurred in 10.5% of patients on topiramate (15/143) and in 0.15% of those on other AEDs (1/688) with p = 0.000. In the topiramate patients who developed hyperthermia, age of occurrence of hyperthermia was 3.77 ± 2.81 years (mean ± sd), and time from starting topiramate until the occurrence of hyperthermia was 0.57 ± 0.53 years. Risk factors for developing hyperthermia in patients receiving topiramate were: the warmer months of the year (May–October; p=0.001), age less than 6 years (p=0.000) and a dose of more than 6 mg/Kg/day (p=0.001). Cooling and hydration were found to alleviate the discomfort associated with the hyperthermia.
Conclusion: Hyperthermia is a potentially common side effect of topiramate. This effect occurs most commonly during warmer months of the year in very young patients receiving relatively high doses of this medication. Patients with these risk factors should be monitored particularly closely for this side effect.

p703
Efficacy and Tolerability of Topiramate
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Purpose: To investigate the efficacy and tolerability of topiramate (TPM) in refractory childhood epilepsy.
Methods: The information about the effects of TPM was collected with the help of a questionnaire filled in by the parents of 66 children with refractory epilepsy. Clinical data were retrieved from medical charts of the patients at Kaunas University Hospital.
Results: Mean duration of epilepsy was 64.3 months. Positive effects were observed in 53 (80.3%) cases, with more than 50% seizure reduction in 64%; in 20% it was temporary. In 21 cases the effect was noticed within the first month of treatment. TPM helped to control 50% of generalised tonic-clonic seizures, 75% of infantile spasms, 20% of simple partial, 27% of complex partial, 30% of myoclonic seizures, 29% of absences. 14% of partial symptomatic and 30% of generalised symptomatic epilepsies did not respond to TPM. 8 out of 10 cases of partial epilepsy with severe bilateral synchrony on electroencephalogram benefited from TPM, so did all 6 cases with photosensitivity. Adverse reactions were reported by 82% of parents, more than one by 58%: 62% complained of somnolence, double vision, or fatigue, 47% noted behavioural changes and irritability, 38% experienced learning difficulties, 40% had weight loss, and 41% reported somatic disorders (nausea, headache, numbness, edema). Despite the adverse reactions, 56% of these parents preferred to go on with TPM treatment because of reliable seizure control.
Conclusion: TPM is a powerful drug in refractory childhood epilepsy, regardless of the relatively high rate of reported adverse reactions.

p704
Open-label Study with Topiramate Monotherapy of Newly Diagnosed Epilepsy in Children
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Purpose: The efficacy and safety of topiramate (TPM) as monotherapy treatment of partial–onset, or primarily generalised seizures in children were evaluated in an open-label trial.
Methods: This was an open label study of six months duration. The major inclusion criteria were: age 3-14 years, a documented history of epilepsy with complex partial seizures (with or without secondary generalisation), or primarily generalised seizures with at least 3 seizures in the past 3 months prior to entering the study. At the baseline visit, the subject underwent a screening that included laboratory tests (haematology and chemistry panels); medical history was recorded and neurological, EEG and CT scan, or MRI of head and physical examinations were performed. The initial TPM dose was 1 mg/kg with a progressive increase of dose until achieving 5 mgr/kg body weight. Adverse events, number and type of seizures was recorded.
Results: 20 patients with at least one seizure per month for 3-6 months prior to the study were included. The patients had a mean age 7.2 years (range 3-13 years), 14 male (70%) and 6 female (30%). The mean topiramate dose was 122 mg/day (range 75-200 mg/day). Median percent reduction from baseline in monthly seizure frequency was 95%, with 19 patients treatment responders (>50% reduction in seizures) and 10 patients (52.6%) were seizure free after 6 months. Safety: Three patients (15%) reported a decrease in appetite. Weight loss was 10%.
Conclusion: Results of this trial strongly suggest that topiramate range dosage 75-200 mgr/day is effective and well tolerated as monotherapy in children with newly diagnosed epilepsy. However, for the number of patients, the results will be carefully evaluated in use of topiramate in these patients.

p705
Topiramate in Drug-resistant Epilepsy in Children: Retrospective Data
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Purpose: Topiramate (TPM) is a new antiepileptic drug (AED) with a wide spectrum in epilepsy. Our purpose is to evaluate the efficacy of TPM in children with drug-resistant epilepsy attending our Service of Neurophysiology, Children Hospital 'Regina Margherita', Torino.
Methods: We revised data of 80 subjects with drug-resistant epilepsy treated with topiramate (TPM) as add-on therapy with other AEDs. We focused on efficacy of TPM and side effects. We used a seizure frequency scale in order to evaluate efficacy of TPM in which score 1 was no seizure and score 7 was high frequency. For statistical analysis we used the non-parametric Wilcoxon test.
Results: The group was made up of 40 females and 39 males, ages ranged from 2 to 33 years, (mean age 10.6, standard deviation 6.5 and median 9). 60% of subjects were diagnosed with symptomatic partial epilepsy, 28.75% with cryptogenic partial epilepsy, 3.75% with symptomatic generalised epilepsy and 7.5% with cryptogenic generalised epilepsy. Age of introduction of TPM ranged from 1 to 28 years (mean age 8.28, standard deviation 6.16, median 7). 35% of the subjects stopped TPM because of non-response or side effects, while 52 (65%) subjects still use TPM in therapy at present. Seizure frequency before having TPM (T0) in therapy and after its introduction (T1) showed a statistically significant reduction ($p< 0.0001$).
Conclusion: We found that TPM is useful in drug-resistant epilepsy because it improves efficacy of other AEDs with a reduction in seizure frequency.

p706
Topiramate (TPM): Efficacy, Tolerability and Pharmacokinetics in Children with Epilepsy Aged from 6 Months to 4 Years
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Purpose: In order to complete the data on refractory epilepsy in the youngest children, we conducted an open label prospective study of children aged from 6 months to 4 years with the main purpose of studying the efficacy, tolerability and pharmacokinetics of TPM as add-on therapy in this age range.
Methods: 22 children aged from 6 months to 4 years of age with a pharmacoresistant epilepsy with any seizure type or epilepsy syndrome were recruited in this open label, prospective study. Children were stratified according to seizure type and by enzyme-inducing or non-enzyme inducing antiepileptic drugs. There was a progressive titration of dose according to weight.
Results: 45% of patients (n=10) were responders (14% with a 50-74% seizure reduction, 17% of patients 75-99% and 14% of patients were seizure free). Two adverse events were considered as probably related to TPM. No olygohydrosis or metabolic acidosis or glaucoma were reported. The TPM plasma concentrations were significantly lower ($p<0.05$) in children with an enzyme-inducing AED.
Conclusion: TPM is useful for patients under four years and it is well tolerated. Children who receive concomitant enzyme-inducing drugs need higher mg/kg doses to achieve the same TPM plasma concentrations as those who do not.

p707
Levetiracetam in the Management of Seizures and Myoclonus in Patients with Neuronal Ceroid Lipofuscinosis
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Purpose: Neuronal ceroid lipofuscinosis (NCL) is one of the most common progressive neurodegenerative diseases of childhood. Levetiracetam (LVT) is a new antiepileptic drug (AED) effective for partial and generalised seizures in childhood epilepsy. It has shown promising results in management of myoclonus of different aetiologies. We used LVT in the treatment of children with NCL.
Methods: We identified 17 patients with Turkish variant of late infantile NCL and used LVT in 7 of them for the management of seizures. 5 patients with a minimum follow-up of 3 months are presented. LVT was administered at 10-40 mg/kg; duration of treatment ranged between 3 months to 1 year.
Results: The age at the onset of symptoms ranged between 2-7 years. The most common initial symptom was seizures. Other neurological features included impairment of motor and language skills, visual problems, developmental regression, and ataxia. Mental regression, myoclonus, loss of vision, and personality disorders developed during the course of the disease. All patients suffered from medically intractable epilepsy. Patients showed remarkable clinical improvement notable at 3 weeks of treatment with LVT. Seizure frequency and severity decreased remarkably as well as improvement of myoclonus, ataxia and attention span. None of the patients suffered from side effects.
Conclusion: LVT can be safely used in paediatric patients with NCL for management of seizures and myoclonus. Additional gains are improved gait and attention span. LVT can be a good option for children with refractory seizures due to progressive neurodegenerative disorders, and could be tried as the first AED in NCL.

p708
Three Year Experience with Levetiracetam in Children with Refractory Seizures
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Purpose: To describe the short and longer term efficacy of levetiracetam in children. Levetiracetam is a newer broad spectrum anti-epileptic drug licensed in 1999. Limited experience has indicated the drug is effective in the management of refractory seizures in children, with a reduction in seizure frequency by 50% or greater for 26% to 52% of the children studied, while seizure freedom varied between 2.6% and 23%. No studies have reported the longer term experience in children with this drug.
Methods: Retrospective analysis of the case notes of 73 children and adolescents treated with levetiracetam at the University Hospital of Wales in Cardiff, Wales. They were aged between 2 and 18 years, and the follow-up period was between 9 months and 3 years.
Results: Of 73 children, 3 (4.1%) were initially seizure free following the introduction of levetiracetam. 48 (65.8%) showed improvement in seizure control, but in 30 (41.1%) this was not sustained beyond a few weeks. In 17 (23.3%) there was no change in seizure frequency and in 5 (6.8%) there was deterioration. In 22 children (30%), levetiracetam was withdrawn because of side-effects (17 children, 23.3%), or because of a deterioration in seizure frequency (5 children, 6.8%). Side-effects included worsening of behaviour, drowsiness and weight loss.
Conclusion: 70% of the children treated with levetiracetam showed a good response following the introduction of the drug, but sustained improvement was only seen in a quarter. An initial good response to treatment with levetiracetam is not usually sustained.

p709
Efficacy and Safety of Levetiracetam as Add-on Therapy in Children with Generalised Epilepsy
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Purpose: To assess the efficacy and safety of levetiracetam (LEV) as adjunctive therapy in children with generalised epilepsy.
Methods: A retrospective chart review of 125 consecutive patients age 6 months to 18 years who were treated with LEV was performed. The data included 40 patients with generalised epilepsy. All patients had concomitant anti-epileptic drugs. LEV was dosed with a starting dosage of 10 mg/Kg/day, increased every 1-2 weeks by 10 mg/Kg up to a maximum of 75 mg/Kg/day, depending on efficacy and tolerability.
Results: In this paediatric population with generalised epilepsy, 60% showed a seizure frequency reduction of more than 50% and 16% of patients were seizure-free. 80% of children with myoclonic seizures had a seizure frequency reduction of more than 50%. Only mild and transient side-effects were observed in 25% of patients. The most commonly reported adverse event was somnolence (20%). In 40% of the children, a positive effect was seen on behaviour and/or alertness.
Conclusion: 1) LEV is effective, safe and well-tolerated in infants, children and adolescents with generalised epileptic syndromes. 2) LEV has a significant effect on myoclonic seizures. 3) LEV has a positive effect on behaviour.

p710
Effects of Lamictal on Seizure Characteristics
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Purpose: To analyse effects of lamictal in children with different characteristics of seizures.
Methods: 91 parents of children receiving lamictal as add-on therapy for resistant seizures were interviewed about seizure control and about their opinion on the effects of treatment on different seizure characteristics.
Results: Data from the group of 53 responders was analysed. The mean age of patients was 9.8 years, the mean duration of treatment was 18 months. Lamictal was effective in 83% of cases. Of the positive responders, full seizure control was achieved in 30% of cases, seizure reduction for more than 50% in 81% cases; 15% of cases did not respond and 4% deteriorated. Parents reported a decrease in seizure duration in 62% of cases, reduction of recovery time in 61%. Loss of consciousness during seizures disappeared in 38%. 29% of parents believed that lamictal prevented their children from seizure-related traumas. Positive effects of lamictal were noticed from the very beginning of the treatment in 14%, by the end of the first month in 39%, by the end of the second month in 16%, whereas only 28% found lamictal effective after having used it for more than 2 months.
Conclusion: Treatment with lamictal as add-on therapy is very much beneficial in children with refractory seizures, both regarding the seizure frequency and the severity: duration, time of recovery, consciousness loss, falls and traumatic injuries attributed to seizures. In the majority of cases the effects are noticed within two months of titration.

p711
Efficacy and Tolerability of Pregabalin in Children with Intractable Partial Epilepsies
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Purpose: To assess the efficacy and tolerability of add-on therapy with pregabalin (Lyrica) in children with intractable partial epilepsies.

Methods: 25 children aged between 5 and 17 years with intractable partial epilepsies were included. Pregabalin dose varied from 3 to 12 mg/kg/day, duration of treatment 1-3 months. Pregabalin was combined with one AED in 8 patients, with 2 AEDs in 12 and with 3 AEDs in 5.
Results: The reduction of seizure frequency of more than 50% was observed in 32% of patients (n=8), in 40% of children (n=10) it was less than 50%. In 3 patients (12%) pregabalin was withdrawn due to seizure increase, and in 4 patients (16%) because of side effects and lack of clinical efficacy. The most frequent side effects comprised sedation and dizziness.
Conclusion: Pregabalin is a rather well tolerated drug and might be a therapeutic option for children with intractable partial epilepsy.

p712
Efficacy of Steroid Therapy for Epileptic Encephalopathies
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Purpose: To evaluate the efficacy of steroid therapy for epileptic encephalopathies.
Methods: Retrospective analysis of treatment and outcome data of patients treated with steroids for epileptic encephalopathies. Outcome was analysed in regard to epileptic syndrome, patient age, duration of seizure disorder, developmental status and type of therapeutic agent.
Results: 60 consecutive patients from six paediatric neurology outpatient clinics were included in the study. The epileptic syndrome and types were as follows: myoclonic epilepsy (n=16), partial epilepsy (n=12), ESES (n=10), Landau-Kleffner syndrome (n= 7), mixed generalised epilepsy (n=5), Rasmussen's encephalitis (n=3), atypical absence (n=2), Lennox-Gastaut syndrome (n =2), spasms (n=2) and behavioural abnormalities in the absence of epilepsy (1). 16 patients were treated with ACTH while 44 were treated with prednisone. Of the second group, 23 were given an initial pulse of methylprednisolone. Complete cessation of seizures or functional improvement was achieved in 16 patients (27%) while improvement of more than 50% was seen in an additional 12 patients (20%). ACTH was found to be significantly more efficacious than prednisone. Initiation of treatment with high dose methylprednisolone did not add to efficacy.
Conclusion: ACTH is superior to prednisone in treating epileptic encephalopathies.

p713
Pentobarbital (Nembutal) for the Treatment of Refractory Status Epilepticus in Children
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Purpose: Refractory status epilepticus (RSE) is treated by clinical and electrographic suppression of seizures using high doses of suppressive anaesthetic agents. In this report we present the outcome of RSE in children treated with pentobarbital.
Methods: We retrospectively reviewed cases of refractory status epilepticus treated at our institution between 1997 and 2004. We evaluated charts for age, neurologic history, aetiology, seizure type, management, electrographic changes and outcome.
Results: 19 patients between the ages of 7.5 months to 17 years were treated in the intensive care unit under neurophysiologic guidance for refractory status epilepticus. 15 of the 19 patients were treated with continuous pentobarbital infusion. 10 patients had complex partial status epilepticus and 5 patients had generalised status epilepticus. The mean dose of pentobarbital was 2.5 mg/kg/hr (range 1-5.5 mg/kg/hr). Duration of treatment ranged from 2-15 days. 13 patients responded to pentobarbital treatment with evidence of burst-suppression pattern on the electroencephalogram. One patient underwent hemispherectomy for refractory status epilepticus and another patient died. Death was not attributed to treatment. Hemodynamic cardiovascular instability occurred in 11 of 15 patients.
Conclusion: Our results suggest that pentobarbital is an effective treatment for refractory status epilepticus in children. Hemodynamic cardiovascular instability is a common side effect of pentobarbital and may limit its use.

p714
Comparing the Effect of Intravenous Midazolam with Rectal Sodium Valproate in Controlling of Children with Refractory Status Epilepticus
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Purpose: Refractory status epileptics is usually defined as a seizure lasting at least 60 minutes and where diazepam, phenytoin or phenobarbital are not effective. In the present study, the effect of intravenous midazolam in controlling refractory status epileptics is compared with rectal sodium valproate.
Methods: 76 children with refractory status epileptics were randomly divided into two groups to receive IV midazolam 400 µg/kg bolus followed by 200 µg/kg/hour through infusion up to 20 minutes and sodium valproate syrup 20 mg/kg diluted with an equal volume of water through rectal enema. The effect of the two drugs was compared in the control of the seizure during the first 20 minutes of treatment, by means of a T-test.
Results: For 84.2% of the children treated with IV midazolam the seizure was under control within 4.5± 0.5 minutes, while for 63% of those receiving sodium valproate, the seizure was completely controlled within 16.5± 0.8 minutes. There was a significant difference between the two drugs ($P<0.00001$).
Conclusion: IV midazolam was more effective than sodium valproate, but sodium valproate can be used in hospitals or child emergency wards without an intensive care unit for controlling refractory status epilepticus, while a midazolam drip can only be used in hospitals with an intensive care unit.

p715
Intermittent Oral Prophylaxis in Preventing Recurrent Febrile Seizures, Diazepam versus Clobazam: A Randomised Study in South Indian Rural Children
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Purpose: This randomised prospective study compared the efficacy of intermittent oral diazepam and clobazam in preventing recurrent febrile seizures (FS).
Methods: Children (0.5 to 3 years) evaluated for FS (simple and complex) were randomised to receive either diazepam (0.3 mg/kg/dose Q 8H- group A) or clobazam (0.25 mg/kg/dose Q 12H- group B) for 48 hours at the onset each febrile episode (> 38 0 C) for 12 months in addition to antipyretics. Number of recurrent FS in 2 groups during 12 months was compared using Chi-Square test. Number needed to treat (NNT) was calculated for each group.
Results: There were 126 febrile episodes (92 treated) in 31 children (M:F 17: 14; mean age 1.561 yrs, sd 0.78) in group A and 142 febrile episodes (110 treated) in 39 children (M:F 21:18 mean age 1.49 yrs sd 0.75) in group B. FS recurred in 14 (15.2%) treated and 12 (35.3%) untreated episodes in group A (overall 20.63%), and in 6 (5.45%) treated and 10 (31.3%) untreated episodes in group B (overall 11.26%). Recurrence of FS was more with diazepam compared to clobazam in 'intention to treat' analysis (odds ratio 2.05; 95% CI: 1.04-4.02) and 'on treatment' analysis (odds ratio 3.1; 95% CI: 1.14-8.46). NNT were 5 (diazepam) and 4 (clobazam).
Conclusion: Though diazepam and clobazam reduced the recurrence of FS, clobazam was more effective than diazepam. Clobazam is a better alternative to diazepam when intermittent oral prophylaxis is considered to prevent recurrent FS in rural children who have no immediate healthcare access.

p716
Evaluation of Thyroid Functions and Thyroid Volumes in Children with Epilepsy in Long Term Administration of Carbamazepine, Oxcarbazepine and Valproic Acid
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Purpose: This study aimed to investigate the effects of carbamazepine (CBZ), oxcarbazepine (OXC), and valproic acid (VPA) on thyroid functions, serum thyrotropin (TSH), and thyroid volumes in children with epilepsy.
Methods: The study was performed at Gazi University Faculty of Medicine, Department of Paediatric Neurology. 53 children with epilepsy (age range 3-17 years) treated with OXC (n=10), CBZ (n=12), or VPA (n=31) at least for one year were evaluated in terms of thyroid hormones, TSH levels, response to TRH stimulating test and thyroid volumes.
Results: The patients in OXC and CBZ groups had similar TT4 and fT4 median levels which were significantly lower than those of the VPA group ($p<0.016$). TT3 median levels were lower in CBZ group compared to the VPA group ($p<0.016$). Basal TSH levels were similar in all groups as thyroid volumes ($p>0.016$). 1 child from the OXC group (10%), 1 from the CBZ group (8.3%), and 6 from the VPA group (19.3%) had hypothyroidic status according to the TRH stimulating test. No statistically significant correlations were found between thyroid gland volume and thyroid function variables and between antiepileptic drug receiving time and thyroid functions or thyroid volume respectively in any of the groups ($p>0.05$).
Conclusion: The results of our study suggested that receiving long-term antiepileptic drugs should be primarily evaluated by TSH for VPA, TT4 for CBZ, and both TT4 and fT4 levels for OXC. Then, the TRH stimulating test should be performed to detect true thyroid status.

p717
Efficacy and Safety of Risperidone vs Tioridazine in the Treatment of Disruptive Behaviours in Paediatric Patients with Epilepsy
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Purpose: To determine the efficacy and safety of risperidone vs tioridazine for the control of disruptive behaviour in children with epilepsy.
Methods: This is a prospective, controlled, randomised study of 46 patients (24 in risperidone group; 22 tioridazine), ages 5-12 years. All patients have disruptive and autistic behaviour, epilepsy (either partial or generalised) and were treated with one or more AEDs. After an aleatorized groups, they starting with an individual flexible titration dose (group 1 risperidone 0.25 mg/day to a max of 1 mg/day; the other with tioridazine at 0.5 mgkg/day to a max of 2 mgkg/day), an individual procedure was used to adjust the dosage for optimal efficacy and minimal untoward effects. The impact was evaluated with a clinical global scale (CGI), peers scales, Conner's test, Yale scale, DSM-IV scale, Overt scale and ESRS. The patients were evaluated at each week the first month, and each month for a year.
Results: 22 patients completed the study in the risperidone group (RG) vs 12 in tioridazine group (TG). 32 of 46 patients were responders according to the definition, and 16/7 patients also showed an enhancement of behaviour/cognition. Side effects were observed in 11 patients (RG) vs 16 (TG); the most frequent were somnolence (22%), increase of appetite weight-gain (19%) and drooling (4%). 2 patients experienced increased seizures (TG), but were controlled with adjustment of their antiepileptic drugs. Antiepileptic levels didn't show a variation in the serum levels. 4 patients (RG) showed a improvement in their seizure control.
Conclusion: In this controlled clinical trial, risperidone appears to be much more effective and safe than tioridazine treatment for children with epilepsy and disruptive-autistic behaviour.

p718
Efficacy of Atomoxetine Treatment in Children with ADHD and Epilepsy
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Purpose: ADHD is a very common problem in paediatric patients with epilepsy. A little research has been undertaken for this population. Atomoxetine is a new ADHD medication with great success for the treatment of these children. The present study evaluates the efficacy and safety of atomoxetine in paediatric epilepsy patients.
Methods: Study subjects were patients, 6 to 15 years old, who meet DSM-IV criteria for ADHD and had concurrent epileptic seizures. The child patients (n=17) were given open-label treatment with atomoxetine (maximum doses to 1.8 mg/kg/day, starting 0.5 mg/kg/day). Responses were evaluated using the Conner's parents ADHD scale and the Clinical Global Impression-Severity (CGI-S) score to examine efficacy, and with an adverse effects chart for secondary side effects, including number of seizures and serum levels of antiepileptic drugs. The evaluation was made after 1, 4, 8 and 12 weeks of treatment.
Results: Significant symptom improvement was noted and maintained though the duration of treatment. There was a significant dose response (1.2 mg/kg/day) in Conner's and CGI after up to three weeks of treatment. In addition, only one patient showed an increase in the number of epileptic seizures during the first two weeks of treatment, without modification of serum levels of antiepileptic drugs. The most frequent side effects for atomoxetine were sedation, loss of appetite and nausea.
Conclusion: In this open clinical trial, atomoxetine appears to be an effective and safe treatment for ADHD in paediatric patients with epilepsy. This can improve the global rehabilitation of paediatric epilepsy patients.

p719
Surgical Treatment of Temporal Lobe Epilepsy in Children: Results, Outcome and Correlations with Clinical Features
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Purpose: To study the outcome and pathology in children operated on for temporal lobe epilepsy (TLE) and their relationship with clinical features.
Methods: We retrospectively reviewed 49 patients operated on for TLE. 17 patients (34%) presented with febrile seizures (FS). The mean age at epilepsy onset was 44 months, mean age at surgery was 10.8 years and mean duration of epilepsy was 6.9 years. Surgical procedures consisted on polar and mesial resection in 30, temporal lobectomy in 11, isolated polar in 3 and other procedures in 5.
Results: Dysplasia was found in 24 patients, hippocampal sclerosis (HS) in 23, developmental tumours in 9 and gliosis in 7. 22 patients had dual pathology (DP) (HS-heterotopia in 15) and 5 had isolated HS. Postoperative outcome disclosed Engel Class I in 43 cases (88%), IIA in 5 and III in 1 (mean follow-up 49.4 months). 88% of patients with FS had HS, either DP or isolated HS. All patients without free interval between FS and first temporal seizure had dual pathology (HS-heterotopia) whereas patients with free interval presented with various pathologies. The mean age of TLE onset according to pathology was 33 months in dysplasia and gliosis, 41 in DP, 50 in tumours and 77 in HS.
Conclusion: As previously described in paediatric reports, we found a high prevalence of dual pathology and dysplasia. Moreover, our results showed that the lack of free interval was highly correlated with heterotopia associated with HS, and that the age of epilepsy onset depended on the pathology.

p720

A French Multicentre and Multidisciplinary Network for Epilepsy Surgery in Children

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Purpose: As clearly stated by the recent ILAE recommendations (Epilepsia 2003), "the success of epilepsy surgery depends on a thorough presurgical evaluation to identify the brain region generating the habitual seizures and to demonstrate that it can be removed safely without causing unacceptable deficits. … Because epilepsy surgery is an elective procedure, the quality standards have to be particularly high … and epilepsy surgery requires close collaboration of a multidisciplinary team of highly trained and experienced specialists…".
In France, no centre exists where all necessary means for early and efficacious evaluation of potentially surgical childhood epilepsies are available on the same site. As a result, selection of candidates to surgery in each centre can only be done on the basis of the locally available means. On the other hand, the French health system allows mobility of the patients. Thus, at least theoretically, patients can have free access to all available evaluation means. At the 23rd ILAE/IBE congress, held in Buenos Aires, we presented the structure and function modalities of a multicentric and multidisciplinary network for epilepsy surgery in children, created in 1995 by C. Munari and Ch. Sainte-Rose. The network provides a prospective database including all patients presented at the monthly meetings of the group. We reviewed and completed the data on children evaluated between January 2000 and December 2004.
Methods: During this 5 year period 143 children (74 boys, 69 girls), aged 16 years or less, were presented for analysis. Depending on the centre of reference, mean age of the patients varied between 6.5 and 13 years. Most of the patients were of French origin (125) and epilepsy was partial in 124/143. In all patients, pre-surgical assessment included clinical history and examination, detailed description of epileptic seizures, MRI findings and interictal scalp EEG. Almost all benefited from a video-EEG investigation before discussion at the network's meeting. For some a second scalp video-EEG was considered necessary. Other investigations, according to the needs for a comprehensive pre-surgical evaluation, included ictal SPECT, FDG PET or fMRI.
Results: Based on these findings patients were considered as being candidates for surgery without complementary investigations when the following criteria were fulfilled: (i) the lesion could be clearly delineated by MRI; (ii) there was a clear-cut concordance with ictal clinical manifestations as described by the patient and/or his family; (iii) interictal EEG abnormalities were concordant (same lobe as the lesion). For these cases the surgical procedure consisted of resection of the lesion (Group 1). In all other cases, video-EEG monitoring with seizure recording was considered mandatory. This latter was considered sufficient to proceed to surgery when it clearly demonstrated an unequivocal electro-clinical correlation (Group 2). For these patients the surgical procedure also consisted in resection of the lesion. However, in temporal lobe cases, in which the onset of the EEG discharge appeared widely extended over the temporal lobe scalp-EEG electrodes, a larger temporal resection could be preferred.
When ictal scalp-EEG data showed anatomo-electro-clinical discrepancies, a long-term stereotactic intracerebral EEG (SEEG) monitoring, using the Talairach and Bancaud method, was performed. Invasive monitoring was considered necessary in only 9 children, 7 of whom have been operated. Extension of the cortical resection was then tailored on the basis of SEEG seizure recordings (Group 3).
Following the first discussion of available data, 62 of the patients were submitted to surgery, 6.5 to 20 months later.
Conclusion:

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Factors Predicting Intractability of Epilepsy during Childhood

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Purpose: To investigate the factors which predict intractability of epilepsy during childhood.
Methods: 337 children with the diagnosis of epilepsy followed for at least 1 year were investigated for intractable epilepsy (İE) (>1 seizure/month, failure of 2 antiepileptic drugs, followed over 12 months).47 children (29 male, 18 female; median age 108±47.4 months) met the criteria of İE. The control group, consisting of 47 children, was randomly selected from 290 children who had epilepsy, followed for at least 1 year but not meeting criteria for İE. All factors including historical data, clinical features, electrophysiological and neuroradiological findings were documented and statistically analysed for the factors which predict intractability.
Results: The following factors were found statistically significant for intractability: abnormal neurological examination, developmental delay/mental retardation, multiple seizure types, status epilepticus, seizure onset under 12 months of age, myoclonic and tonic-astatic seizures, abnormal background activity on EEG, symptomatic epilepsy and abnormalities on MRI ($p<0.05$). However, abnormal prenatal, natal, postnatal and family history, seizure onset after 12 months of age, focal discharge on EEG were not statistically significant ($p>0.05$).
Conclusion: Children with symptomatic epilepsy, developmental delay/mental retardation, neurological findings, status epilepticus, multiple seizure types, abnormal background activity on EEG, and MRI findings are at high risk for intractable epilepsy.

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Case-control Study of Risk Factors of Intractable Epilepsy in Children

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Purpose: This study is to determine the risk factors of intractable epilepsy in children.
Methods: The intractable epilepsy patients were those who had one or more seizures per month over a period of 12 or more months and experienced trials of at least two antiepileptic drugs with adequate compliance. Non-intractable epilepsy patients were those had never met the definition of intractable epilepsy and had been seizure free for more than one year. Potential predictors studied included: birth history, developmental status, family history of epilepsy, age of seizure onset, initial seizure type, EEG, clinical neurological examination and neuroimaging, aetiology of epilepsy, seizure frequency. The odds ratio was used to indicate the association between each factor and intractable epilepsy. Multiple logistic regression analysis was performed to exam the relationship of predictors and intractable epilepsy.
Results: There were 120 patients (mean age 3.9 years) and 120 control subjects (mean age 4.1 years) compared in this case-control study. All of them were collected from the Epilepsy Centre of Children's Hospital of Fudan University from 1 January 2000 to 1 January 2004. Multivariate analysis indicated that perinatal asphyxia (OR=13.51, 95%CI: 14.82~9.17), neurologic impairment (OR=10.2, 95%CI: 13.9~8.79), the age of seizure onset (OR=9.26, 95%CI: 10.77~7.11), mental retardation (OR=6.73; 95%CI: 8.12~4.65); complex partial seizures (OR=3.21, 95%CI: 5.47~2.63) and abnormal EEG background (OR=2,69, 95%CI: 4,19~1,77) were independent predictors of intractable epilepsy.
Conclusion: Perinatal asphyxia, neurologic impairment, the age of seizure onset, mental retardation, complex partial seizures and abnormal EEG background were independent risk factors of intractable epilepsy.

p723
Epilepsy in Hypoxic-ischemic Encephalopathy: Correlations with Clinical, EEG and Neuroimaging Data
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Purpose: This retrospective study was designed to assess the correlations existing between epilepsy and clinical, EEG or neuroimaging data in a large group of patients with cerebral palsy due to a prenatal or perinatal hypoxic-ischemic encephalopathy (HIE).
Methods: The study group consisted of 102 patients (40 females, age range 2.67 – 42 years, mean age 11.92, SD ± 8.8) with a defined history of prenatal or perinatal HIE. All the subjects underwent neurological examination, brain MRI (0.5 T), psychometric tests, wakefulness and sleep EEG recordings. Seizures and epilepsy were classified according respectively to the 1981 and 1989 ILAE Classification criteria. MRI images were visually evaluated and classified on the basis of the type, the location, and the severity of the lesions. Statistical analyses of the correlations between data were carried out by means of chi-square, and other non parametric tests.
Results: 57 patients (56%) presented seizures, and 82% of them reached a >50% reduction of seizures with antiepileptic drugs. Seizures resulted significantly more frequently in the group of patients with cortical involvement ($p<.01$), and in the group of subjects with gestational age (GA) $\geq$ 36 weeks ($p<.035$). In the group with involvement of the white matter only, the patients with EEG paroxysmal abnormalities +/- seizures presented a higher score of MRI alteration; in the group with cortical lesions, the presence of seizures determined a higher score of MRI alteration.
Conclusion: In patients with HIE, presence of seizures is clearly correlated with cortical involvement and with the severity of the MRI picture.

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Outcome of New Referrals to a Paediatric Epilepsy Clinic in a District General Hospital
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Purpose: The new establishment of a paediatric epilepsy clinic run by a general paediatrician generated the need to audit the outcome of such clinics. The aim was to calculate the number of new referrals and from that, deduce the percentage of those given the final diagnosis of epilepsy. As there are no previous similar studies, a standard of 50% of correctly diagnosed referrals was deemed acceptable.
Methods: Outcomes of referral to a paediatric epilepsy clinic were studied using a retrospective audit for the previous 30 months at the DGH. All patients who had been newly referred within the designated time period were selected using the health trust computer record system.
Results: The total number of patients selected for the study was 104. After the application of exclusion criteria this was reduced to 76. Patients were excluded because: 12 already had an established diagnosis by a paediatric neurologist; 5 had unobtainable notes or on-going diagnosis; 6 due to continuous DNA; 5 not yet seen. Our audit revealed that an overwhelming majority of the referrals came from GPs; 47 patients (62%), with an additional 20 patients (26%) of referrals coming from other paediatric services, and only a minority from A & E, 9 patients (12%). It also showed an over referral of non-epileptic children to the specialist clinic with only 29 patients (38%) being given a final diagnosis of epilepsy (standard 50%). Other diagnoses included febrile convulsions, RAS, syncope and "under investigation".
Conclusion: Less than 50% of referrals were diagnosed with epilepsy. This indicates the need for guidelines and support material for GPs due to the distressing implications that an epilepsy referral has on the child and family.

p725
Treatment of Epilepsy in Patients with Mental Retardation and Related Disabilities
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Purpose: The aim of this study is to determine the effectiveness of drug therapy for patients with epilepsy in a middle and severe mental retardation group.
Methods: We studied 38 patients of the previous group aged 2-30 years old instituted in a protectory of our region (16 of them had also quadriplegia). 20 of them suffered from epilepsy; 9 had focal crisis beginning and secondary generalisation.
Results: The median age of the first crisis was 4 months (1-24 months old). None of these children had responded to the first drug therapy. Two years later epilepsy was controlled in all children. We administered 2 drugs to 15 children and 3 to the rest.
Conclusion: Epilepsy is difficult to control in children with disabilities and the spasms rarely respond to the first drug therapy. 2-3 drugs were needed to control epilepsy in this group of children.

p726
Outcome of Patients with Infantile Spasms at School Age
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Purpose: Infantile spasm (IS) is an epileptic encephalopathy with onset during infancy and with severe mental and neurological consequences, in the long-run. We studied the present status of a group of children who were followed by us, until the start of school age.
Methods: Among 240 patients with past or present diagnosis of IS, 76 patients at or older than 7 years of age, or who were deceased before that age were included in the study. All patients had regular sleep-and waking EEGs with at least yearly intervals that contributed to the diagnosis of type and course of epilepsy. Aetiologic diagnoses were confirmed by cranial MRI and other relevant laboratory data.
Results: Main aetiological diagnoses were perinatal hypoxic-ischemic insult, post-natal CNS infection, tuberous-sclerosis, and metabolic disease. 15 patients were classified as cryptogenic IS. There were a total of 76 patients, 24 of whom died before 7 years of age. 8 patients who had no or mild epilepsy, were able to attend normal primary schools, but some received educational support. 25 children who had epilepsy and mental/motor deficits received special education and only 18 were ambulatory. Only 1 of the remaining 19 patients with the poorest clinical course seemed to benefit from education. They all had intractable epilepsy and a severe neurological condition that necessitated home or institutional care. 19 of the 52 patients were seizure-free for at least one year.
Conclusion: Epilepsy and motor retardation may be major concerns for parents during the early years, whereas mental deficits take priority on the approach of school age.

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Apgar Scores and Long-term Risk of Epilepsy: A Population-based Cohort Study
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Purpose: We examined if a low Apgar score can predict epilepsy in childhood and early adulthood. An association between low Apgar scores and epilepsy could support the view that pre- or perinatal factors play a role in the aetiology of epilepsy.

Methods: We carried out a population-based cohort study of 1,538,732 infants born alive in Denmark between 1 January 1978 and 31 December 2002 by using national registers. The one- and five-minute Apgar scores were recorded by midwives following standardised procedures. The endpoint was registered hospitalisations and outpatients with epilepsy according to International Classification of Disease (ICD-8 before 1994 and ICD-10 from 1994). Outpatients were included in the register from 1995.
Results: The incidence rate of epilepsy increased with decreasing one- and five-minute Apgar scores and the incidence rate decreased when the Apgar scores improved from one to five minutes. The incidence rate of epilepsy was 628 per 100,000 person-years for those with five-minute Apgar scores of 1 to 3 and 86 for those with a score of 10 (incidence rate ratio: 7.14, 95% CI: 5.79-8.81). The risks of epilepsy associated with low Apgar scores were particularly high in early childhood. The association between Apgar scores and epilepsy did not change in children without cerebral palsy, congenital malformation or a parental history of epilepsy.
Conclusion: The Apgar score was strongly associated with the risk of epilepsy throughout childhood and early adulthood. More attention should be given to the pre- and perinatal time period when evaluating causes of epilepsy.

p728
Seasonal Presentation of Epileptic Seizures in a Community Based University Hospital in Sao Paulo, Brazil
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Purpose: Seasonal variation of several pathologies is described including cardiac, vascular, and respiratory diseases. Epileptic seizures present seasonal presentation according to aetiology. The seasonal variation of those considered as idiopathic forms, which occur at school age, is less studied.
Methods: We studied the monthly distribution of the diagnosis 'not specified convulsions and epilepsy' (CID R56.8 and G40.9, respectively) in an emergency unit of the University of São Paulo Hospital, which attends neighbourhood patients of Butantã district in the city of São Paulo, SP, Brazil, in the period of January to December 2003. The diagnosis was codified by professional people of the medical system of data and statistics of the same institution after analysis of the medical data. The patients were divided in groups regarding their ages: bellow 5 yrs, between 5-15 yrs, older than 15 yrs (groups I, II and III, respectively).
Results: Total number of consultations because of convulsions or epilepsy in 2003 was 527, which corresponds to 0.6% of all admissions in the emergency unit for paediatrics and general medicine. The monthly mean in the studied groups was: group I 10 (sd 5.22), group II 11.16 (sd 4.42) and group III 22.66 (sd 6.06). In group I, we observed two peaks, in December and January (summer) and the other in June and July (winter), which corresponds probably to the higher number of symptomatic aetiologies in these cases. In group II, there was only one peak in the months of November and December (end of spring and beginning of summer). In group III, there was a slight increase of cases in the second half of the year, especially in the period of August to October (spring).
Conclusion: We conclude that in this study of 527 admissions because of convulsions and epilepsy in 2003 in a community based university hospital of São Paulo, Brazil, there was a tendency to seasonal presentation of cases, with higher prevalence in the second half of the year, mainly in spring and beginning of summer, specially in patients aged between 5-15yrs; below 5yrs, there was a higher incidence of convulsions in summer and winter.

p729
Outcome in a Group of Children and Adolescents with Focal Epilepsy
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Purpose: The aim of this study was to determine the outcome in a group of patients with focal epilepsy.
Methods: 204 children and adolescents newly diagnosed with epilepsy (two or more unprovoked seizures) aged 1 month to 15 years, mean 5.2 years, were prospectively studied. Patients were admitted to the Department of Child Neurology. 182 patients were followed-up from 1 to 9 years, mean 2.8 years. The epileptic seizures and the aetiology were classified according to the New Proposed Scheme for People with Epileptic Seizures and Epilepsy of ILAE(2001). Remission from seizures was analysed during the last year of this study. A period of more than one year seizure free was considered as criteria for remission. The effects of seizure type, age (at the time of the diagnosis), aetiology, initial EEG and CT scans on remission from seizures, were evaluated. Chi-square test with a level of significance of 5% (a=0.05), was used as statistical analysis.
Results: 135 (74.2%) of patients remained seizure-free. Focal seizure types had no significant difference for predicting remission of seizures (p=0.8472). There was a predominance of remissions in the group aged between 10-14 years (78.3%), followed by the group aged between 5-9 years (77.1%) (p=0.0201). 85.6% of patients with idiopathic epilepsy were seizure free, followed by the group of patients (68%) with cryptogenic epilepsy (p=0.0375). 93.6% of patients with abnormal EEG were uncontrolled (p=0.038). 84.2% of patients with a normal CT scan were seizure-free (p=0.0332).
Conclusion: Our results indicate that age (at the time of the diagnosis), aetiology, initial EEG and CT scans showed a good predictive value in children and adolescents with focal epilepsy.

p730
Outcome of Epilepsy Service at a District General Hospital
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Purpose: The study aimed to establish an overall assessment of our epilepsy service, and the standard of our current management. Epilepsy is the commonest neurological disorder of childhood; it has been highlighted that misdiagnosis, under or over investigation and mismanagement are known to be problematic. Paediatric epilepsy clinics run by paediatricians with an interest in epilepsy are a new establishment. The standard and outcome of such service has not been evaluated.
Methods: A retrospective case review study of all known children diagnosed with epilepsy over a two year period (August 1999 to August 2002). A relevant data collection tool was designed based on regional guidelines.
Results: Currently 156 patients are on treatment; 52% male, 48% female. Only 4% presented in the neonatal period. One third were 5 years old or younger. Only 8% presented as status epilepticus. The majority of patients (87%) were seen within 6 weeks of referral. The epilepsy nurse specialist saw almost all patients (96%). Seizure description was adequately described in only 32%, most commonly with absent seizures. Febrile convulsions were noted in 22%, particularly in tonic clonic seizures. Half of the patients had one type of seizure. Abnormal EEG was reported in 60%. MRI scan of the brain was conducted in 53% of patients of whom 43% were abnormal. Only 33% had ECG. Over two thirds (77%) were on monotherapy. The majority of patients with generalised epilepsy (82%) were on sodium valproate. A quarter (24%) attended special schools. Of those who attended main stream schools, 24% needed special classes or extra help. 1 patient was misdiagnosed and medication withdrawn within 2 months. No deaths were reported in the last 5 years.

Conclusion: The majority of our patients have been seen within a reasonable time. A high percentage of our patients had abnormal results at investigation and the majority were on monotherapy. This makes misdiagnosis and mismanagement less likely.

p731
Partners in Epilepsy (PIE): International Epilepsy Management with Electronic Records Registry System: Data Analysis in Paediatrics
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Purpose: A study, based on naturalistic data, to investigate current practices and clinical outcomes, as well as identify needs in epilepsy management.
Methods: Electronic record management in daily clinical practice (demographics, aetiology, syndrome and treatment) in epilepsy centres in Belgium, France, Portugal, Spain, Switzerland and the United Kingdom: data were analysed from 979 children.
Results: Aetiology was entered in 29% of records: cortical/development disorders/malformations were the most frequent causes (48/281), 35% did not fall into a predefined category. Epilepsy syndrome was defined in 32% of cases, of which 47% had partial epilepsy, 35% generalised, 14% undetermined, and 3% special syndromes. At date of last consultation (median 6 months), 42% were seizure-free. Among the children with persisting seizures, partial seizures were the most frequent, present in 52% (median range: 2 (0-600)/month). Antiepileptic drugs (AEDs) were prescribed in 96% (most common AEDs: valproic acid (59%), carbamazepine (37%), lamotrigine (23%), topiramate (15%)); 82% were on monotherapy, 12% on two, 5% on three, and 1.4% on four AEDs. The most common AED combinations were lamotrigine/valproate (11%), topiramate/valproate (9%), carbamazepine/lamotrigine (4%), carbamazepine/valproate (4%). Side effects were not commonly reported; at lower incidence than according to adult records.
Conclusion: Registry analyses provided valuable information on epilepsy characteristics, outcome and AED use in children. Partial epilepsy was the most common type identified. In the majority, however, the epileptic syndrome was not recorded. 4 in 10 were seizure-free at the last consultation. The majority received monotherapy. Side effects were not often reported. (PIE is supported by Janssen-Cilag.)

p732
Learning Difficulties in Children with Epilepsy: An Innovative French Educational Service Available within the Child's Total Environment
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Purpose: Epilepsy in infancy can be responsible for learning difficulties and scholastic under-achievement. The SESSAD was founded to address these specific needs of evaluation and treatment. The SESSAD is a multidisciplinary team which assesses the different factors responsible for under-achievement (neurological, cognitive or psychological). Its goal is to allow children with epilepsy and learning difficulties to attend school in optimal conditions (i.e. social integration, academic success) in partnership with parents and school.
Methods: We gathered medical, academic, cognitive and behavioural information for every child admitted between September 2001 and 2004. Calls from families whose child was not admitted were also collated.
Results: 45 children (21 girls and 24 boys), with a median age of 6 (extremes: 3-14) at admission were included. 23 children had localisation-related epilepsy: symptomatic/cryptogenic (22), idiopathic (1). 16 had generalised epilepsy: cryptogenic/symptomatic (11), idiopathic (5). 6 had unclassified epilepsy. 42 children were attending a normal school, but 25 were at least one year behind. 21 children had an IQ>70, with a significant dissociation between verbal and performance IQ in 14 cases. 21 had an IQ< 70. Behavioural difficulties were present in a majority of cases: inhibition (20/45), instability (25/45), difficulties in socialisation (37/45), immaturity (40/45). We were contacted by 131 families whose child was not admitted because of imposed geographical limits or the limited number of cases allotted.
Conclusion: The SESSAD is an innovative means to help children with epilepsy and learning difficulties but our experience emphasises the lack of specific structures for these children.

p733
Health-related Quality of Life and Epileptic Syndrome of 88 Children in Two Specialised Institutions for Children with Epilepsy
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Purpose: Health-related quality of life in epilepsy is an important aspect for the evaluation of psycho-social consequences of this chronic disease. However, there are very few studies that assessed the impact of a specific epileptic syndrome on quality of life (QOL). The following data are the first results of an epidemiological study ongoing in a French department (1.2 million inhabitants) and concerning all children with epilepsy aged from 3 to 16 years during 2005, focusing on the impact of paediatric epilepsy on QOL.
Methods: All children aged 3 to 16 years in two specialised institutions for children with epilepsy were included (N=88). Complete medical data including epileptic syndrome and treatment were recorded. The parents completed a questionnaire including QOL scales emphasising on the burden of epilepsy on development, schooling and family life. The Vineland adaptative behavioural scale was also completed for each participating child by take carers in the institution. Statistical analysis focused on the impact of the specific epileptic syndrome on QOL
Results: The distribution of QOL scores for each epileptic syndrome as well as relationships between QOL scores, Vineland scores and different indexes of gravity of the epileptic condition will be presented .
Conclusion: QOL is a subjective but important dimension in analysing the psycho-social impact of children's epilepsy. This dimension is different from more objective measures of gravity of the epileptic condition or measures of child's autonomy.

p734
Prospective Study on the Impact of a Child's Epilepsy on their Quality of Life and their Family
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Purpose: The aim of this prospective study was to determine the relationship between seizure type, seizure frequency and epilepsy syndrome on the quality of life of both the child and family over a 1 year period.
Methods: The sample was drawn from a population of children with epilepsy attending a tertiary paediatric neurology service in Dublin. Data was collected on seizure type and frequency, epilepsy syndrome, physical and cognitive ability, behaviour, co-morbidities, demographic and socio-economic variables. The attending parent completed the Child Health Questionnaire 50-item version (CHQ-50) for children >= 5 years. The Impact of Paediatric Epilepsy Scale (IPES) was used to measure the burden on families.

Results: 132 children were enrolled and complete data was available on 127. The median age was 8.8 years and 54% were male. 63% had partial seizures and 61% had cryptogenic or symptomatic epilepsy. 53% had frequent seizures (> 10/month). 93 children >= 5 years were included in the QOL analysis. Children with frequent seizures scored significantly worse than those with no/infrequent seizures on 10/14 and 11/14 of the CHQ-50 subscales tested and both IPES scores at baseline and 12 months respectively. Children with cryptogenic/symptomatic epilepsy scored significantly worse than those with idiopathic epilepsy. No such differences were found between seizure types and there were no differences between findings at baseline and 12 months.
Conclusion: The burden of epilepsy to children and their families is substantial. Seizure frequency and epilepsy syndrome rather than seizure type appears to affect this outcome.

p735
Development of the Multi-cultural DISABKIDS Quality of Life Questionnaire and Epilepsy Module for Children
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Purpose: To develop a multi-cultural quality of life questionnaire for children (8-16 years) with epilepsy.
Methods: Focus groups with children were conducted in seven countries to obtain statements for inclusion in the generic questionnaire. Children with epilepsy were included in three countries (Sweden, France and the UK). Following cognitive debriefing and pilot testing the final version of the DISABKIDS generic questionnaire (37 items; 6 domains) was tested in seven countries. The epilepsy module (10 items; 2 domains: impact of epilepsy and social stigma) was evaluated in five countries (Sweden, France, the UK, the Netherlands and Germany), and validated against standard QoL questionnaires (KINDL, DUCAT). A test, retest procedure was conducted in a subgroup and a proxy survey carried out.
Results: Completed questionnaires were received from 181 children and their proxies. The internal consistency values were between α =.70 and .90. The epilepsy domains had an internal consistency of α =.90 (impact) and .83 (social); 21.7% (impact) and 28.3% (social) of participants reaching the top of the scale. The intraclass correlation coefficient for the child and proxy versions were 0.601 (impact); 0.669 (social). Comparisons between counties showed similar results for all domains.
Conclusion: The DISABKIDS generic questionnaire and epilepsy module can be shown to be a robust measure of quality of life for this child population with consistent results across Europe. Further analysis of the behaviour of the questionnaire will be needed in other countries and languages to assess the reliability of results across a wider inter-cultural base.

p736
Evaluation of Familial, Social, Physical and Psychological Problems in Children that Conflict with Epilepsy Diseases
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Purpose: Epilepsy is one of the disorders with chronic, recurrent and sudden changes in neurological function due to an electrical dysfunction in the cerebrum. Previous studies indicated that this disorder may be induced by familial, social, physical and psychological problems in children with epilepsy. The aim of this study was evaluation of familial, social, physical and psychological problems in children that conflict with epilepsy diseases.
Methods: This is a clinical trial study during which we investigated children that conflicted with epilepsy. At the first time we recorded demographic data including age, sex and so on. Then we collected data regarding familial, social, physical and psychological problems using a questionnaire.
Results: The results indicated that the mean age was 13 years, 57% were female, 27% had a family history and 45% had psychological problems (anxiety, depression and...). 16% have familial problems (in relation to brothers and sisters), 35% have social problems (in relation to students and teachers) and 16% have physical problems (fatigue, weakness). Also, there was no significant correlation ($p>0.05$) between quality of life and age or sex.
Conclusion: The above findings have shown that some children and their families were not able to adapt to epilepsy. Also they have problems in their lives that can be create stressful situations for them.

p737
Eyelid Myoclonia with Absences Associated with an Argininosuccinic Aciduria: Which Relationship between the Metabolic Defect and this Presumed Idiopathic Epileptic Syndrome?
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Purpose: Eyelid myoclonia with absences (EMA) is a well documented entity, clearly recognised as a specific epileptic seizure type. According to ILAE 2004 classification, EMA is not yet defined as a separate syndrome. Nevertheless, most authors consider it as an idiopathic epileptic syndrome (ILAE 2004), although EMA may occur in symptomatic generalised epilepsies.
Methods: We report a case of an 8 year old girl diagnosed with argininosuccinic aciduria at the age of 3 (lethargy, mild hyperammonemia) with a favourable evolution under low protein diet and arginine therapy. Slightly after, the parents reported eyelid blinking considered as tics and subsequently not treated. Because of developmental language delay, we performed an electroencephalogram at the age of 8.
Results: The EEG revealed many generalised, irregular 3-5 Hz polyspikes and polyspike-slow wave complexes concomitant with myoclonic jerks of the eyelids. The video-EEG monitoring confirmed the diagnosis of eyelid myoclonia with absences. Eye closure induced similar prolonged epileptiform discharges associated with a variable impairment of consciousness. Photosensitivity was unclear.
Conclusion: Argininosuccinic aciduria is an autosomal recessive disorder of the urea cycle. Neurologic features can include motor milestones delay and cognitive impairment but epilepsy is rather uncommon. This observation highlights a possible relationship between a specific neurometabolic disorder and EMA. Because myoclonic jerks are frequently observed in different inborn errors of metabolism, we suggest that EMA may be part of the neurologic manifestations of metabolic defects. Note: video-EEG is available.

p738
Benign Myoclonic Epilepsy of Infancy followed by Juvenile Myoclonic Epilepsy: A Case Report
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Purpose: To present a girl with benign myoclonic epilepsy of infancy (BMEI), who later in her adolescence, after about 10 years seizure-free, developed JME. As far as we know, according to published data,

no patient with these two successively appearing syndromes has been described, even though one unpublished case was suggested
Methods: The case history and EEGs records were analysed for a period of 14 years during which the patient developed both forms of idiopathic generalised epilepsies; BMEI and JME.
Results: We describe a 15 year old girl who had suffered since the age of 8 months from daily myoclonic seizures involving mainly the upper limbs and the head. At that time sleep EEG showed generalised spikes and polyspike-waves. Clinical and EEG features were typical for BMEI. Seizure remission was observed within a few days on valproate treatment (introduced at the age of 18 months) that was tapered off within two years (since the age of 3 years and 5 months). The patient had been seizure free until the age of 11 years when absence and myoclonic seizures occurred. The EEG showed normal background activity. During hyperventilation and photic stimulation generalised polyspikes and spike-waves were observed. During video-EEG a generalised tonic-clonic seizure (GTCS) was recorded. Based on both clinical and EEG features JME was diagnosed. Seizure remission was achieved during three years valproate treatment. Neurodevelopmental outcome of the patient was normal.
Conclusion: Coexistence of two idiopathic generalised epileptic syndromes in one patient is not common but its occurrence strongly suggests a common genetic background of both syndromes. As we know, no patient with BMEI and JME successive appearance has been yet described. The question whether BMEI and JME constitute either the clinical continuum of the same epileptic syndrome or two distinct syndromes of IGEs still remains open until molecular diagnosis might confirm it .

p739
Generalised Epilepsy and Classical Spike-wave Discharges Associated with Unilateral Thalamic Lesions
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Purpose: Idiopathic generalised epilepsy (IGE) is a heterogeneous condition with a predominantly genetic aetiology. Clinical hallmarks for IGE syndromes include generalised spike and wave discharges, and normal brain imaging. We report on two patients with clinical presentation compatible with IGE, but whose imaging studies revealed a unilateral thalamic lesion.
Methods: The medical record of each patient was reviewed with interest on age of onset, seizure types, response to anticonvulsants, electrophysiological and imaging studies.
Results: The first patient presented with nocturnal generalised tonic-clonic seizures and occasional diurnal myoclonic seizures at age 12, which were well controlled with topiramate (not having tolerated valproic acid). The second patient had absences and eyelid myoclonia starting at age 6, that were refractory to valproic acid, lamotrigine, and ethosuximide. EEG findings in both individuals revealed classical generalised spike and slow wave discharges, at 4-5 and 3-4 Hz respectively. In the first patient, MRI revealed a 6mm non-enhancing lesion over the right thalamic pulvinar, whereas in the second case, a 6mm lesion over the medial and lateral dorsal nuclei was found. Coherence and cross-phase-spectral analysis of EEG applied to the latter case showed high interhemispheric coherence values. SISCOM images performed during an asymptomatic prolonged burst of epileptic activity showed hyperperfusion over the left cingular gyrus, subcallosal and bilateral orbitofrontal regions.
Conclusion: In rare cases, clinical features compatible with IGE may be associated with structural thalamic lesions.

p740
Correlation Between Clinical Manifestations and EEG/MEG Features in GLUG-1 Deficiency Syndrome
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Purpose: Glucose transporter-1 deficiency syndrome (Glut-1DS) is a neurological disorder appearing as intractable epileptic encephalopathy in infancy with various neurological symptoms caused by a low cerebral glucose level. We tried to clarify the relationships between clinical symptoms and EEG/MEG features in 4 Japanese Glut-1DS patients.
Methods: EEG was recorded and analysed by BESA 5.04 version of Nihon Kohden Corporation, and MEG was recorded by 64 channel whole head type of CTF Corporation and analysed by single dipole method.
Results: EEG was normal in all patients at onset. In 2 patients with intractable epilepsy, partial seizures in infancy followed by frequent absence seizures in childhood, EEG changed into focal slow waves, focal spike-and-slow waves, and finally diffuse spike-and-slow waves. EEG of one patient with only partial seizures showed only focal spikes, but equivalent current dipoles of MEG spikes were distributed over wide areas of the bilateral frontal lobes. EEG of the last patient with severe ataxia and rare epileptic seizures was normal throughout the course. Fast Fourier Transform analysis of EEG revealed a reduction of delta and theta waves after taking foods.
Conclusion: Topography, extent and chronological changes of EEG and MEG abnormalities corresponded to clinical manifestations of epileptic seizures for all 4 patients. These manifestations are considered to reflect the pathophysiology of Glut-1DS.

p741
Encephalitis Rasmussen: Diagnostic and Therapeutic Dilemmas
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Purpose: To present the diagnostic and therapeutic dilemmas in a child with epilepsia partialis continua, encephalitis Rasmussen.
Methods: A 10 year old child is presented with the clinical feature of uncontrolled seizures, mostly simple partial motor seizures, namely intractable unilateral seizures, paroxysmal disorder manifested with epilepsia partialis continua, with a developmental and motor regression, and progressive neurological symptoms with a predominance of hemiparesis.
Results: The clinical feature started 3 years before, with focal motor seizures exclusively during sleep, as sudden onset in a previously healthy child with good performance at school. With time these seizures progressed to epilepsia partials continua, and motor and mental deterioration, and delineation of hemiparesis. Different investigations were performed in the differential diagnostic procedures for confirming or negation of other disorders of hereditary degenerative aetiology, cerebrovascular or tumours of the central nervous system, presented by progressive neurological symptoms. Laboratory results were normal: routine ones, aminoacidaemia, aminoaciduria, screening test of aminoacids in urine, the copper levels in serum, the ceruloplasmin levels in serum, electrolytes in serum, enzymes levels in serum (SGOT, SGPT, LDH, CPK), serum IEPh, LP and cytochemical analysis of CSF. EMG was normal. Serial of EEGs demonstrated localised spike foci in the beginning, than generalised spike-wave, and at last slow-wave disturbances with changed background activity. The diagnosis of encephalitis Rasmussen was supposed and than confirmed by clinical features of progressive

neurological symptoms, motor and mental delay, and a serial of neuroimaging MRIs that showed progressive focal and with time, hemispheric cortical brain atrophy.
Conclusion: We presented a 10 year old child, with epilepsia partialis continua, progressive neurological symptoms of hemiparesis, motor and mental regression. The diagnosis of encephalitis Rasmussen was confirmed with the clinical features, and evidence of progressive changes on MRIs. Different AEDs as mono and polytherapy were ineffective. We can report that the treatment procedure with bolus corticosteroids, every month, the last six months, and chronic corticosteroids orally administered were of benefit in seizure reduction, and with that, stabilisation of neurological signs, motor and mental, was achieved.

p742
Epilepsy in Cystic Lesions of the Pineal Region in Childhood
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Purpose: To present clinical characteristics of epilepsy and EEG findings in 5 children with cystic lesions of the pineal region.
Methods: The patients are 2 boys and 4 girls aged 11 to 15 years with epilepsy as the presenting symptom. All examinees had MRI verified cystic lesion of the pineal region. Diagnostic work up excluded all other possible aetiologies for symptomatic epilepsy. The size of the lesions varied from 8x8x10 mm to 15x12x10 mm in diameter.
Results: Three children had generalised epilepsy (absence, grand mal), one had secondarily generalised and one partial complex seizures. All the children had abnormal epileptic EEG recordings ranging from focal spike or sharp-waves to diffuse paroxysmal polyspike, spike-waves complexes and were put on valproate therapy. Stabilisation of epileptic seizures in all children was obtained over 6 months to 2 years follow-up period. On subsequent MRI examination at six monthly intervals no changes were noticed in comparison to initial findings. Therefore, neurosurgical intervention wasn't considered as yet necessary and clinical, EEG and MRI follow up was recommended.
Conclusion: Epilepsy may occur as the less common symptom of cystic lesions of the pineal region. So far details of epileptic seizures were not presented. In our patients, children with MRI verified cystic lesions of the pineal region, epileptic seizures were absence, grand mal, partial complex and partial seizures with secondary generalisation. Epilepsy was stabilised by administration of antiepileptic drugs.

p743
Mesial Temporal Sclerosis and Chemotherapy in Children
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Purpose: We report on 2 patients with specific development of mesial temporal sclerosis (MTS).
Methods: The first patient had acute leukaemia when he was 4 years old. He received chemotherapy (daunomycin, vincristine, L-asparaginase). During treatment he sustained a febrile status epilepticus. MRI performed 15 days later revealed abnormality of signal in the left hippocampus (T2 and FLAIR increase). Six months later, an acute episode of cyclosporine A toxicity was noted. One year later he developed a temporal lobe epilepsy and brain MRI revealed left hippocampal sclerosis. The second patient had Wiskott Aldrich syndrome and received bone marrow transplantation when he was 1 year old, because of severe thrombocytopenia. Ten years later temporal lobe seizures occurred. Brain MRI revealed right mesiotemporal sclerosis with hippocampal atrophy and T2 increase.
Results: Retrospective studies of MTS have demonstrated a high incidence of "initial precipitating incidents", including febrile seizures, trauma hypoxia and intracranial infection, usually before age 5 years. In a recent review of MTS, Goyal et al. Epilepsia 2003;44:131-134) identified three children treated for acute leukaemia with MTS secondary to chemotherapy. The authors hypothesized that chemotherapy was the IPI event in their small cohort. Four other children underwent allergenic haematopoietic stem cell transplantation and developed cyclosporine A toxicity within the first three months and MTS one year later. MTS could be a consequence of CSA toxicity or of the underlying disease and its treatment (Faraci et al. Bone Marrow Transplantation 2003;31:919-922).
Conclusion: This unusual association may contribute to the understanding of the underlying mechanisms of MTS development.

p744
Kohlschütter Syndrome: An Inherited Epileptic Encephalopathy?
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Purpose: To further define the clinical and epileptic phenotype of Kohlschütter syndrome (OMIM 226750); a rare autosomal-recessive disorder of unknown aetiology with epilepsy, mental retardation and yellow teeth.
Methods: We studied 3 patients with Kohlschütter syndrome: one boy (patient 1, 8 years) and two siblings from a consanguineous family, a boy (patient 2, 4 years) and a girl (patient 3, 20 months).
Results: Seizures started before the end of the first year of life in all 3 children. Although psychomotor development before epilepsy onset had been normal (patients 1 and 2) or only slightly delayed (patient 3), it then stagnated or even regressed before at least motor development slowly continued again. All children are now severely mentally retarded. Seizure semiology was manifold and comprised atonic seizures with perioral cyanosis, mild tonic seizures, generalised tonic-clonic seizures, myoclonic seizures and atypical absences. EEG showed multiregional sharp waves in the 2 older children and one left frontotemporal sharp wave focus in the youngest patient. Cerebral MR imaging was normal.
Conclusion: Kohlschütter syndrome is a clinical diagnosis and should be suspected if children present with epilepsy and yellow teeth. In this syndrome epilepsy is difficult to treat and leads to stagnation of development or even regression at manifestation, before slow developmental progress is resumed. Epilepsy therefore seems to be essential for the pathogenesis of the severe mental retardation which could be interpreted as an epileptic encephalopathy. A similar phenomenon has been found in at least some of the few published cases affected with this rare disorder.

p745
Factors Associated with Behavioural Disturbance in an Epidemiological Study of Children with Epilepsy
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Purpose: To determine factors associated with behavioural disturbance in an epidemiological study of children with epilepsy.
Methods: Families of 127 children with epilepsy in a defined inner-London area were sent questionnaires which included Rutter behavioural scales and a wide range of other parameters. Statistical analyses were performed with SPSS software.
Results: 59% of the questionnaires were returned. Sufficient data for analysis of the behavioural scales were obtained in 54 children (43% of the total of 127 children). Behaviour was disturbed in 57% of this subgroup. The following factors were statistically significantly associated with disturbed behaviour: learning difficulties $p<0.001$,

quality of life p<0.001, age at first seizure p=0.001, adverse medication effects p=0.001, injury in seizures p=0.002, being teased/bullied p=0.003, polytherapy p=0.015 and seizures in last 3 months p=0.016. Factors such as gender, seizure duration, recovery time and number of emergency room admissions were not statistically significantly associated with behaviour in this study.
Conclusion: Behaviour is disturbed in a high proportion of children with epilepsy. The factors associated with behavioural disturbance in this sample included: learning difficulties, quality of life, age at first seizure, adverse medication effects, injury in seizures, being teased/bullied and seizures in the last 3 months.

p746
Evaluation of Children with Transient Loss of Consciousness: Syncope or Epilepsy?
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Purpose: Syncope, nonepileptic paroxysmal manifestation, is characterised by a transient loss of consciousness, associated with tonic-clonic movements resulting from cerebral anoxia and can be misinterpreted as epilepsy. The aim of this study is to evaluate children with transient loss of consciousness and to determine the causes: syncope or epilepsy.
Methods: We used a group of 593 children evaluated in our clinic or in our emergency room, from 2002-2004, with transient episodes of loss of consciousness. The patients had no history of recent trauma, fever, infection, intoxication, or psychiatric disorder. The study protocol included general physical and neurologic examination, paroxysmal manifestation characterisation, EEG, ECG, psychological examination.
Results: 241 (40.67%) patients had the final diagnosis of nonepileptic paroxysmal manifestation and 87 (36.09%) of these children had the final diagnosis of syncope. 43.67% of children with syncopal episodes have a positive family history for syncope, 22.98% for headache, 12.67% for epilepsy and 8.04% for febrile seizures. Also 6 patients have in the past experienced febrile seizures and 14 headache. Clinical features were loss of consciousness without other symptoms in 21% of cases and with generalised hypotonia (3.7%) or hypertonia (34.5%), clonic (11%) or tonic-clonic movements (2.8%), head and eye deviation (3.2%), urinary loss (2.5%), facial pall (31.5%) or cyanosis (12.6%). The tests used (EEG, ECG) lead to the diagnosis of vasovagal syncope.
Conclusion: Of the manifestations of syncope, clonic or tonic-clonic movements are potentially the most confounding, as they raise the question of epileptic seizures in many cases. Syncopal convulsions are common but are not a form of epilepsy. Diagnosis of syncopal episodes is based on history, physical examination, ECG findings and absence of EEG ictal discharges.

p747
Study on Differentiation between Migraine and Epilepsy in 43 First Visit Children with Complaints of Headache
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Purpose: To differentiate migraine and epilepsy in 43 children with headache.
Methods: 43 first visit children complaining mainly of headache, from November 2002 to October 2004 were included. Range of age: 4-15 years (8.57±3.21 years). Electroencephalogram (EEG) with photic stimulation was carried out at their first visit. The patients with definite EEG abnormalities were given computerised tomography (CT) examinations.
Results: 12 (27.9%) had no EEG abnormalities. Among the 31 (72.1%) who had EEG changes, 12 (27.9%) showed irregular alpha activities or high build-up with a little asymmetry during hyperventilation. They and the 12 with normal EEGs were diagnosed with migraine. 19 (44.2%) had definite EEG abnormalities: 6 (13.9%) had occipital spikes. 2 (4.6%) had occipital spikes during photic stimulation. 4 of them had either visual abnormalities or eyes/head deviation accompanied by headache. They were diagnosed with occipital lobe epilepsy. 4 (9.3%) had frontal spikes, and 2 of them had sleeping disorders before the headache occurred. They were suspected as having frontal lobe epilepsy. 3 (7.0%) showed central-temporal spikes, and 1 had GTCS during sleep three weeks later. This was affirmed as benign childhood epilepsy with centrotemporal spikes (BECT). 4 (9.3%) had continual asymmetric high build-up during hyperventilation. On the CT of these 19 patients, 2 (4.7%) showed occipital cortex dysplasia. 1 (2.3%) was found to have vascular malformation.
Conclusion: In children, occipital lobe epilepsy may be indicated by headaches. When it is difficult to make a diagnosis, it is better to re-examine. The comorbidity of migraine and epilepsy should also be recognised.

p748
Incidence of Epilepsy after Bacterial Meningitis in Children
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1) University Children's Hospital, Belgrade, Serbia and Montenegro

Purpose: Determining the incidence of epilepsy in children after bacterial meningitis.
Methods: Retrospective analysis of children treated for bacterial meningitis at University Children's Hospital in Belgrade from January 1999 to September 2002. Follow-up period was 2 years.
Results: 118 children were included in this study (52.5% male). None of the children had afebrile seizures before the meningitis. Children's age was between 2 months to 14 years: infants 49.1%; 2-6 years 40.7%; 7-14 years 10.2%. Aetiology: haemophilus influenza type b 28 children/23.7%; neisseria meningitides 29/24.6%; streptococcus pneumonia 14/11.9%; unknown 45/38.1%; others 2/1.7%. Inappropriate antibiotic oral treatment was established in 53 children/44.9% (before appropriate diagnosis). During the 2 year follow-up period, 9 children (7.6%) had epilepsy and 2 (1.7%) had febrile seizures. 4 children had generalised convulsive seizures, 3 had partial seizures and 2 had infantile spasms. Study showed that the main predictor factors for epilepsy were convulsions during meningitis (8/9) and age, (infants 7/9). Other predictors for epilepsy in this study were not statistically significant (period to adequate antibiotic therapy, clinical signs of increased intracranial pressure, consciousness disorders, focal neurological signs, neuroradiological finding, aetiology). Other sequels (locomotor dysfunction, mental retardation, hearing loss) were found in 25 children (21.2%); 6 children (5.1%) had subdural effusions without neurological sequels.
Conclusion: Incidence of epilepsy and other sequels after childhood bacterial meningitis is still high. The most significant predictors for epilepsy after bacterial meningitis are age and convulsions during the meningitis. Although it is not statistically significant, the percentage of inadequate antibiotic therapy before diagnosis of meningitis is still very high. The vaccination for Hib in Serbia and Montenegro is still not being performed. Therefore, introduction of effective Hib conjugate vaccine into a national program of vaccination in Serbia and Montenegro would lead to a lower incidence of epilepsy and other sequels after childhood bacterial meningitis.

p749
Excessive Daytime Sleepiness among Children with Epilepsy
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Purpose: Adults with epilepsy were shown to experience excessive daytime sleepiness (EDS) and poor sleep quality, which may be due to anticonvulsant use, seizures, and/or primary sleep disorders (Foldvary, Journal of Clinical Neurophysiology. 19(6): 514-21, 2002). Similar studies, however, are lacking in children. We hypothesized that children with epilepsy have worse daytime sleepiness compared to controls.

Methods: Children with epilepsy (treated with non-benzodiazepines, non-barbiturate anticonvulsants) and age/sex matched controls between ages 8 and 18 were recruited for this pilot study. All subjects completed the Paediatric Daytime Sleepiness Scale (PDSS) and parents completed the Paediatric Sleep Questionnaire (PSQ). Two tailed t-tests were used for group comparisons and regression analysis to identify independent predictors of daytime sleepiness among patients. Marshfield Clinic institutional review board approved the study.
Results: 50 children with epilepsy (30 male; 20 female), and 30 age/sex-matched controls (18 male, 12 female) were enrolled in the study. Parents of children with epilepsy reported significantly worse daytime sleepiness on PSQ (p=0.01). Furthermore, these parents more often reported complaints of sleep apnea (p= 0.007) and parasomnias (p=0.005) compared to controls. On the PDSS, children with epilepsy reported significantly worse daytime sleepiness compared to controls (p=0.002). Seizure frequency, epilepsy syndrome and anticonvulsants used were not significant predictors of EDS among patients.
Conclusion: EDS is common among children with epilepsy, which may be due to an underlying sleep disorder such as sleep apnea or parasomnias. Further studies are needed to determine factors underlying EDS, and whether treatment of underlying sleep disorder improves EDS among children with epilepsy.

p750
Epilepsy in Children with Cerebral Palsy Born in Rijeka from 1982 to 1992
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Purpose: Determination of prevalence, particularities, risk factors and prognosis of epilepsy among children with CP (cerebral palsy).
Methods: The study included children with CP and epilepsy diagnosed according to standard criteria, born in Rijeka from 1982 to 1992 and systematically followed at the Centre for children with neurodevelopmental problems. The follow-up issues were: type of CP, timing of occurrence of epilepsy, results of neuroimaging tests (CT, MRI), electroencephalography, antiepileptic treatment modalities, prognosis of epilepsy.
Results: Among 89 children with CP, 32 (35.2%) have an associated epilepsy; 60% of them with occurrence of epilepsy in the first two years of life. Neonatal seizures, sepsis and meningitis (46.9%), pathologic neuroimaging results (84.3%) and mental subnormality (78%) increase the risk of epilepsy in children with CP. Epilepsy is much more frequent among children with spastic tetraplegia (84.5%). Infantile spasms and partial secondary generalised seizures represents more than 50% of the epilepsy variation among these children. 53% of the patients were treated with two or more antiepileptic drugs. Although severe epilepsy refractory to treatment was observed in 26.6% of patients, it is surprisingly that 40% of children had seizure-free periods lasting for more than 5 years.
Conclusion: Although in children with CP epilepsy is a life-long condition, the use of new antiepileptic drugs which increase the seizure free periods, as well as the possibility of neurosurgical treatment, bring more optimism to their families and promise a better quality of life.

p751
Clinical Study of Epilepsy in Children with Cerebral Palsy
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Purpose: To study the spectrum of epilepsy in children with cerebral palsy.
Methods: A total of 93 consecutive patients with cerebral palsy (CP) were retrospectively studied. Criteria for inclusion were follow-up periods for at least 2 years. A correlation between the incidence of epilepsy and the seizure types in the different forms of CP was examined. Other factors associated with epilepsy such as the age of first seizure, the occurrence of abnormalities on brain imagings, and the electroencephalogram (EEG) were also analysed.
Results: The prevalence of epilepsy in children with CP was 46.2%. Incidence of epilepsy was predominant in patients with mixed, diplegic, and quadriplegic palsies: 55.5%, 51.6%, and 50.0% in frequency. The first seizure occurred during the first year of life in 48.8% of patients with epilepsy. Generalised tonic-clonic seizures were the most common seizure type (44.2%), predominant in diplegic patients (64.3%). Infantile spasms and myoclonic seizures took up the main cause of seizure in quadriplegic children (60% and 40%, respectively). The occurrence of epilepsy was more in the group with abnormal brain imagings, especially encephalomalacia and cortical atrophy. All children with epilepsy in this study showed abnormal EEG findings: generalised abnormalities were observed in 55.8% of children with epilepsy; more dominantly in quadriplegic children (80%) and 40% of children with diplegia showed focal abnormalities.
Conclusion: Cerebral palsy is associated with a higher incidence of seizure disorders, which, in a majority, has its onset the first year of life; brain imaging and EEG in most affected in epilepsy in children with CP.

p752
Beyond Brain Tumours and Cognition: Neurological Complications in Long-term Survivors of Childhood Non-central Nervous System Malignancies
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Purpose: Non-cognitive neurological complications of the original disease and treatment in children treated for malignancies other than CNS tumours have not been well documented in the literature. We reviewed survivors of paediatric non-cns malignancies (including leukaemia) to determine the type and frequency of non-cognitive, neurological complications.
Methods: Retrospective audit of 865 Late Effects Clinic visit records. 638 patients with a variety of malignancies were included. Follow-up ranged from 5-30 years from completion if treatment. Data including: diagnosis, age, treatment and neurological complications, were collected and descriptively analysed.
Results: 99 neurological complications occurred in 85 patients. The majority (70%) of complications occurred in patients who were diagnosed at age less than 5 years. The most common complication was seizure (23 patients), followed by hearing loss (18 patients), neuropathies (17 patients), cavernous angiomas (8 patients) and cerebral vascular accidents (7 patients).
Conclusion: Significant and sometimes debilitating non-cognitive neurological complications occur in survivors of paediatric non-cns malignancies. For this paper, I will concentrate on those who developed seizures and those who presented with seizure as a complication of cavernous haemangioma. Treatment strategies must be created that continue to improve survival and minimise long-term complications. Information on these complications needs to be disseminated more widely in the medical community.

p753
Autoantibodies Against NMDA-GluR Epsilon 2 in Patients with Acute Encephalitis
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Purpose: We found autoantibodies against the NMDA GluR epsilon 2 subunit in sera and CSF from patients with Rasmussen's encephalitis. To reveal the pathophysiological mechanisms in intractable epilepsy after acute encephalitis, we studied the autoantibodies in such patients.
Methods: We established stable NIH3T3 transformant cell lines expressing NMDA GluR epsilon 2 as antigens. We analysed autoantibodies against GluR epsilon 2 in the CSF of 46 patients with acute encephalitis or encephalopathies, categorised into localised encephalitis (24 patients) and widespread encephalitis (22 patients) by clinical symptoms in the initial stage. Patients with localised encephalitis showed psychic symptoms, solitary seizures and very mild impairment of consciousness in the initial stage. On the other hand, those with widespread encephalitis showed profound unconsciousness and convulsive status in the initial stage.
Results: In patients with localised encephalitis, IgM autoantibodies in CSF tended to appear in the acute stage (0-20 days after onset of neurological symptoms) or the recovery stage (21-60 days after onset). In patients with widespread encephalitis, IgM autoantibodies in CSF tended to appear in the chronic stage (over 60 days after onset) or the recovery stage. These data may suggest that two different types of GluR autoimmunity contribute to the pathogenesis of localised and widespread encephalitis. In patients with widespread encephalitis, the presence of the autoantibodies in CSF correlates significantly with onset of epilepsy after encephalitis (p=0.01), and with mental impairment (p=0.03).
Conclusion: Autoantibodies against GluR epsilon 2 may have a causal relation with epileptogenesis after widespread encephalitis.

p754
Correlation of Seizure Characteristics and Hippocampal Volumetric MRI Findings in Children with Idiopathic Partial Epilepsy
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Purpose: The aim of this study was to investigate the hippocampal volumes in children with idiopathic partial epilepsy using volumetric MRI and to correlate the radiological findings with seizure characteristics.
Methods: 30 patients with idiopathic partial epilepsy between 3-18 years of age were studied. Thirteen age and sex matched healthy children served as the control group. Patients with a history of any perinatal insult, intracranial infection or neurodegenerative disease were excluded. The age of seizure onset, the severity and the frequency of seizures and antiepileptic drug duration and response were noted. The total, right and left hippocampal volumes of the study and control patients were evaluated using volumetric MRI by the same paediatric radiologist.
Results: The corrected right, left and total hippocampal volumes were found significantly decreased in the study of patients compared with the control subjects (p=0.000). Hippocampal volumes were not found to be correlated with the age of onset of epilepsy, the frequency or the severity of the seizures, the response to antiepileptic drugs or the duration of the treatment (p=0.000, r<0.5).
Conclusion: Our results suggest that the reduction of hippocampal volumes were not influenced by seizure characteristics in children with idiopathic partial epilepsy. Thus, other factors than seizure characteristics might be present which determine hippocampal volumes in these patients.

p755
Quantitative 1HMRS and MRI Volumetry Indicate Neuronal Damage in the Hippocampus of Children with Focal Epilepsy and Infrequent Seizures
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Purpose: Whether and at what stage the hippocampus is affected in children with focal, temporal, non-intractable epilepsy is poorly known. We have now studied eventual metabolic and volume changes in the hippocampus of children with non-symptomatic focal epilepsy under antiepileptic medication but still having infrequent seizures.
Methods: Quantitative proton magnetic resonance spectroscopy (1HMRS) and volumetric MRI were used to study the hippocampal region of 11 paediatric outpatients (10 to 17 years) with cryptogenic localisation-related epilepsy and their 8 healthy controls (9 to 16 years). The spectra were obtained bilaterally from the hippocampi using the 1.5 T MR imager. The spectral resonance lines of N-acetyl group (NA), creatine and phosphocreatine group (Cr), choline-containing compounds (Cho) and myo-inositol (mI) were analysed quantitatively. The volume of the hippocampus was semiautomatically calculated.
Results: The mean concentration of NA was significantly decreased (p=0.024, one way-ANOVA) both in the focus-side (9.02 ± 2.00 mM) and in the non-focus-side (8.88 ± 2.09 mM) of the patients compared to the control persons (10.76 ± 1.86 mM), in particular if the children had a history of generalised tonic clonic seizures. In accordance, the mean hippocampal volume of the focus- side of the patients (2.65 +0.53 cm3) was significantly reduced compared to that of the controls (3.25 + 0.46 cm3). The mean concentration of Cho, Cr and mI did not differ significantly between the patients and controls.
Conclusion: Metabolic changes in the hippocampi were detected in children with non-symptomatic localisation-related epilepsy and infrequent seizures. Reduced NA could reflect neuronal metabolic dysfunction and/or neuronal damage as indicated by our volumetric findings.

p756
Neuroimaging in Neurocutaneous Syndromes: Clinico-aetiological Correlations
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Purpose: Neuroimaging in paediatric epilepsy was used for an early aetiological diagnosis and a better understanding of epileptiform EEG pattern activity, and of symptoms in an appropriate management carried out by a multi-disciplinary team. Our paper will illustrate correlations between particular aspects of brain-scans (magnetic resonance imagining - MRI) computerized tomography CT, arteriography with electroencephalogram EEG aspects and clinical neurological, dermatological, psychological symptoms of children and families with genetic neurocutaneous syndromes.
Methods: Clinical examination in the multidisciplinary team was followed by blood tests, EEG, MRI, CT and arteriography, in order to find correspondence between epileptiform EEG patterns, drug therapy and the outcome regarding seizure control, cognition and quality of life in childhood. Family counselling and psychotherapy for parents was necessary to adjust reactions to a diagnosis and reach the stage of acceptance for treatment.

Results: In our 5 cases (neurofibromatosis type II – 1 case, tuberous sclerosis type II – 2 cases, and angiomatosis Struge-Weber – 2 cases) the clinical neurological, dermatological, psychological examinations followed by EEG, MRI and arteriography had been done in all cases to find correlations between clinical symptoms, the pattern of epileptic seizures and brain transformations. Some particular aspects will be documented in depth with images.
Conclusion: The role of neuroimaging is important for a multidisciplinary approach as well as in the appropriate management in working with parents to accept drug treatment and a certain lifestyle for family and child.

p757
11C-Flumazenil in Evaluation of Intractable Epilepsy in Children
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Purpose: The purpose of the study was to evaluate the add-on information of positron emission tomography using 11C-flumazenil as a tracer (FLU-PET) in the pre-operative evaluation of childhood intractable epilepsy. 11C-flumazenil is a GABA-A agonist and as a PET tracer has proved to delineate the epileptic focus more accurately than tracers of brain metabolism in adults, being especially useful in extratemporal lobe epilepsy and in detecting dual pathology.
Methods: The study population consisted of 14 children aged 2 to 17 years. All participants had intractable epilepsy (3 suspected temporal, 11 extratemporal lobe epilepsy) and had had routine pre-operative evaluations (video-EEG, MRI, ictal SPECT (6 of the patients), and FDG-PET (7)) and were referred to FLU-PET because of nonconfirmatory results in the previous investigations. The children underwent a static 20min FLU-PET investigation using a GE Advance PET scanner, starting 30-40 min after the 11C-flumazenil injection (3.7MBq/kg). Four studies were performed in propofol anaesthesia. The studies were visually analysed by two independent investigators (LM,ES). 2 of the patients were subsequently operated on.
Results: There was a localising finding in nine of the FLU-PET studies. An abnormal focal accumulation of 11C-flumazenil was seen in 4 out of the 6 patients with normal MRI and in 1 of the 3 patients with nonlocalising ictal SPECT. In 1 patient out of the 2 with no localising findings in FDG-PET, there was a focal hyperaccumulation of FLU.
Conclusion: FLU-PET detects focal findings in young epilepsy patients who lack structural or metabolic focal cerebral lesions.

p758
Spectrum of Epilepsy in Children with Malformations of Cortical Development
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Purpose: Review of cases with malformations of cortical development (MCD), after being classified according to Barkovich criteria and characterisation of the clinical spectrum of epilepsy.
Methods: We carried out a retrospective study of clinical reports and cerebral MR of patients with MCD followed in our department. They were grouped according to Barkovich criteria by two neuroradiologists. Tuberous sclerosis, neoplasic and megalencephalies were excluded. From the clinical reports we took these data: age of onset and type of epilepsy, pharmacoresistance, follow-up time, presence of mental retardation.
Results: We found 71 cases, corresponding to 81 types of MCD. Microlissencephaly was present in 5, hemimegalencephaly in 3, lissencephaly/subcortical band heterotopia (SBH) spectrum in 8, cobblestone complex in 2, heterotopia in 13, schizencephaly in 7, polymicrogyria in 39, cortical dysplasia in 3, S. Aicardi in 1. Epilepsy was present in 61 patients, focal in 30, generalised in 20 and 11 had West Syndrome. Epilepsy was refractory to drug treatment in 30 patients. 1 child with hemimegalencephaly was submitted to surgery. Follow-up time ranged from 1 to 17 years. Mental retardation was found in 67 patients.
Conclusion: The more frequent MCD were those related to abnormal cortical organisation. Epilepsy was present in 86% without a predominant type of epilepsy although West Syndrome was present in 15%. Patients with schizencephaly, even if bilateral, had focal epilepsy. Intractable seizures occurred in 100% of children with microlissencephaly, hemimegalencephaly and SBH. MCD are an important cause of epilepsy and neurodevelopment disorders, particularly in the first year of life.

Wednesday 31st August and Thursday 1st September 2005
13:15 – 14:15
Poster Session
Genetics

p759
Idiopathic Epilepsies with Seizures Precipitated by Fever: Clinical and Genetic Study of 85 Patients
C. Marini[1], D. Mei[1], T. Temudo[2], A.R. Ferrari[1], D. Buti[3], A. Moreira[4], L. Parmeggiani[1], P. Bonanni[1], C. Dravet[1], S. Seri[5], H. Cross[6], B. Neville[6], J. Narbona[7], A.I. Dias[4], E. Calado[4], D. Battaglia[8], F. Guzzetta[8], E. Reid[6], A. Pelliccia[1], R. Guerrini[1]

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Purpose: Idiopathic epilepsies have a predominant genetic aetiology. Several genes coding for subunits of ion channels or GABAA receptor have been associated to generalised and focal epilepsies in single patients and/or families.
Methods: We performed a clinical and genetic study of 85 patients in whom most seizures occurred during febrile episodes. The aim of this study was to achieve a better definition of the spectrum of phenotypes that might be associated with mutations of a1 subunit sodium channel gene (SCN1A).
Results: We classified patients as follows: severe myoclonic epilepsy on infancy (SMEI) = 36; sporadic myoclonic astatic epilepsy= 3; generalised epilepsy with febrile seizures plus (GEFS+) spectrum= 16; febrile seizures= 7; idiopathic generalised epilepsies= 11; atypical benign rolandic epilepsy=1; idiopathic focal epilepsy= 1; benign neonatal seizures= 1; undetermined focal or generalised epilepsies=5; prolonged febrile convulsive seizures and symptomatic temporal lobe epilepsy = 1. The remaining 3 patients, due to lack of clinical information, were unclassified. DHPLC screening of SCN1A revealed mutations in 28 patients: 26 with SMEI, 1 with GEFS+, 1 with prolonged febrile convulsive seizures and symptomatic temporal lobe epilepsy. Mutations were: 14 missense (3 familial) and 14 truncating (1 familial).
Conclusion: Our study confirms the causative role of SCN1A in SMEI with 72% of patients positive to the analysis. A de-novo mutation was found in a patient with prolonged febrile convulsive seizures and symptomatic temporal lobe epilepsy extending the spectrum of phenotypes associated with SCN1A mutations. Amongst GEFS+ phenotypes the rate of SCN1A mutations was around 6%.

p760
Mutation Analysis of the SCN1A Gene in The Netherlands: First Results
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Purpose: Mutations in the SCN1A gene are associated with GEFS+ (generalised epilepsy febrile seizures+) and SMEI (severe myoclonic epilepsy in infancy. We report the first results of mutation analysis of the SCN1A gene in The Netherlands.
Methods: Analysis of the SCN1A gene was performed in one family with GEFS+, patients with benign febrile and afebrile convulsions (n=2), classical SMEI-phenotype (n=6), severe epilepsy and psychomotor retardation (n=6), myoclonic-astatic seizures (n=1) and progressive myoclonic epilepsy with normal intelligence (n=1).
Results: In the GEFS+ family a novel missense mutation was found (Asp332Gly). The mutation cosegregated with the disease. The aspartic acid at position 332 is highly conserved and located in a functionally important domain of the protein. In 4 of the 6 patients with SMEI mutations were found: three truncating mutations (982insG, 3370-3371delTT and 3509delT) and one missense mutation (Gly1433Glu). An uncertain variant (Arg931His) was found in a boy with severe psychomotor retardation and therapy-resistant epilepsy. Family and functional studies will be performed to determine the pathogenicity of the missense mutation and the uncertain variant.
Conclusion: Five mutations and one uncertain variant were found in 16 patients and one family (29%). Most of the patients without a mutation did not have a classical GEFS+ or SMEI phenotype.

p761
Generalised Epilepsy with Febrile Seizures Plus: Clinical and Genetic Analysis in Three Serbian Families
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Purpose: Generalised epilepsy with febrile seizures plus (GEFS+) is an inherited epileptic syndrome with an autosomal dominant pattern of inheritance, incomplete penetrance and various phenotypic expressions. Few point mutations on four different genes were described but only 1.7-10% of GEFS+ families demonstrate mutations in known genes.
Methods: 5 members of OM pedigree, 26 members of MM pedigree, and 6 members of KS pedigree were interviewed. Detailed clinical evaluation was performed on 33 members of all three families (of 77 live members) and data on clinical history, seizure types, semiology, syndromology and frequency, possible aetiology and comorbidity were obtained as well as EEG recording and brain MR imaging. Mutation analysis of the SCN1A, SCN1B and GABRG2 genes was performed on affected individuals.
Results: MM pedigree. There are 20 affected members in 4 generations. In second generation 66% of members were affected, as well as 63.6% and 47.6% in third and fourth generation, respectively. Prognosis of epilepsy was good in 66.6% (8/12). Severe epilepsy was revealed in 2 subjects. In 5 out of 12 affected members, seizures other than GTCS were found. OM pedigree. Over half of affected members had febrile seizures during childhood. Pharmacoresistant afebrile GTCS and associated absence seizures in variable frequency were clinical features of proband. Proband's daughter has a 'milder' form of the similar phenotype. Penetrance in this pedigree is approximately 30%. KS pedigree. No other seizure type than febrile and afebrile GTCS was observed in this small pedigree. No mutation in the exons of the SCN1A, SCN1B and GABRG2 genes were found.
Conclusion: Recognition of GEFS+ on clinical grounds contributes to better integration of this syndrome into already defined epileptic syndromes.

p762
Association Between GEFS+3 Locus and GEFS+ Syndrome in Two Affected Tunisian Families
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Purpose: We describe 2 Tunisian families with generalised epilepsy with febrile seizures plus (GEFS+). The aim of this report is to search for a linkage and/or association between the known FS and GEFS+ loci and GEFS+ syndrome in affected Tunisian families.
Methods: A total of 14 patients with GEFS+ and 55 controls belonging to two Tunisian families affected with GEFS+ syndrome had clinical and genetic studies. Genetic analysis of genomic DNA has been performed using microsatellite markers spanning the FS and GEFS+ loci. Statistical analysis has been realised by intrafamilial association test (FBAT) and by parametric linkage (LOD scores) and non-parametric linkage (NPL) tests. In addition, a transmission disequilibrium test (TDT) has been performed using the computer program GENHUNTER v 2.1.
Results: Epilepsy phenotypes included FS in 4 patients (A-IV:10; A-IV:3; A-IV:18; A-IV:22). Median age at FS onset was 2 years (range, 6 months to 5 years). One patient (B-V:3) had FS+ (onset seizures at 6 years). FS+ associated with generalised tonic clonic seizures were found in 3 patients (A-V:27; A-V:30; A-VI:13); FS+ with myoclonic seizures in 1 patient (B-V:6). 5 patients had idiopathic generalised epilepsy (A-IV:24; A-V:5; A-V:7; A-V:25; B-V:3). Median age at afebrile seizure onset was 17 years (range 14 to 25 years). The result of FBAT test revealed an association between GEFS+3 locus and GEFS+ syndrome in these 2 Tunisian families with a very significant p value. This association was also confirmed by results of TDT test. A search of mutation in GABRG2 gene is ongoing.
Conclusion: Our study showed a heterogeneity of epilepsy phenotypes and a probable association with GEFS+3 locus in 2 Tunisian families.

p763
Spanish Family with Generalised Epilepsy with Febrile Seizures Plus (GEFS+): Clinical and Genetic Analysis
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Purpose: Generalised epilepsy with febrile seizures plus (GEFS+) is a familial epilepsy syndrome characterised by the association of febrile seizures and diverse generalised and focal epilepsy phenotypes. The aim of this study is to characterise the clinical features of a four generation GEFS+ Spanish family and to perform linkage analysis to the known GEFS+ loci.
Methods: We identified a GEFS+ family including 9 affected individuals. Personal interviews and DNA samples were obtained from 17 individuals. Microsatellite markers in chromosomes 5q34, 19q13.1 and 2q21-q24 were genotyped and linkage analysis was performed.
Results: Of 9 affected individuals, 5 presented febrile seizures, 1 febrile seizures plus, 1 persisting childhood absence epilepsy and 2 focal epilepsy not preceded by febrile seizures (1 presented déjà-vu sensations, plus generalised tonic-clonic seizures and the other one complex partial seizures consisting of staring, mouth deviation and left tonic convulsions). The mode of transmission was consistent with an autosomal dominant pattern with incomplete penetrance (69%).

Linkage analysis excluded linkage to the previously described GEFS+ loci.
Conclusion: We describe a family with GEFS+ in which 2 affected members present focal epilepsy. Linkage analysis in this family suggests the existence of additional, undescribed loci for GEFS+.

p764
Evidence that not MASS1 but Another Gene is Mutated in a Belgian FEB4 Family
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Purpose: Generalised epilepsy with febrile seizures plus (GEFS+) is a familial epilepsy syndrome with a spectrum of phenotypes including febrile seizures (FS), atypical febrile seizures (FS+) and afebrile generalised seizures. The study aims to identify the locus in a multiplex GEFS+ family.
Methods: A 10 cM density genomewide scan was conducted in a three-generation Belgian family with GEFS+. Mutation analysis of VLGR1 was performed in 3 affected family members. 41 additional small Belgian FS or GEFS+ families were genotyped for markers encompassing the FEB4 locus.
Results: A three-generation GEFS+ family shows parametric linkage to the FEB4 locus on chromosome 5q14-q15 with a maximal logarithm of odds score of 3.18. Previously, a heterozygous nonsense mutation in the monogenic audiogenic seizure susceptibility gene (MASS1) has been reported in a single small Japanese GEFS+ family as a possible cause of FEB4. MASS1 consists of exon 6-39 of the very large G protein-coupled receptor gene (VLGR1). No VLGR1 mutation was found in the FEB4 family. Nonparametric multipoint linkage analysis in 41 small FS or GEFS+ families provided no evidence of linkage with markers located in the FEB4 locus.
Conclusion: This study confirms the existence of a locus for FS and GEFS+ on chromosome 5q14-q15. The absence of a mutation in VLGR1 adds to the growing evidence that mutations in another gene within the FEB4 locus may be involved. No evidence of linkage to FEB4 locus in 41 small FS and GEFS+ families suggests a small contribution of this locus to FS and GEFS+ in the Belgian population.

p765
Phenotypic and Genetic Analysis of Families with Idiopathic Generalised Epilepsy
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Purpose: The aims of the study were to better characterise different clinical features in patients with idiopathic generalised epilepsies (IGE) trying to identify phenotypically defined subgroups; and to evaluate the presence of an already described mutation in CACNB4 (arg-482-ter) in our population.
Methods: 51 patients meeting the inclusion-exclusion criteria were submitted to a systematic clinical assessment and detailed family history. Whenever possible, neurophysiologic evaluation and extraction of blood samples for genetic testing were performed, both in probands and their relatives. Search for arg-482-ter mutation was performed according to the original description (Escayg et al, Am J Hum Genet 2000;66(5):1531-9).
Results: Population: 21 males, 30 females; with a mean age of 23.7+ 7.4 years; 42 juvenile myoclonic epilepsies (JME); 7 absence epilepsies (AE). A family history of IGE or febrile seizures in first degree relatives was found in 35% of probands. Relevant findings included the association of absence seizures in JME patients not evolving from AE, with an earlier age of onset (T test; p=0.033). In a subpopulation of 14 probands and 21 first-degree relatives in which a video-EEG was performed, we found a high prevalence of asymmetric photic driving (57%), with significant association with photosensitivity (x2; p=0.018). The pattern of either symmetric or asymmetric photic driving showed intra-familiar consistency. Mutation in CACNB4 was not found in our population.
Conclusion: It is still possible to delineate more precise phenotypic subtypes, as may be the case of the subpopulation with asymmetric photic driving described here. This could enable the performance of more specific molecular genetic studies.

p766
Analysis of Two-locus Linkage Interactions in Epilepsy Related Photosensitivity
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Purpose: Photosensitivity or photoparoxysmal response (PPR) is an abnormal cortical reaction of spikes or spike and wave discharges triggered by intermittent photic stimulation. It is an epilepsy-related EEG trait with prevalence of ~2% in the general population of paediatric age, but highly prevalent in idiopathic epilepsies, especially in common idiopathic generalised epilepsies (IGEs), such as CAE and JME. This degree of co-morbidity suggests that PPR is involved in the predisposition to IGE. The identification of genes for PPR would therefore aid dissecting the genetic basis of IGE.
Methods: We conducted a genome-wide screen in 16 PPR-multiplex families with prominent myoclonic epilepsy background and found empirical genome-wide significance for linkage at 7q32 (HLOD =3.47, PNPL = 3.39 x10-5) and 16p13 (HLOD =2.44, PNPL =7.91 x10-5) (Pinto D et al Hum Molec Genet. 2005; 14: 171-178). Both these genomic regions contain genes that are important for neuromodulation of cortical dynamics, and could therefore play a role in PPR. To gain more information about the genotype-phenotype relation, we currently explored interactions between the two loci, assuming multiplicative, heterogeneity and additive models.
Results: Besides enabling modelling of interactions and increasing the power to detect linkage, two-locus linkage analysis also leads to more accurate estimates of the disease-locus positions than single-locus linkage analysis, reducing the effort involved in fine-mapping.
Conclusion: Preliminary results show that a multiplicative two-locus model best fits the data, suggesting that the loci underlying our linkage peak may be functionally related.

p767
Complex Co-occurrence of Craniofacial Dysmorphisms, Mental Retardation and Photosensitive Epilepsy in One Family
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Purpose: To study a core family with craniofacial dysmorphism, mental retardation (MR) and photosensitive epilepsy (PE).
Methods: All members presented mild (father, mother and son) or more severe MR (daughter). No presence of consanguinity between the parental branches. The mother, 45 yrs, had PE since she was 13. The daughter, 25 yrs, IQ 40, has PE with auto induced seizures since the age of 1 yr. Their son, 23 yrs, IQ 66, has nocturnal seizures since he was 4. All but the father are under AEDs treatment. All family members had craniofacial abnormalities. We performed EEG examination with extensive IPS, MRI of the brain and X-ray skeletal examination.
Results: EEG-investigations: the mother had an asymmetrical background (R>L) and a localised photo paroxysmal response (PPR). The father had a bi-frontal epileptic focus (L>R) and a localised PPR.

The daughter had an R fronto-temporal focus and surprisingly no clear PPR. The son bi-frontal spontaneous epileptiform activity (L>R), generalised PPR. MRIs showed a mild asymmetrical ventricle for the son (R>L) and the father (L>R). Both children showed skeletal abnormalities. Karyotype of the children were normal.
Conclusion: This family shows a bi-parental inheritance of PPR, epilepsy, developmental delay as well as gross skeletal abnormalities. The EEG helps in characterising the phenotypes. Most likely there are complex interactions between the genes involved. Although there are some similarities with the Niikawa-Kuroki or the Borjeson-Forssman-Lehmann syndrome, they do not fit into these syndromes, and there are no obvious candidate genes for the specific components of the phenotype.

p768
Possible Association Between a Haplotype of the GABA(A) Receptor Beta3 Subunit Gene and Childhood Absence Epilepsy
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Purpose: Childhood absence epilepsy (CAE) is considered to be a genetic disease, but genes responsible have not yet been identified. In a previous study of our group, association between the GABA(A) receptor beta3 subunit gene (GABRB3) and 48 CAE cases was found (Feucht M et al. Biol Psychiatry 1999; 46(7):997-1002). Subsequently, we identified several SNPs (single nucleotide polymorphisms) in the coding, non-coding and gene regulatory sequences of the GABRB3 gene. In the present work, we performed an association study with haplotypes of the GABRB3 gene and we examined the transcriptional activity of the promoter haplotypes using a luciferase reporter assay.
Methods: Haplotypes were determined by cloning and sequencing of the respective DNA fragments and tag-SNPs were genotyped in 45 CAE core families using PCR-RFLP (restriction fragment length polymorphisms) analysis or allele specific PCR. Further, exon1a promoter haplotypes were cloned in front of the reporter gene luciferase. These constructs were transfected into human NT-2 cells and luciferase activity was measured.
Results: Five haplotypes were defined and a subsequent association study showed significant association (p=0.003017) between the GABRB3 gene and CAE. We further verified that the promoter haplotype 2 associated with CAE has a significantly lower activity in an in vitro luciferase expression assay compared with those haplotypes overrepresented in the normal controls.
Conclusion: These data suggest a role for the exon1a promoter haplotype variant 2 in the pathogenesis of CAE. Supported by the Jubiläumsfonds of the Austrian Nationalbank.

p769
EEG and Mutational Analysis of the GABA-A Receptor 1 Subunit Gene (GABRA1) in Girls with Idiopathic Gonadotropin Dependent Precocious Puberty
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Purpose: To investigate functional mutations or polymorphisms of gene GABRA1 in girls with idiopathic gonadotropin dependent precocious puberty (IGDPP) and normal brain MRI and to correlate with EEG findings. GABA is important as an inhibitory neurotransmitter in the intrinsic mechanism of pubertal onset, cortical hyperexcitability and epilepsy.
Methods: We studied 31 girls with clinical and hormonal diagnosis of IGDPP (6 familial and 25 sporadic) and 73 unrelated controls. 2 patients also had idiopathic generalised epilepsy and 23 performed EEG. Genomic DNA was extracted from peripheral blood and the entire coding region (exons 3-11) was amplified using specific intronic primers and direct automatic sequencing. Two polymorphisms were studied by Genescan software, PCR and enzymatic restriction analysis.
Results: EEG revealed abnormalities (spike, sharp-wave and spike and slow-wave paroxysms, intermittent delta-wave rhythm) in 6 (4 without epilepsy) of 23 girls with IGDPP. Automatic sequencing did not show potential functional mutations. We identified 7 polymorphisms (2 exonic variants, 156T>C and 1323G>A; 5 intronic variants, IVS2-712(GT)n, IVS3+12A>T, IVS8+45T>G, IVS9+76T>G and IVS10+15G>A). Genotype distribution and allele frequency of polymorphisms were not statistically different between unrelated patients and controls, and patients with and without EEG abnormalities.
Conclusion: GABRA1 functional mutations or polymorphisms do not seem to be involved in premature GnRH-secretion and precocious puberty in girls. In addition, EEG abnormalities reflecting cortical hyperexcitability were found in patients without epilepsy, which suggests that other GABA receptor particles may be involved in IGDPP and EEG should be part of the investigation.

p770
Molecular Analysis of Idiopathic Generalised Epilepsy in Volga-Ural Region of Russia
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Purpose: We aimed to study the association of some polymorphic DNA-loci, linked to an epilepsy gene, with an increased risk of developing epilepsy.
Methods: In this study we carried out analysis of polymorphic DNA-loci D5S402 and D5S422, linked to the GABRG2 (γ2 subunit of γ-aminobutyric acid receptor) gene, DNA-loci D2S124 and D22330, linked to SCN1A (α1 subunit of neuronal sodium channel) gene, STR-polymorphism and SNP polymorphism A522C in the GRIK1 (kainite-selective GluR5 receptor) gene. Genotyping of these loci were determined on DNA samples of 125 IGE patients and 150 healthy donors.
Results: The analysis of D5S402 polymorphisms showed that allele 2 (169 bp) is frequent in epilepsy patients in comparison with controls (OR=1.49; $p<0.05$).The research of D2S124 revealed significant differences in the distribution of allele and genotype frequencies between IGE patients and healthy donors (OR=1.7; $p<0.05$). The frequencies of prevalent 107 bp and 115 bp alleles of STR-polymorphism in GRIK1 gene in IGE-patient were 15% and 6%, and in control group - 23% and 39% ($p<0.05$). No significant differences in the distribution of allele and genotype frequencies in D5S422, D2S2330 polymorphic loci and A588C polymorphism of GRIK1 gene were found between patients with IGE and healthy donors.
Conclusion: Our results suggest that GABRG2, SCN1A and GRIK1 genes may be involved in epileptogenesis of common forms of IGE in Volga-Ural region.

p771
Frequency of Mutations in the EFHC1 Gene in a Large Group of Patients with Juvenile Myoclonic Epilepsy
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Purpose: To perform mutation screening in the candidate gene EFHC1 in a large group of patients with juvenile myoclonic epilepsy (JME). The EFHC1 gene contains an EF-hand motif, suggesting a role

in neuronal calcium equilibrium. Recently, putative mutations were described in exons 2, 3, 4 and 5 of this gene in a few Mexican families segregating JME.
Methods: We performed mutation analysis of the EFHC1 gene in 53 patients with JME, and 54 controls. Individuals were genotyped by PCR using seven pairs of primers that amplified the entire coding region and exon/intron boundaries of exons 1 to 5 of the EFHC1 gene. PCR products were analysed by the single-stranded conformation polymorphism (SSCP) method and DNA sequencing.
Results: SSCP analyses detected different patterns of migration for exon 3, in 1 JME patient and 2 control subjects, and for exon 4, in 3 patients. Sequence analysis for exon 3 of the fragments with SSCP band shifts showed an intronic change (A-G) in one control (SNP rs9349626) and a modification in the coding region resulting in an aminoacid substitution (R182H) in another control subject.
Conclusion: To date, our results failed to identify EFHC1 gene variants that could be related to the JME phenotype in our large group of patients. Besides, sequencing analyses found a nucleotide substitution in exon 3 of a control subject, which was previously described in JME affected individuals of the large Belize family (Suzuki et al. Nat Genet. 2004 Aug;36(8):842-9). Therefore, our results confirm that this aminoacid substitution is probably not related to JME.

p772
Juvenile Myoclonic Epilepsy: Antelepsini 1/EFHC1 Functions
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Purpose: In 2004 we showed that myoclonin1/EFHC1 is an epilepsy and polyspike wave-causing gene in chromosome 6p12.1 in 21 affected members of 6 out of 24 JME Hispanic or European American families (Suzuki et al., 2004). Myoclonin1/EFHC1 increased R-type calcium currents that were reversed by JME mutations. Overexpression in hippocampal cells in culture induced apoptosis that was reversed by JME mutations. To further explore the functions of myoclonin EFHC1 in cells, we studied EFHC1 in drosophila melanogaster.
Methods: We performed blast searches of drosophila databases using the human protein sequences of myoclonin1/EFHC1. We expressed the gene EFHC1 ubiquitously as well as specifically to drosophila brain and neuromuscular synapse.
Results: Two drosophila proteins revealed extensive homology with their human counterpart, myoclonin 1/EFHC1 and myoclonin2/EFHC2. One of the disease-causing missense mutations occur in a conserved aminoacid residue of drosophila. Human myoclonin EFHC1 maps to chromosome 6p12.1 and myoclonin 2 to Xp11.4. Myoclonin EFHC1 homologue expressed ubiquitously, drosophila expires. Expressed specifically in brain, cell death produces problems in walking and flying.
Conclusion: Myoclonin 1/EFHC1 has cell death and cell deleterious activities in drosophila brain similar to EFHC1 effects in hippocampal cells in culture. Studies of EFHC1 deleterious effects in neuromuscular synapse of drosophila are ongoing.

p773
Andreas Rett and Benign Familial Neonatal Convulsions
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Purpose: In 1964 Rett and Teubel published a detailed account of a family having neonatal seizures, a condition later called benign familial neonatal convulsions (BFNC). Since then BFNC has been mapped to chromosomes 20 and 8, and two genes have been identified, KCNQ2 and KCNQ3. It becomes important to determine if Rett's family (the first report) actually fits currently accepted views of BFNC.
Methods: We traced the family through the birth registry in Vienna by initials and birth dates. Three family members consented to medical interview, neurological examination, EEG recordings and DNA analysis. All exons from KCNQ2 and KCNQ3 were sequenced by standard methods in the proband. Variants were examined for familial segregation by sequencing the other two family members.
Results: Two brothers had seizure onset at day 3 and remission, respectively, by one month and 3-4 months. Their seizures were generalised tonic at onset with cyanosis, and occurred during wakefulness and sleep, with a brief postictal period. 7 other family members had neonatal seizures. 3 of the total of 9 developed tonic-clonic seizures on awakening, from ages 2-3 to 13-14 years (adding to our knowledge about BFNC). None of these seizures were provoked by any stimulus (except once by fever). Recent EEGs were normal. DNA analysis of 2 affected individuals showed a single-base deletion in the C-terminus of KCNQ2.
Conclusion: The ages at onset, clinical history, and DNA results are compatible with a diagnosis of BFNC. We conclude that Rett's astute description of BFNC semiology has withstood the test of time.

p774
Mutation Analysis of the LGI1/Epitempin Gene in 48 patients with Distinct Epilepsy Syndromes
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Purpose: We describe a mutation analysis of the LGI1 Gene in 48 unrelated patients with distinct epilepsy syndromes to investigate whether disease-causing mutations in LGI1 are also responsible for other epilepsy syndromes than autosomal dominant partial epilepsy with auditory seizures (ADPEAF).
Methods: The coding exons and the intron-exon boundaries of LGI1 were PCR amplified. The BigDye® Terminator Cycle Sequencing kit (version 3.1) was used for sequencing. The resulting DNA-fragments were separated by the ABI PRISM® 3730 DNA analyser and the sequences analysed with the ABI DNA Sequencing Analysis software. Pyrosequencing was used to screen control individuals for the identified genomic variations.
Results: We detected 3 intronic polymorphisms (IVS1-55T>C, IVS2-37A>C and IVS6-18T>C), one exonic polymorphism (F219F) and two polymorphisms in the 3'UTR (c.1854G>A and c.1889T>C), but no coding mutations were identified. Unfortunately, all SNPs were detected in several control individuals or did not segregate with the phenotype.
Conclusion: We can conclude that genomic variations in the LGI1 gene are not likely to be involved in the aetiology of epilepsy patients other than ADPEAF patients. Screening of non-ADPEAF patients for

LGI1 mutations appears not useful in genetic counselling of these patients.

p775
Searching for a New Locus for Autosomal Dominant Lateral Temporal Lobe Epilepsy (ADLTLE)
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Purpose: To perform linkage studies in the candidate regions surrounding the LGI2, LGI3 and LGI4 genes in a kindred with ADLTLE with no mutations in the LGI1 gene and no linkage to chromosome (ch) 10q.
Methods: We studied 23 affected individuals in a single family segregating ADLTLE. All individuals recruited for the study were interviewed and examined by a neurologist. In addition, all 23 family members had high resolution MRI scans. A total of 42 family members were genotyped for 9 polymorphic dinucleotide repeat markers flanking the LGI2, LGI3 and LGI4 genes. Two-point lod scores (Z) were calculated using the LINKAGE package.
Results: Auditory auras were reported by 18 of 23 patients (78%). Deja-vu phenomena, associated to auditory auras, were reported by 13/18 (72%). 3 individuals had only isolated frequent deja-vu episodes, and 2 individuals had only generalised tonic clonic seizures. MRI scans of all 23 patients in this kindred were normal and two-point lod scores were significantly negative ($Z < -2.00$) for all markers tested.
Conclusion: Most affected individuals in this kindred have deja-vu phenomena suggesting involvement of mesial aspects of temporal lobe structures as well. This clinical characteristic is not a common feature in ADLTLE families with mutations in the LGI1 gene. In addition, we found that mutations in the LGI2, LGI3 and LGI4 genes are not causing ADLTLE in the family studied. A wide genome search is under way in order to identify the causative gene in this kindred.

p776
Multiparametric MRI in Patients with Familial and Sporadic Temporal Epilepsy with Auditory Auras
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Purpose: We performed a multiparametric MRI study in patients with autosomal dominant lateral temporal epilepsy (ADLTE) and idiopathic partial epilepsy with auditory features (IPEAF) in order to find out focal abnormalities not detectable with conventional MRI techniques.
Methods: We included 11 patients (4 with ADLTE associated with epitempin mutations, 4 with ADLTE without epitempin mutations and 3 with IPEAF) and 24 age and sex-matched healthy controls. All patients had a detailed routine and sleep EEG investigation. Each patient and control underwent conventional MRI, voxel-based morphometry (VBM), diffusion tensor imaging (DTI) and magnetisation transfer imaging (MTI).
Results: Overall the EEG showed temporal lobe abnormalities (localised over the left side in 7 cases). Conventional MRI was negative. VBM demonstrated significantly reduced grey matter volume in the left mesial temporal region (mainly parahippocampal gyrus) and left thalamus (inferior-posterior region) in the whole patient group as compared to controls. In addition, the fractional anisotropy (FA) in patients was significantly reduced in the white matter of the left parahippocampal gyrus and the splenium of the corpus callosum.
Conclusion: Our study demonstrates that a multiparametric MRI study may disclose otherwise undetectable focal grey and white matter abnormalities in the temporal lobe of patients with genetically-related forms of lateral temporal lobe epilepsy. These abnormalities are consistent with a malformative rather than an acquired origin.

p777
Focal Cortical Dysplasia: Family Studies Provide Evidence for a Genetic Basis
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Purpose: Whilst considerable progress has been made in understanding the clinical and pathological features of focal cortical dysplasia (FCD), little is known regarding the aetiology. Most cases of FCD occur sporadically and familial cases are not recognised apart from a single family reported with FCD and schizencephaly. Here, we present the familial occurrence of FCD and malformations of cortical development (MCD).
Methods: Three families where probands had FCD and a relative had a MCD were ascertained. We studied the family history of seizure disorders in family members and imaging was performed in affected individuals. Histological examination was available on 5 patients.
Results: The probands all had pathologically confirmed FCD. In family 1, the first cousin had a ganglioglioma. The first cousin of the proband in family 2 had a confirmed dysembryoplastic neuroepithelial tumour (DNET). The nephew of the proband in family 3 had MRI-diagnosed FCD. All affected individuals presented with seizures with mean onset 7.5 years (range 3-12 years). Partial seizures were intractable, sometimes with secondary generalisation leading to epilepsy surgery in 5. The malformations were located in the occipital lobe in one family and the temporal lobe in another.
Conclusion: These families add clinical genetic evidence that FCD may have a genetic basis. Although no susceptibility genes for FCD are currently known, mutations in such genes could lead to a spectrum of malformations including FCD, DNET and ganglioglioma. Identification of causative genes would lend valuable insights to the neurobiology of these disorders.

p778
Familial Frontal Lobe Epilepsy with Versive Seizures
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Purpose: To characterise the genetic and clinical features of a three generation Spanish family with an epileptic syndrome characterised by versive seizures and myoclonus.
Methods: We identified an extended family including 11 affected individuals presenting partial epilepsy with versive seizures. Personal interviews and DNA samples were obtained from 21 individuals. A whole-genome-screen using microsatellite markers and haplotype and linkage analysis were performed.
Results: The proband presented a phenotype characterised by palpebral myoclonus, oculoencephalic versive seizures, photosensitivity and psychomotor delay. Age of seizure onset ranged from 6 to 21 years (mean 13 years). EEGs showed focal discharges and seizures were frequently secondary generalised. The mode of inheritance was consistent with an autosomal dominant pattern with incomplete penetrance. We excluded linkage to the benign adult familial myoclonic epilepsy (BAFME) loci. Linkage to a specific chromosome region with a maximum lod score of 2.67 (theta=0) was found.

Conclusion: We describe a family that may represent a previously undescribed form of familial partial epilepsy. A suggestion of linkage to a specific chromosome region in this syndrome was found.

p779
Partial Epilepsy and 47 XXX Karyotype: Report of Four Cases
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Purpose: Epilepsy can be part of the phenotypic spectrum of various types of chromosomal aberrations. Trisomy X is one of the most common chromosome abnormalities characterised by great clinical variability. Up until now, epilepsy has rarely been described in patients with 47 XXX karyotype.
Methods: We report the case of 4 girls with epilepsy with 47 XXX karyotype identified by R-banded chromosome analysis performed according to standard procedures on lymphocytes from peripheral blood cultures.
Results: Our four 47 XXX patients are characterised by moderate to severe mental deficiency, and partial epilepsy with various degrees of severity. The epileptic phenotypes of our patients share many common features: childhood onset, partial seizures with prolonged duration, ictal motor manifestations with head or eye deviation and/or clonic jerks, occurrence of the seizures in clusters, limited electroencephalographic information.
Conclusion: Although a specific electro-clinical pattern could not be defined, our report suggests that the association of partial epilepsy in 47 XXX girls is not fortuitous and reinforces the recommendation for karyotype analysis in patients and adults with epilepsy and cognitive disorder, even without dysmorphic features. Our report also enlarges the clinical spectrum of 47 XXX phenotype. Recognition of chromosomal aberrations in epilepsy patients is important for clinical follow-up, familial information, and genetic counselling.

p780
Polyalaniane Tract Analysis in the ARX Gene: Looking for Mutation Associated with West Syndrome
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Purpose: It has been known for a long time that aminoacids homopolimeric tracts are abundant in eukaryotic proteins. In the 1990s the new type of mutation, "dynamic mutation", expansion of CAG repeats coding for polyglutamine (poly-Q) tracts was described, as a cause of the group of human neurodegenerative disorders. Recent findings have also pointed to the polyalanine (poly-A) stretches expansion as a pathogenic mechanism in some congenital malformation, skeletal dysplasia and nervous system abnormalities. Expansion/duplication one of the two polyA tracts in the 2 exon of the ARX gene represents the most frequent mutation in patients with ARX-associated West syndrome (WS, MIM 308350), but this mutation also has a different clinical manifestation as X-linked mental retardation and Partington syndrome. In about 40% of West syndrome probands with any ARX mutation, the duplication of poly-A tract [428-451dup(24bp)] has been described, so this gene region could be denoted as a "mutational hotspot" for cryptogenic/idiopathic WS and the place of first choice for mutation analysis. The purpose of this study was to analyse the polyA tracts in the ARX gene in a selected group of Polish patients with cryptogenic WS.
Methods: West syndrome represents a particular type of seizure (infantile spasms), hypsarrythmia on EEG and mental retardation. Among patients referred to our Clinic with West syndrome, the group of 7 affected boys was selected, fulfilling the strict diagnostic criteria of cryptogenic/idiopathic form of disease. All patients were the firstborn to healthy parents, with delivery at 37 week gestation. They all presented normal psychomotor development before seizure onset. Patients' EEG showed symmetric hypsarrhythmia with absence of focal abnormalities. Brain MR images, routine blood, metabolic, CSF and urine tests were normal. DNA was extracted for all selected subjects. Molecular analysis of the one prone to expansion, polyA coding stretches in ARX gene [428-451dup(24bp)] was performed. To check second polyA expanding region (GCG)10+7 the part of exon2 covering both polyA regions was analysed. In both cases the PCR reactions were performed according to already published methods.
Results: Analysis of the both polyA stretches in the exon 2 of ARX gene, did not show expansion/duplication in any of them for all selected subjects. The next step of mutation analysis is checking the other, already known mutations (1058C>T/P3532) and 5(IVS4-816_Ex5701/del/R483fs) and sequencing of the whole exonic regions to search for new alterations
Conclusion: Epilepsy is often associated with mental retardation (MR) and vice versa. The ARX gene is an example when genetic abnormalities not only in the same gene, but also of the same type, may be an underlying combination of MR and epilepsy, given the evidence for association between those two manifestations. There is still not enough information about genotype/phenotype correlation for ARX associated disorders. Detailed analysis of this gene in patients with clinically characterised ARX associated syndromes/disorders seems to be valuable for better understanding their pathophysiology and could have also diagnostic value. Mutation analysis of the ARX gene in the cases of boys with cryptogenic/idiopathic West syndrome, may reveal the cause of the disease. Detection of the mutation is important for the proband's family for the reason of accurate genetic counselling. As we did not find mutations in polyA coding tract, further analysis is necessary to confirm/exclude alteration of ARX gene in all WS patients under consideration.

p781
Brain Derived Neurotrophic Factor (BDNF) and Multidrug Resistance (MDR) Gene Polymorphisms in Patients with Mesial Temporal Sclerosis (MTS)
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Purpose: The association between partial epilepsy and BDNF gene polymorphisms is shown. In a study it is argued that in patients with MTS, MDR proteins are upregulated, which contribute to their role in drug resistance. The cell distribution patterns may not solely be linked to critical drug resistance but suggest different cellular functions. No reports about both BDNF and MDR in patients with MTS have been seen in the literature. We investigated the gene polymorphism on BDNF and MDR in patients with medial temporal lobe epilepsy and MTS to better understand their functions.
Methods: 50 patients with MTS and 50 patients with medial temporal lobe epilepsy without MTS were included in this study. A control group of 50 healthy individuals was also constituted. The 50 healthy controls were matched for their age and sex ratios. The mean age of the patients at admission was 19 years (17-76). There were histories of febrile seizures in 31 patients. Aura was described in 43 patients; the most defined auras were abdominal epigastric sensation and psychic. Simple and complex partial seizures were most frequently seen while secondarily generalised seizures were rarely observed.
Results: Genomic DNA was extracted from peripheral blood leukocytes using standard protocols. BDNF and MDR gene polymorphism were analysed using a PCR-restriction fragment length polymorphism method.
Conclusion: BDNF and MDR gene polymorphism in patients with MTS and without MTS are discussed. Among patients of epilepsy, a complex interplay between genetic and acquired risk factors result from multiple genetic polymorphisms.

p782
Single Nucleotide Polymorphisms
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Purpose: P-glycoprotein 170 encoded by the multidrug resistance 1 (MDR1) gene, exports various antiepileptic drugs out of the cell of BBB, which confers multidrug resistance. This study was performed to elucidate the relationship between single nucleotide polymorphisms (SNPs) of the MDR1 gene and drug resistance in some Koreans with epilepsy and to reveal the genetic characteristics of SNPs in healthy Koreans.
Methods: Three known SNPs in the MDR1 gene of T1236C, G2677T/A, and C3435T (each in exon 12, 21, and 26) were genotyped in 322 enrolled subjects, classified as 'RS' group (n = 99) with drug resistant epilepsy, 'RP' (n = 108) with drug responsive epilepsy, and control of health volunteers (n = 115). The frequencies of genotype, haplotype and combined polymorphisms (CPs, associations of genotypes of each polymorphism) were compared among three groups, and the frequencies in Korean volunteers were compared with other ethnic data.
Results: At the three SNPs, the genotype frequencies had no difference between RS and RP groups. In comparison with the control group, only at the position 1236 in exon 12, TC was more frequently observed in RS than control (41.2% vs 56.2%, p = 0.0466). Neither CPs nor haplotypes showed any difference among the three groups. Korean volunteers shared similar genetic characteristics of the SNPs to Asians but different from Caucasians.
Conclusion: For three SNPs in the MDR1 gene, there was no difference of genotype and haplotype frequencies between drug resistant and responsive groups in epilepsy. Koreans shared similar genetic characteristics of the SNPs to Asians but different from Caucasians.

p783
Pharmacogenetics in Epilepsy: An Australian Prospective Study
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Purpose: To report initial data of a prospective study assessing pharmacoresistance (PR) and adverse drug reactions (ADR) in newly treated epilepsy patients and the relationship to genetic variability in candidate genes.
Methods: Data was collected on side effects (ADR) and pharmacoresistance (PR) at 3 and 12 months. Polymorphisms were assessed in genes involved in drug transport, metabolic pathways and sites of action (sodium channel).
Results: Of 165 patients (carbamazepine, n=75 and valproate, n=56), 40 (24%) experienced ADRs and 22 were pharmacoresistant (PR). A number of interesting trends were observed. Variant of UGT1A gene (AA genotype), known to decrease valproate metabolism by glucoronidation, showed an increased incidence of ADRs (OR6, AA9/18 vs GG3/22). The CC genotype of multi-drug transporter receptor (MDR1) gene showed an increase in pharmacoresistance (OR5, CC 5/16 Vs TT 2/24) and increased ADRs was associated with the TT genotype (OR4, TT 8/24 Vs 2/16). SCN1 AA genotype, known to alter the alpha unit of the sodium channel, was associated with increased ADRs (OR3, AA5/20 Vs GG1/12) and the SCN1GG genotype associated with pharmacoresistance (OR 4, AG 2/25; GG 3/12), which is interesting in light of the recent publication of an association with the SCN1 GG genotype with high maximal doses of carbamazepine. We found an association with maximal valproate dose (mg/day) (AA=1070 n of 10, AG=840 n of 15, GG=913 n of 8) but not with carbamazepine dose.
Conclusion: Preliminary data analysis indicates trends for an association between genotypes and the outcome of antiepileptic drug treatment.

p784
CYP2C9 Polymorphism in Patients on Phenytoin Therapy
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Purpose: CYP2C9, a major enzyme in the liver, is responsible for the metabolism of numerous clinically important drugs, such as phenytoin, with a narrow therapeutic index. Polymorphism of CYP2C9 has been reported previously. In this preliminary study, the frequency of CYP2C9*2 & CYP2C9*3 allelic variants were examined in Turkish epilepsy patients who received phenytoin treatment.
Methods: A group of 25 male and female subjects was studied after obtaining written informed consent; they have all been treated with phenytoin for at least two weeks. After the isolation of DNA from peripheral blood the allelic variants were studied by polymerase chain reaction and restriction fragment length polymorphism. Plasma phenytoin concentrations were determined utilizing fluorescence polarisation immunoassay (FPIA) on Abbott AxSYM system.
Results: The frequencies of CYP2C9 genotypes in the study group were found to be 76%, 12%, 12% for CYP2C9*1/1, CYP2C9*1/2, and CYP2C9*1/3 respectively. The mean phenytoin serum concentrations were determined to be 6.71 ug/ml for genotype CYP2C9*1/1, 9.23 ug/ml for CYP2C9*1/2 and 15.77 ug/ml for CYP2C9*1/3.
Conclusion: The results show that there is a strong correlation between CYP2C9 genotypes and phenytoin dose requirement. It is suggested that the CYP2C9 genotyping can be used routinely to obtain efficient phenytoin therapy and to lower the risk of concentration dependent intoxications of phenytoin in mutated carriers.

p785
Foetal Valproic Acid Syndrome: Is a Common Mutation in the Methylene-tetra-hydrofolate Reductase Gene a Genetic Risk Marker?
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Purpose: Women with epilepsy carry a higher risk of malformations in their offspring than do women in the background population. The risk has been shown to be related to intra utero exposure of antiepileptic drugs (AED), in particular valproic acid (VPA). Previous

studies have drawn attention to the possibility of a hereditary susceptibility to the teratogenic effect of AED, with specific focus on the common 677 C-T mutation in the methylene-tetra-hydrofolate reductase (MTHFR) gene. We wanted to investigate whether the mutation can be used as a genetic marker for the risk of foetal VPA syndrome in women on VPA monotherapy.
Methods: Based on neuropsychological testing and the appearance of specific minor and major malformations, we confirmed the diagnosis of foetal VPA syndrome in 4 children exposed to VPA in utero. We then performed genetic testing on the mothers (n=4).
Results: Only 1 of the mothers (25%) were heterozygote for the mutation, none were homozygous (0%).
Conclusion: The common 677C-T mutation cannot in any practical sense be used in the clinic as a genetic risk marker.

Wednesday 31st August and Thursday 1st September 2005
13:15 – 14:15
Poster Session
Drug Therapy

p786
Differential Role of Y2 and Y5 Neuropeptide Y Receptors in Suppression of Seizures
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Purpose: Neuropeptide Y (NPY) is considered to be a powerful antiepileptic agent in different animal models. However, it still remains controversial which NPY receptors mediate this effect.
Methods: We used a gene knockout strategy for Y2 and Y5 NPY receptors in mice to explore the antiepileptic effect of NPY in different in vivo and in vitro epilepsy models.
Results: In vitro, in both Y2 and Y5 knockout (Y2-/- and Y5-/-) mice, NPY exerted partial anti-epileptiform effect on 0Mg2+-induced bursting activity in the hippocampal CA3 area. In contrast, in slices from double knockout (Y2Y5-/-) mice, NPY was ineffective. The frequency of epileptiform discharges in Y2Y5-/- mice was higher than in wild-type (WT) and other mutant mice, suggesting increased excitability. In vivo, systemic kainate induced more severe seizures in Y2Y5-/- mice than in WT mice. Similarly, Y5-/- but not Y2-/- mice displayed more severe seizures than WT animals. During hippocampal kindling, another in vivo epilepsy model, Y5-/- mice developed generalised seizures faster than WT mice. Kindling afterdischarges in amygdala, but not in hippocampus, were significantly longer in Y5-/- mice. We also found decreased Y1 receptor binding in hippocampal areas of all three mutant strains. In vitro, in both Y2 and Y5 knockout (Y2-/- and Y5-/-) mice, NPY exerted partial anti-epileptiform effect on 0Mg2+-induced bursting activity in the hippocampal CA3 area. In contrast, in slices from double knockout (Y2Y5-/-) mice, NPY was ineffective. The frequency of epileptiform discharges in Y2Y5-/- mice was higher than in wild-type (WT) and other mutant mice, suggesting increased excitability. In vivo, systemic kainate induced more severe seizures in Y2Y5-/- mice than in WT mice. Similarly, Y5-/- but not Y2-/- mice displayed more severe seizures than WT animals. During hippocampal kindling, another in vivo epilepsy model, Y5-/- mice developed generalised seizures faster than WT mice. Kindling afterdischarges in amygdala, but not in hippocampus, were significantly longer in Y5-/- mice. We also found decreased Y1 receptor binding in hippocampal areas of all three mutant strains.
Conclusion: (i) Both Y2 and Y5 receptors mediate NPY's antiepileptic effect in a synergistic manner in vitro. (ii) In systemic seizures, antiepileptic effect of NPY can be mediated via activation of extra-hippocampal Y5 receptors alone. (iii) Since Y1 receptor activation might be proconvulsive, decreased Y1 receptor binding could be a compensatory reaction to increased excitability in these mice.

p787
Antiepileptic Drugs-induced P-glycoprotein Overexpression in Madin-Darby Canine Kidney (MDCK) Cells
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Purpose: The prime objective of therapy of epilepsy is the complete suppression of all seizures without impairment of CNS functions. It is commonly accepted that many epilepsy patients are significantly benefited by currently available pharmacotherapy. Unfortunately, epilepsy is resistant to drug treatment in about one-third of cases, and this intractable epilepsy may be due to multidrug resistance induced by conventional antiepileptic drugs. The phenomenon is sometimes associated with an overexpression of multidrug resistance gene 1 (MDR1), which is located on chromosome seven and encodes P-glycoprotein (Pgp), a transmembrane protein of 170 kDa. The purpose of this study was to determine if the overexpression of Pgp could be induced in MDCK cultures by some commonly used anticonvulsants.
Methods: MDCK cells were treated with topiramate (10 and 100 mM), phenobarbital (30 and 300 mM), carbamazepine (30 and 100 mM), levetiracetam (30 and 300 mM) and phenytoin (30 and 100 mM) for 72 h. Drug-containing medium was replaced every 24 h. Western blot analysis was performed to compare the P-glycoprotein immunoreactive protein levels in control and drug-treated MDCK.
Results: Topiramate, phenobarbital, carbamazepine, levetiracetam and phenytoin induced overexpression of Pgp in MDCK cells. This upregulation of Pgp was dose-dependent, but different for each used antiepileptic drug. Significantly higher levels of Pgp were detected at 30 and 100 mM of carbamazepine and phenytoin. Lower expression of Pgp was present in topiramate, levetiracetam and phenobarbital treated cells.
Conclusion: Treatment with antiepileptic drugs may contribute to the expression in MDCK of MDR1 and its protein product, Pgp.

p788
Multidrug Tolerance is One of the Important Mechanisms of Pharmacoresistance to Antiepileptic Drugs
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Purpose: The responses to antiepileptic drugs are heterogeneous among patients. There is totally no effect among some patients, whereas among others seizures are completely or partially controlled initially but after some time (tolerance development latency), there is no effect any more even though the dosage is increased (functional drug tolerance). Structurally and pharmacologically different drugs have similar responses even to the same patient (multidrug tolerance). We investigated clinical features of multidrug tolerance.
Methods: Epilepsy cases between 1999 to 2004 at our epilepsy clinic were retrospectively analysed.
Results: There were 23 cases who developed multidrug tolerance. The age of development of multidrug tolerance is 2 to 26 years (median 7.5 years). The disease history was 0.92 to 18 years (median 5 years). The epileptic seizures or epilepsy syndromes were variable. They had at least 1-22 attacks each month (median 3 attacks per month, n=9) and most had 1-11 attacks daily (median 3 attacks daily, n=18). Most patients had mental retardation or development regression (this series had hereditary metabolic errors screened). The major feature was that they developed multidrug tolerance to at least two antiepileptic drugs. During the tolerance development latency, seizures were partially controlled among 3 cases and among others completely controlled. The tolerance development latency was 17 to 225 days (median 40 days). Finally almost all antiepileptic drugs available in China failed to control their seizures.
Conclusion: Research on the fundamental mechanisms of pharmacoresistance focused on this multidrug tolerance patient subgroup may be a new strategy needing to be considered

preferentially. Key words are epilepsy, intractable, drug tolerance, pharmacoresistance, antiepileptic drugs.

p789
Our Experience in the Treatment of Catamenial Epilepsy with CBZ
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Purpose: To evaluate the effectiveness of CBZ in catamenial epilepsy.
Methods: We studied the protocols of 37 patients with catamenial epilepsy treated with CBZ. In 12 patients (32.4%) the epilepsy attack is on the first day of the menstrual cycle, in 25 patients (67.6%) it is during the menstrual cycle. In 5 patients epilepsy began at the first menstrual cycle. The age of patients was from 12 to 45 years. All the patients were followed for ten years of treatment with carbamazepine. In all the patients diagnosis was made clinically, and in 30 patents the EEG pattern was paroxistic. The maintenance treatment for 15 patents was 400 mg of CBZ daily, and for 22 of them 600 mg of CBZ daily. For all of the patients, three days before and after the menstrual cycle the dose of CBZ was increased by 200 mg daily.
Results: 13 patients (35%) are now free of epileptic seizures, 7 patients (19%) have had one epileptic attack in seven months, and 17 patients (46%) have had one epileptic attack in five months.
Conclusion: The treatment of catamenial epilepsy with a maintenance dose of 400 mg daily of CBZ, plus an increase of dose of 200 mg daily during the menstrual cycle has a satisfactory effect.

p790
Attempt for Treating Catamenial Epilepsy with Acetazolamide as Add-on Therapy
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Purpose: Catamenial epilepsy (Greek katomenios - monthly) is a disorder that affects a lot of women with epilepsy. It is characterised by seizures that appear at specific points in the menstrual cycle. Cyclical changes in the circulating levels of estrogens and progesterone are important factors of the condition. Estrogens are proconvulsant, while progesterone has the opposite effect. Imbalance of fluids and electrolytes can also play a role. Other possibilities are a lower level of antiepileptics, or an increase of affective stress prior to menstrual cycles. There no specific treatment; conventional therapies often have a disappointing lack of effect. In our study we tried to evaluate effectiveness of acetazolamide as add-on therapy for treating women with catamenial epilepsy.
Methods: The study assessed patients treated as having catamenial epilepsy from 1998-2004. All patients had a full investigation for their epilepsies, including electroencephalographic studies, neuroimaging and laboratory findings.
Results: 26 patients aged from 16-30 years (mean age 20.96, median 19 years) were assessed. Prior to introduction of acetazolamide 16 were on monotherapy (11 on carbamazepine and 5 on valproate) and 10 on polytherapy (carbamazepine, valproate, vigabatrine). 17 had partial seizures (partial complex seizures mainly) and 9 had primarily generalised seizures. After the introduction of acetazolamide, 2 days before menstrual cycles, during menstrual cycles and 2 days after, 16 patients (61.54%) were seizure free during a follow up period of 6 months to 2 years. In 4 patients we had no effect (15.38%), and in 6 patients we had reduction of seizures from 25-75%.
Conclusion: We conclude that intermittent treatment with acetazolamide can be helpful in some patients with catamenial epilepsy.

p791
Seizure Control in the Course of Pregnancy under Treatment with Lamotrigine, Carbamazepine and Valproic Acid in Monotherapy: Observations from the German EURAP project.
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Purpose: Antiepileptic drugs (AED) underlie modified pharmacokinetics during pregnancy. Regarding lamotrigine (LTG) a clinically relevant decrease of serum concentration levels has been reported. EURAP (European Registry of Antiepileptic Drugs and Pregnancy) enables a comparison of seizure frequency during pregnancy.
Methods: EURAP is a prospective study to investigate pregnancies with AED-exposition. Women taking AED at the time of conception are included until the 16th week of gestation time and were observed until one year post partum. We compared the first and third trimesters regarding seizure frequency and dose modification in patients, who got pregnant while treated with LTG, carbamazepine (CBZ) or valproic acid (VPA) in monotherapy.
Results: Until January 2005, 388 pregnant women were enrolled in Germany, 171 have already given birth. 81% of patients were treated with monotherapy. The three most frequently used AED were LTG (n=44), CBZ (n=36) and VPA (n=48). In the first trimester 25% of the women had seizures (20% of LTG patients, 22% of CBZ patients, 31% of VPA patients). In the third trimester 25% of the patients had seizures (23% of LTG patients, 22% of CBZ patients, 25% of VPA patients). In 22% of the patients dose modifications were performed (in 34% of LTG patients, 14% of CBZ patients, 17% of VPA patients).
Conclusion: An increased seizure risk under LTG treatment during pregnancy cannot be confirmed. Relatively many dose modifications in LTG monotherapies compared to CBZ and VPA are remarkable. The highest seizure frequency was observed with VPA in the first trimester. A causal non-compliance cannot be excluded, as serum concentrations are not monitored by EURAP.

p792
Congenital Malformation in Children of Mothers with Epilepsy
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Purpose: To identify the frequency of congenital malformations (CM) in children of mothers with epilepsy (EM) and some related risk factors.
Methods: Prospective study of 370 children of EM carried out from January 1995 - January 2005. A questionnaire was designed to register demographic, clinical and genetic data. Final results were recorded on a data base to make statistical analysis, and results were compared to a control group of 500 children from mothers who did not have epilepsy (NEM).
Results: CM were diagnosed in 9.85% children from EM (36/370) 4.20% (21/500) in children from NEM (odd ratio=2.7; IC of 95%= 2.01-3.3) rate of CM with only one antiepileptic drug (DAEs) was 3.1% to 1.2% of the control (RR=2.1; IC 95%; 1.3-3.5%) rate was 4.9% when taking 2 DAEs (RR=3.6; IC 95%; 2.1-6.5%) and 9.7% if taking three or more DAEs (RR= 6.3; IC 95%; 2.5- 16.3) most common CM were cardiac defects (1.63 % to 0.4%) cleft palate (1.15 %to 0.18%) urogenital abnormalities (1.80% to 0.61%) and defects of the neural tube (1.30% to 0.50%) CM were more frequent in children under valproic acid (14.38%) than those under other DAEs (2.7%) ($p < 001$) daily dose of valproic acid was higher in children with CM than those without CM (1750 to 1000 mg; $p < 0.01$) 37.5% of MC were diagnosed in children from EM with tonic clonic seizures during the first trimester of pregnancy.

Conclusion: CM occurred more frequently in children from EM use of DAEs in pregnancy. Polytherapy, high doses and seizures during the first trimester are some risk factors of CM in children from EM.

p793
Cardiac Malformations are Increased among Infants of Mothers with Epilepsy
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Purpose: To estimate the risk of cardiac malformations and their relationship to intrauterine exposure to anti-epileptic drugs (AED).
Methods: All infants born to women with epilepsy enrolled in this registry were prospectively evaluated by clinical and echocardiograph examinations at 3 months of age by a cardiologist blinded to the AED exposure. Atrial Septal defects (ASD) <4mm and patent foramen ovale were excluded from defects.
Results: We examined 427 live born babies. The mothers had generalised (44.8%) or localisation related (51.2%) epilepsy. AED exposure was monotherapy in 237 - phenobarbitone (38), valproate (65), carbamazepine (103), phenytoin (29), clonazepam (2) and polytherapy in 116, while 73 infants had no AED exposure. Cardiac malformations were identified in 37 infants (8.7%) - atrial septal sefect 26 (70.3%), tetralogy of Fallot 3 (8.1%), patent ductus arteriosus and pulmonic stenosis 2 each (5.4%), ventricular septal defect, tricuspid or mitral valve defect, transposition of great arteries 1 each (2.7%). There was no correlation between cardiac defect and maternal age, epilepsy syndrome, seizures during pregnancy or folate use. Cardiac defects were significantly more among those with birth weight < 2.5 Kg ($p=0.013$) and abnormal maturity ($p<0.001$). Polytherapy was associated with a higher frequency of malformations (12.3%) than monotherapy (6.8%). Among the monotherapy group, cardiac defects were more frequent with valproate (12.3%) and phenobarbitone (7.9%) compared to others (3.7%).
Conclusion: Cardiac defects were observed in 8.7% of all infants of mothers with epilepsy, ASD constituting 70% of the defects. Phenobarbitone and valproate carried a higher risk of cardiac defects when compared to other AEDs.

p794
Antiepileptic Drugs, Folic Acid and Congenital Abnormalities: A Nation-wide Hungarian Case-control Study
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Purpose: Folic acid supplementation in pregnancy reduces the risk of neural tube defects and maybe other abnormalities. Carbamazepine (CBZ), phenytoin (PHT), phenobarbital (PB) and primidone (PRI) decrease blood folate levels and may therefore counteract the effects of exogenous folate supplementation. We evaluated whether folate supplementation reduced the risk of congenital abnormalities (CAs) after exposure to these antiepileptic drugs (AEDs) during early pregnancy.
Methods: The Hungarian Case-Control Surveillance of Congenital Abnormalities (1980-1996) contains disease and exposure data on mothers of 22,843 children with CAs (cases) and 38,151 children without CAs (controls). We assessed the effect of drugs taken in the second and third month of pregnancy, i.e. the time of organogenesis.
Results: Children exposed to CBZ, PHT, PB and PRI, but no folic acid, had an increased risk of CAs (odds ratio 1.5; 95% CI 1.2-1.9). This risk was reduced with folic acid supplementation (odds ratio 1.2; 95% CI 0.8 – 1.8). The risk of CAs increased with the number of AEDs used. The odds ratios for CAs when exposed to 1 AED was 1.57 (95% CI 1.33-1.87) and with folic acid 1.26 (95% CI 0.94-1.68); in children exposed to 2 or more AEDs the risk of CAs were 4.10 (95% CI 1.42-11.8) and with folic acid 2.62 (95% CI 0.59-11.7), all compared to offspring of mothers taking only folic acid. No statistically significant effect modification by folic acid use was found.
Conclusion: Folic acid supplementation in second and third gestational months may have a protective effect on developing congenital abnormalities, also in offspring of mothers taking CBZ, PHT, PB and PRI.

p795
Effect of Anti-epileptic Drugs on Foetal Behaviour
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Purpose: To examine movements in foetuses of women taking the anti-epileptic drugs carbamazepine, valproate and lamotrigine. Selected anti-epileptic drugs have been associated with a higher risk of congenital anomalies and with cognitive development. To date no study has examined the effects of anti-epileptic drug therapy on foetal behaviour.
Methods: Foetuses of 30 women taking three anti-epileptic drugs (carbamazepine: n=10; valproate: n=10; lamotrigine: n=10) and of 20 women unaffected by epilepsy were studied. Foetal movements were observed by ultrasound for 30 minutes at 12-15 weeks gestation. The number of arm, leg, startle and head movements was recorded off-line for each foetus.
Results: Results revealed more movement by foetuses in the carbamazepine group (M=9.62+/-3.15[s.d.]) and less movement by foetuses in the valproate group (M+6.06+/2.37) than by those in the control group (M=6.96+/-3.010). Movement scores of foetuses in the lamotrigine group (M=7.75+/3.03) were similar to those in the control group.
Conclusion: Foetal activity is affected by anti-epileptic drugs and these effects are drug specific. Anti-epileptic medications have been associated with cognitive delay in children. Observation of foetal behaviour reveals the effect of these medications on central nervous functioning during the prenatal period. Evaluation of foetal behaviour may enable the mechanisms by which anti-epileptic drugs exert their long term neurodevelopmental consequences to be determined. Ethical approval was obtained from Queens University Medical Ethics Committee and all participants provided full consent.

p796
Prognosis for Patients with Newly Diagnosed Epilepsy after Status Epilepticus
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Purpose: In approximately 10% of patients, the first unprovoked epilepsy seizure occurs as status epilepticus (SE). Some patients have recurrent seizures, necessitating anti-epileptic therapy. Reports on therapeutic outcomes for this group are scarce.
Methods: The comparison included therapeutic results achieved with 86 epilepsy patients aged 7-82 years with SE as the first manifestation of the condition and the outcome observed in 86 newly diagnosed patients with epilepsy matched for age and seizure type. The analysis included the first monotherapy effectiveness, the percentage of

patients with 3-year remissions during the 5-year treatment course, the percentage of patients cured and the percentage of patients with recurrent seizures following the initial event-free period.
Results: Therapeutic results in newly diagnosed patients with epilepsy with and without prior SE were respectively: the first monotherapy effectiveness (%) 48.8 vs 51.2, 3-year remission (%) 41.9 vs 69.8, drug discontinuation (%) 2.3 vs 16.3, seizure recurrence (%) 17.4 vs 5.8.
Conclusion: Epilepsy with SE as the presenting syndrome has a poorer prognosis than epilepsy with isolated seizures with respect to seizure remission achievement and possibility of curing the patient. These patients manifested more frequent recurrent seizures following an initial remission. No difference has been found in the effectiveness of the first monotherapy employed.

p797
Management of Prolonged Seizures using Intranasal Midazolam
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Purpose: To ascertain the impact of intra-nasal midazolam (INM) on managing prolonged seizures. In particular, parental confidence and preference on using an emergency anti-convulsant, rationale for that preference, perceived speed of action of preferred anti-convulsant, and impact on emergency department attendances.
Methods: 347 parents/carers completed a questionnaire or interview. As the relevant questions and the researcher collating results were common to both, results were combined.
Results: Of 131 children and adults each given 1-20 doses of INM, seizures were controlled in 95.4%, increasing to 97% with increased dose based on weight. The protocol was the same for all, with plastic ampoule 5 mg/1 ml, midazolam dripped directly into the nostrils, and dose 0.2-0.3 mg per kilo administered for a seizure over 3 minutes in children, 5 minutes in adults. There were no respiratory arrests (one slowing of breathing possibly due to the seizure), or nasal symptoms post seizure, nor have there been adverse dental reports. Emergency department attendances are currently being audited, but on parent report attendances have reduced with INM. Of the 347 respondents, 55 had administered rectal diazepam (RD) and 70 had administered INM. Of the 47 who had administered both RD and INM, 33 (70.21%) preferred INM, and 39% considered INM to be effective within 2 minutes, compared with only 8.8% for RD.
Conclusion: INM administered according to our protocol is a safe and reliable means of managing prolonged seizures in the community. Users feel more in control, with cost savings from reducing the number of attendances at emergency departments.

p798
Concentration of Homocysteine in Epilepsy Patients
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Purpose: Recently a theory was established on the cytotoxic effect of homocysteine excess. There was also found a higher homocysteine concentration in epilepsy patients. The aim of the study was to establish whether there is an incidence between hyperhomocysteinemia and receiving anticonvulsant drugs.
Methods: The concentration of homocysteine was measured by using fluorescence polarisation immunoassay. The blood concentration of homocysteine, folate and vitamin B12 was measured in 40 patients. These measurements were made in 15 patients after the first epileptic seizure, in 16 on monotherapy and 9 on polytherapy. The same measurements were made in the control group of patients suffering from low back pain.
Results: Patients on monotherapy had a mean plasma homocysteine concentration 14.85 umol/l ± 6.35 and was higher than in the control group in which it was 12.58 umol ± 3.03. The highest homocysteine concentration had patients receiving phenytoin. Also, a slightly higher plasma homocysteine concentration was found in patients on polytherapy, and after the first epileptic seizure.
Conclusion: The longer the patients suffer from epilepsy the higher the concentration of homocysteine.

p799
Plasma Antioxidant Activity in Elderly Epilepsy Patients on Monotherapy
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Purpose: Increase in oxidative stress has been related both with some types of epilepsies and with antiepileptic drugs. On the other hand, age increases significantly the vulnerability to free radical-induced damage. The objective of the present study was to investigate the total antioxidant status (TAS) of plasma in elderly epilepsy patients, treated with valproic acid, carbamazepine, phenytoin or phenobarbital as monotherapy.
Methods: Our sample included 129 epilepsy patients, aged 60-93 years (mean: 71±7.5), and 40 healthy controls (age range: 60-90, mean: 67±6.5 years). Patients were receiving valproate (N=38), phenytoin (N=38), carbamazepine (N=34) or phenobarbital (N=19). Total antioxidant plasma status was measured by spectrophotometry by using a standardised technique (Randox Laboratories).
Results: As could be expected with this age range, mean TAS values, both in healthy subjects and patients, were lower than reference values for younger adults. No relevant differences in TAS were found between controls (0.751±0.12 µmol/l) and patients (0.774±0.19 µmol/l), nor when comparing the later as a group or when separately analysing each treatment group (VPA: 0.801±0.17µmol/l, PHT: 0.759±0.18 µmol/l, CBZ: 0.728±0.19 µmol/l, and PB: 0.829±0.26 µmol/l). Among controls, women had significantly lower TAS values than men, but this difference was not observed among epilepsy patients.
Conclusion: Our data indicate that neither epilepsy nor antiepileptic treatment significantly decrease the total antioxidant serum activity in elderly patients.

p800
Bone Mineral Density and Calcium Metabolism in Ambulatory Children Receiving Antiepileptic Drug Therapy
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Purpose: Antiepileptic drug (AED) therapy can adversely affect bone health in ambulatory children with epilepsy. The aim of the study was to investigate the influence of carbamazepine, valproate or phenobarbital as single or multiple therapy on bone mineral density (BMD) and calcium levels in our patients.
Methods: We prospectively examined spinal BMD by dual-energy X-Ray absorptiometry and serum total and ionized calcium values in 34 patients, aged between 6-12 years who had seizures, on long-term AED therapy. 10 patients received valproate, 11 carbamazepine, 5 phenobarbital and 8 multiple AEDs. Comparisons were made with a sex and age-matched control group of 35 healthy children. For statistical analyses we used student t-test, Mann-Whitney U-test and Pearson correlation. Significance was at $p< 0.05$.

Results: BMD in the lumbar spine region (L2-L4) is lower in both boys and girls, but significantly in girls with epilepsy ($p<0.05$). The decrease in BMD was not dependent on the duration of therapy, but was in direct correlation with the age and the commencement of therapy. The boys on AET had significantly lower serum total calcium values ($p<0.05$), but patients from both sex groups had significantly lower serum ionized calcium values ($p<0.005$) as compared to controls. The multiplicity of AED therapy was a significant negative determinant of BMD and serum total and ionized calcium values. Significant direct correlation was between BMD and serum total and ionized calcium values in both sex groups.
Conclusion: Children with epilepsy who receive AED therapy may have reduced BMD and serum total and ionized calcium values.

p801
Adverse Effects of Antiepileptic Drugs on Bone Mineralization in Children with Epilepsy
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1) Kyungpook National University Hospital, Daegu, Korea

Purpose: Chronic use of antiepileptic drugs in children with epilepsy may cause a disturbance of bone metabolism. The aim of this study is to evaluate the effects of antiepileptic drugs on bone mineralization in children with epilepsy.
Methods: 75 children with epilepsy were enrolled in the study. They had been on antiepileptic drugs for at least one or more years. Bone mineral density was measured by dual-energy X-ray absorptiometry on the lumbar spine and whole body along with other blood works. Statistical analysis for bone mineral density of subjects was compared with the results of the published data.
Results: Bone mineral density was significantly decreased in the antiepileptic drug treated group as compared with the control group at all ages ($p<0.05$). However, BMD among groups by a variety of different antiepileptic drugs was not significantly different ($p>0.05$).
Conclusion: Because chronic administration of antiepileptic drugs in growing children may cause the disturbance of bone mineralization, early detection and intervention of abnormal bone metabolism should be considered in the management of children with epilepsy.

p802
Evaluation of Side Effects of Antiepileptic Drugs in Marrakech Epilepsy Out-patients
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Purpose: Within the framework of the coverage of epilepsy, the practitioner is brought to prescribe antiepileptic drugs (AED), with different dosages and during a long time. The AED can cause many side effects (SE). Authors analyse the profile of SE of AED in Marrakech out-patients.
Methods: The authors undertook a retrospective study of 240 patients for a period of 3 years and analysed SE noticed during the duration of treatment and its management.
Results: The age of our patients varied between 4 and 64 years (male predominance), mean treatment duration was 14 months. Among the patients under phenobarbital (25), we noticed a high percentage of SE, 15 cases (60%), dominated by cognitive effects, followed by gingival hypertrophy and gastrointestinal SE. In the 94 patients under carbamazepine, 17 presented SE (18%), dominated by sedation, than cutaneous allergy, followed by memory dysfunction. Among the 88 patients under valproic acid, 18 showed SE (24%): dominated by sedation, then memory dysfunction and gastrointestinal SE. In the 23 patients under phenytoin, many SE were noticed (52%), dominated by gingival hypertrophy. With new AEDs very few SE were noticed.
Conclusion: Classical AEDs are responsible for many SE, especially PB and PHT; the new ones have less, but are seldom used due to socio economic difficulties and low coverage of social security; there are also some old habits of many users of AED, especially general practitioners. That is why good management of epilepsy is needed to assure a good quality of life for our epilepsy patients.

p803
Usefulness of the System for Prescribing Anti-epileptic Drugs by Using the Diagram of Clinical Course with Medical Treatment
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Purpose: We drew the diagram of clinical course with medical treatment of epilepsy patients on the computer, and displayed it on the screen of prescription form. We examined the usefulness of this prescription system for adjustment of the drugs.
Methods: Subjects were 82 epilepsy patients with severe motor and intellectual disabilities. We drew the diagram using ClarisWorks ver.4 (Claris Corp.) on the computer and inserted it in the prescription form. The fit frequency was displayed by the bar graph every month. The dose, the administered period and the data of drug concentration were diagrammed. The prescription form was created using FileMaker Pro5 (FileMaker Inc.). We elaborated the treatment strategy referring to the diagram, and adjusted the drugs. We compared the changes of drugs in both periods of 20 months before and after introducing this prescription system.
Results: The alteration of dose was performed only to 25 patients in the former period, but to 48 patients in the latter period. The resumption of drug was not performed to anybody during the former period, but performed to 3 patients during the latter period. The addition of a new drug was performed to 12 patients during the former period, but to 15 patients during the latter period. The discontinuation of drug was performed to 10 patients in both periods.
Conclusion: It became easy to write a prescription referring to clinical course with medical treatment. We showed that it was useful to adjust the dose and re-evaluation of the drug by using our prescription system.

p804
Epilepsy Action Packaging Survey: A Study of the Consistency of Supply of Anti-epileptic Drugs
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Purpose: Over several years, Epilepsy Action members have contacted the charity with complaints of seizure breakthroughs and worsening side effects due to a change in the version of their anti-epileptic drug (AED). This change can be due to switching between branded, generic and parallel imported versions of AEDs.
Methods: To assess the extent of the problem, Epilepsy Action compiled a survey, which was sent to 17,500 members. Responses were received from 1,851 people (response rate of 10.6%).
Results: 31% (576) of respondents had been offered a different version of their usual AED. Of these 23% (168) believed their epilepsy had worsened as a result; 18% (131) experienced more side effects; 14% (103) experienced different side effects. 24% (137) of respondents had been given mixed bundles of AEDs from more than one manufacturer. 34% (625) had their medication repackaged in plain or unprinted packs. 53% (333) of these patients did not receive a Patient Information Leaflet (PIL) with their medication.
Conclusion: Epilepsy Action has identified several key areas for action. 1) The need to recognise in all information that consistency of supply is vital in the effective treatment and control of epilepsy. 2)The UK pharmacists' payment system may need to change to avoid financial disadvantage. 3) The introduction of tamper-proof packaging for prescription medication. 4) An end to the dispensing of mixed bundles of different versions of the same medication. 5) Europe-wide consistency in the naming of drugs. 6) A guarantee that every package of medication contains an accurate PIL.

p805
Pharmacoeconomic Evaluation of Pharmacotherapy of Epilepsy
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Purpose: Pharmacoeconomic studies for chronic medical illnesses are becoming important due to an increase in the number of newer drugs, with epilepsy being no exception. Studies involving economic issues related to epilepsy are limited, but the burden of epilepsy is huge.
Methods: A prospective, non-interventional, observational study, was carried out at the neurology out patient department of a tertiary care hospital, to examine economics of the pharmacotherapy of epilepsy. Demographic, disease and treatment data were collected for one year from epilepsy patients, in a specially designed proforma. Parametric, non-parametric tests and multivariate analysis was used to determine direct and indirect treatment costs.
Results: Among 410 patients, males were more than females ($p < 0.05$), with mean age 28.80 ± 15.60 yrs, and an average of two visits. Primary generalised seizures (58.50%) and neurocysticercosis (73.50%) were frequent causes. Monotherapy was seen among 72%, and polytherapy in 28.0% patients. Pattern and extent of AED monotherapy was phenytoin, oxcarbazepine, carbamazepine-CR, sodium valproate-CR and others. Pharmacoeconomic evaluation revealed annual treatment costs per patient of INR 8,518.74. Extrapolation of costs to the 5 million population with epilepsy in India, revealed an economic burden of INR 42.6 billion constituting 0.2% GNP. Cost minimisation analysis showed a higher absolute annual cost of new vs old AEDs ($p < 0.05$). Multivariate analysis of patient sample model fit the data well ([$R2 = 0.71$, $F=43.036$, $p = < 0.001$).
Conclusion: A significant increase in direct and indirect treatment costs compared to normal individuals in the present study, suggests the need to design a comprehensive treatment plan to encourage cost effective AED use, to reduce the economic burden of epilepsy.

p806
Phenobarbital: Is Tolerability a Problem in Developing Countries - The Patients' Perspective
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Purpose: Finding an efficient and cost effective antiepileptic drug is a continuous endeavour of any epilepsy program in a developing country. Phenobarbital has remained an effective antiepileptic agent over the decades, but doubts over its tolerability have limited its use in urban settings. This pilot study collected the responses of patients who were taking phenobarbital for epilepsy.
Methods: 60 patients were evaluated who presented to the Refractory Epilepsy Clinic at our institute. 32 were taking phenobarbital at the time of presentation and 28 were taking other standard antiepileptic drugs (including valproate, carbamazepine, phenytoin etc). The patients were given a questionnaire regarding their perception of side effects of the antiepileptic drugs they were taking; these side effects included cognition, memory, daily activities, sedation, school performance etc.
Results: 20 of the 32 patients (62.5%) on phenobarbital reported no significant effect on their daily activities as compared to other antiepileptic drugs in which 20 of the 28 patients (71%) tolerated the antiepileptic drug well. The most common side effect encountered in phenobarbital group was sedation (35%).
Conclusion: In our setup we have a lot of patients who do manual work for whom carrying on the activities of daily life is more important than subtle cognitive changes. We may be able to identify a group of patients in whom phenobarbital may be a cost-effective antiepileptic drug without causing significantly perceived side effects. But as it was just a pilot study, we plan to undertake a longer randomised planned prospective study to reach the goals we set out to achieve

p807
Juvenile Myoclonic Epilepsy Worsened by an Inappropriate Therapy
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Purpose: Juvenile myoclonic epilepsy (JME) is a benign epilepsy of childhood which requires a long therapy. Add-on therapy (especially with phenobarbital (PB) and carbamazepine (CBZ)) can worsen the clinical symptoms of JME. The authors tried to underline a worsening risk of JME by inadequate drugs that may cause diagnostic difficulties; and to insist on the fact that valproate (VPA) was effective as monotherapy.
Methods: The authors report 3 cases of JME worsened by inadequate polytherapy (CBZ and PB added to VPA).
Results: Patients were brothers and one sister: aged 17, 35 and 20 years old; descended from consanguineous parents with normal pregnancy, delivery and psychomotor development. Myoclonic jerks and generalised seizures started at the age of 8 to 12. Neurological examination found severe generalised myoclonic jerks prevented the patients from standing up and they experienced moderate concentration and memory difficulties with a clear slowing of cognitive functions. These clinical data suggest myoclonic encephalopathy (Lafora, Unvericht-Lundborg…); but a JME could not be excluded; paraclinical investigations were done to clarify the diagnosis: EEG (with a normal back ground activity), biological parameters, cerebral CT-Scan and bilateral axillary coetaneous biopsy were normal. After reducing CBZ, then PB, and keeping all the patients only under VPA, their situation improved remarkably and they became seizure free. Diagnosis of JME was made and initial cognitive and neuropsychiatric signs were the results of the long therapy with CBZ and PB.
Conclusion: These cases show that inappropriate antiepileptic drugs can exacerbate myoclonia in JME and affect cognitive functions and sometimes can be a misleading in the diagnosis of JME; sodium valproate remains the most effective drug in monotherapy. Our medical students meanwhile have found some basic sound information about epilepsy, and significant false information. These results underline the necessity to sensitise the general population about epilepsy, to consolidate the basic background and to fill the major deficiencies in medical school teaching programmes.

p808
Comparison of Add-on Valproate and Primidone in Carbamazepine-unresponsive Patients with Partial Epilepsy: A Randomised Open Trial
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Purpose: The purpose of this study was to evaluate the efficacy of add-on valproate (VPA) or primidone (PRM) when carbamazepine (CBZ) could not control partial epilepsy.
Methods: The trial was prospective and open. Patients (partial epilepsy) who did not become seizure-free on CBZ were randomised to either VPA add-on (group 1, n=68) or PRM add-on (group 2, n=68). The doses of VPA and PRM were escalated in a stepwise fashion (200mg/day, 400mg/day and 600mg/day for VPA; 25mg/day, 50mg/day, 75mg/day for PRM). The doses weren't increased when patients were seizure-free or experienced adverse effects such as dizziness and nausea. The baseline period was three months. The evaluation period was at least three months in both groups. The proportion of patients with 100%, 75-99%, 50-74%, <50% reduction in seizure frequency and with seizure worsening were determined. Comparison of the efficacy of the two groups was by nonparametric test.

Results: In the VPA group, 27.9% of patients became seizure-free, 22.1% had a seizure reduction of 75-99%, 10.3% had a seizure reduction of 50-74%, 26.5% had a reduction of <50% and in 13.2% of patients seizures worsened. In the PRM group,17.6% of patients became seizure-free, 16.2% had a seizure reduction of 75-99%, 5.9% had a seizure reduction of 50-74%, 42.6% had a seizure reduction of <50% and in 17.7% of patients seizures worsened. The efficacy of group 1 was significantly different from group 2 ($p<0.05$).
Conclusion: The efficacy of add-on VPA was significantly greater than that of add-on PRM in patients with partial epilepsy who did not become seizure-free on CBZ.

p809
Reason for Using Sustained Release Formulation of Valproic Acid as Epilepsy Therapy
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Purpose: Epilepsy is a chronic disorder that requires not only drug safety, efficacy or tolerability, but also patient adherence to long term therapy. Sustained-release formulations (SRF) of some anticonvulsants have been developed to reduce dose frequency, to maintain constant plasma drug concentrations, and to minimise adverse effects.
Methods: An epidemiological, observational, retrospective study of 31 patients (both genders, age ranging from 24 to 84 years), 22 receiving valproic acid (VPA) in monotherapy for primary generalised epilepsy or cryptogenic generalised tonic clonic seizures, and 9 receiving add-on therapy for refractory epilepsy. 18 patients began drug therapy with SRF and 13 switched from intermediate-release to SRF (same dose once or twice daily).
Results: 3 patients were withdrawn for side effects (incapacitating tremor or gastric intolerance). 28 patients finished the study with a mean body weight of 83 Kg. Drug doses ranged from 1000 to 2500 mg/day with mean daily dose of 21.5 mg/Kg. In all but 2 patients plasma drug levels were over 50 mcg/ml (normal: 50-100). In these 2 patients , dose intake was not changed because of good clinical control.
Conclusion: Using a SRF of valproic acid resulted in therapeutic plasma drug levels, allowing dose frequency reduction and improved patient compliance.

p810
Acceptability and Tolerability of a New Microsphere Formulation of Sodium Valproate (Depakine® Chronosphere®) in Monotherapy for Children with Epilepsy
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Purpose: A new microsphere formulation of slow-release valproate (Depakine® Chronosphere®; Sanofi-Aventis) was developed to be administered sprinkled on food or directly swallowed with a drink. The objective of this study was to evaluate the acceptability and safety of this new formulation for children with epilepsy treated with monotherapy.
Methods: An open-label study was performed on 301 children aged between 3-16 years. 102 subjects were newly treated and 199 switched from another formulation of valproate. At inclusion, children started the microsphere formulation and were followed for a further ninety days. Subjects were assessed at D0 and D90 with the Hedonic Visual Analogue Scale for treatment acceptability. Adverse events, compliance and seizure occurrence were recorded.
Results: Compliance was good, with 80% of subjects not missing a dose. Acceptability was considered good or very good by 52.3% of children under five and by 67.6% of older children, compared to 25.7% and 40.0% respectively for the acceptability of the previous treatment in switched patients. The proportion of subjects remaining seizure free rose from 54.3% at inclusion to 62.0% at D90 ($p=0.0006$; c2 test) for children under five and from 59.0% to 67.1% ($p=0.0010$; c2 test) for children between five and ten. The most common adverse events reported were pulmonary, neurological, gastrointestinal or general.
Conclusion: The new microsphere formulation of sodium valproate was better accepted than previous formulations by children with epilepsy. Use was acceptably tolerated and associated with good compliance and improved seizure control. Financial support for this study was provided by Sanofi-Aventis.

p811
Effect of Valproic Acid on Depression in Epilepsy Patients
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Purpose: Depression is very common and clinically important psychiatric disorder in patients with epilepsy. Valproic acid (VPA) is not only an anticonvulsant, but also a mood-stabiliser used in the treatment of affective disorders. The aim of the study was to evaluate the effect of VPA on depression in patients with epilepsy.
Methods: 73 adult epilepsy patients with clinical symptoms of mild or moderate depression were observed. The primary assessment included medical history, seizure frequency and evaluation with Beck Depression Inventory (BDI) and Montgomery-Asberg Depression Rating Scale (MADRS). Then valproic acid was administered as monotherapy or add-on therapy. Antidepressants were not used. After 6 months this assessment was repeated for 69 patients.
Results: 54 (78.3%) patients showed significant improvement in mood state reflected in decrease of mean values of BDI and MADRS. This group of patients also had satisfactory seizure control (50% or more seizure reduction). 9 (13%) patients had unchanged or increased seizure frequency but their mood state improved according to BDI and MADRS results. 6 (8.7%) patients had no positive changes in mood state and required further treatment with antidepressants.
Conclusion: Valproic acid causes a positive influence on depression in patients with epilepsy and may preferably be administered to epilepsy patients with comorbid mood disorders.

p812
Parkinsonism in Epilepsy Patients on Anti-epileptic Drug Treatment
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Purpose: Parkinsonism has been reported as a side effect of valproate. There is little data on the prevalence of valproate-induced Parkinsonism amongst a cohort of epilepsy patients who are managed in epilepsy clinics. We determine the occurrence and spectrum of Parkinsonism among patients with epilepsy in Singapore.
Methods: The UPDRS was used to assess signs of Parkinsonism in epilepsy patients seen at our epilepsy clinic over a 20-week period. Seizures and epilepsy syndromes were classified according to ILAE classification. Patients with post-encephalitic epilepsy or secondary causes of Parkinsonism were excluded. Patients with suspected valproate-induced Parkinsonism had their valproate dose reduced or switched to another AED and assessed again with UPDRS.
Results: 183 patients (85% Chinese, 9% Indians, 6% Malays) were studied. The mean age was 37 (25-49) years, with 103 (56%) females. Mean duration of epilepsy was 17 (5-29) years. Majority (83%) had localisation-related epilepsy. 101 patients (55%) were on valproate monotherapy or with other AEDs. 4 patients (2.2%), all Chinese, had signs of Parkinsonism, with a mean UPDRS score of 14. They were on valproate, for an average of 6-7 years, in combination with other AEDs: lamictal (1), carbamazepine (2) and phenytoin (1). 3 patients had normal neuroimaging while 1 had left mesial temporal sclerosis. Parkinsonism improved in 2 patients after the valproate dose was reduced.
Conclusion: Although the frequency of probable valproate-induced Parkinsonism in our population is low, our study highlights the need

for a high index of suspicion for this complication in epilepsy patients who present with bradykinesia or tremors.

p813
Mechanism of Valproate-induced Red Cell Macrocytosis
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Purpose: Increased red cell mean corpuscular volume (MCV) and macrocytosis without anaemia were reported to be induced by the administration of valproate (VPA). The mechanism of VPA-induced red cell macrocytosis remains unknown. The aim of this prospective study was to evaluate folate and vitamin B12 status in children receiving VPA monotherapy.
Methods: I evaluated red cell indices, serum folate, serum vitamin B12, and red cell folate levels in 20 newly diagnosed children with epilepsy (13 boys and 7 girls), aged 7.7±4.8 years, who were treated with VPA monotherapy, that were measured by competitive protein-binding radioassay using commercial kits. Statistical analysis was performed using the paired t test.
Results: After 12 months of therapy, MCV in red cells increased significantly from 81.7 ± 4.4 fl to 83.7 ± 5.4 fl (p=0.0043). Serum folate and vitamin B 12 levels were not changed. However, the concentration of folate in red cells decreased significantly from 247.2 ± 72.6 ng/ml to 210.5 ± 71.0 ng/ml (p=0.0089).
Conclusion: The results demonstrate that there is an increase in MCV and evidence of red cell macrocytosis in patients treated with VPA. VPA-induced macrocytosis is determined to be caused by decreased red cell folate levels and not by decreased serum folate levels. A decrease in red cell folate levels is unequivocal evidence of folate deficiency and/or a disturbance of folate metabolism. VPA-induced macrocytosis may be attributable to marginal folate deficiency, as red cell folate levels appear to be an appropriate index for evaluating folate status.

p814
Prevalence of Polycystic Ovaries in Epilepsy Patients using Valproic Acid
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Purpose: To investigate the frequency of occurrence of polycystic ovaries (PCO) in women taking valproic acid (VPA) as monotherapy for epilepsy.
Methods: 163 epilepsy patients were seen at the outpatient neurology clinic at Princess's Basma Teaching Hospital, Irbid, and Basheer Hospital, Amman, Jordan. A detailed medical history was taken from the patients followed by a clinical examination and vaginal ultrasonography of the ovaries.
Results: 102 patients (62.5%) had primary generalised seizures, 46 patients (28.2%) had partial seizures and 15 patients (9.2%) had partial secondary generalised seizures. Mean age ± standard error of the mean (SEM) was 29.8 ± 0.97 years. The duration of epilepsy and treatment with VPA were (mean ± SD) 9.1 ± 0.48 and 7.9 ± 0.4 years, respectively. The dose and serum concentrations of VPA were (mean ± SD) 983.9 ± 101.96mg and 52.7 ± 4.7 mg/L, respectively. Mean body mass index (BMI) was 25.6 ± 0.92 kg/m2. The mean weight gain was 6.6 ± 1.3kg (range 2–24kg). Menstrual abnormalities were detected in 58 (35.6%) patients. 12 patients (7.4%) had PCO; these patients were compared with 17 patients without PCO selected randomly. There was a statistically significant difference in testosterone level and BMI values in patients with PCO compared with those without negative PCO. Patients with PCO had a mean ± SEM serum testosterone level of 1.2 ± 0.18 g/L and BMI values of 29.24 ± 1.75 kg/m2. However, patients without PCO had a serum testosterone level of 0.61 ± 0.1 g/L and a BMI of 21.91 ± 0.7 kg/m2. Menstrual abnormalities were detected in all patients with PCO and in 8 patients without PCO. Hirsutism was found in 4 cases with PCO and in 1 case with no PCO. There were no statistically significant differences in the duration of therapy, doses and serum concentrations of VPA in patients with PCO compared with those without PCO.
Conclusion: These results suggest an association between the use of VPA and PCO, hyperandrogenism, obesity and menstrual abnormalities. For women receiving VPA therapy, clinicians should consider performing an assessment of ovarian structure and function, especially if these patients develop menstrual cycle disturbances during treatment.

p815
Clinical Relevance of Drug Interaction Between Valproate and Phenprocoumon
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Purpose: A combined therapy with the antiepileptic drug valproate and the oral anticoagulant phenprocoumon is common, especially for patients suffering from ischemic stroke and symptomatic seizures. There are no reports of clinically relevant interactions between these drugs.
Methods: We reviewed the data of all in- and outpatients of our neurological department within the last 38 months. Two groups of patients were identified: group 1 was treated with valproate in addition to an established phenprocoumon therapy, group 2 received phenprocoumon at the same time or in addition to an existing valproate medication. For group 1, the latest available International Normalized Ratio (INR) values were achieved, means calculated for each patient and correlated to the maximum INR values shortly after initiation of valproate. Patients were excluded if the dosage of the drugs during the relevant time was unknown or compliance was insufficient.
Results: 18 patients received a combined treatment with valproate and phenprocoumon. Three patients met exclusion criteria, the remaining were divided into group 1 (n=11) and group 2 (n=4). Means of INR values in group 1 before treatment with valproate ranged between 1.6 and 3.2 (SD 0.05-1.22) and raised significantly after initiation of valproate (mean +77%, range from +45 to +138%). In group 2, the intended INR values were reached with low doses of phenprocoumon.
Conclusion: There is a clinically relevant interaction between valproate and phenprocoumon. Patients on valproate need unusually low doses of phenprocoumon for active anticoagulation. In patients receiving valproate with pre-existing phenprocoumon a potentially hazardous rise of INR has to be observed.

p816
Low-doses of Selective Serotonin Re-uptake Inhibitors (SSRIs) Improve Behavioural Disorders in Children and Adults with Epilepsy: A Prospective Open-label Study
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Purpose: A prospective study was performed to evaluate the effect of selective serotonin re-uptake inhibitors (SSRIs) on behavioural disorders in children and adults with epilepsy.
Methods: Patients with epilepsy and behavioural disorders that interfered with their social life were recruited from the outpatient clinic of our centre. They were administered low doses of SSRIs (either fluvoxamine 25–50 mg or paroxetine 5 mg per day). They were followed for 2–4 years and their behaviour was assessed by a 5-point scale based on the observations of the first author and the caregivers.
Results: 23 patients (including 8 children < 15 years) entered the study after informed consent. Age at entry was 2-39 years (18.0 ± 7.8). The epilepsies were: 14 localisation-related, 2 undetermined and 7 symptomatic generalised. 22 patients took fluvoxamine and 1 patient

paroxetine. 20 out of 23 patients (87%) showed improvement in their behavioural disorders: aggression (4), obsessive-compulsive disorders (5), impulsive actions (4), insomnia with dysphoria (4), perverseness (2) and stereotyped behaviour (1). The effects of SSRIs were more prominent in children, and appeared within 22 days after introduction except in 1 patient. The effect continued more than 2 years in 13 patients (65%). In the remaining 7, SSRIs were discontinued due to lack of effect (5), aggravation of seizures (1), and dropout (1). Adverse effects were: increased seizures (1), transient sleepiness (2) and decreased appetite (1).
Conclusion: SSRIs, even in low doses, improve emotional and behavioural disorders in patients with epilepsy, especially in children.

p817
Side Effects of Antiepileptic Drugs and Depressive Symptoms: What is the Importance of Screening in Clinical Treatment of Patients with Epilepsy?
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Purpose: The identification of depressive symptoms and side effects of antiepileptic drugs (AED) may be one of the most important aspects of care to improve patients' health status. Using a valid and reliable instrument, the Adverse Events Profile (AEP) and the Beck Depression Inventory (BDI) we can assess depressive symptoms and side effects of AED in outpatient clinic visits. The objective of this study is to assess the incidence of depressive symptoms and adverse effects of AED and to correlate the variables depression, adverse events and seizure frequency.
Methods: 40 patients, 20 with temporal lobe epilepsy (TLE) submitted to surgical treatment and 20 with juvenile myoclonic epilepsy (JME), answered the AEP, BDI and a brief interview about clinical and demographic variables.
Results: Among patients with TLE, the most frequently used AED were carbamazepine (95%) and clobazam (80%). Memory impairment (45%) was the most common adverse event. In the JME group valproate (70%) was the most frequently used AED, and upset stomach was the most common adverse event (30%). Depressive symptoms were found in 30% of the TLE patients and in 70% of the JME group. No statistic association was observed between seizure frequency, depression symptoms and adverse effects of AED.
Conclusion: Significant adverse events are frequently observed in patients with TLE and JME. In this series, depressive symptoms were more common among patients with JME. The regular use of AEP and BDI in outpatients may help identify depression and toxicity of medication, with improvement in health status.

p818
Levetiracetam Decreases Spontaneous Spiking Activity and Increases EEG Gamma Frequencies in DBA2J Mice: Role of GABAB Receptors
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Purpose: DBA2/J mice present spontaneous spindling of spike-wave discharges (SWDs) which are originated by thalamic-cortical altered oscillators and modulated by GABAB receptors. Since such mechanism not only affects SWDs but also involves the background EEG activity, it was of interest to investigate the role played by GABAB receptors in the pathophysiology of the spontaneous spiking activity of DBA2/J mice in correlation with cortical rhythms. In this contest, the action of levetiracetam as a potential anti-absence drug was also studied.
Methods: EEG signals digitised in a bandwidth of 0.1-100 Hz, at 1024 Hz sample-frequency were analysed off-line (EEG-LAB, The Mathworks). Mice were treated intraperitoneally (i.p.) with: vehicle (control, 10 ml/kg); the reference GABAB agonist baclofen (1.0-10 mg/kg), the selective GABAB antagonist SCH 50911 (12.5-100 mg/kg); γ-butyrolactone (GBL; 25-100 mg/kg), the putative antagonist of GHB-binding site NCS 382 (100-400 mg/kg), and levetiracetam (LEV; 25-100 g/kg).
Results: GABAB agonists worsened spontaneous spiking and decreased gamma frequencies, while both GABAB antagonists and LEV reduced spontaneous and GABAB-induced increase of SWDs and determined a rapid improvement (> 25%) of gamma frequencies suggesting a possible common anti-synchronising action [1].
Conclusion: The results indicate that GABAB receptors play a significant role in the pathogenesis of spontaneous spiking activity (e.g. generalised absence seizures) in DBA2J mice as well as in modulating gamma rhythms. Moreover, since LEV shared some mechanisms of action with known GABAB antagonists in suppressing SWDs, our study also suggests the possible use of this drug in typical absence. [1] Medvedev AV, Brain Res Bull. 2002;58: 115-128.

p819
Levetiracetam Intravenous Infusion: Safety, Tolerability and Bioavailability versus Oral Tablet
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Purpose: An intravenous (i.v.) formulation of the antiepileptic drug (AED) levetiracetam (LEV) has been developed for patients in whom oral administration is temporarily not feasible. A phase-I two-way crossover, single-dose study was conducted to compare the bioavailability of LEV i.v. infusion to that of oral tablets. This was followed by a placebo-controlled parallel trial to determine i.v. LEV tolerability and pharmacokinetics.
Methods: 18 healthy subjects (9 male, 9 female) were randomised to receive a single 1500 mg dose of LEV given as a 15-minute i.v. infusion or 3 x 500 mg oral tablets. After a 7-day washout, subjects were crossed over to the other formulation. After a further 2-day washout, subjects were randomised in a 2:1 ratio to i.v. LEV 1500 mg or placebo twice daily for 4.5 days. Plasma LEV concentrations were used to assess LEV pharmacokinetics.
Results: The rate and extent of systemic exposure to LEV after 15-minute i.v. infusion were equivalent to those after oral intake (Cmax: 50.5 vs 47.7 µg/mL; AUC: 392 vs 428 µg.h/mL). Geometric mean ratios (i.v./oral) were 92% and 104%, respectively, with 90% confidence intervals within the 80%-125% range, demonstrating bioequivalence of the two formulations. Safety and tolerability did not differ between the two routes of administration. Local tolerability of i.v. infusion was good. Somnolence and postural dizziness were the most common adverse events.
Conclusion: LEV 15-minute i.v. infusion is bioequivalent to oral intake. It represents a well tolerated, safe and valuable alternative for patients unable to take the drug orally. Study supported by UCB S.A. Belgium

p820
Efficacy of Levetiracetam in Pharmacoresistant Continuous Spike-wake Activity During Slow Sleep
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Purpose: To evaluate the efficacy and safety of levetiracetam (LEV) as add-on therapy in refractory continuous spike-wake activity during slow sleep (CSWS).
Methods: We introduced LEV as add-on therapy in 20 children age 22 months to 18 years affected by pharmacoresistant CSWS. 12 patients had partial-onset seizures and 8 patients had atonic seizures and/or

atypical absences. We evaluated clinical, neuropsychological and electroencephalographic outcome.
Results: 50% of patients showed a seizure frequency reduction of more than 50% and 25% became seizure-free. 4 children (16%) had a complete electroencephalographic response, 3 showed mild to moderate reduction of spike-wave activity during slow sleep and 13 patients had no evidence of electroencephalographic response. In 35% of children we observed a significant improvement in behaviour, attention, verbal responses and/or alertness. Only 5 patients showed adverse events.
Conclusion: 1) LEV is a safe alternative as add-on therapy in children with refractory CSWS. 2) LEV was highly effective in partial-onset seizures associated to CSWS. 3) There was an irregular electroencephalographic response not related to seizure control. 4) LEV had a positive neuropsychological effect not related directly to seizure control.

p821
Efficacy of Levetiracetam in Patients with Generalised Epilepsy and Myoclonic Seizures
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Purpose: To evaluate the efficacy and tolerability of levetiracetam (LEV) as either de novo (monotherapy) or add-on therapy in patients with different generalised epilepsies characterised by myoclonic seizures.
Methods: 35 patients (21 female, 14 male), mean age 24.7 (±10.5) years were enrolled. 21/35 had juvenile myoclonic epilepsy (JME); 4 severe myoclonic epilepsy of infancy (SMEI); 2 Lennox-Gastaut syndrome (LGS); 1 myoclonic-astatic epilepsy (MAE); 1 myoclonic absences (MA); 1 benign myoclonic epilepsy in infancy (BMEI). 5 patients had unspecified epileptic syndromes. Patients received LEV as de novo monotherapy or add-on therapy. Seizure frequency changes and adverse events (AEs) were assessed. Follow-up was for more than 12 months.
Results: Patients received LEV 2000-3000 mg/day; 8 receiving LEV de novo, 27 as add-on therapy to other drugs (e.g. lamotrigine, valproate). In total, 29 (82%) of the 35 patients achieved ≥50% seizure reduction. 15 (42%) patients achieved seizure freedom: 62% (5/8) de novo patients (all JME); 37% (10/27) receiving add-on (8 JME, 1BMEI, 1 other). A further 14 (40%) patients achieved ≥50%-99% seizure frequency reduction: 12% (1/8) receiving LEV de novo (JME), 48% (13/27) receiving add-on (4 other, 3 SMEI, 3 JME, 1 LG, 1 MA). 6 (17%) patients discontinued LEV for inefficacy (2 JME, 1 LG, 1 SMEI) or seizure worsening (2 JME). No further patients discontinued due to AEs.
Conclusion: Our results confirm that LEV as de novo (monotherapy) and add-on therapy at doses between 2000-3000mg/day effectively reduces myoclonic seizure frequency in patients with generalised epilepsy. LEV was also very well tolerated.

p822
Efficacy and Tolerability of Levetiracetam in Generalised Epilepsy
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Purpose: Evaluation of the efficacy and tolerability of levetiracetam (LEV), in primary and secondary generalised epilepsy, as add on therapy and the possibility to convert to monotherapy.
Methods: This is a single centre, post marketing, retrospective study. Between 2001 and 2004 we investigated 30 patients (18 women, 12 men) suffering from either secondary generalised epilepsy (SGE), idiopathic generalised epilepsy (IGE), Lennox Gastaut syndrome (LGS), juvenile myoclonic epilepsy (JME), generalised epilepsy with febrile seizures plus (GEFS+) or progressive myoclonus epilepsy (PME). Patients were treated with LEV either as add on therapy or as secondary monotherapy. During a mean treatment period of 12.8 months (range 1-30) LEV serum levels were controlled with high performance liquid chromatography (HPLC).
Results: Of 30 patients (mean age 38.1 +/- 12 yr) were 9 IGE, 3 JME, 4 PME, 7 LGS, 6 SGE,1 GEFS+, all drug resistant under antiepileptic treatment with either VPA, PRM, PB, LTG, DPH, TPM, Benzodiazepine, vagus nerve stimulation or any combination of these. Under treatment with LEV on a mean dosage of 2666.7 mg (+/- 723.2 mg) and serum blood levels of mean 43.1 µg/ml (+/- 22.6 µg/ml) we found 15 responders with seizure reduction of 50% in 3 (2 LGS, 1 IGE), of 75% in 6 (1 SGE, 4 IGE, 1LGS) and 100% in 6 patients (1 IGE, 3 SGE, 2 JME). 15 patients (4PME, 2SGE, 3IGE,1 JME, 4 LGS, 1GEFS+) were non responders. Serum blood level did not differ significantly between the two groups. 3 patients (all IGE) could be converted to monotherapy successfully. 6 patients dropped out of the study due to side effects (3) or lack of efficacy (3).
Conclusion: Levetiracetam is a new option in the therapy of drug resistant generalised epilepsy. Drop outs due to side effects are rare.

p823
Levetiracetam as Monotherapy in Refractory Myoclonic Epilepsy
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Purpose: Levetiracetam is a last generation AED, S-etil-2-oxo-1-pirolidin-acetamide (Keppra), a derivate of piracetam; a drug known many years ago as nootropic (formerly used for treating AD as it potentially improves cognitive functions and is still in use for post-anoxic myoclonic jerks). Mechanism of action is essentially unknown. It's not effective against electrical or pentylenetetrazol induced seizures, but in animal models has a protector effect against kindling. It doesn't seem to interact with other drugs. The most relevant sites of binding are the neurons of brain, hippocampus, and cerebellum. The pharmacokinetic profile seems to be very safe, with fast absorption when taken orally, it is not altered by foods, has lineal elimination, mostly renal. Half life is about 6–8 hrs, with an increase in older aged and renal failure patients. There are a few side effects such as dizziness, sedation or somnolence. It is effective against partial, photosensitive and generalised seizures. We tried to replace drugs which fail to control myoclonic seizures in a group of patients for LEV as monotherapy.
Methods: Long-term continuation, efficacy, and safety of the new antiepileptic drug levetiracetam (LEV) was evaluated in all patients with myoclonic epilepsy of the idiopathic-remote symptomatic group, aged 8-21 years, with at least 3 seizures each week, and a history of 5 years from the start of disease. They were exposed to the drug during its developmental program (n = 23), after failing with sufficient time on treatment with at least two drugs, always including VPA. Doses were in the range of 1000–3000 mg./day, with titration in 1–2 months.
Results: Good tolerance and wellbeing were almost the rule. The efficacy rate was estimated to be 63% after 1 year and 47% after 3 years. Thirty-nine percent (23/46) of patients had a seizure reduction of 50%, and 13% (8/51) became seizure-free for at least 6 months. Frequently psychiatric or behavioural problems associated with epilepsy showed an improvement, and sleep function was better.
Conclusion: LEV seems an effective and well tolerated new antiepileptic drug for use in monotherapy against myoclonic epilepsy of the idiopathic-crypto-remote symptomatic group, with a long lasting history of disease and well established refractory condition. LEV could be considered a first choice drug for that particular epileptic syndrome.

p824
Open-label Prospective Study of Efficacy and Safety of Levetiracetam: One Year Follow-up
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Purpose: To analyse the efficacy and safety of levetiracetam by means of a one year follow-up, prospective, open-label study.
Methods: Patients with any type of seizure and epilepsy in whom treatment with levetiracetam was started in our clinic were included in this study. The study included a baseline visit and follow-up visits at 1, 3, 6 and 12 months. Levetiracetam was discontinued if lack of efficacy or intolerable side effects appeared. The following data were analysed at baseline: age, gender, age at seizure onset, seizure types, type of epilepsy, aetiology, monthly seizure frequency and number of antiepileptic drugs (AEDs) tried. During follow-up visits efficacy, side effects (type and duration) and concomitant AED use were analysed.
Results: 101 patients were included in the study. The majority of patients presented complex partial seizures (63.4%) and partial epilepsy (86%). The most frequent aetiology was mesial temporal sclerosis (14.9%). At baseline, the mean seizure frequency was 15.66±35 seizures per month and the mean number of AEDs tried 3.72±2.14. 80 patients (79.2%) completed the one year follow-up. At the 12 month visit or at discontinuation 37 patients (36.6%) were seizure-free for the last 6 months, 29 patients (28.7%) showed a > 50% improvement in seizure frequency, 32 patients (31.7%) showed no improvement and 3 patients (3%) showed worsening of seizure frequency. Prolonged side effects were observed in 21 patients (20.8%), and 13 patients (12.9%) had to discontinue levetiracetam. The most frequent side effect was somnolence. Monotherapy was achieved in 17 patients (16.8%) at the end of the study.
Conclusion: Levetiracetam proved to be an efficient AED for 65.3% of the patients and 16.8% achieved monotherapy. Tolerability was good and side effects were rarely severe enough to discontinue medication.

p825
Levetiracetam as Adjunctive Treatment in Refractory Partial Epilepsy: A Prospective Open-label Long-term Evaluation
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Purpose: To evaluate the efficacy and safety of levetiracetam as add-on therapy in patients with refractory partial epilepsy.
Methods: Patients with partial epilepsy refractory to > 2 antiepileptic drugs (AEDs) were recruited. Three periods were considered: baseline (8 weeks); titration (2 weeks): levetiracetam up to 1000 mg/day; follow-up (up to 24 months): levetiracetam up to 3000 mg/day if clinically indicated. The main effect was the probability of achieving 6-month and 12-month remission, assessed by Kaplan-Meier survival curves. Differences were tested with the log-rank test. The secondary end-point was tolerability, evaluated at each visit as type, duration and intensity of the adverse events.
Results: The sample included 157 patients (90 F, median age 42 years, range 11-77) with refractory partial epilepsy (59 cryptogenic, 96 remote symptomatic, 2 undetermined), previously treated with a median of 6 AEDs (range 2-11). Mean follow-up duration was 63 (SD 35) weeks, median levetiracetam dose was 2000 mg/day (range 500-3000). The cumulative probability of 6-month and 12-month remission was 19-24-25-26% and 13-16-17-20% at 12-24-36 and 48-weeks. 20 patients (12.7%) became seizure-free after treatment start, remaining seizure-free for a mean period of 89 weeks. Patients with < 6 seizures/month had the highest chance of remission (p=0.017). Adverse events were reported in 75 patients (48%), with 25 drop-outs (16%). Somnolence, nervousness, aggression and vertigo, mostly mild and transient, were the commonest complaints.
Conclusion: In this prospective, open-label, long-term study levetiracetam add-on therapy appears to be effective and fairly safe, with up to 20% of patients with refractory partial epilepsy achieving 12-month seizure remission.

p826
Use of Levetiracetam in a General Neurology Unit
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Purpose: To demonstrate the efficacy, retention curve and side effect profile seen in patients treated with levetiracetam (LEV, Keppra®); to establish the number of patients, their demographics and epilepsy/seizure types.
Methods: This is a retrospective review of a patient population with epilepsy, who attended a general neurology unit in a district general hospital. Patient records, including clinic letters (written by consultant neurologists, specialist registrars and epilepsy specialist nurse), were retrieved using key search words, 'epilepsy' and 'levetiracetam (Keppra)'. Patients who commenced LEV treatment between December 2000 and August 2004 were included.
Results: Our completed review is of 184 patients (equating to 263 patient years), 59 (32%), 82 (45%), 26 (14%) on one, two and three antiepileptic drugs, respectively, when LEV commenced. This data shows that 140 (76%) patients remain on treatment with 68 (37%) reporting side effects, 44 (24%) discontinuing LEV; 40 (22%) due to side effects, 2 (1%) due to pregnancy, and 2 (1%) due to diagnosis change. Improved seizure control was reported, with 27 (15%) patients becoming seizure-free (dose range of LEV 500-3750 mg), 19 (10%) having 75% seizure reduction, 17 (9%) having 50% reduction and 33 (18%) having improved control or feeling of well being. We will present our completed findings at the IEC 2005 Congress.
Conclusion: Our preliminary results indicate that LEV was well tolerated by this patient group and there was significant improvement in seizure control in 96 (52%) of the patients audited. Project sponsored by a grant from UCB Pharma, UK.

p827
Positive Impact of Adjunctive Levetiracetam on Health-related Quality of Life in Patients with Partial Epilepsy
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Purpose: To evaluate, in an open-label study, the effect of levetiracetam (LEV) on health-related quality of life (HRQOL) in community-based patients in Belgium.
Methods: The QOLIE-10-P (Patient Weighted Quality of Life in Epilepsy Inventory) was completed by 185 adult patients with uncontrolled partial epilepsy at baseline and after 16 weeks of treatment with adjunctive LEV. The QOLIE-10-P is an expanded version of the QOLIE-10 designed to measure overall distress, change in overall quality of life, and priority of importance of each domain. QOLIE-10-P scores range from 0 to 100 (best HRQOL). Treatment effect was assessed using paired t-tests.
Results: Median reduction of weekly partial seizure frequency was 59% after 16 weeks of LEV adjunctive therapy. Statistically significant increases from baseline (i.e., improvement in HRQOL) were observed in all QOLIE-10-P scores (all $p<0.05$) except energy-fatigue ($p=0.06$). Greatest improvements were found for seizure worry (9.7), overall QOL (9.4) and cognitive functioning (8.7) among domains and for role function (7.3) among factors. The increase in

total score was 7.11 ($p<0.001$). The new distress item demonstrated significant reduction (-12.2, $p<0.001$). Interestingly, the cognitive functioning domain showed large enhancements not only in patients whose condition improved but also in patients with stable disease according to the investigator's evaluation (7.4) and in patients with less than 50% decrease in seizure frequency from baseline (6.5).
Conclusion: Addition of LEV to standard medication had a positive impact on all components of HRQOL. Improvement in cognitive functioning was observed even in subjects for whom the condition was considered unchanged.

p828
Levetiracetam in Partial Epilepsy: A Retrospective Analysis of its Usefulness in an Outpatient Clinic
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Purpose: Levetiracetam was released in 2000 as an antiepileptic drug for add-on treatment of focal epilepsies. Several controlled studies have demonstrated its usefulness. We perform a retrospective study on its efficacy and tolerability in an outpatient Neurology unit (i.e. 'real life' conditions).
Methods: Effects of add-on treatment with levetiracetam on seizure frequency and side effects were analysed retrospectively in 40 consecutive patients with focal epilepsy (focal and/or secondary generalised seizures) in which levetiracetam was used.
Results: 40 patients analysed, mean follow-up of 14.1 months. 22.5% patients became seizure-free, 17.5% had more than 75% reduction in seizure frequency, 7.5% had more than 50% seizure frequency. Dosage range 2000 - 5000 mg/day. Increasing dosage to more than 4000 mg/day did not improve efficacy in general but could induce an increase in psychic side effects, except for a patient who had a significant improvement with 5000 mg/day. Efficacy against all seizure types independent of focus localisation. No evidence for development of tolerance with longer periods of treatment. Most common adverse effects were somnolence and aggressiveness; one case developed hallucinations. Tolerability did increase slightly with slow titration (considering slow titration an increasing speed of less than 500 mg/48h).
Conclusion: Levetiracetam is a potent and generally well tolerated new antiepileptic drug; it is also efficacious in patients with refractory focal epilepsies. Sometimes high doses are needed to observe a clear benefit.

p829
Levetiracetam Monotherapy in Focal and Generalised Epilepsy. An Open-label Post Marketing Study
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Purpose: To evaluate the efficacy and tolerability of levetiracetam (LEV) as monotherapy in focal and generalised seizures and to investigate the correlation of LEV serum levels with dosage of daily intake and outcome.
Methods: This is a single centre, post marketing, retrospective study. We investigated 40 patients with regard to seizure reduction (100%, >75%, >50% or unchanged) suffering from focal and generalised epilepsies under control of LEV serum levels measured with high performance liquid chromatography (HPLC).
Results: 85% had focal epilepsy, 15% had generalised epilepsy. Mean age of patients was 36.4 yr □ 12.8 (13-65 yr), f:m = 19:23. During an observation period of 21.4 □ 11.2 mo 40 patients were on LEV-monotherapy for 15.7 □ 10.9 mo, 2 patients (5%) dropped out of the study due to side effects (seizure aggravation). Daily dose ranged from 1500-4000 mg (mean 2837.5 □ 603.3, median 3000), serum level ranged from 5-176.9 µg/ml (mean 44 □ 26.8, median 42). 60% of patients (23 focal, 1 generalised) were seizure free, 10 after being converted to lev-mono therapy. 7 (17.5%) focal and 2 (5%) generalised epilepsy patients were not free of seizures on LEV-mono therapy, and received add on therapy with either clobazam, carbamazepine, lamotrigine, or topiramate without reduction of seizure frequency. 3 of these focal patients were operated and rendered seizure free. LEV-dosage and serum level did not differ between seizure free patients and non-responders. 3 (7.5%) focal and 2 (5%) generalised epilepsy patients had 75% reduction (one focal after conversion to monotherapy, rendered seizure free after surgery), and 1 (2.5%) focal and 1 (2.5%) generalised epilepsy patient had 50% reduction of seizures.
Conclusion: LEV exerts a potent anticonvulsive effect on both focal and generalised epileptic disorders. Several open label studies proved its efficacy in monotherapy even in generalised epilepsies. Lack of efficacy is not related to low serum levels of LEV but a lack of effect per se.

p830
Comparison of Levetiracetam and Lamotrigine in Late-onset Epilepsy
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Purpose: To compare the efficacy and safety of add-on treatment of levetiracetam (LEV) and lamotrigine (LTG) in elderly patients with epilepsy.
Methods: LEV or LTG were randomly assigned (1:1) to aged epilepsy patients clinically uncontrolled on antiepileptic drug (AED) monotherapy regimens. Patients were assessed for a 12 month follow-up period by means of diaries, side-effect scales, EEG and neuropsychological tasks.
Results: At 12 month evaluation 5 (25%) patients undergoing LEV and 2 (10%) undergoing LTG were seizure-free. Seizure reduction > 50% was seen in 14 of 20 (70%) patients receiving LEV and in 4 of 20 (20%) receiving LTG. 2 patients prematurely discontinued LEV due to side effects and 5 discontinued LTG for lack of efficacy or side effects. At the end of the study seizure-free subjects, after discontinuation of the first AED, underwent a further 12 month monotherapy follow-up.
Conclusion: Our evidence suggests that efficacy/safety of LEV in elderly patients may be in some instances superior to those observed for LTG. LEV could also have substantial potential use in the elderly as monotherapy proposal because of its easy and fast titration and lack of drug interactions.

p831
Cost-effectiveness Analysis of Levetiracetam Add-on Therapy for the Treatment of Partial Onset Seizures: A Comparative Analysis Versus Topiramate
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Purpose: To assess the cost-effectiveness of adjunctive levetiracetam (LEV) in terms of cost per seizure-free patient gained per year in comparison to adjunctive topiramate (TPM).
Methods: A two-year dose escalation decision model comparing LEV add-on to TPM add-on was designed. The Portuguese Health Care system perspective was adopted. Direct medical cost parameters included physician visits (both GP and specialist), accidental injuries and emergency visits, hospitalisation, LEV and TPM drug costs, seizure and adverse event related costs. The effectiveness measure was the proportion of patients achieving seizure freedom at the end of the year and was derived from the Cochrane review of the two

antiepileptic drugs. Extensive sensitivity analyses were conducted to evaluate the effect of uncertainty and to quantify the robustness of the model.
Results: After the second year of treatment and for a cohort of 10,000 refractory patients, LEV treatment would result in 151 additional seizure-free patients with cost savings of 1,177,500 € (18,427,800 € vs. 19,605,300 €) leading to incremental cost-effectiveness ratio (ICER) of - 7798 € per seizure-free patient achieved. This negative ICER indicates that adjunctive LEV is dominant over TPM add-on therapy.
Conclusion: When used as add-on therapy for patients with refractory partial seizures, levetiracetam is more effective at lower cost than topiramate and could lead to cost savings from the Portuguese Health system perspective.

p832
Benefit of Levetiracetam in a Group of Patients with Very Refractory Partial Seizures
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Purpose: The aim of this review was to determine the efficacy of levetiracetam on a refractory group of patients with partial seizures who were poorly controlled despite a trial of several available antiepileptic medications and were not considered surgical candidates.
Methods: 19 patients with a long history of poorly controlled partial seizures and failing to respond to a number of antiepileptic medications were followed up for three years after being commenced on levetiracetam up to a dose of 3,000mg/day. This was performed in an open label, uncontrolled fashion and were reviewed every three to six months for three years.
Results: 11 out of the 19 (53%) had a greater than 50% reduction in their seizure frequency that was maintained over the three year period. One patient has remained seizure free for three years. 5 (26%) did not have any benefit and were weaned off the levetiracetam. The retention rate was 74% after three years.
Conclusion: Levetiracetam is an antiepileptic medication that has a very good response rate, even for a very refractory group of patients who have failed a number of other antiepileptic drugs, and should be considered for this group of patients.

p833
Prospective Evaluation of Efficacy and Tolerability of Levetiracetam for Children and Teenagers with Epilepsy and Learning Disability
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Purpose: To evaluate efficacy and tolerability of levetiracetam in young patients with refractory epilepsy and learning disability.
Methods: Levetiracetam was prescribed and titrated according to clinical criteria for this open label, prospective study. Monitoring included baseline seizure counts, frequency of emergency medication, AED levels, behaviour questionnaires and EEG.
Results: 17 patients were enrolled (10 males, 7 females, aged 7-20 yrs (mean 15 years 9 months). 11 reached a maintenance dose of levetiracetam. Levetiracetam was discontinued in 5 because of adverse effects or increase in seizures. In 1 case consent was withdrawn. Levetiracetam was added to treatment in 16 cases and monotherapy in 1. The maintenance dose was 14-63mg/kg (mean 35mg/kg). Duration of maintenance was 98-378 days (mean 200 days). Seizure counts were reduced by: less than 50% in 1; 50%-75% in 4; 87% in 1; 100% in 4 and unchanged in 1. Overall, the group showed an 87% reduction in the use of emergency treatment compared to baseline. EEG was unchanged in 4, improved in 4 and worsened in 3. Four of 5 withdrawals experienced an increase in seizures of 36-73% (median 42%) and seizures decreased in 1. Adverse events included somnolence in 1, fluctuation in mood in 1, challenging behaviour in 3 and headache in 1. Pre-morning-dose levetiracetam plasma levels ranged from 5.6-32.7 mg/L.
Conclusion: 56% of this patient group had a reduction in seizures of at least 50%. Levetiracetam was well tolerated in 70% of cases. The decreased requirement for emergency treatment indicates that seizure severity is also reduced. Levetiracetam should be considered in children and teenagers with learning disabilities and epilepsy resistant to other anti-epileptic drugs.

p834
Efficacy and Tolerability of Levetiracetam for Epilepsy Patients with Acquired Progressive Cognitive Impairment
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Purpose: Efficacy and tolerability of Levetiracetam (LEV) in elderly patients with seizures and cognitive impairment are not defined. We attempt to evaluate these questions in a 2-year open-label study.
Methods: 25 epileptic patients (11 male, mean age 76.5 years, SD 6.8) with a clinical and supported neuropsychological diagnosis of progressive cognitive impairment or dementia (DSM-IV-R criteria) were treated with LEV as add-on therapy or alternative monotherapy. Assessments and outcome measures comprised Folstein mini-mental status examination (MMSE), clinical dementia rating (CDR), neuropsychiatric inventory (NPI), geriatric depression scale (GDS), Katz activities of daily living (ADL), Lawton's instrumental activities of daily living (IADL), cognitive subscale of the Alzheimer's disease assessment scale (ADAS-cog), Udvalg for Kliniske Undersogelser (UKU) scale, and Alzheimer's disease cooperative study-clinician's global impression of change (ADCS-CGIC).
Results: Mean follow-up was 11.4 months (SD 8.8) with 18 patients completed 6 months, 12 completed 1 year and 5 completed 2 years of observation. At the last follow-up visit 21 subjects (84%) were on LEV therapy. LEV and change in antiepileptic regimen improved CIBG score in more than half the patients. NPI, MMSE, ADL, IADL and ADAS-cog scores were stable or slightly modified. During follow-up 2 patients died (considered unrelated causes) and 2 were institutionalised. Emerging related adverse events considered moderate according to the UKU scale were: somnolence/sedation and reduced duration of sleep akatisia, epileptic tonic-clonic seizures, nausea/vomiting, weight loss, increased sexual desire, and others were rare and considered mild.
Conclusion: LEV is an effective and well-tolerated drug for elderly subjects with epilepsy and cognitive impairment.

p835
Use of Levetiracetam in Epilepsy Patients with Associated Learning Disabilities Seen Within a General Neurology Unit
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Purpose: To demonstrate the efficacy, retention curve and side effect profile seen in patients with epilepsy and associated learning difficulties treated with levetiracetam (LEV, Keppra®); to establish the number of patients, their demographics and epilepsy/seizure types.
Methods: Whilst undertaking a retrospective review of a patient population with epilepsy who attended a general neurology unit in a district general hospital, a number of patients with associated learning disabilities were identified. Records were reviewed for patients who commenced LEV treatment between December 2000 and August 2004.
Results: Our completed study has 32 patients (equating to 47 patient years) presenting with mid to severe learning difficulties and epilepsy. Results show that 28 (88%) patients remain on treatment and while 8

(25%) reported side effects only 4 (13%) withdrew from treatment. Commonly reported side effects were mood swings in 3 (9%) patients and increased seizures in 2 (6%) (not confirmed by seizure records). Improved seizure control or feeling of well being was reported by 16 (50%) patients, with 1 (3%) becoming seizure-free and 4 (13%) others reporting a 75% seizure reduction. We will be able to present our full findings at the IEC 2005 Congress. Along with specific information relating to LEV, we will include general data on patient demographics, epilepsy and seizure type.
Conclusion: Our preliminary results indicate that LEV was well tolerated by this patient group and that there was a significant improvement in seizure control in 16 (50%) of the patients audited. Project sponsored by a grant from UCB Pharma, UK

p836
Effectiveness, Tolerability and Safety of LEV in the Treatment of Epilepsy Associated with Liver Diseases
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Purpose: Levetiracetam (LEV) has a good pharmacological profile. It can be considered for patients with comorbidity of epilepsy with other medical disorders.
Methods: We selected 10 patients affected by partial or generalised epilepsy associated with liver diseases consisting of chronic or acute hepatopathies in which the treatment with old AEDs led to complications. Unfavourable metabolism or complex drug interactions caused a worsening of medical disease or a decrease in the plasmatic level of concomitant drugs. After an assessment of EEG clinical and blood parameters, we introduced LEV with a starting therapeutic dose and we withdrew the previous therapy in the cases in which old AEDs had been used.
Results: In this special population, 8 patients suffered from partial epilepsy, 2 from generalised epilepsy; in almost all cases seizures were not fully controlled by previous therapy. Concomitant liver pathology consisted of HCV chronic hepatopathies in 7 cases and acute toxic hepatitis in 3 cases. Reasons for therapeutic change were liver failure or increased hepatic values in those patients treated with AEDs in which acute or chronic hepatotoxic effects were documented and/or interactions of specific drugs (i.e. interferon) with enzyme inducer AEDs. The daily doses were 1000-2000 mg. LEV was effective and safe (seizure recurrence after a 6-12 month follow-up was not observed. An improvement in basal medical conditions was verified).
Conclusion: LEV, an effective and well tolerated new AED, could be a first choice drug in the treatment of epilepsy associated with acute or chronic hepatopathies.

p837
Medical Resources Utilisation, Associated Costs and Adverse Events of Levetiracetam and Topiramate in a Retrospective Claims Analysis
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Purpose: To compare medical resources utilisation, associated costs and adverse events (AEs) in patients initiating levetiracetam (LEV) or topiramate (TPM).
Methods: A retrospective cohort study was conducted using a U.S. claims database. Patients diagnosed with epilepsy having no prescription for LEV or TPM for 6 months prior therapy initiation were followed between 3 months and one year (July 2001-December 2003). Patients were matched by epilepsy/therapy types and propensity score including clinical and demographic characteristics. Comparison of utilisation and costs was performed using Wilcoxon rank-sum tests. Risk of AEs was assessed with Cox proportional hazards models.
Results: Matching resulted in 955 patients in each group with similar characteristics: mean age ~31 years, ~64% women, 70% generalised seizures, 71% adjunctive therapy. Utilisation (mean/patient/year) was lower in LEV than TPM for physician office visits (16.4 vs 18.4, $p=0.004$), medications other than anti-epileptics (20.3 vs 25.0, $p<0.001$) and outpatient visits (ns). Consequently, total pharmacy cost was significantly lower for LEV ($3,708 vs $4,153, $p<0.001$). Use and cost of diagnostic tests and hospitalisations were lower in TPM. However, overall costs (pharmacy, outpatient, inpatient) were comparable between groups. Absence of AE during follow-up was 44% for LEV versus 39% for TPM. Risk of AEs was significantly lower in LEV than TPM: Hazard Ratio: 0.87, 95% CI: [0.77-0.98], $p=0.018$; median time to first AE: 47 days LEV; 42 days TPM.
Conclusion: LEV showed significantly less utilisation and cost of common healthcare services than TPM. Rate and risk of AEs were lower in LEV. Overall costs were comparable.

p838
Effects of Carbamazepine and Levetiracetam on Gaze and Posture Control
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Purpose: To compare objective measures (nystagmography, posturography) of side effects of slow release carbamazepine (CBZ) and levetiracetam (LEV) on gaze and posture control.
Methods: Eye movements and posture control were investigated prospectively before (baseline) and 1 hour, 4 hours and 8 hours after a single dose of 1000mg LEV and 400mg CBZ in 12 healthy volunteers in a double-blind cross-over randomised trial.
Results: LEV reached maximum plasma levels at 17.6mg/l 1 hour after intake, whereas CBZ reached maximum plasma levels at 4.8 mg/l 8 hours after intake. CBZ impaired posture control by 670% of the baseline body sway ($p<0.001$). In contrast, LEV showed only an increase of body sway of 18.2%. Peak saccade velocity was significantly slower with CBZ (15.7%) ($p<0.024$), whereas the slowing caused by LEV was not significant. Smooth pursuit was not significantly influenced by either drug.
Conclusion: CBZ markedly impairs posture control and to a lesser extent gaze control which is not the case with LEV.

p839
Mode of Action of Topiramate and Levetiracetam in Relation to Behavioural Side-effects
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Purpose: It is hypothesised that that the anticonvulsant mechanisms of drug action are also responsible for mood modulating characteristics. Mood modulating profiles of antiepileptic drugs (AEDs) have been classified into two classes. The first class is assumed to have deactivating effects related to potentiation of GABA and the second class is assumed to have activating effects that are associated with the attenuation of glutamate. The aim of this study is to test this hypothesis by reviewing the multiple mechanisms of action of topiramate (TPM) and levetiracetam (LEV) in collaboration with clinical behavioural side-effects of patients with therapy resistant epilepsy.

Methods: We retrospectively analysed the side-effects (activating, deactivating, tired/sleepy, total deactivating, headache, rest CNS, food problems) of all treatment resistant patients who had been treated with TPM and LEV in the epilepsy centre Kempenhaeghe, a tertiary referral centre for epilepsy.
Results: LEV has not been found to have a predominant activating or deactivating effect. We found TPM to act as a deactivating AED with tired/sleepy side-effects being predominant compared to other deactivating side-effects such as depression or anhedonia. TPM in comparison to LEV was found to be associated with a high incidence of side-effects, and was associated with a higher drop out rate during the first 6 months of treatment.
Conclusion: The deactivating effects of TPM may be coupled to a predominance of potentiation of GABA as both LEV and TPM inhibit glutamate but only TPM consistently enhances GABA.

p840
Follow-up Study of Topiramate as a First-line Therapy in Newly-diagnosed Infantile Spasms
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Purpose: The aim of this study was to establish the efficacy, tolerability and problems associated with the use of topiramate as a first-choice drug in newly-diagnosed infantile spasms.
Methods: This was an open-label study with an open follow-up period. 54 patients with West syndrome (infantile spasms) were given topiramate as monotherapy. If spasm-freedom was not obtained after 20 days topiramate therapy, nitrazepam 0.1~0.2 mg /kg /d, was added. The follow-up ranged from 24 to 36 months.
Results: Results: 31 cases□57.4%□showed seizure freedom for more than 24 months. There was a greater reduction from baseline in seizure frequency shown in 44 cases (81.4%), poor or null response 10 cases (18.6%). The average dose was 5.2 mg/kg/day, the maximal dose of 26 mg/kg/day and minimal dose 1.56 mg/kg/day. There were negative reactions include poor appetite 3 cases, absent sweating 3 cases, to not sleeping 3 cases.
Conclusion: Topiramate proves to be an effective and safe drug as a first-choice drug in the treatment of West syndrome.

p841
Topiramate (TPM) Monotherapy, Efficacy and Tolerability: Clinical Experience in Childhood Epilepsy
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Purpose: To assess the efficacy and tolerability of topiramate monotherapy in 17 children with recently diagnosed 'naïve' treated epilepsies or switched from bi-therapy in a retrospective open-label survey.
Methods: Topiramate was licensed in Italy for use in childhood epilepsies from 2001 and as monotherapy in epilepsy from 2002. We retrospectively evaluated 17 patients, 7 males and 10 females, aged between 2 and 16 years, selected from our epilepsy data base, according to the following criteria: subjects on monotherapy with TPM as first AED in recent diagnosed epilepsies or subjects converted to TPM monotherapy. Switch to monotherapy reasons were analysed. Neurological status, neuroimaging, epilepsy type and seizure frequency were considered. The patients were followed for up to 6 months. Seizure freedom and absence of side effects were considered favourable indices of efficacy and good tolerability.
Results: Epilepsy types were classified according to I.L.A.E criteria and scheduled as follows: 9 focal symptomatic epilepsies with or without secondary generalisation, 5 idiopathic focal epilepsies, 3 idiopathic generalised epilepsies. The current maintenance dosages of TPM ranged from 4 to 9 mg/kg/die. Monotherapy with TPM was achieved from previous bi-therapy in 9 patients; in 3 of them to simplify therapy after reaching good seizure control, in 3 patients because of side effects caused by previous AED and in 3 owing to inefficacy of previous first drug. One of these turned to another AED because of relapse after a period of good seizure control. All other subjects obtained or maintained complete seizure control at follow up without expressive side effects. 8 subjects received TPM as first AED, only 1 of these switched to bi-therapy because of inefficacy; no important adverse events were experienced.
Conclusion: Topiramate monotherapy seems quite effective and well tolerated in an broad spectrum of epilepsies in childhood.

p842
Topiramate in Paediatric Epilepsy
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Purpose: The last years have brought many advances in the treatment of epilepsy, including many new AEDs. Among these, topiramate has demonstrated a broad spectrum of activity, with a significant reduction in seizure frequency over baseline, few drug interactions and a good tolerability. We sought to evaluate the efficacy and safety of TPM in childhood epilepsy, as adjunctive therapy for several different types of seizures and as stand-alone (monotherapy) treatment for recently diagnosed epilepsy.
Methods: We retrospectively evaluated 57 patients (29 males and 28 females) suffering from partial (50 subjects) and generalised (7 subjects) epilepsy. Among these, 9 patients were treated with topiramate as monotherapy, 47 in add-on. We analysed age at onset, duration of epilepsy, manifestations and frequency of seizures, before and after treatment, tolerability and adverse effects.
Results: 19 patients (33.3%) experienced over a 50% reduction of seizure frequency, 12 of those (21%) were seizure free. 20 patients (35.10%) improved, but seizure frequency decreased less than 50% while it was unvaried in 13 patients (22.8%). Seizure frequency worsened in 5 patients (8.8%), after an initial improvement. With regard to tolerability, the most common adverse effects, occurring in 34 patients, were appetite decrease, often in association with weight loss, somnolence, headache and agitation. However, the symptomatology was mild and only 6 subjects discontinued treatment due to adverse events.
Conclusion: Topiramate has a broad spectrum of activity. It's effective as an add-on but also as monotherapy for many different types of seizures. It's well tolerated with few adverse effects and minimal drug interactions.

p843
Response to Topiramate (TPM), Carbamazepine (CBZ) or Valproate (VPA) by Seizure Type in Newly Diagnosed Epilepsy
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Purpose: We report post-hoc analyses of relative effectiveness vs baseline seizure type in a double-blind trial of TPM (100 or 200 mg/day), CBZ (600 mg/day) and VPA (1250 mg/day) in newly diagnosed epilepsy.
Methods: Patients ≥6 years were eligible if epilepsy diagnosed <3 months before screening. Investigators individualised therapy by selecting CBZ or VPA as preferred agent based on presentation. Patients then randomised to double-blind treatment with chosen treatment or to one of two TPM dosages. Patients unable to achieve assigned dose or requiring therapy change exited. Primary efficacy endpoint in protocol-defined analyses was time to exit; secondary efficacy endpoints were time to first seizure and patients seizure-free for last 6 months of treatment. In the primary data analysis, TPM was at least as effective as CBZ or VPA. In post-hoc analyses, patients were grouped by baseline seizure type.
Results: 382 intent-to-treat patients had partial-onset seizures (POS), 211 generalised onset seizures (GEN). TPM did not differ

significantly from CBZ and VPA in time to exit among patients with POS (P=0.803) or GEN (P=0.720). Overall, differences between TPM and CBZ and VPA were not statistically significant. Discontinuation rates due to adverse events were: TPM 100, 19%; TPM 200, 28%; CBZ, 25%; VPA, 23%. Adverse events differed according to their known profiles.
Conclusion: TPM monotherapy is at least as effective against partial-onset and generalised-onset seizures as CBZ and VPA. Study sponsor: Johnson & Johnson Pharmaceutical Research & Development, LLC.

p844
Quality of Life in Treatment of Epilepsy: Efficacy and Tolerability of Topiramate as Monotherapy
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Purpose: To evaluate the efficacy and tolerability of topiramate as monotherapy in adult patients with epilepsy.
Methods: The study was an open-labelled, randomised, prospective, 12 month trial, dose response, including 62 patients, divided into two groups, to receive topiramate 100 mg/day and 200 mg/day. Different types of seizures were analysed. To evaluate efficacy, primarily we compared change in seizure frequency throughout 48 weeks of treatment, with the baseline. Secondly, we evaluated the effects on QUOLIE-89 scores. Safety and tolerability were assessed evaluating the adverse effects of topiramate.
Results: 64% of the patients had partial, 30% had generalised seizures, and 6% were unclassified. Seizure reduction >75% compared to baseline was achieved in 54.3% of the patients ($p<0.05$), a reduction >50% in 32.5% patients and 13.2% were seizure free, with similar improvement rates for both partial and generalised seizures. Improvement of QUOLIE scores was found in psychological, physical, social relationships and level of independence domains. Adverse events were recorded in 30% of patients, mainly evident in the higher dose group.
Conclusion: Topiramate monotherapy (100mg/day) is effective and well tolerated, with minor adverse effects, in the treatment of epilepsy, independent of seizure type.

p845
Effectiveness of Topiramate in Patients with Epilepsy
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Purpose: To evaluate the long-term effectiveness of Topiramate as mono- or add-on therapy for patients with refractory epilepsy.
Methods: Retrospective study of 229 patients of median age 33.4 and median duration of disease 18 years for a period of 5 years. 44.98% had partial epilepsy; 55.02% had generalised epilepsy. Median per month frequency of seizures is 19.2 for partial, 15.32 for generalised and 20.83 for cases with both partial and generalised. According to applied doses of topiramate, 5 groups are defined: <100mg/d, 100mg/d, 125-150mg/d, 175-200mg/d and >200mg/d. In 6.99% topiramate is used as monotherapy; in the rest, as add-on therapy, most often with valproate - 31.88%, carbamazepine - 14.41%, valproate + carbamazepine - 13.1%, oxcarbazepine - 3.49%. In the course of observation the accompanying therapy was reduced or stopped for 9.6%.
Results: There was a general reduction of seizures >50% in 79.62% of cases. The most frequent dose is 175-200mg/d with which the highest reduction of >50% is reported - in 86.25%. In 3.88% there is no change in seizure frequency. In the course of observation the clinical effect is most marked in the 6th month, followed by gradual seizure frequency reduction by the end of the 5th year and is most pronounced in patients with both partial and generalised seizures - by >50% in 88.6% compared to those with generalised - 84.71% and with partial - 80.92%.
Conclusion: Topiramate has high and long-term effectiveness as monotherapy or add-on therapy in patients with refractory idiopathic and symptomatic, partial and generalised epilepsies.

p846
Long Term Effectiveness of Lower Dose Topiramate as Adjunctive Therapy for Refractory Epilepsy Patients
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Purpose: To evaluate the long-term efficacy and safety of topiramate as adjunctive therapy titrated to clinical response in patients with refractory epilepsy.
Methods: 115 patients (62 adults and 53 children) enrolled in this open-label, self-controlled prospective study which was designed to adopt a slower dosage escalation schedule with lower initial and target dosage of topiramate. The titration strategy mostly responds to patients' complaints. The long-term efficacy, safety and retention rate of topiramate, and their relationship with dosage and titration method were evaluated.
Results: The median percentage reduction was 56.0%, 75.8%, 76.1%, 77.3% and 78.1% after 8 weeks, 6 months, 1 year, 2 years and 3 years topiramate treatment respectively for adults, and 32.1%, 66.7%, 68.9%, 70.1% and 70.8% respectively for children. The overall efficacy for partial seizures (70.6%) was higher than that for generalised seizures (37.5%, p=0.035). 10 patients achieved a 3 year remission. The mean dosage in responders was 129.3±54.3mg/d for adults and 3.1±1.4mg/kg/d for children. 33 patients (28.7%) experienced adverse events (AEs). Most of the AEs (24.3%) were found during the titration period. The most common symptom of AE was appetite disorder (18.3%). Retention rate was 90.4%, 72.2%, 62.5% and 56.1% after 6 months, 1 year, 2 years and 3 years respectively. At 3 years, 6 patients had discontinued topiramate for AEs, 16 patients for inadequate control.
Conclusion: Topiramate was showed to be effective for refractory epilepsy as adjunctive therapy in this long-term study, especially for partial seizures. AEs were mild and well-tolerated when titration strategy is individual and responds to patient complaints.

p847
An Open-label, Self-controlled Study of Topiramate as Add-on Therapy with Lower Dose for Treatment of Refractory Epilepsy
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Purpose: To find the appropriate dosage and titration method for using of topiramate (TPM) as add-on therapy for patients with refractory epilepsy.
Methods: 50 patients entered this open-label, self-controlled study which was designed to adopt a slower dosage escalation schedule with lower initial and target dose. Dosage was titrated for each patient with a criteria for pause of titration or decreasing of dose. The efficacy and safety of TPM, and it relationship with dosage and titration method was evaluated.
Results: Seizure frequency reduction by ≥50% was found in 58.0% of all patients. 11 patients (22.2%) became seizure-free. The average dosage in responders was 123.9±47.9 mg/day for adults and 3.6±1.2 mg/kg/day for children, which were much lower than that reported previously. Better seizure control was achieved in 9 patients after decreasing the dosage from their maximally achieved dosage. Treatment-emergent adverse events (TEAEs) were observed in 18 (36%) patients, which was 23% (7 cases) for adults and 55% (11 cases) for children. The most frequent symptom was anorexia, which occurred in 16.7% of adults and in 45.0% of children. Weight loss, language disturbance and other CNS-related events were also clinically noteworthy. In patients with more than one concomitant

AED there was a significantly lower responder rate and higher incidence of AEs.
Conclusion: Topiramate has been confirmed to be effective and safe as add-on therapy for refractory epilepsy with a lower dose in the present study in China. Anorexia is the most frequent AE in this trial, different from the data of western countries.

p848
Topiramate in Elderly Patients with Epilepsy
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Purpose: To evaluate the efficacy and tolerability of flexible doses of topiramate (Topamax®, TPM) in elderly patients with epilepsy.
Methods: In this prospective multicentre observational study, patients >60 years of age were evaluated at baseline and after 12 and 24 weeks. Doses of TPM and concomitant antiepileptic drugs could be adjusted individually.
Results: 113 patients (54% female, mean age 71±8 years, 81% partial epilepsy) were enrolled. The most frequent seizure types were generalised tonic-clonic (73%), complex partial (26%), simple partial (18%) and absence seizures (12%). 58 patients received TPM in monotherapy (mean dose at endpoint 95±11 mg/day), 55 patients in combination with 1–3 other antiepileptic drugs (mean dose 95±9 mg/day). Mean baseline seizure frequency was 7.1±10.4 (12 week retrospective baseline) and decreased to 1.6±3.3 at endpoint. The responder rate was 84%, and 53% of the patients remained seizure-free for at least 3 months. 83% of the patients completed the study. Main reasons for discontinuation were lack of tolerability (8.7%) and loss to follow-up (4.4%). No patient discontinued due to lack of efficacy. The only AE >5% was dizziness (5.3%). Psychomotor slowing was reported in 2 (1.8%) and memory difficulties in 1 patient (0.9%).
Conclusion: In elderly patients with epilepsy, TPM was associated with a significant reduction of seizure frequency. Monotherapy doses used for elderly patients were slightly below the recommended target dose of 100 mg/day, while in combination therapy a considerably lower dose was used compared to the recommended target dose of 200 mg/day for adults.

p849
Topiramate for Migraine Prevention: A Prospective Observational Study
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Purpose: There is expanding use of antiepileptic drugs across a range of neurological disorders. Topiramate, at daily doses of 100 mg to 200 mg, has been shown to be efficacious for the prevention of migraine attacks in randomised trials. We explored the efficacy and safety of topiramate for this indication in routine clinical practice.
Methods: 34 unselected patients (all women, aged 22-60 years) with migraine fulfilling the diagnostic criteria of the International Headache Society were recruited consecutively from two general neurology clinics and commenced on topiramate. All patients had at least 2 migraine attacks during the previous 28 days. Patients were assessed at baseline and 4, 8, and 12 weeks after starting topiramate. Migraine intensity was measured by a visual analogue scale ranging from 0 (no pain) to 100 (most severe pain) points.
Results: Among the intent-to-treat population, mean daily dose of topiramate during the treatment period was 74.4 mg (SD 30.5). 21 patients (62%) completed the whole treatment period while 8 (24%) withdrew early due to adverse events. The most common adverse events resulting in withdrawal were paresthesia and somnolence. During the treatment period, the mean number of days per month with migraine attacks decreased by 2.6 ($p=0.007$), and mean intensity of migraine attacks decreased by 10.1 points ($p<0.001$).
Conclusion: In routine clinical practice, topiramate was efficacious and well tolerated for migraine prevention, even at doses lower than those used in randomised trials.

p850
Topiramate Reversed AED-induced Weight Gain
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Purpose: Most antiepileptic drugs (AEDs) frequently cause weight gain in some patients. As overweight is a risk factor for many medical illnesses, proper weight control is critical for certain patients. Also, weight gain induced by AEDs may cause poor compliance.
Methods: 36 patients over 16 years of age who experienced weight gain more than 5% of their baseline body weight after the initiation of carbamazepine or valproic acid were included. After 8 weeks of add-on therapy of topiramate, 4 weeks of observation and 8 weeks of previous AED withdrawal was completed. After an additional 8 week maintenance period (28 weeks of topiramate), final body weight was checked.
Results: 32 patients (M:F=12:20) completed this study. Initial body weight was 82.1 Kg in men and 68 Kg in women. 4 patients dropped out because of insufficient seizure control (2 patients), adverse effects, and lost to follow-up (1 patient each). Mean age was 29.6 years (± 11.2 years). Weight loss occurred in 31 patients. Mean weight loss in men was 5.0 Kg (± 4.2 Kg) and greater in women (5.1 Kg vs. 4.8 Kg). Also, compared with initial body weight, % weight loss was greater in woman (7.4% vs. 5.8%).
Conclusion: Consideration of weight change as a selecting factor of AEDs may improve the general health and compliance of epilepsy patients. Topiramate may be a useful substitute AED for patients who gained weight induced by AEDs.

p851
Clinical Analysis of Hypohidrosis in Epilepsy Patients Receiving Topiramate Treatment
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Purpose: To investigate the correlation between hypohidrosis and topiramate (TPM) treatment in patients with epilepsy.
Methods: 239 epilepsy patients taking TPM as monotherapy or add-on therapy were included. Morbidity, clinical features, medication and prognosis of hypohidrosis were studied.
Results: 15.1% (36/239) of patients developed hypohidrosis; 23.1% (34/147) of those under 12 years and 2.2% (2/92) of those over 12 years. The clinical features included hypohidrosis, skin dryness, fever and intolerance of exercise, which tended to be mild or moderate and always occurred when the dosage of topiramate was increased. It's not necessary to withdraw topiramate, however, it is recommended that the dosage be reduced. Improvement of the environment and avoidance of exercise challenge helped to ameliorate the symptoms. Antipyretics were useless.
Conclusion: Hypohidrosis associated with TPM treatment was generalised, and mostly applied to patients less than 12 years. The incidence of hypohidrosis during topiramate treatment was closely related to the age of patients.

p852
High Performance Liquid Chromatography Detection of Lamotrigin in Therapeutic Drug Monitoring: Marmara University Experience
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Purpose: Lamotrigine as a new antiepileptic drug is currently being used in mono and polytherapies and striking results demonstrate that lamotrigine is becoming an important drug in the pharmacotherapy of epilepsy. In this study, we attempted to measure the steady state plasma concentrations of lamotrigine, to incorporate the analyses in the routine tasks of our 'Therapeutic Drug Monitoring Unit'. The epilepsy patients treated in Marmara University and Cerrahpasa Medical School Hospitals were included in the analysis.
Methods: Plasma lamotrigine levels were detected using a high performance liquid chromatography (HPLC) technique with UV detection at 214 nm. Upon the completion of extraction procedures using chloroform, either the samples or the external standards containing chloramphenicol as an internal standard were injected onto HPLC system with isocratic elution of 0.01 M KH2PO4 (pH: 6.7), acetonitrile, methanol (70:20:10%, v/v/v). For the interpretation of the results, the therapeutic level for lamotrigine was accepted as 3-14 ug/ml. Patient data like age, weight, height, sex, other illnesses and concurrent use of other drugs were also gathered, together with the dose and duration of lamotrigine.
Results: 45% of the patients were found to be within the accepted therapeutic levels, 52% were detected being below and 3% above the announced therapeutic levels (3-14 ug/ml).
Conclusion: This study demonstrates that HPLC can be used for routine lamotrigine monitoring. However, it is important to note that accepted therapeutic levels for lamotrigine changed recently and clinical outcome of the patients should be evaluated together with the analytical measurements to guide the epileptologists in their reasoning.

p853
Comparative Study of Sodium Valproate and Lamotrigine as Monotherapy in the Management of Typical Absence Seizures
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Purpose: To see the efficacy of sodium valproate and lamotrigine as monotherapy in typical absence seizure.
Methods: 30 patients were included (males 16; females 14 – age between 5 to 14 years). Typical absence seizures were diagnosed clinically and supported by EEG. Patients with any form of other premorbid conditions were excluded. A randomised, open label, parallel group design was made to give sodium valproate and lamotrigine (15 patients in each group). The doses of both the drugs were escalated according to the clinical response, starting from a low dose. Lamotrigine was titrated very slowly at 2 weekly intervals to avoid unwanted side effects (maximum 10 mg/kg/day). Patients were followed up once a month for the subsequent 12 months with their seizure diary. Various haematological and biochemical parameters were checked during these follow ups. Repeat EEGs were done whenever required. Primary efficacy of the drug was considered where no clinical and electroencephalographic evidence of seizure was found.
Results: After one month of treatment 9 patients (60%) were seizure free with sodium valproate and none receiving lamotrigine. After 3 months 11 patients (73.3%) receiving sodium valproate and 8 patients (53.3%) receiving lamotrigine were seizure free. After 12 months 12 patients (80%) receiving sodium valproate and 10 patients (66.6%) receiving lamotrigine were seizure free respectively ($p>0.05$). Minimal side effects were noted: in 26.6% with sodium valproate and 20% with lamotrigine. No drop out was observed.
Conclusion: Lamotrigine was found to be as efficacious in controlling typical absence seizures as was sodium valproate. But lamotrigine has a slower onset of action, possibly due to slow titration of doses. Both drugs were well tolerated.

p854
Efficacy and Tolerability of Lamotrigine in Children with Treatment-resistant Epilepsy
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Purpose: To investigate the efficacy and tolerability of Lamotrigine (LTG) as add-on therapy for children with treatment-resistant epilepsy.
Methods: 20 children, age 3-14 years, were studied retrospectively for 12 months. Patients were on an average of 1.6 concomitant anticonvulsants at entry. Seizure frequency was compared before and after treatment. Doses ranged from 20-400 mg daily. All subjects had physical and neurological examinations, and routine baseline haematological, biochemical, and urinary investigations prior to entry.
Results: 9 patients (45%) became seizure free. 3 patients (15%) had seizure reduction by 75% or greater. 3 patients (15%) had seizure reduction by 50% or greater. 5 patients (25%) had no significant change from baseline or became worse. Lamotrigine was discontinued in 3 patients representing a withdrawal range of 15%. A reduction of 50% on the number of concomitant anticonvulsants was reported compared to baseline. 6 children (30%) were converted to Lamotrigine monotherapy at the end of our study period. There was an overall 87.1% seizure frequency reduction after one year of treatment with LTG. Lamotrigine was generally well tolerated. 40% of patients reported no side effects. 3 (15%) reported decreased concentration. 3 (15%) reported headaches. 2 (10%) reported rash and one patient was withdrawn because of this. No patient showed significant changes from baseline haematological, urinary and biochemical parameters.
Conclusion: Lamotrigine was an effective drug with a substantial rate of seizure-free patients in our population. It was also generally safe and well tolerated in the majority of our patients.

p855
Lamotrigine in Paediatric Patients with Refractory Epilepsy
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Purpose: New generation antiepileptic medications improved seizure outcome in patients with intractable epilepsy. We studied efficacy and the side effect profile of lamotrigine (LTG) in paediatric patients with refractory epilepsy.
Methods: We reviewed the database of our prolonged video-EEG monitoring laboratory retrospectively and identified 75 patients with refractory epilepsy who had been on LTG either alone or in combination for at least three months.
Results: The age at onset of seizures ranged between the newborn period-13 years (mean: 3.28±3.16). The age at the time of evaluation ranged between 1-24 years (mean:12.54±5.79). 30 patients (40%) had generalised seizures; 39 patients (52%) had partial onset seizures with or without secondary generalisation; 6 patients (8%) had two or more types of seizures. Overall 16% of patients had idiopathic epilepsy, 24% had cryptogenic epilepsy and 60% had symptomatic epilepsy. MRI was available for 64 patients and 38 (60%) had abnormal findings. LTG reduced seizure frequency by 30-50% in 46% of patients with partial seizures, and in 60% of patients with primary generalised seizures. Patients with symptomatic epilepsy owing to perinatal asphyxia had the least favourable outcome. Most common side effects were mild skin rashes and gait disturbances; less frequent side effects included deterioration of seizures, vertigo and insomnia.

Conclusion: Lamotrigine has shown efficacy in paediatric patients with both generalised and partial seizures; the most favourable results regarding seizure outcome are obtained in patients with generalised seizures. None of our patients suffered from major adverse events. However, patients should be closely monitored regarding side effects of LTG.

p856
Lamotrigine Therapy of Epilepsy Associated with Angelman's Syndrome
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Purpose: Angelman syndrome is a neurogenetic disorder characterised by developmental delay and a frequently refractory epileptic condition. Valproate, clonazepam and/or phenytoin are said to be the most effective. Experience with the newer antiepileptic drugs (AEDs) is very limited despite their better safety profile and tolerability. We hypothesized that lamotrigine might be more efficacious and better tolerated.
Methods: Potential patients for this retrospective study were identified from the epilepsy clinics at Notre-Dame, Sainte-Justine, and Yale New Haven hospitals. Patients were included in the study if they had Angelman syndrome along with refractory seizures. The medical record of each patient was reviewed with interest on seizure types, previous AEDs and response to lamotrigine.
Results: 5 patients (2M, 3F, 10-35yo) were included in this study. All had 2 or more seizure types: generalised tonic-clonic (5), complex partial (4), myoclonic (3), and atypical absences (2). Previously failed AEDs included valproate (5), carbamazepine (3), phenytoin (5), clonazepam (4), clobazam (3), topiramate (2), nitrazepam (1), phenobarbital (1), and gabapentin (1). 1 patient had pancreatitis on phenytoin, 1 had worsened seizures on carbamazepine, and 1 developed hepatic encephalopathy on valproate. 3 patients became seizure-free with lamotrigine (9, 20 and 36 months FU), 1 was seizure-free for one year with subsequent loss of efficacy, and 1 showed >90% reduction in myoclonic seizures (20 months FU). No side effects were reported.
Conclusion: Lamotrigine can be effective and well tolerated in patients with Angelman's syndrome.

p857
Comparison of Valproate and Lamotrigine for Treatment of Newly Diagnosed Epilepsy: Interim Report
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Purpose: Comparison of efficacy and tolerability of lamotrigine (LTG) and valproate (VPA) in patients with newly diagnosed epilepsy. Interim analysis is performed to evaluate predetermined criteria for drug discontinuation.
Methods: A prospective, open, parallel group trial for patients with newly diagnosed epilepsy, previously untreated, randomised to monotherapy with LTG or VPA, and followed up for a minimum period of 6 months. The protocol was designed to conform with standard clinical practice. End point variables were seizure freedom and retention on treatment for study period. Statistical analysis was performed for alpha = 0.05; results are expressed as confidence intervals.
Results: 73 patients with newly diagnosed epilepsy (median age 34 years, range 18-76), were randomised to VPA (n=38) or LTG (n=35). 51 patients (59-79%) had partial seizures with/without secondarily generalised seizures, and 22 (21-41%) had generalised seizures without partial onset. 55.26%, (40-70%) patients with VPA have remained seizure free for the study period, as have 54.29% (38-70%) patients on LTG. Efficacy of each drug in various seizure types didn't differ significantly. 68% (53-81%) patients randomised to VPA were still taking it at the end of study period as were 69% (52-81%) patients randomised to LTG.
Conclusion: Interim analysis didn't find any statistical significant difference neither for efficacy nor for safety of VPA and LTG monotherapy in newly diagnosed epilepsy. Further results in respect to greater power and follow up period will be submitted.

p858
Randomised Double-blind Trial of Lamotrigine Versus Sustained-release Carbamazepine in Newly Diagnosed Elderly Epilepsy Patients: A Preliminary Analysis
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Purpose: To compare the efficacy and tolerability of lamotrigine (LTG) and sustained release carbamazepine (CBZ) in elderly patients with newly diagnosed epilepsy.
Methods: This multicentre, double-blind, double-dummy 40 week study (five European countries) included newly diagnosed elderly patients (65 years or older) who had presented with two or more unprovoked epileptic seizures (partial with/without secondary generalisation, or primary generalised tonic-clonic). The dosage of LTG or CBZ (1:1 randomisation) was escalated over 4 weeks, then adjusted according to efficacy and tolerability. Starting, initial maintenance, and maximum dosages were 25, 100 and 500 mg/day for LTG, and 100, 400 and 2000 mg/day for CBZ, respectively.
Results: Of 179 patients (median age 73) evaluable at this interim analysis, 92 (46 M, 46 F) received LTG and 87 (53 M, 34 F) received CBZ. 43 LTG patients (47%) and 31 CBZ patients (36%) experienced at least one seizure during follow-up. Mean time to first seizure among patients who had at least one seizure was 9.6 weeks (SD 10.5) in the LTG group, compared with 5.7 weeks (SD 8.7) in the CBZ group. Median time to first seizure was 4 weeks (range 0-38) on LTG, and 2 weeks (range 0-33) on CBZ.
Conclusion: No statistically significant differences were found regarding seizure freedom rates and time to first seizure. There was a trend for less patients on CBZ experiencing further seizures, but time to first seizure among those who had at least one seizure was longer in the LTG group. Ongoing analysis of adverse events and treatment withdrawal rates will allow more meaningful interpretation of efficacy data.

p859
Lamotrigin Monotherapy Outcome in Outpatients of a Tertiary Referral Centre
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Purpose: Evaluation of lamotrigin monotherapy outcome in epilepsy outpatients, with respect to the therapeutic threshold.
Methods: 88 seizure-free patients on lamotrigin monotherapy, followed in the outpatient clinic during 2004, were registered, and monitored by serum lamotrigin levels. It was possible to determine the therapeutic threshold for 55 patients (=N), age 4-73 years, localised epilepsy: 42, generalised epilepsy: 11, and unclassified epilepsy: 2.
Results: Range of lamotrigin therapeutic threshold: for all patients: 4.0 - 48.5 micromole/l, for the group with localised epilepsy: 5.5 - 42.0 micromole/l, for generalised epilepsy: 4.0 - 31.0 micromole/l. In the group of unclassified epilepsy one patient had a therapeutic threshold of 4.0, and the other one of 48.5 micromole/l. Across all patients we found a lamotrigin therapeutic threshold < or = 10 micromole/l in 18%, < or = 20 micromole/l in 60%, < or = 30 micromole/l in 80%, and < or = 40 micromole/l in 93%.
Conclusion: Lamotrigin therapeutic threshold shows a rather wide range, with higher values for a proportion of localised epilepsy

patients than for generalised. In 7% of the patients evaluated, lamotrigin therapeutic threshold is higher than 40 micromole/l.

p860
Generic Substitution of Antiepileptic Drugs: Preliminary Observational Reports of Lamotrigine Switching in Canada
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Purpose: Switching patients from older branded antiepileptic drugs (AEDs) to generic versions can increase the risk of breakthrough seizures and side-effects (Crawford P et al, Seizure 1996;5:1-5; Wilner AN, Epilepsy Behav 2004;5:995-998). Less is known about the consequences of substituting newer AEDs. Here, outcomes associated with substituting generic lamotrigine for brand (Lamictal®; GlaxoSmithKline) in Canada were assessed.
Methods: Observational data was collected from spontaneous reports of lamotrigine-associated adverse reactions filed to Health Canada's Adverse Drug Reaction Monitoring Program (CADRMP), a survey of Ontario pharmacists and a physician chart audit.
Results: Reports of lamotrigine-associated adverse reactions to CADRMP rose from 30 during the 16 month period before generic versions became widely available to 56 in the 16 months following wide generic lamotrigine availability. 29 of the 56 reports were linked specifically to generic lamotrigine, and 14 of these involved lack of seizure control. Loss of seizure control was also identified as the primary reason for patients being switched back to brand from generic lamotrigine following an adverse event, in both the pharmacists' survey (11/14 patients) and the physician chart audit (8/9 patients). Control was regained for the majority of patients, following a return to branded lamotrigine.
Conclusion: These initial reports of loss of seizure control in some patients following brand-to-generic lamotrigine switching, build upon existing similar experiences with older AEDs. Physicians have a vital role in educating their patients as to the potential risks and benefits of AED generic substitution. Study supported by: GlaxoSmithKline Research & Development

p861
Efficacy and Tolerability of Valproate-Lamotrigine Combination Therapy in Refractory Seizures
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Purpose: About 60-70% of newly diagnosed epilepsy patients may achieve adequate seizure control with a single antiepileptic drug. However, for one-third of epilepsy patients polytherapy must be initiated. The combination therapy of valproate and lamotrigine has shown promising results in patients with refractory seizures. Our aim is to determine efficacy and tolerability of the valproate-lamotrigine combination therapy in patient with refractory seizures.
Methods: In open-label, non-randomised, add-on trial we analysed efficacy and tolerability of valproate-lamotrigine therapy in 185 patients (median age 28 years) with seizures refractory to other therapies. The follow-up period was minimum of one year. Efficacy was classified as: 1) remission without adverse effects; 2) remission with adverse effects; 3) >50% seizure reduction; 4) < 50% seizure reduction 5) seizure worsening. Adverse effects were classified as acceptable and unacceptable.
Results: The median doses of lamotrigine was 300 mg and of valproate 1500 mg per day. Remission without adverse effects was obtained in 37 patients (20%); remission with adverse effects in 6 patients (3.2%); seizure reduction of >50% in 59 patients (31.9%); seizure reduction of <50% in 80 patients (43.2%); and seizure worsening in 3 patients (1.7%). Acceptable adverse effects were present in 21 (11.4%), and unacceptable adverse effects requiring discontinuation in 30 patients (16.2%). The most frequent adverse effects were tremor (24.9%), dizziness (12.4%), rash (10.8%), weight gain (10.3%), and double vision (7.0%). Therapy was withdrawn in 79 patients (42.7%), mainly due to the lack of efficacy.
Conclusion: Our data suggest high efficacy and good tolerability of valproate-lamotrigine combination in patients with refractory seizures.

p862
Evaluation of Antiepileptic Drug Therapy for Refractory Focal Epilepsy
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Purpose: To evaluate the clinical results of medical therapy for refractory focal epilepsy.
Methods: A retrospective review of 55 patients with refractory focal epilepsy. We analysed and compared the type of seizures, performed neurological examinations using EEG, CT scan and/or RMI, and identified the antiepileptic drugs used and the maximum seizure-free interval for each patient.
Results: There were 55 patients with focal refractory epilepsy, cryptogenic or symptomatic; 21 of them were males and 34 females, aged from 18 months to 18 years. 54.5% of cases had symptomatic focal refractory epilepsy and 45.5% of cases were cryptogenic. In 58% of cases focal seizures were associated with generalised seizures. All patients were tried on more of the antiepileptic drugs in mono or polytherapy and in some cases corticotherapy and even ketogenic diet were used. Seizure-free intervals were between o1ne day and 2 years, 10 months. In 67, 28% of the cases the best control of the seizures were with valproate as monotherapy or in association. Lamotrigine in monotherapy was administrated in 3 cases followed by a seizure free period of 3–12 months. 8 patients had received carbamazepine in monotherapy with a seizure-free period between 5 days–34 months
Conclusion: According with preliminary results for our group with refractory focal epilepsy, VPA monotherapy or in association with CBZ or LTG had better results regarding length of seizure control. There is a necessity for controlled prospective studies to confirm this hypothesis.

p863
Status Epilepticus as a Result of Acute Lamotrigine Intoxication
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Purpose: It has been suggested that lamotrigine has proconvulsive activity at higher doses. In addition there is not much known about the effects of acute lamotrigine intoxication e.g. due to suicidal ingestion.
Methods: We report a case of convulsive status epilepticus as a result of acute lamotrigine intoxication due to a suicidal gesture.
Results: A 41 year old woman with intractable epilepsy of parietal lobe origin ingested 4100 mg of lamotrigine in a suicidal gesture. Prior to the event she had a miscarriage and became increasingly depressed. She had only simple partial seizures with pain and dystonic motor activity of the left hand. Her seizures were mainly nocturnal and she never had a convulsive seizure. Her antiepileptic regimen consisted of lamotrigine (500 mg per day) and phenobarbital. About 30 min after the patient ingested the pills she went into convulsive status epilepticus. She acquired multiple facial and tongue lacerations due to the seizure activity. Treatment with high dose benzodiazepines was required to terminate seizures. Her lamotrigine level after admission was 47.7 µg/ml (normal range 4-18 µg/ml). Other symptoms of intoxication included severe ataxia, confusion and headaches that were most prominent shortly after admission. Those symptoms, however, resolved completely within five days. As the patient had never had a convulsive seizure, and due to the close temporal relationship, the lamotrigine intoxication most likely triggered status epilepticus.
Conclusion: This reports confirms the suspicion that lamotrigine at higher doses can have a proconvulsant effect. Symptoms of suicidal lamotrigine intoxication include ataxia, confusional state and headache, all of which are completely reversible.

p864
Cross Sensitivity of Skin Rash with Current Antiepileptic Drugs
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Purpose: To investigate cross sensitivity with new antiepileptic drugs (AEDs).
Methods: Retrospective survey of medical records concerning all AED treatment in consecutive patients.
Results: 663 patients were included comprising 2567 exposures to AEDs. Rashes occurred in 93 patients, caused by more than one AED in 18 cases. 50% (4/8) of patients with phenytoin (PHT) rash also exposed to oxcarbazepine (OCBZ), developed OCBZ rash, whereas 80% (4/5) of patients with OCBZ rash had experienced PHT rash ($p < 0.0005$). 29% (7/24) of patients with carbamazepine (CBZ) rash also exposed to OCBZ, developed OCBZ rash, whereas 78% (7/9) of patients with an OCBZ rash had experienced a CBZ rash ($p < 0.0005$). 13% (4/31) of patients with CBZ rash also exposed to lamotrigine (LTG), developed LTG rash, whereas 24% (4/17) of patients with LTG rash had experienced CBZ rash (n.s.). 40% (2/5) of patients with LTG rash also exposed to OCBZ, developed OCBZ rash, and 22% (2/9) of patients with OCBZ rash had LTG rash (n.s.). 27% (3/11) of patients with PHT rash also exposed to LTG, developed LTG rash, and 27% (3/11) of patients with LTG rash had experienced PHT rash ($p = 0.037$).
Conclusion: The risk of OCBZ rash in patients with previous CBZ rashes is low (<1:3), compared to the risk from CBZ in patients with OCBZ rashes (4:5). The cross sensitivity between LTG and CBZ appears to be lower than between CBZ and OCBZ.

p865
Risk Factors for Lamotrigine-induced Rash in Children and Children and Adolescents with Epilepsy
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Purpose: To analyse risk factors for the occurrence of LTG-induced rash.
Methods: A retrospective analysis of the incidence of LTG-induced rash in children and adolescents with mainly intractable epilepsy was performed. Between January 2000 and October 2004, a total of 298 out-patients were treated with either LTG add-on (223) or in monotherapy (65).
Results: Rash occurred in 11 (3.7%) patients with either idiopathic generalised or focal epilepsy (male 7, female 4) with a mean age of 14 years (range, 4 to 22 years). Moderate diffuse macular-papular or morbilliform rash appeared in 9 patients while severe urticarial skin eruption was observed in 2 children. No life-threatening condition was seen. All these patients but one, were treated with LTG as add-on therapy, in co-medication with valproate. 1 patient received LTG in monotherapy. Rash occurred within 2 to 4 weeks (x =18 days) of starting LTG. In 2 patients, initial dose of LTG was higher than recommended (>0.15 mg/kg/day for children taking valproate) and in another two dose of LTG was increased faster than recommended. One patient had a past history of multi-drug hypersensitivity reaction (rash) on carbamazepine, tetracycline and cephalosporine. LTG was discontinued in all patients. All rashes resolved after withdrawal of lamotrigine. Seizures increased in 4 of 11 patients during skin eruption or after the drug withdrawal.
Conclusion: Valproate co-medication was reported in all but one of our patients with LTG induced rash. Fast dosage escalation and initial LTG dose, higher than recommended were concluded in only one third of these children.

p866
High-Affinity Binding of Pregabalin at Alpha-2-Delta (α2–δ) Subunits of Voltage-Gated Calcium Channel: Contribution to Anticonvulsant Action
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Purpose: Pregabalin shows anticonvulsant, analgesic-like and anxiolytic-like actions in animal models and positive results in clinical studies of partial seizures, neuropathic pain and anxiety disorders. This presentation summarises results investigating the role of α2–δ binding on the anticonvulsant action of pregabalin.
Methods: Receptor binding studies using radioligands, behavioural analysis using DBA/2 anticonvulsant test in wild type vs. α2–δ type 1 mutant mice were used.
Results: Pregabalin binds with high affinity to recombinant α2–δ type 1 and type 2 proteins (KD=6 +/- 1 and 7 +/- 1 nM; Mean +/- SEM). These properties are very similar to binding studied with membranes isolated from native mouse, rat, porcine or human brain. Pregabalin did not significantly alter radioligand binding at 38 other commonly studied drug sites, indicating that α2–δ proteins are the primary binding sites for pregabalin. Since a knockout mutation to α2–δ type 1 caused lethality at birth in mice, alternative approaches were required. A single amino acid mutation was incorporated into the native α2–δ type 1 gene sequence to convert arginine 217 to alanine (R217A). The R217A mutation reduced binding affinity for radioligand in vitro by 20-fold. R217A mice had reduced binding of radioligand to neocortex (KD increased from 10 +/- 3 to 238 +/- 29 nM, Mean +/- SEM), hippocampus and other forebrain structures, but relatively unchanged binding in cerebellum. R217A mice had reduced potency of pregabalin for anticonvulsant action. Experiments with compounds structurally related to pregabalin showed a correlation between affinity for binding to α2–δ and in vivo activity in the DBA/2 anticonvulsant test.
Conclusion: These results suggest that high affinity binding to the α2–δ protein is required for the anticonvulsant activity of pregabalin. Together with gabapentin, binding at α2–δ protein defines a novel class of CNS drugs.

p867
Pharmacokinetic Properties of Pregabalin and Gabapentin: Differences and Similarities
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Purpose: To compare the pharmacokinetic (PK) properties of pregabalin and gabapentin; two compounds characterised by high-affinity binding to the α2-δ protein in the CNS. Despite that similarity, pregabalin and gabapentin have been found to exhibit different anticonvulsant, analgesic, and anxiolytic properties.
Methods: The PK properties of pregabalin and gabapentin were assessed using pharmacology studies measuring absorption, bioavailability, metabolism, and drug-drug interaction properties.
Results: Significant PK differences between pregabalin and gabapentin were found. Pregabalin is absorbed rapidly (peak concentrations ≤1hr) yielding plasma concentrations that increase linearly with increasing dose while gabapentin is absorbed slowly (peak concentrations ~3-4hr) yielding plasma concentrations that do not increase proportionally with dose. Significant differences in bioavailability were also encountered: pregabalin bioavailability is ≥90% irrespective of clinical dose whereas gabapentin bioavailability drops from 60% to 33% as dose increases from 900 to 3600mg/day. Pregabalin and gabapentin can be given without regard to food intake. Apparent volumes of distribution for pregabalin and gabapentin are 0.5 and 0.8L/kg respectively. Neither pregabalin nor gabapentin are metabolised, inhibit the enzymes responsible for the metabolism of other drugs, nor bind to plasma proteins. Both drugs are eliminated

renally (t1/2~6hr). Pregabalin renal clearance is <GFR (~70mL/min) indicating net tubular re-absorption. Gabapentin renal clearance is similar to GFR (~120 mL/min). Pregabalin can be administered BID or TID while gabapentin is given TID.
Conclusion: Pregabalin, a second generation α2-δ ligand, has distinct PK advantages over gabapentin. Pfizer funded.

p868
Tiagabin-HCL (Gabitril®): The Treatment of 161 Patients with Partial Epilepsy over a Period of Six Months
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Purpose: In the present investigation, Tiagabin-HCL, a novel anti-epileptic agent, was tested as add-on therapy in an open-label, multicentre study for ongoing treatment of patients with partial epilepsy. Primary objectives consisted of tolerance, compliance and efficacy.
Methods: Tiagabin was administered as add-on therapy to an ongoing anticonvulsive therapy in 161 epilepsy patients (83 male, 72 female) with partial, complex partial and secondary generalised seizures. At the study onset, 39.8% of the patients were treated with monotherapy, 50.3% with combination therapy, 79% of those were treated with 2, 21% with 3 antiepileptic drugs. Reasons for the add-on therapy consisted of inadequate control of seizures and/or adverse effects of the previous therapy. Carboxamide derivatives, lamotrigine and valproic acid were the most frequently used first-line treatments. The titration phase lasted about 6 weeks; after 6 months the median dose was 30 mg/day. Compliance was good; after 6 months 75% of the patients were still included in the study.
Results: At the end of the study there was a 64% reduction in simple partial seizures, 67% reduction in complex partial seizures and a 76% reduction in secondary generalised seizures. Adverse reactions in the first 3 months were seen in 18.6% of patients, and within the following 3 months in only 6.2%. Serious adverse-events were not observed, especially non-convulsive status or visual field defect.
Conclusion: Tiagabin-HCL is a good choice for add-on therapy of epilepsy. It is well tolerated and reduces the frequency of focal and secondary generalised epileptic seizures

p869
Treatment of Infantile Spasms with Vigabatrin as the First Drug
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Purpose: Vigabatrin was proved to be a promising drug for treatment of IS with response rate of 43 to 68%. We conducted the a centre, prospective, observational, uncontrolled study of treatment of newly diagnosed patients with infantile spasms (IS) to assess the efficacy of vigabatrin.
Methods: From September 1995 to September 2004, 164 infants with IS were diagnosed at the Institute. We included 116 previously untreated infants in the study. After 2 basal days for registering the spasms, vigabatrin was given through the same protocol: 50 mg/kg for 1 day, 100 mg/kg 2 days, and 150 mg/kg for 7 days until 1999, and 14 days thereafter before assessing the therapeutic response. Neurologic status, psychometric testing, fundus oculi, metabolic investigation, CT or MRI of the brain were done to reveal the aetiology. EEG was done at admission, on the 7th and 14th day.
Results: There were 75 male and 41 female infants with onset of spasms at 5.6 months mean (range 10 days to 11 months). There were 83 infants with symptomatic, 17 with cryptogenic and 16 with idiopathic IS. Cessation of spasms and resolution of hypsarrhythmia was registered in 64 (55%) patients during 14 days, reduction of spasms for >50% in 24 (20%), reduction of spasms< 50% or persistence 17 (14.5%) and worsening in 11 (9.4%). Positive therapeutic response was registered in 42 (50%) patients with symptomatic, in 9 (52%) with cryptogenic and 13 (81%) with idiopathic IS ($p>0.01$, x^2 test). Worsening of IS during vigabatrin treatment and relapses after cessation of spasms were not seen in the idiopathic group.
Conclusion: Vigabatrin demonstrated significant efficacy as the first drug in infants with IS regardless of aetiology with quick therapeutic response within 2nd and 14th day of treatment.

p870
Vigabatrin Neuro-retinal Toxicity: How to Monitor?
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Purpose: To decide if peripheral neuro-retinal toxicity in people with epilepsy on vigabatrin (VGB) is best monitored subjectively using visual fields or objectively using the wide field multifocal electroretinogram (WF mfERG).
Methods: A long term longitudinal study is ongoing to objectively assess the progression of neuro-retinal toxicity associated with VGB therapy at the Epilepsy Unit, Western Infirmary, Glasgow. 180 patients have been assessed so far, 51 of whom have had repeat assessments. These patients have been placed into four groups, current VGB, ex-VGB, other GABA-ergic, GABA naïve. Patients were matched for age, sex, duration of epilepsy and seizure control. All patients had WF mfERGs, logMar visual acuity, colour vision assessment, visual fields (static perimetry) and electroretinograms (ERGs) performed. In addition visual quality of life and epilepsy-related quality of life were assessed using questionnaires VFQ-25 and QUOLIE-31 respectively.
Results: The difference in P1 latency between central and peripheral responses on WF mfERG is the best correlation with visual field defects, 97.5% sensitivity and 95% specificity. There is little difference between the groups in visual acuity, colour vision and ERG results. The questionnaires show people on VGB have a more negative change in their QOLIE-31 than the other groups whereas VFQ-25 change in the VGB group is similar to other groups.
Conclusion: The difference in P1 latency between central and peripheral responses on WF mfERG is the best correlation with visual field defects and is a good way to monitor progressive visual dysfunction in people on VGB.

p871
Effect of Zonisamide on Urine
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Purpose: Urolithiasis is a rare side effect of zonisamide. Since alkaline urine and crystalluria have been demonstrated to be risk factors for urolithiasis (Go T J Neurol 2003;250:1251-1252., Go T Pediatr Neurol 2005;32:113-115., Go T Childs Nerv Syst in press), the relationship between urine and zonisamide was investigated.
Methods: Urinary pH and the degree of crystalluria were retrospectively studied in epilepsy patients one month after the addition or withdrawal of zonisamide as part of their antiepileptic treatment regimen for the last three years. A total of 27 patients on zonisamide, aged 1 to 25 years (10.1 +/- 5.7 years), 15 males and 12 females and 16 patients not taking zonisamide, aged 2 to 21 years (11.4 +/- 5.3 years), 10 males and 6 females were enrolled in this study. The degree of crystalluria was graded according to the presence of crystalluria per high power field (HPF), as +1 (1-4/HPF), +2 (5-9/HPF) or +3 (> 9/HPF). Patients with pyuria, bacteriuria, hematuria, proteinuria or abnormal serum electrolytes, creatinine, urea nitrogen

were all excluded from the study. Statistical analysis was performed using Wilcoxon signed-rank test.
Results: Urinary pH did not change after the addition or withdrawal of zonisamide to the antiepileptic treatment regimen. However, the degree of crystalluria significantly increased after addition ($p < 0.003$) of zonisamide and decreased after its withdrawal ($p < 0.02$).
Conclusion: Urolithiasis induced by zonisamide might not be due to alkalinization of urine. Crystalluria should be carefully monitored in patients treated with zonisamide to prevent urolithiasis.

p872
New Anticonvulsant Retigabine Opens Kv7.2 (KCNQ2) Channels by Binding to the Activation Gate
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Purpose: Retigabine (RTG) is an anticonvulsant drug with a novel mechanism of action. It activates neuronal KCNQ-type K+ channels by inducing a large hyperpolarising shift of steady-state activation. To identify the structural determinants of KCNQ channel activation by RTG, we constructed a set of chimeras using the neuronal, RTG-sensitive Kv7.2 (KCNQ2) channel and the cardiac, RTG-insensitive Kv7.1 (KCNQ1) channel.
Methods: Functional expression in X oocytes was used to characterise the effects of RTG on mutant channels.
Results: Substitution of either the S5 or the S6 segment in Kv7.2 by the respective parts of Kv7.1 led to a complete loss of activation by RTG. Trp-236 in the cytoplasmic part of S5 and the conserved Gly-301 in S6 (Kv7.2), considered as the gating hinge (Ala-336 in Kv7.1), were found to be crucial for the RTG effect: mutation of these residues could either knock-out the effect in Kv7.2 or restore it partially in Kv7.1/Kv7.2 chimeras.
Conclusion: We propose that RTG binds to a hydrophobic pocket formed upon channel opening between the cytoplasmic parts of S5 and S6 involving Trp-236 and the channel's gate, which could well explain the strong shift in voltage-dependent activation.

p873
Short-term Evaluation of Thyroid Functions and Volumes in Children with Epilepsy Treated with Oxcarbazepine and Valproic Acid
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Purpose: The aim of this study was to evaluate the effects of short term administration of oxcarbazepine (OXC) and valproic acid (VPA) on thyroid metabolism.
Methods: 55 children aged 3-17 years with newly diagnosed epilepsy were included. OXC (n=25) and VPA (n=30) were started as monotherapy. Those who were clinically or subclinically hypothyroid were excluded. Free (f) and total (t) T3, T4, thyroid stimulating hormone (TSH), reverse T3 (rT3) and thyroid volumes were measured before, at the third and sixth months of therapy.
Results: The number of patients having abnormally low hormone levels at the third and/or sixth months in the OXC and VPA groups were as follows; tT4; 8 (32.0%) vs 1 (3.3%), fT4; 5 (20.0%) vs 2 (6.6%), tT3; 4 (16.0%) vs 1 (3.3%), fT3; 3 (12.0%) vs 1 (3.3%) respectively. Serum rT3 values decreased in the OXC group, being significant at the third month. TSH levels were significantly elevated in the VPA group compared to the baseline (p=0.023). Thyroid volumes were not effected in either group.
Conclusion: Although clinically euthyroid, patients under OXC or VPA showed altered thyroid functions at a relatively short therapy interval. With relatively normal thyroid hormone and higher TSH levels, patients taking VPA therapy seem to compensate the side effects of the drug. Relatively lower thyroid hormone levels, especially rT3 which reflect tissue levels of thyroxin and uneffected TSH levels in the OXC group can be explained by either rearranged metabolism with even low levels being enough and no TSH elevation is needed, or by blunted TSH response to relatively low hormone levels.

p874
Status Migranosus Induced by Oxcarbazepine in Three Women With Epilepsy and Migraine
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Purpose: To present 3 cases of status migranosus (SM) induced by oxcarbazepine (OXC) during switchover from carbamazepine (CBZ) to oxcarbamazepine.
Methods: Case Reports: Patient 1: 33y/o, female, with symptomatic temporal lobe epilepsy, secondary to a left temporal dysembryoplastic neuroepithelial tumour, presenting with secondarily generalised seizures. Migraine attacks occur every 1-3 months, responsive to sumatriptan. During switchover from CBZ 1200mg/day to OXC 2100mg/day the patient complained of a pounding headache, nausea and vomiting, lasting over 4 days, unresponsive to sumatriptan, rizatriptan, metoclopramide, rofecoxib, dexamethasone and chlorpromazine. SM subsided after OXC was quickly discontinued and replaced by CBZ. Patient 2: 38 y/o, female, developed secondarily generalised seizures following embolization and surgery due to a right occipital arteriovenous malformation. Seizures were controlled by CBZ 1600mg/day and clobazam 10mg/day. Migraine attacks started at the age of 13y/o and were generally mild. During switchover to OXC (2400mg/day) developed a pounding headache and vomiting, lasting 3 days, unresponsive to diclofenac, metoclopramide, dexamethasone, chlorpromazine. Relief was obtained after OXC discontinuation and CBZ reintroduction. Patient 3: 30 y/o, female, with generalised idiopathic epilepsy, generalised tonic-clonic seizures, controlled by CBZ 1200mg/day. Migraine attacks started as a teenager, controlled by isometepteno, dipirone and caffeine. Patient was switched over to OXC 1800mg/day and on day-7 developed SM lasting 4 days, responsive to OXC discontinuation and CBZ reintroduction.
Results:
Conclusion: Headache may occur during OXC treatment for epilepsy. However, SM has not been reported during the switch over from CBZ to OXC, calling for caution on patients presenting with a history of both conditions.

p875
Effect of Gender on the Pharmacokinetics of Eslicarbazepine Acetate (BIA 2-093), a New Voltage-gated Sodium Channel Inhibitor
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Purpose: Eslicarbazepine acetate (BIA 2-093) is a novel voltage-gated sodium channel blocker in development for the treatment of epilepsy and bipolar disorder. Following chiral analysis, it has been found that eslicarbazepine acetate is metabolised to the S(+) enantiomer of licarbazepine (also known as eslicarbazepine), the main active metabolite. This study aimed to determine the effect of gender on the pharmacokinetics of eslicarbazepine acetate.
Methods: Single-centre, open-label, non-randomized, parallel-group study in 12 female and 12 male healthy subjects. The study consisted of a single-dose (600 mg) period and a multiple-dose (600 mg, once-daily, for 8 days) period, separated by 4 days.
Results: Eslicarbazepine acetate was rapidly and extensively metabolised to eslicarbazepine. Following a 600 mg single-dose, mean maximum eslicarbazepine plasma concentrations (Cmax) and area under the plasma concentration-time curve from 0 to infinity (AUC0-∞) were respectively 9.3 µg/mL and 171.9 µg.h/mL in male subjects,

and 10.1 µg/mL and 205.0 µg.h/mL in female subjects. At steady-state, mean Cmax and AUC0-∞ of eslicarbazepine were 15.5 µg/mL and 295.8 µg.h/mL in male subjects, and 16.8 µg/mL and 295.2 µg.h/mL in female subjects. Steady-state plasma concentrations were attained at 4 to 5 days of administration in both groups. Following single-dose, eslicarbazepine Cmax, AUC0-24 and AUC0-∞ geometric mean (and 95% confidence intervals) ratios (female/male) were 1.09 (0.87, 1.43), 1.16 (0.95, 1.48) and 1.17 (0.90, 1.63), respectively. Following last dose, eslicarbazepine Cmax, AUC0-24, and AUC0-∞ ratios were 1.10 (0.98, 1.27), 1.04 (0.88, 1.28), and 1.01 (0.83, 1.30), respectively.
Conclusion: The pharmacokinetic profile of eslicarbazepine acetate was not affected by gender. Supported by BIAL (Portela & Cª, SA)

p876
Effect of Eslicarbazepine Acetate (BIA 2-093) on the Steady-state Pharmacokinetics of Digoxin in Healthy Subjects
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Purpose: To investigate the effect of eslicarbazepine acetate (BIA 2-093) on the steady-state pharmacokinetics of digoxin.
Methods: Single-centre, randomised, double-blind, placebo-controlled, two-way crossover study in 12 healthy subjects. The study consisted of two 8-day treatment periods separated by a washout of 10 or more days. On each period, subjects received either a daily oral dose of eslicarbazepine acetate 1200 mg once-daily or placebo concomitantly with a digoxin once-daily dose of 0.5 mg/day on days 1 and 2 and 0.25 mg/day on days 3 to 8.
Results: Maximum digoxin plasma concentration (Cmax) was reached (tmax) at 1.0 h (median) post-dose both after reference (digoxin plus placebo) and test (digoxin plus eslicarbazepine acetate) treatments. Mean steady-state digoxin area under the plasma concentration-time curve over the dosing interval (AUCτ) was 17.6 ng.h/mL and 16.6 ng.h/mL with reference and test treatments, respectively. Digoxin AUCτ test/reference ratio presented a point estimate (PE) of 0.96 and a 90% confidence interval (90%CI) of 0.90-1.03. Mean digoxin Cmax was 2.4 ng/mL and 1.9 ng/mL with reference and test treatments, respectively, and PE and 90%CI of the Cmax test/reference ratio were 0.85 and 0.68-1.07. The 15% decrease in digoxin Cmax, when digoxin was administered concomitantly with BIA 2-093, is not expected to affect digoxin efficacy because the extent of exposure (as assessed by AUCτ) was similar and Cmax decrease may reduce the probability of adverse events related with digoxin peak exposure.
Conclusion: Eslicarbazepine acetate, at the dose of 1200 mg once-daily, has no relevant effect on the steady-state extent of systemic exposure to digoxin. Supported by BIAL (Portela & Cª SA).

Wednesday 31st August and Thursday 1st September 2005
13:15 – 14:15
Poster Session
Adult Epileptology

p877
Frequency of Epilepsy Idiopathic Generalised with Variable Phenotypes in the External Consultation of Neurology at Merida, Venezuela
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Purpose: Epilepsy in our environment represents a problem of public health, which agrees with studies that reveal a high prevalence in developing countries. Generalised idiopathic epilepsy is a syndrome determined genetically. In 2001 a new proposal of classification of epilepsy and epileptic syndromes includes the new category of Generalized Idiopathic Epilepsies with Variable Phenotypes (EGIFV): 1) Epilepsy Absence (EA), 2) Juvenile Myoclonic Epilepsy (JME) and 3) Epilepsy with only generalised tonic-clonic seizures (GTCE). Our objectives were to determine the EGIFV frequency and to establish the familiar pattern in our population. Neurology, 61(11): 1576-1581. Rev Neurol, 35(1): 82-86. Epilepsia, 42:1-8.
Methods: We used retrospective research through the revision of charts from neurology consultations, during 2004, and included patients who had an EGIFV diagnosis in all its semiological variants.
Results: 509 epilepsy consultations were included; there were 68 consultations with a diagnosis of EGIFV (13.35%). There were 38 cases with diagnosis of GTCE that corresponded to 55.8% of the cases evaluated with EGIFV. There were 18 cases (26.47%) with a diagnosis of JME. There are 12 cases (17.64%) with a diagnosis of EA. We found that EGIFV appeared in several members of 3 large families.
Conclusion: EGIFV frequency is relevant (13.35%) in our population. A familiar pattern was observed in three large families, suggesting genealogical research is necessary to provide a population pool for genetic characterisation of EGIFV.

p878
Myoclonus, as an Atypical Phenotype in Familial Early Onset Alzheimer's Disease
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Purpose: Although epilepsy is not rare in sporadic Alzheimer's disease (AD), only 5 cases of familial early onset AD (EOAD) with mutations in Presenelin 1 gene (PSEN1) were reported to be associated with myoclonus. The objective of this study is to describe the phenotype of an EOAD patient with myoclonus and established L250V/PSEN1 mutation.
Methods: A Bulgarian family with two observed and 7 affected cases in 3 generations was studied. DNA sequencing of PSEN1, electroencephalogram (EEG), and clinical, neuropsychological and neuroimaging examinations, were performed in the observed patients.
Results: The initial symptom of the first observed patient was forgetfulness at the age of 40 years. The disease course was characterised by slowly worsening of cognitive problems accompanied by myoclonus jerks and behaviour disturbances. EEG showed diffuse changes with generalised sharp wave discharges. She died at the age of 51 years. The AD diagnosis was confirmed histopathologically. The initial symptoms of the second patient were memory deficits and behavioural abnormalities, at the age of 46 years. By age of 50, he had severe dementia. EEG was normal. Neuroimaging in both patients revealed severe atrophy with white matter changes. Their fathers and grandfathers had dementia with a similar clinical course.
Conclusion: We describe L250V/ PSEN1 mutation associated with pathologically confirmed familial EOAD. The phenotype was characterised by behavioural changes in all patients and myoclonus in one of them. Our findings concur with previous report (Furuya et al, Neurol Sci, 2003:209), where the clinical phenotype of myoclonus without behavioural changes was described.

p879
'Withdrawal-approach' Behaviours During Epileptic Seizures
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Purpose: We previously described the act of biting, a behaviour occurring during human epileptic seizures with an instinctive and aggressive valence (Tassinari et al. Epilepsia 2005). We now extend our analysis to individuate and better define the characteristics of

other displays directed to the examiner during or after the 'seizure' event.
Methods: We analysed the Video-EEG recordings of patients, candidates for epilepsy surgery, who presented gestures, facial expressions or vocalization with a 'withdrawal-approach', meaning during or after seizures, and described the semiological features of each of these behaviours.
Results: We observed: a) aggressive-withdrawal behaviours: arm/hands behaviours (grabbing, hitting, threatening, challenging); organized violent behaviour; 'feline-like' hissing and cowling; facial expression of anger; b) approach-appetitive behaviours: behaviours directed to obtaining forgiveness and sympathy or appearing as a need of help and protection in a context of fear; c) joke-play behaviours associated with facial expression of happiness. Vocalization or change in vocal tone resembling sudden variations of feelings and intentions were also observed. These behaviours occur both during the ictal and postictal period and could be spontaneous or clearly 'evoked' by examiner's action. Aggressive behaviours are often seen in association with biting while approaching behaviours often followed a previous withdrawal behaviour.
Conclusion: Our data show that during epileptic seizures instinctive withdrawal-approach behaviours can emerge. The expression of these behaviours could depend on the perception and evaluation of the environment that seemed to be altered during seizures involving the fronto-limbic structures.

p880
Paroxysmal Motor Phenomena During Sleep: Study of the Frequency of Parasomnias in Patients with Nocturnal Frontal Lobe Epilepsy and their Relatives
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Purpose: To verify whether patients with NFLE and their relatives have a higher frequency of parasomnias, in particular arousal disorders, to shed light on the still unknown physiopathological mechanisms underlying NFLE.
Methods: Patients with NFLE: patients aged >1 year with video-EEG recording of at least 1 hypermotor seizure or 2 paroxysmal arousals; relatives of patients with NFLE: at least 7 members of the proband family; control subjects: aged > 1 year, matched for age, sex, education and geographic origin. Relatives of control subjects: at least 7 members of the control family. Each subject underwent a standardised interview, applying the International Classification of Sleep Disorders–Revised (ICSD-R) minimal criteria to diagnose the main parasomnias occurring at any time in the subject's life.
Results: 358 individuals were interviewed: 26 patients with NFLE (M/F: 13/13), 161 relatives of probands, 20 control subjects and 151 relatives of controls. The following parasomnias were more frequent in the NFLE group: probands vs controls: bruxism ($p<0.05$) and arousal disorders such as sleep walking and sleep terror, even if the rarity of the latter and the small cohort precluded any statistically relevant conclusion. Proband relatives vs control relatives: arousal disorders ($p=0.0186$) and nightmares ($p=0.002$).
Conclusion: We confirmed the original hypothesis of a higher frequency of arousal disorders in patients with NFLE and their relatives suggesting a possible common physiopathological mechanism. The study also disclosed two 'unexpected' findings: a higher frequency of bruxism in NFLE patients and nightmares in their relatives.

p881
Asymmetric Seizure Termination of Generalised Tonic Clonic Seizures in Focal versus Generalised Epilepsies
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Purpose: An asymmetric seizure termination (AST) of secondarily generalised tonic clonic seizures (sGTCS) in temporal lobe epilepsy (TLE) has been shown to lateralise seizure onset to the ipsilateral side of longer lasting clonic jerks. Our aim was to compare its prevalence in focal epilepsies (FE) versus generalised epilepsy (GE), where focal signs sometimes are misleading in the diagnostic process. In focal epilepsies we assessed the positive predictive value (PPV) of AST for lateralising the seizure onset.
Methods: Videos of 84 consecutive patients (41 TLE, 24 frontal lobe epilepsy (FLE), 19 GE) showing 177 generalised tonic clonic seizures (92 TLE, 47 FLE, 38 GE, mean 2, range 1-10) were analysed retrospectively. All patients underwent intensive video-monitoring, MRI, neuropsychological testing and SPECT/PET when feasible. Two investigators assessed frequency and side of the last clonic jerks, blinded for diagnosis, EEG and imaging data.
Results: AST occurred in all three patient groups, with a prevalence of 63.4% in TLE (46.7% of seizures), 70.8% in FLE (59.6% of seizures) and 42.1% in GE (21.1% of seizures) (for patients NSD; for seizures TLE vs FLE NSD, TLE vs GE and FLE vs GE $p<.001$). The PPV for the side of seizure onset was 74.4% ($p=.003$) in TLE and 75.0% ($p=.008$) in FLE respectively.
Conclusion: AST has a similar prevalence in both TLE and FLE, lateralising seizure onset to the ipsilateral hemisphere. Although less common than in FE it also may occur in GE. Focal signs should not inevitably lead to the assumption of focal seizures.

p882
Reflex Epilepsy with Writing, Tooth-brushing and Hot Water
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Purpose: Reflex epilepsies are a relatively rare group of seizure disorders and encompass only 5% of all epilepsy patients. Complex precipitating mechanisms as well as other cognitive tasks are defined as praxis induced seizures. Sensory reflex epilepsy is relatively uncommon.
Methods: Our objective is to describe a patient with three types of reflex epilepsy including writing, tooth-brushing and hot water induced seizures.
Results: A 24 year old male patient was referred to our clinic because of tooth-brushing and writing induced seizures. His history reveals that he also had hot-water induced seizures. He was born after an uneventful pregnancy, labour and delivery. All developmental milestones were achieved. At age 17, he had his first right focal motor secondarily generalised seizure. After this first unprovoked seizure he began to seize whenever he wrote or brushed his teeth. His seizure begins with focal myoclonias involving his right arm. If he does not stop the activity as soon as possible the seizure becomes secondarily generalised. At the age of 20, he developed hot water induced epilepsy with the same ictal semiology of his other seizures. He undertook valproic acid treatment. His ictal EEG showed left posterior temporal spikes with secondary involvement of homologous areas of the right hemispheres. Ictal SPECT revealed no perfusion defect in this patient without any lesion on MRI.
Conclusion: To our knowledge this is the first case where three types of reflex-induced seizure occurred in the same person. Complex and

sensory induced reflex seizures would have a common pathway which waits for explanation.

p883
Rostral Cingulate Motor Area and Paroxysmal Alien Hand Syndrome
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Purpose: Alien hand syndrome is characterised by abnormal motor behaviour of the contralateral upper limb, which is subjectively experienced as involuntarily or 'alien' induced.
Methods: We report a patient with a paroxysmal form of this rare syndrome resulting from an ischemic lesion within the rostral part of the right cingulate motor area (CMA).
Results: FDG-PET investigation disclosed focal hypermetabolism of the right CMA (corresponding precisely to the structural MRI lesion). Video-EEG monitoring clearly revealed the ictal epileptic mechanism of the 'alien hand' seizures. Paroxysmal complex motor activities in the left upper limb completely disappeared immediately after establishing antiepileptic pharmacotherapy (LEV).
Conclusion: Rostral CMA very probably plays a crucial role in the production of the ictal automatic motor behaviour of the contralateral hand. This finding may implicate the participation of this part of the caudal anterior cingulate cortex in the genesis of ictal limb automatisms in epilepsy patients.

p884
Ictal Bradycardia and Cardiac Asystole during Temporal Lobe Seizures: A Video-EEG Documentation
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Purpose: To present the video-EEG documentation of ictal bradycardia (IB) and cardiac asystole (CA) during temporal lobe seizures.
Methods: Two patients (case 1: 39 year-old female; case 2: 54 year-old male) suffering from drug-resistant temporal lobe epilepsy underwent long-term video-EEG monitoring from presurgical evaluation. EEG (10-20 International montage) and EKG were simultaneously recorded. Brain MRI in case 1 was unremarkable, in case 2 showed right mesial temporal sclerosis. Both patients underwent cardiologic examination, echocardiography, head-up tilt test, and continuous heart rate/blood pressure monitoring.
Results: Case 1: video-EEG recordings of her seizures showed psychomotor arrest, loss of consciousness, head turning to the left, then fall of the patient. Ictal EEG showed rhythmic theta activity on the left side, rapidly spreading contralaterally. About 25 seconds after EEG seizure onset, heart rate slowed down to about 16 beats/min for about 20 seconds: this EKG change was associated with fall. Cardiologic investigations were unremarkable. Case 2: video-EEG recordings showed seizures characterised by loss of contact, oro-alimentary automatisms, paleness, and fall of the patient. Ictal EEG showed a right temporal rhythmic theta activity; a few seconds after ictal EEG onset, CA occurred lasting up to 10 seconds; at the end of CA, the fall occurred. Head-up tilt test resulted positive for neuromediated syncope.
Conclusion: IB/CA during epileptic seizures have been anecdotally reported; possibly their occurrence is underestimated. Recognition of IB/CA is relevant to disclose a condition that can be involved in sudden unexpected death in epileptic patients and to avoid misdiagnosis with non-epileptic falling fits.

p885
Relationship between Sleep Disorders and Epilepsy in Patients at the Unit of Neurology of the University Hospital of the Andes
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Purpose: To study the relationship that exists between sleep disorders and epilepsy. To determine the frequency of sleep disorders in patients with epilepsy compared with healthy controls. To establish the type and classification of sleep disorders experienced by the patients with epilepsy. To determine the frequency of snores, breathing pauses and drowsiness in the patients with epilepsy.
Methods: Study of observational analytic transverse type in 45 patients with epilepsy and 45 healthy controls. Two structured surveys were applied: format sleep disorders (FTS-6-02) and the Scale of Epworth.
Results: Insomnia was observed in 58% ($p < 0.05$) of patients with epilepsy. Difficulty in going to sleep appeared in 39% ($p < 0.01$); difficulty to maintain the sleep appeared in 40% ($p < 0.038$) of the patients with epilepsy. Nightmares were evident in 27% ($p < 0.05$) and the relationship with anguish, anxiety or stress was 42% ($p < 0.005$). In reference to breathing pauses during sleep, 36% were affected ($p < 0.006$). Day drowsiness appeared in 36% of patients with epilepsy ($p < 0.005$). The frequency of sleep dysfunctions in general in patients with epilepsy was 98% ($p < 0.0001$).
Conclusion: Patients with epilepsy present a probability 37 times greater of suffering one or more sleep disorders than do people who don't have epilepsy.

p886
Algorithms for the Diagnosis and Pharmacotherapy of Migraine Comorbid with Epilepsy
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Purpose: The purpose of this paper was to assess the use of algorithms for the diagnosis and pharmacotherapy of migraine comorbid with epilepsy.
Methods: Patients with migraine preceding the onset of epilepsy were included in this prospective study which used a diagnostic algorithm comprising the entities of the International Classification of Headache Disorders (ICHD-II, 2005), and a pharmacotherapy algorithm based on the best available data regarding acute treatment and prophylaxis of migraine. All patients kept a migraine diary and a seizure diary throughout the study. Treatment results at 9 months and 12 months follow-up were compared with a one month baseline period before the onset of treatment.
Results: Of 24 patients (age range 10-48 years, 19 females and 5 males) migraine worsened after the seizure onset and necessitated prophylactic pharmacotherapy in 18 (75%) patients. After 6 and 9 months of treatment with antiepileptic drugs (valproate in 12, topiramate in 4 and gabapentin in 2 patients) migraine frequency and intensity were significantly decreased when compared to baseline period ($p<0.01$). The postictal headache was significantly better when relieved with sumatriptan than with a combination of ibuprofen and metoclopramide ($p<0.01$). At the 9-months follow-up, seizure reduction occurred in all patients of whom 15 (62.5%) became seizure-free for the last three months.
Conclusion: Although the sample studied is small, the results seem to justify further prospective use of algorithms for the diagnosis and pharmacotherapy of migraine comorbid with epilepsy.

p887
Paroxysmal Kinesigenic Movement Disorders and Epilepsy
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Purpose: To observe the clinical features of paroxysmal kinesigenic movement disorders (PKMD) and to explore their relationship with epilepsy.
Methods: Clinical data, imaging and electroencephalograms (EEG) changes in 41 patients with PKMD were investigated in detail.
Results: All cases were paroxysmal kinesigenic, among which 30 presented as paroxysmal kinesigenic choreoathetosis (PKC) and 11 complained of paroxysmal kinesigenic dystonia (PKD). All patients were alert throughout the ictus. Abnormal imaging change occurred in 6 cases; epileptiform discharges in EEG examination in 12 cases. Antiepileptic drugs took effect on all patients.
Conclusion: Dysfunction of the reflex centre between the sensory afferent pathway and the motor efferent pathway might contribute to dyskinesia which presented some characteristics similar to epilepsy. It was suggested that PKMD shares similar biological changes with epilepsy.

p888
Seizure-related Injuries in Patients with Epilepsy
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Purpose: Patients with epilepsy are reported to have an increased risk of physical injuries. Seizure-related injuries are defined as any injury - trauma, resulting from a seizure, sufficient for the patient to seek medical attention. The aim of this study is to evaluate the risk, type and circumstances of injuries during the epileptic seizures.
Methods: A questionnaire regarding lifetime seizures and their traumatic consequences was administered to 245 consecutive patients with epilepsy (newly diagnosed patients were excluded), 135 female and 110 male, age 18-64 years (M 32.5) admitted to the University Clinic. Generalised tonic-clonic seizures (from onset), complex partial, partial with secondary generalisation and myoclonic seizures, were the most common seizure types.
Results: Out of 245 patients, 95 (38.8%) had had at least one traumatic event during a seizure. 60 reported head trauma (63.2%) as follows: cranial soft tissue contusions or lacerations 46, dental fractures 11, epidural haematoma 1, subdural haematoma 1 and cranial fracture 1. Burns were experienced by 12 (12.7%), blunt injury 8 (8.4%), body wounds 7 (7.3%), bone fractures and dislocations 5 (5.3%), and traffic accidents 3 (3.1%) patients (poly trauma). Domestic accidents prevailed (56.8%), followed by street (29.5%) and work accidents (10.5%).
Conclusion: Head trauma (contusions and lacerations) are commonest types of injuries during seizures. Burns occurred frequently among females at home. In 2 patients injuries during driving occurred as a result of legislation irreverence. Data showed significant risk associated with seizure-related injuries and so facilitates sensible patient counselling about how the risk of such injuries could be minimized.

p889
Cardiac Symptoms in Epilepsy: Monitoring Strategies
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Purpose: Cardiac symptoms can occur in epilepsy, mostly demonstrated by arrhythmias. Severe effects were observed in two cases, demonstrated here to describe potential strategies.
Methods: Patient 1 is a 50 year old woman with previously sparse attacks of altered consciousness initiated by an auditory sensation. She presented with attacks identical to angina pectoris repeatedly followed by generalised seizures, often with urination. Thorough cardiac investigation revealed no objective dysfunction; Printz-metal angina was suggested. Later epilepsy with an atypical aura was suspected and the patient was successfully treated with antiepileptic drugs. Patient 2 is a 40 year old woman with partial complex seizures with dysphasia and secondary generalisation. Once, treated in the intensive care unit in a postictal state, the cardiac monitoring suddenly revealed prolonged asystolia, later AV block III.
Results: Patient 1 became seizure free with no cardiac symptoms on 100 mg Topiramate. Results from simultaneous EEG and ECG registrations will be demonstrated. Patient 2 got a cardiac pace maker. Due to persistent seizures in spite of heavy pharmacological treatment, the decision was taken to implant a vagal nerve stimulator, a procedure which can be performed, given that the cardiac pace maker initially is adjusted.
Conclusion: Cardiac symptoms in epilepsy can be expressed differently and are difficult to identify. The increased occurrence of sudden death in epilepsy as well as arrhythmias during seizures should increase our attention to potential warning signs and appropriate methods for surveillance should be discussed.

p890
Labour and Professional Satisfaction in Patient with Epilepsy
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Purpose: To determine the patients' level of professional and job satisfaction. To detect possible deficits in shaping professional motivation as a special feature of personality.
Methods: 60 patients with diagnosed epilepsy were studied by means of the Washington Psychosocial Inventory (WPSI). Other techniques were also used, such as interviews and autobiographies.
Results: Evidence was collected on the existence of prejudices and wrong ideas concerning epilepsy, which hinder a solid motivational forming in this area. The testimony from one of the patients is also presented to illustrate misunderstandings and limitations these people with epilepsy face from school days to working times.
Conclusion: Consequently, there is job and professional dissatisfaction in most of the studied subjects.

p891
Non-Caucasians with Epilepsy Report Lower Health Related Quality of Life
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Purpose: To determine whether ethnicity is independently associated with health related quality of life (HRQOL) in epilepsy patients.
Methods: Patients enrolled in an epilepsy clinic completed a self-administered survey consisting of quality of life in epilepsy (QOLIE-31, primary outcome), depression, and anxiety scales. A subsequent interviewer-based survey assessed sociodemographics, attitudes

toward self-care, social-support, trust in healthcare, self-efficacy, and health-literacy. Ethnicity was self-reported. Epilepsy-specific assessments included seizure frequency, seizure control, focal vs generalised, and compliance. The bivariate relationship between potential predictors and QOLIE-31 was evaluated using correlations for continuous variables and the t-test for categorical variables. Predictors with $p<0.20$ in bivariate analysis were entered into a stepwise multiple linear regression analysis designed to determine the independent association between ethnicity (Caucasian/Non-Caucasian) and QOLIE-31. Ethnicity-interaction terms were also evaluated.
Results: To date, 81 epilepsy patients (mean age 42+/-16, 72.8% Caucasian, 72.8% focal epilepsy) have completed baseline surveys. The mean QOLIE-31 score was 61.1+/- 19.0. Bivariate analysis identified non-Caucasian ethnicity ($p<0.05$), depression ($p<0.001$), higher seizure frequency ($p<0.10$), poor seizure control ($p<0.20$), anxiety ($p<0.001$), focal epilepsy ($p<0.20$), low compliance ($p<0.01$), low social-support ($p<0.001$), low self-efficacy ($p<0.001$), unemployment ($p<0.01$), low compliance ($p<0.05$), and exercise ($p<0.20$) as potential predictors of lower QOLIE-31 score. Multivariate analysis identified non-Caucasian ethnicity ($p<0.05$), depression ($p=0.001$), anxiety ($p<0.001$), and low self-efficacy ($p<0.01$) as independent risk factors for lower QOLIE-31 scores. There was significant interaction between ethnicity and anxiety ($p<0.05$).
Conclusion: Non-Caucasian ethnicity is independently associated with lower HRQOL in epilepsy. Furthermore, anxiety appears to have a more detrimental effect on HRQOL among non-Caucasians compared to Caucasians.

p892
Surveillance Study of Hot Water Epilepsy in Istanbul, Turkey
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Purpose: The aim of this study is to screen hot water epilepsy (HWE) in people aged between 1 and 34 in Istanbul and to determine the relationship between demographic properties and the condition.
Methods: Four groups were selected for simple random sampling in four districts on the European side of Istanbul. A standardised form including 6 items related to HWE symptoms, individual and family history and bathing habits has been administered to 639 healthy volunteers for this epidemiological study.
Results: 50.2% (n:321) of volunteers were women and 49.8% were men (n:318). The mean age was 12+6.33 years. 28 cases (4.4%) responded by saying yes for at least one of the symptoms that are defined for HWE. Symptoms were respectively: deja vu, dreamy state, discoloration of the face and a feeling that there are environmental changes. Among the people who had complaints, discrimination of gender was not statistically significant ($\chi 2$:1.40, $p=0.24$). Family history for epilepsy was significant in these cases ($\chi 2$:4.31, $p=0.04$). Bathing habits and the water temperature were investigated separately. 18 of the cases were evaluated by 2 neurologists. 12 of them were male. 1 case and the mother of another case were diagnosed as HWE and 2 cases as probable HWE. Interictal EEG revealed no epileptiform abnormality in 3 of them. Long-term follow-up was started.
Conclusion: Due to the high detection rate (0.3%) found in this study, epidemiological studies with a larger sample size and long term follow-up will further contribute to exploring the real frequency and understanding the pathogenetic mechanisms of the disease.

p893
Southern Indian Study on Iatrogenic Seizures
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Purpose: Iatrogenic seizures are uncommon disorders due to treatment with drugs, biological agents, radiation, drug withdrawal, diagnostic tests, procedures and operations. Only a few studies are available recording this entirely in developing countries like India.
Methods: This prospective case series study was done to find out the incidence, clinical presentation, and cause for iatrogenic seizures in a Southern Indian rural population. Patients with a history of seizures admitted in Trichy KAPV Medical College's AGM hospital and ABC hospital for a period of 3 years from 2002 were used for this study.
Results: Iatrogenic seizures constituted 57 (2.35%) of the total number of 2,421 cases of seizure disorder patients admitted during the study period. 38 were male (66.66%) and 19 were female (33.33%). The age of these patients ranged from 7 to 63 years. None had a history suggestive of an active epilepsy, or any recent onset of seizures. 5 (8.77%) patients had a seizure during childhood and another 19 (33.33%) patients had a positive history of epilepsy in their family. Of 57 patients with iatrogenic seizures 9 (15.78%) had motor partial seizures on treatment with anticysticidal treatment with albendazole for neurocysticercosis. 12 (21.05%) patients on anti-diabetic medication with hypoglycaemic episode had a generalised tonic clonic seizure (GTCS). On treatment with atropine for organophosphorus poisoning 5 (8.77%) patients had GTCS. 10 (17.54%) who had treatment for bronchial asthma from a traditional healer with indigenous medicine on theophylline injection had GTCS. 5 (8.77%) had GTCS with a tramadol injection. 3 (5.26%) with chlorpromazine had GTCS. 1 woman (1.75%) who was on oral lorazepam for more than a year for anxiety disorder had GTCS on abrupt withdrawal of the drug. 10 (17.54%) had GTCS with crystalline penicillin (7patients) and Benzathine penicillin (3 patients). 2 (3.50%) with carbamazepine for trigeminal neurologia had GTCS.
Conclusion: In this series, iatrogenic seizures were reported in 2.35% of patients. Presence of a positive family history (33.33%) of seizure or epilepsy can cause people to get iatrogenic seizures. Due to lack of hypoglycaemic awareness 21.05% of patients had GTCS. Patients with focal brain lesions got more partial seizures than generalised seizures. Patients with asthma on indigenous medicine with emergency allopathic medication had more iatrogenic seizures, probably due to a synergic effect. In developing countries children and adults having had a penicillin injection also had a higher incidence of iatrogenic seizures. To prevent these seizures physicians should take caution in administering drugs associated with proconvulsant potency, to patients with a positive family history of seizures or epilepsy, with a previous history of seizures, neuro psychiatric disorders or with underlying brain conditions.

p894
Prognostic Factors and Recurrence Rate of a First Non-provoked Epileptic Crisis on Patients from 1 Month to 16 Years Old who Consulted the San Vicente of Paul Hospital between 1997 and 2004
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Purpose: Determine the recurrence rate and the prognostic factors related to the recurrence of a first unprovoked epileptic crisis.
Methods: A study of retrospective and descriptive cohort, 52 children who consulted between 1997 and 2004 with a first unprovoked epileptic crisis were under observation for a minimum period of 6 months or until a recurrence was presented. Children with early symptomatic and febrile seizures, new born, myoclonic, atonic seizures, or absence, were excluded.
Results: All 52 patients were under observation for an average of 19 months (range 2 and 72 months). The age of the first crisis was on

average 6.9 years (range 6 months to 7 years). 16 (31%) patients presented recurrence crisis, of whom 7 (43.7%) had family background of epilepsy and only 1 (16.2%) had a previous febrile seizure. Neurodevelopment retard was found in 4 (25%) cases, crisis of partial onset in 11 patients (60.7%), abnormal neurological exam (EEG) in 50% of the cases, abnormal neuroimages in 4 patients (25%). No differences were found on the range of ages and the aetiologies.
Conclusion: Principal recurrence factors were found in those patients with a family background of epilepsy, neurodevelopment retard, abnormal neurological exam, disturbed EEG and crisis of partial onset. No differences were found in the age of initiation or the aetiology of the seizures.

p895
First Unprovoked Seizure: Problems and Questions of Diagnosis and Treatment in Tashkent
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Purpose: We studied 46 adult patients after first unprovoked seizure.
Methods: EEG were performed on 25 of them within the first 48 hours of the first seizure, 6 of them in 7 days, and 5 patients in 10 days after the seizure.
Results: The standard EEG was abnormal in 68.7% of early performance and significantly associated with increased risk of seizure recurrence, especially for patients with focal epileptiform activity. Only 2 patients had epileptiform discharges in the standard EEG, on whom EEG was performed later than 48 hours. EEG with sleep deprivation was abnormal in 43.8% of all cases and revealed epileptiform patterns in 11.8% of patients who had no epileptic activity in the standard EEG. Routine EEG revealed nonspecific focal slowing in 12 of 38 patients who presented with normal neurological status on admission. Further neuroradiological examination detected previously unknown brain lesions in 9 of these cases, particularly brain tumours (n=2), AVM (n=3), posttraumatic scars (n=3), chronic subdural haematoma (n=1).
Conclusion: Thus, the early performance of EEG is important for early detection of focal nonepileptic and epileptic abnormalities after a first unprovoked seizure and may provide valuable information on previously unknown disorders. But we can suppose that a relatively low rate of incidence of single seizure in the Tashkent population could be explained by cultural particularities (fear that it could be known to relatives and friends, especially for young unmarried persons) and also absence of specialised epilepsy units with qualified specialists in epileptology in Uzbekistan.

p896
Prevalence and Pattern of Epilepsy in Student Community in West Bengal: A Study from India
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Purpose: Epilepsy, a global health problem, is also a significant neurological burden for students. The aim of this study was to estimate the frequency of epilepsy and syndrome classification among the student community of West Bengal.
Methods: Students attended the Neurology O.P.D. of Students Health Home (SHH), were evaluated by a group of neurologists to confirm the diagnosis and were evaluated with history, examination and appropriate investigations. The study was carried out between March 2002 and February 2004.
Results: The total number students enrolled were 330,120. There were 1,794 persons with active epilepsy with a crude prevalence rate of 5.41 per 1000 population. Generalised epilepsies and epileptic syndromes constituted 6.7%, localisation-related epilepsies constituted 34.03% and epilepsy undetermined whether focal or generalised constituted 3.21%. Semiologic classification showed generalised tonic-clonic (43.%), absence (8.9%), myoclonus (6.02%), atonic (4%), partial seizure (34.24%), and multiple seizure type (3.06%). 86% seizures were controlled with either mono or polytherapy
Conclusion: Frequency of active epilepsy among the student community does not differ from that of the general population. The study highlights that proper evaluation and good seizure control can be achieved in a well-structured centre even with limited resources.

p897
Women, Epilepsy and Pregnancy
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Purpose: The aim of the investigation was to carry out an epidemiological study of epilepsy in Belarus.
Methods: We performed a population-based case ascertainment of all available sources of medical care (including the State Belorussian Register of people who were subjected to radiation exposure after Chernobyl disaster) from January 2002 until December 2004. Women of all ages were analysed. 37% of patients were girls under 18, 51% were women aged between 18 and 50 and 12% were women over 50 years old. Pregnancies, their outcomes and children born of women suffering from epilepsy, were also analysed. Only cases with active epilepsy (at least one seizure during the last 5 years regardless of treatment) were included. All patients were examined by a psychiatrist or a neurologist.
Results: The incidence rate of epilepsy (registered newly-diagnosed patients) among women suffering from the Chernobyl disaster in 2002-2004 varied from 16.4 to 24.5 per 100,000 of population. The prevalence rate of epilepsy among women who underwent radiation exposure in 2002 was 142.7 and in 2004 - 151.7 per 100,000 of population.
Conclusion: We analysed case reports of 28 pregnant women suffering from epilepsy. One of them, 32-weeks of gestation women, have died at home together with foetus during status epilepticus. Blood level of phenobarbital was found to be 50 mg/l. Another 12-weeks of gestation women had non-progressive pregnancy. Blood level of carbamazepine found to be 30 mg/l. 30% of patients received carbamazepine and valproates. 20% received benzonale and last 50% of patients received phenobarbital. Caesarean section was performed in 30% of cases. There were no malformations in children born from women, suffering from epilepsy.

p898
Preventable Epilepsies and their Significance: A Study from Eastern India
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Purpose: Epilepsy is one of the most common neurological problems with a significant socio-economic burden not only to patients and their families but also to society and the nation. With recent advances in neuroimaging and molecular biology we can establish the aetiology of epilepsy in a number of cases, among which a significant proportion are preventable. The aim of this study was to identify the preventable factors causing epilepsy, so that necessary intervention could be taken.
Methods: Patients attending OPD and Epilepsy Clinic of the Institute and Rural Health camps were evaluated by a group of neurologists to confirm the diagnosis of epilepsy. The patients were then evaluated with detailed history, clinical examination and appropriate investigations to find the aetiology.
Results: A total 475 (345 patients from the Institute and 130 from Rural Health camps) were included in the study. Although the majority had idiopathic epilepsies, we could establish aetiologies in 45.6% of patients from the Institute and in 36% of cases in the rural group. Preventable aetiologies were found in 28.3% of patients from the Institute and in 25.5% from the rural group. Birth asphyxia and

perinatal insult, neurocysticercosis, other CNS infection, head injury, drugs and toxins, and cerebrovascular accidents were identified. A significant proportion of refractory epilepsies from the Institute were due to preventable causes.
Conclusion: We conclude that a significant number of cases of epilepsy are due to some preventable causes in India that can be tackled by a few public health measures.

p899
Epidemiological Profile of Epilepsy in the University Hospital in Bogota, Colombia
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Purpose: Epilepsy is a chronic disorder with important personal and social consequences. Its epidemiology has received widespread attention in numerous studies concerning the general population, but in other regions, the population differs in the way it must be handled and followed-up. The main purpose of this study was to determine the characteristics of patients with a diagnosis of epilepsy and the frequency of the different types of epilepsy and syndromes according to age groups.
Methods: We conducted a descriptive study of 291 patients with a diagnosis of epilepsy who were attended in the Neurology Unit at the Hospital Universitario Samaritana between December 2003 and September 2004. The variables obtained were age, sex, age of onset of seizures, antecedents, the kind of seizure and syndrome. The mean, standard deviation and variance analysis were employed, according to the type of variable used.
Results: The patients were between 10 and 89 years old (mean: 34.5 years), the male/female ratio was 170/121 (1.4:1). Age at onset of the seizures varied from 0-89 years (mean: 22.87). Predominance of focal seizures (83.85%), followed by generalised seizures (16.151%). Of the epileptic syndromes, 52.58% were symptomatic focal, 28.87% were cryptogenic focal and 15.81% were idiopathic generalised.
Conclusion: The epidemiological profile is similar to that observed in other populations.

p900
Epilepsy as a Risk Factor for Cancer
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Purpose: Epilepsy and long-term use of antiepileptic drugs have been suggested to be associated with an increased risk of cancer. We therefore set out to analyse previous diagnoses of epilepsy as a risk factor for certain cancer forms in a case-control study.
Methods: Incident cases of leukaemia, lymphoma, myeloma and pancreatic cancer were identified from the Swedish Cancer Registry 1987–1999, in total 54,000 cases. Controls (n=138,000) were randomly selected from the Swedish Population Registry stratified on age, sex and year of cancer diagnosis. Cases and controls were linked to the Swedish Hospital Discharge Registry for 1969-1999 to identify first time hospital discharge for epilepsy.
Results: While an epilepsy diagnosis the same year as a cancer diagnosis carried an elevated risk of non-Hodgkin lymphoma, odds ratio (OR) 2.89, 95% confidence interval (CI) 1.89-4.41, Hodgkin's disease, 4.77 (1.77-13.30), leukaemia, 2.55 (1.50-4.32), and pancreatic cancer, 2.05 (1.22-3.45), discharge with a diagnosis of epilepsy two years or more before the diagnosis of cancer was not associated with an increased risk of any of the types of cancer included in this analysis. The lack of association was evident also for individuals with an epilepsy diagnosis preceding malignancy/reference-year by >10 years.
Conclusion: Clinical examinations prompted by seizures probably explain the observed association between epilepsy diagnosis the year before a cancer diagnosis. However, our results lend no support to the suggestion that epilepsy, and presumably long-term exposure to antiepileptic drugs, is associated with an increased risk of the types of cancer included in the present study.

p901
Predictive Factors of Short-Term Outcome in Patients with Status Epilepticus
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Purpose: Short-term outcome in patients with status epilepticus (SE) is usually favourable despite severe derangement of homeostatic functions during prolonged episodes of SE. The aim of the study was to determine the predictive factors of short-term outcome in patients with SE.
Methods: All consecutive adult patients with an episode of SE admitted to the Institute of Neurology in Belgrade during a 10-year period were prospectively included in the study. Clinical characteristics of SE were correlated with the outcome of a patient using multivariate logistic regression. Risk factors and predictive value for the outcome of each characteristic were determined. Outcome was defined as favourable if there was no difference, or unfavourable if there was a difference between the neurological, cognitive or psychiatric functioning of a patient before and after the episode of SE at the time of discharge.
Results: There were 920 patients with SE. There was a favourable outcome in 698 (76%) and unfavourable 222 (24%) patients. A later group included new sequels of the underlying disease in 81 (8.8%), death in 120 (13%), and other outcomes in 21 (2.2%) patients. Only serious aetiology was significantly associated with the unfavourable outcome (risk factor: 370, CI 77-1774, $p<0.00001$). In an analysis of patients who died, we found that serious aetiology led to death in 106 patients while in 14 (12%) the death was due to the complication of convulsions, therapy, and/or prolonged coma.
Conclusion: Serious aetiology was the only factor with a significant predictive value for the short-term outcome of patient with SE. There was a hint that in a small group of patients who died after SE, the outcome was influenced by the complications of convulsions, therapy, and/or coma.

p902
Epilepsy in the Elderly Latin-American population: A Systematic Review of its Prevalence
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Purpose: The elderly is the most rapidly growing segment of the population. In the northern hemisphere, the prevalence of active epilepsy is about twice that of younger adults. But approximately 85% of the global burden of epilepsy is in the developing world. A systematic review and analysis of prevalence studies of epilepsy in the elderly Latin-American population was conducted, in order to establish its magnitude.
Methods: MEDLINE, IMBIOMED, and LILACS (Latin-American and Caribbean biomedical database) were searched. We included studies exploring the prevalence of epilepsy in the elderly through standardised data collection questionnaires, with reports of population numbers for data confirmation, and with a clear definition of epilepsy. Reviews, abstracts, letters to the editor, duplicate studies, and studies on subpopulations were excluded. Type of population (urban/rural), gender, year of study, and method of ascertainment were collected.
Results: The search yielded 1518 publications in MEDLINE, 96 in LILACS, and 99 in IMBIOMED. Application of the exclusion criteria resulted in 32 studies; but only 7 presented prevalence in the elderly population. The median prevalence was 13.5 per 1000 people (range: 0-32.8). The method of ascertainment was similar in all: questionnaire

and evaluation, with the exception of one study (health records). Four studies were performed in rural and three in urban settings. Information was available only for Bolivia, Brazil, Ecuador, Chile, Guatemala, and Panamá.
Conclusion: Albeit substantially variable, the median prevalence of epilepsy in the elderly Latin-American population was similar to that in the northern hemisphere. Sources of variability in prevalence rates will be explored.

p903
Seizure Recurrence Following First-ever Seizure from Sleep in Adults
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Purpose: A first-ever seizure arising from sleep has been reported to be associated with a higher risk of seizure recurrence in selected patient populations. This may have implications in identifying patients who should be treated after a first-ever seizure.
Methods: Prospective analysis of adult patients attending a hospital based first seizure clinic. Patients with prior seizures were excluded. The clinical characteristics of patients with a first-ever seizure from sleep were compared to those with a first-ever seizure during wakefulness. The occurrence of a second seizure was analysed in all patients with a minimum of one year follow-up.
Results: Seizures arose from sleep in 91 of 475 patients (19%). Focal epileptiform abnormalities were more frequent in the seizures-from-sleep group whereas generalised epileptiform abnormalities were more frequent in those with a first ever seizure during wakefulness. The demographic and clinical data including proportion treated were similar between the two groups. Seizure recurrence occurred in 43 patients (47%) with a first-ever seizure arising from sleep compared to 163 patients (42%) presenting with a seizure during wakefulness ($p=0.41$). The time to second seizure and the proportion with seizure recurrence at one year were also similar. If the first seizure occurred during sleep the second seizure was highly likely to also arise from sleep (79% versus 13%, $p<0.0001$).
Conclusion: A first-ever seizure from sleep was not associated with a higher risk of seizure recurrence and when present the second seizure was highly likely to also occur while asleep. These findings may have implications for treatment decisions and the counselling of patients with first-ever seizures.

p904
Epilepsy Prevalence in Bursa City Centre
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Purpose: This study is designed to find the epilepsy prevalence in the city centre of Bursa, a city situated in the west of Turkey. The study design was in accordance with the advice of the World Health Organisation (WHO) and study criteria were set up according to principles of ILAE Epidemiology and Prognosis Commission.
Methods: Out of 1,195,000 population, 2,124 people were asked to complete a standard questionnaire during a semi-structured face-to-face interview carried out by two neurology residents. Epilepsy patients filled another questionnaire after which they were examined by the same residents in order to classify the seizures.
Results: During the first interview, out of 190 suspected epilepsy cases, 26 (15 male, 11 female) were found to have epilepsy. Point prevalence of active epilepsy in this area was 8.4 per 1000. Life-long prevalence ratio was 12.2 per 1000. 61.50% of 26 patients had generalised, 11.50% partial, 11.50% both generalised and partial seizures and 7.60% had reflex epilepsy. Seizures started during the first decade of their lives in 50% of the patients. Only 34.60% were using antiepileptics regularly.
Conclusion: Since there are few prevalence studies in our country, multi-centred studies from different regions of the country should be planned. Some new questions should be added to the standard questionnaire of WHO for epilepsy to make practitioners in our society diagnose epilepsy more accurately. This will help identify patients who should be diverted to tertiary care centres.

p905
Clinical and Aetiological Profile of New Onset Seizures in an Emergency Department in Northwest India
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Purpose: To determine the clinical and aetiological profile of new onset seizures presenting to the emergency department (ED) of a secondary-care, teaching, general hospital in North West India.
Methods: Patients over 12 years of age, with new onset seizure/seizure clusters in the 72 hours preceding presentation to the ED from 8 January 2003 to 30 June 2004 were evaluated using a tailored protocol with various biochemical, microbiological, neuroimaging and EEG investigations. The seizures were classified, according to the ILAE semiologic, syndromic and aetiologic classifications.
Results: New onset seizures comprised 110 (1.03%) of all admissions to the ED. Aetiological diagnosis was established in 83 (74.5%) cases. Aetiological diagnoses included: neurocysticercosis (12.7%), acute infarct (8.2%), uremia (7.2%), CNS infections (7.2%) and hyponatremia (5.4%). Computerised tomography (CT) (plain & contrast) was done on 88 patients and was found to be abnormal in 44 (50.0%). EEG was done on 20 (18.2%) of patients and was abnormal in 9 (45%) of these.
Conclusion: Neurocysticercosis, cerebral infarct, metabolic abnormalities and CNS infections were the most common causes of new onset seizures in the ED. CT scan has a high yield in the evaluation of new onset seizures presenting to the ED.

p906
Epidemiological Aspects of Adult Epilepsy in Libreville, Gabon
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Purpose: Epidemiological surveys indicate that the prevalence of epilepsy is higher in developing countries than in industrialised countries. The purpose of this study was to gain insight into the impact of epilepsy on adults in terms of frequency and risk factors in a Central African country.
Methods: A retrospective study was carried out in a department of neurology of Hospital Centre of Libreville, on patients hospitalised between 1 January 2000 and 31 December 2003. All patients with a diagnosis of epilepsy (ILAE criteria) confirmed by a neurologist and neuroradiological examination (EEG, CT scan or MRI) were included.
Results: 153 (12.5%) epilepsy patients were found among 1259 subjects admitted during the study period. 90 patients were males (sex-ratio= 1.4) and the mean age was 37.3 years. Generalised seizures were observed in 80.4% of cases and partial seizures in 19.6% of cases. 31 cases had idiopathic epilepsy, 27 had cryptogenic epilepsy and 95 had symptomatic epilepsy. The causes of epileptic seizures were: infection of the CNS (42.1%), stroke (30.5%), alcohol (15.8%), intracranial tumours (8.4%) and post-traumatic epilepsy (3.2%). Lastly 12 patients with a family history of epilepsy were identified. Treatment administered was: phenobarbital (55.5% of cases), valproic acid (38.6% of cases) and carbamazepine (5.9% of cases).

Conclusion: This study shows that epilepsy is major public health problem in Gabon. Therefore, other studies are necessary to quantify the impact of each aetiology in this infliction in this country.

p907
Epilepsy Pattern in Bangladesh
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Purpose: Bangladesh has no National statistical data about epilepsy, but our observations reveal that there are at least 5-6 million people with epilepsy in our country. This study aims to identify the main characteristics of a cohort of patients with epilepsy attending the Neurology Foundation Hospital (NFH).
Methods: 3557 patients with a clinical history of more than 2 convulsive attacks seen at the NFH, Dhaka, between May 1997 and December 2004 were the study population. For each patient, the main demographic and clinical variables were recorded. Patients were seen and followed-up by the same neurologist. EEG, brain CT and MRI were performed on selected cases.
Results: The main findings were: male predominance (67% : 33%). The majority of patients were between 16-31 years (40%). Seizure type: tonic-clonic 79%, complex partial 7.7%, focal epilepsy 6.2%, absence seizure 3.9% and juvenile myoclonic epilepsy 3.2%. 81% of patients were on polytherapy and 19% on monotherapy. Phenobarbitone (42%) and carbamazepine (25%) were the commonest prescribed drugs. 65% of patients were well controlled. Deep-rooted prejudices among the lay people, inadequate treatment, difficult access to the hospital and unavailability of the common drugs were the main challenges to treatment.
Conclusion: This study reveals the main characteristics of a large cohort of epilepsy patients in Bangladesh, as well as the main problems involved in their treatment: deep-rooted stigma and lack of knowledge about epilepsy among the public and even the physicians and unavailability of facilities for diagnosis and treatment of the epilepsy patients.

p908
The Epidemiology, Clinical Characteristics and Management of Adults Referred to a Teaching Hospital First Seizure Clinic
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Purpose: There is little data describing the epidemiology of patients who present to the Emergency Department (ED) with a first seizure. There continues to be lack of clarity as to the level of investigation, including the use of neuroimaging, that should be performed in the ED, and which patients require admission for further management. The aim of this study was to describe the epidemiology, clinical characteristics and management of adults with a suspected first seizure.
Methods: Data was collected on consecutive adults referred to the first seizure clinic at the Royal Infirmary of Edinburgh between 4 February 2003 and 10 February 2004.
Results: 232 patients were studied. Median age was 32 years (mean 37; range 13-84). 53% were male. Lower socio-economic groups were more likely to present with a first seizure. 19% of patients with a suspected first seizure were admitted to hospital. Appropriate driving advice was documented in 64% of driver's notes. 72% of patients were seen at the follow-up first seizure clinic within six weeks of being referred. 8% of patients had a further suspected seizure whilst waiting to be seen at the clinic. 52% of patients were diagnosed as having a first seizure at the clinic, of which 50% were provoked by either alcohol, drugs or sleep deprivation. Computer tomography and electroencephalogram were the most common investigations ordered at the first seizure clinic.
Conclusion: Patients who present to the ED with a suspected first seizure can in general be safely managed as an outpatient. First seizures are often precipitated by drugs and alcohol.

p909
Seizures in Acute Stroke: A Prospective Study from India
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Purpose: Seizures following cerebro-vascular accidents are of increasing importance as the population ages and are of growing contribution to symptomatic epilepsies. The purpose of the study was to assess prospectively the incidence of seizures in patients with acute stroke.
Methods: 277 consecutive patients with acute stroke admitted to the neurology ward were included in the study. CT scan and/or MRI of brain and other relevant investigations were carried out on all patients. Patients were followed up for one year for occurrence of seizures. Mean follow up period was 10.8 months.
Results: There were 204 cases of ischaemic stroke and 73 cases of haemorrhagic stroke. 13 patients (4.7%) had seizures (Ischaemic stroke – 9 and intracerebral haemorrhage – 4). 11 cases had early onset seizures (at onset 7 and 4 between 4th and 7th days) and 2 patients had seizures after 6 and 11months from acute stroke. None had a positive family history or past history of seizures. Seizures were partial with secondary generalisation in 85% cases. Imaging showed large cortical infarct in 62% cases with evidence of cardioembolic cause in 46%. The patients with seizures were younger (mean age 49.5 vs 54.9 years among patients without seizures). EEG was carried out on 13 patients and was abnormal for 9 patients.
Conclusion: Post stroke seizures are mostly partial in onset and occur in about 4.7% patients with acute stroke. The seizures are more common in relatively younger patients having larger infarcts and cardioembolic stroke.

p910
Seizure Recurrence After Antiepileptic Drug Withdrawal: Correlation with Presence and Degree of Hippocampal Atrophy
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Purpose: Various factors influence the proportion of patients with epilepsy who were previously seizure-free under medication, and will experience a recurrence after antiepileptic drug (AED) withdrawal. Structural abnormalities are believed to be one of the most important variables. The objective of this article is to determine the presence and degree of hippocampal atrophy (HA) in a group of patients with at least two years seizure freedom who underwent AED withdrawal and to correlate HA with seizure recurrence.
Methods: From a group of 99 patients followed in a protocol for AED, we performed a hippocampal volumetric study in 84 patients who had high resolution MRI. Hippocampal volumes (HcV) were determined in 3mm T1-IR coronal images using NIH software, with correction for the variation of total intracranial volumes. Data was compared to those from a control group and HA was determined for HcV below two standard deviations from the mean of the control group.
Results: A total of 50/84 patients (59.5%) had seizure recurrence after AED withdrawal and 31/84 patients (37%) had HA. HA was present in 23/50 (46%) patients with seizure recurrence and 8/34 (23.5%) of those who remained seizure-free ($\chi 2$, p=0.036). Survival analysis (Kaplan-Meier) demonstrated a significant difference of seizure recurrence between patients with or without HA (Mantel, p=0.029). Patients with seizure recurrence had smaller HcV than those who remained seizure-free (ANOVA, p=0.024).
Conclusion: Although patients with partial epilepsy and HA may have good seizure control with appropriate AEDs, MRI evaluation of Hc abnormalities should be taken into account when deciding on AED discontinuation in seizure-free patients.

p911
Prevalence of Post-traumatic Epilepsy Among People with Epilepsy in a Developing Country
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Purpose: The aim of the present study was to find out the prevalence of seizures caused by head injury among epilepsy patients attending an epilepsy centre in a developing country, and the various contributing factors responsible for the development of such seizures.
Methods: This study was conducted retrospectively on epilepsy patients who visited me in my clinic. The medical records of the index cases were reviewed for details of head trauma; type of injury, severity of injury.
Results: We screened 1300 epileptic patients; 101 patients had a past history of head trauma. Road traffic accidents were responsible for 80% of the head trauma, followed by falls from a height (15%). Most of the patients (90%) had their seizures within five years of the head trauma. The shortest time between trauma and onset of seizures was 6 months; the longest time was 7 years following severe head trauma. Partial seizures with secondary generalisation were the commonest type of seizures found in 49.5% of patients followed by generalised tonic-clonic seizures (25.7%), while complex partial were found in 12.87% and simple partial seizures in 11.88%. EEG was positive in 85 % of the cases and helped in classification of the type of epilepsy.
Conclusion: Post-traumatic epilepsy represents about 7% of the epileptic population in my study. Most of the cases are caused by road traffic accidents. Improving the quality of safe driving could prevent a high percentage of head injuries and subsequent epilepsy.

p912
A Study of Epilepsy in the Elderly Population of India
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Purpose: Approximately one third of new onset epilepsies occur over 65 years of age. In order to study the characteristics of epilepsy in the elderly population, we evaluated 51 consecutive patients with epilepsy who were over 60 years of age.
Methods: The study was conducted in the epilepsy clinic of a tertiary referral teaching hospital, over 22 months. A detailed history, clinical evaluation, brain imaging and EEG were performed. Patients were followed up for minimum of 3 months and drug levels were obtained whenever deemed necessary.
Results: Elderly patients accounted for 6.5% of all the patients with epilepsy. Of the 51 cases post stroke seizures were seen in 23.5%, tumours in 17.6%, dementias in 3.9%, infective causes in 5.9% and other causes in 7.8% of cases. In 15.7% the cause was presumed to be idiopathic and in 25.5% the cause remained unknown. Males predominated (68.6%); seizure type was mostly partial (73%), 20% being complex partial. Prolonged postictal confusion, postictal paralysis and status epilepticus were common (12%, 10%, 14% respectively). Epilepsy was easy to control (77% were seizure free at 3 months). Most were on monotherapy (82%), phenytoin being the commonest. Adverse events were seen in 23%, ataxia and rash being the commonest. The mortality (11.8%) was high.
Conclusion: Epilepsy is common in the elderly. Different causes, higher mortality, drug related adverse events and complications (eg. status epilepticus) make this group more vulnerable. With growing life expectancy and an increasing elderly population, epilepsy is likely to pose a big challenge to the developing world.

p913
Risk Factors of Epilepsy through a Case-control Study in a Tertiary Referral Centre in Eastern India
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Purpose: To study the risk factors in patients with epilepsy by comparing them with an age and sex matched control population.
Methods: 100 consecutive subjects suffering from active epilepsy were recruited from the Epilepsy Clinic of Bangur Institute of Neurology from January to December 2004. 300 age and sex-matched subjects without any past history of epilepsy were included in the control group. Their demographic profiles, history of febrile convulsions, history of head injury, central nervous system (CNS) infection in the past, birth hypoxia and injury, family history of epilepsy, etc. were recorded. Using a multivariate analysis we calculated and adjusted the odds ratio (OR) and 95% confidence intervals (CI) for each factor.
Results: We found a positive association between epilepsy and positive family history [OR=6.67(1.98-32.61)], history of significant head trauma [OR=5.37(1.78-16.14)], history of birth hypoxia [OR=13.2(1.69-104)] and history of febrile convulsion [OR=19.95(5.03-162.25)] in multivariate analysis. However, birth hypoxia, cerebral palsy, pre- and peri-natal maternal illnesses and CNS infections were found to be significantly associated with epilepsy in univariate analysis.
Conclusion: After correcting the effects of all other factors, history of significant head trauma, birth hypoxia, a positive family history and history of febrile convulsions in the past were found to be significantly associated with epilepsy in our population.

p914
Incidence of Epileptic Seizures of Neurological Patients Admitted to the Emergency Room
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Purpose: To establish the incidence of epileptic seizures in patients hospitalised in the Neurology Department of the Emergency City Hospital over 3 years, and to study their aetiological and clinical polymorphism.
Methods: Retrospective study of medical cases with history, clinical, biochemical, CT and EEG results analyses.
Results: In our clinic 322 patients with epileptic seizures were urgently hospitalised; 238 men and 84 women, with age range from 16 to 76 years. The number of such patients tends to increase each year, from 9.26% of the total number of urgently hospitalised patients to 9.84%, and 14.25%. In 202 cases seizures appeared for the first time; the other 120 cases represented repeated seizures. 292 patients demonstrated generalised seizures, while focal seizures appeared only in 14 cases, nonconvulsive seizures in 9 patients, and polymorph seizures in 12 cases. aetiological factors were represented by trauma in 75 cases, alcohol withdrawal in 66 patients, vascular in 36, infections in 11, cerebral tumour in 5, parasites in 4 cases. In 97 cases aetiology was mixed, and in 28 patients aetiological factor was unknown.
Conclusion: Patients with epilepsy represent 9,26 to 14,25% of all neurological patients hospitalised because of emergency causes. The majority (74%) were men. The main aetiological factors were head trauma, alcohol abuse, and cerebro–vascular failure. 63% presented with initial seizures, and in 90.7% cases they were generalised.

p915
Stroke and Partial Epilepsy
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Purpose: Partial seizures occurring during the evolution of stroke can lead to various complications, and can increase mortality. The objective of our study was to achieve an early diagnosis of partial seizures developed during stroke and to apply the appropriate treatment, thereby improving the prognosis of diseases.
Methods: We studied 1,000 patients with stroke admitted in County Hospital of Constantza, Department of Neurology between 1 February 2000 and 1 January 2004. We analysed the following parameters: age, sex distribution, clinical manifestations, paraclinical investigations, treatment response, prognosis, mortality. Seizures were classified in accordance with ILAE classifications.
Results: In our group 120 patients presented partial seizures: 20% motor partial seizures, 15% sensitive partial seizures; 60% were age 50-60 years, 40% 40-49 years; 30% had ischaemic stroke, 70% haemorrhagic type; 95% improved after treatment and 5% become worse with generalised epilepsy, status epilepticus, coma and a poor prognosis.
Conclusion: Early diagnosis and treatment of partial seizures during stroke are important, and can decrease mortality. Ischaemic stroke is a more frequent cause of death than haemorrhagic stroke. Cortical or extensive lesions are at a higher risk of developing seizures than subcortical lesions and those that involve only one lobe.

p916
Ictal Epileptic Facial Pain in Two Patients with Malformation of Cortical Development in the Contralateral Postcentral Cortex
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Purpose: To report two patients with ictal epileptic facial pain, a rare occurrence during epileptic seizures.
Methods: Patients FLO and MDI are described together with clinical data, interictal scalp electroencephalogram (EEG) and magnetic resonance imaging (MRI). Patient MDI was evaluated for epilepsy surgery including video scalp electroencephalographic (VEEG) monitoring, interictal glucose metabolism positron emission tomography (PET), magnetoencephalography (MEG) and subdural ictal recording.
Results: FLO is a 41-year-old right-handed woman with a painful ictal sensation in the left face and complex partial seizures since age 37. She was seizure-free at last follow-up with sodium valproate and tiagabine. The interictal EEG recorded sharp waves and theta activity in the right parietal and temporal regions. MRI showed large right parietal perisylvian polymicrogyria. MDI is a 29-year-old left-handed woman with medically intractable left face ictal pain since age 9. Interictal EEG recorded right epileptiform activity at the centro-parietal and vertex regions. Ictal VEEG analysis showed rhythmical 7-8 Hz activity at the parietal vertex and right parietal regions. PET indicated glucose hypometabolism over the right parietal lobe. MEG showed epileptiform magnetic source imaging in the right parietal, and MRI showed possible right focal parietal polymicrogyria. Video-EEG with an 8x8 subdural grid covering the right lateral parietal area demonstrated ictal origin in the right inferior postcentral gyrus. Resective surgery was performed without seizure recurrence.
Conclusion: Facial pain may be an ictal epileptic symptom arising from the contralateral postcentral areas. The parietal cortex may play a role in the generation and processing of focal trigeminal pain.

p917
Corpora Amylacea (CoA) in Refractory Mesial Temporal Lobe Epilepsy: Clinico-Pathological Correlations
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Purpose: Although corpora amylacea (CoA) is a recognised marker of mesial temporal sclerosis (MTS), its significance in mesial temporal lobe epilepsy (MTLE) is uncertain. In the present study we have tried to define the prevalence and significance of CoA in surgical specimens of patients with MTLE.
Methods: We scored, on a semi quantitative scale, the presence of CoA in CA1, CA3, dentate gyrus and end folium of the hippocampus and graded as >10/high power field (HPF) (grade 3), 6-10/HPF (grade 2), <5/HPF (grade 1) and none (grade 0). We compared the demographic, clinical, neuropsychiatric, electrophysiological and outcome data of patients with (CoA+) and without (CoA-)
Results: Out of 373 temporal lobectomy specimens from MTLE patients with >1 year post-operative follow-up, CoA was present in 129 (34.5%) specimens. The mean age at surgery in the CoA+ group was significantly higher than that of the CoA- group (24.5 years vs 31.8 years, p-0.0001). The mean duration of epilepsy prior to surgery in the CoA+ group was longer (21.7 years vs. 15.5 years, p-0.000). Other variables like age at seizure onset, history of febrile seizures, interictal and ictal EEG data, pathology in MRI other than MTS, and post-operative seizure outcome did not differ between the two groups. Psychiatric symptoms occurred more in the CoA+ group. 17 of the 21 (80.9%) patients with major psychosis, had grade 2-3 CoA, schizophrenia being the commonest.
Conclusion: Our results lend support to the progressive nature of pathology in MTS, and the pathogenic role of CoA in TLE related psychosis indicating that it is probably a surrogate marker.

p918
Malformation Caused by Abnormalities of Cortical Development (MCD)
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Purpose: To find a correlation between epilepsy and malformation caused by abnormalities of cortical development (MCD) in an Albanian patients cohort.
Methods: We studied the charts of 755 patients, 428 (56.7%) males, 327 (43.3%) females, presented at the outpatient clinic of Epilepsy, University Service of Neurology, Tirana, Albania, between January 2004 and February 2005. We concentrated on the age of disease, its gravity, clinical forms, EEG and imaging performed and AED treatment used.
Results: 93 (12.3%) of these patients had at least one MRI performed. We found 17 (18.2%) patients with MCD among them. According to Brakovich we classified the cases in: heterotopia, ganglioglioma, poly microgyria with schizencephaly, schizencephaly and cortical dysplasia. The mean age of MCD epilepsy patients is 27 years old (15-34 years). The mean disease duration is 20.3 years. Computerised EEG registrations are performed in all cases. The main epilepsy form diagnosed is secondary generalised epilepsy. 5 patients are on monotherapy, 8 on polytherapy (2 AEDs), and 4 on polytherapy (3 AEDs). 10 (58.8%) of these patients have drug resistant epilepsy.
Conclusion: MCD is one of the most important aetiologies of chronic and drug resistant epilepsy.

p919
Dual Pathology in Epilepsy: Experience from Peruvian Referral Centre
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Purpose: Most frequent lesions associated with refractory epilepsy are cortical dysplasia, vascular malformation, cerebral tumour and mesial temporal sclerosis (MTS). Previous studies have described simultaneous presence of MTS and extrahippocampal lesions; this clinical presentation is called 'dual pathology'. We report our experience with the frequency and clinical characteristics of dual pathology in epilepsy in-patients.
Methods: We made a prospective study of 87 epilepsy patients from March 2002 to December 2004. The patients were hospitalised in the biggest Peruvian reference centre and had at least a cerebral organic lesion and cerebral IRM with coronal slices.
Results: We selected 38 patients with the following pathologies: neurocysticercosis (15), vascular malformation (9), tumour (6), cortical dysplasia (5) and gliotic lesions (3). We found simultaneous hippocampal atrophy (HA), inclusion criteria for dual pathology, in 7 patients (18.4%). Age of onset and duration of epilepsy, and febrile convulsions didn't participate in presence of HA. Dual pathology was present in patients with cortical dysplasia and gliotic lesions.
Conclusion: Some possible common pathogenic mechanisms during pre or perinatal development can explain the association between MTS and other structural lesions; this hypothesis is based on the observation of the frequent relation of HA with developmental diseases in our study. This association can have surgical therapeutical implications if we can determine the responsible lesion of refractory epilepsy.

p920
Sudden Death after Brain Injury: Role of Post-traumatic Epilepsy
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Purpose: Sudden death is a rather neglected late complication in brain-injury patients. Its incidence, mechanism and possible prevention give rise to certain questions.
Methods: We present a retrospective study of 6 brain-injury patients, followed-up in Nantes, who have suffered sudden death at least 2 years after their brain injury (mean 12 years later). Their mean age at the time of injury was 25.3 years old. Basal characteristics, type and severity of initial lesion, as well as co-existence of endocrinologic disorders and/or epilepsy have been studied.
Results: In our population, 5 patients initially had a GCS inferior to 8. Haemorrhagic contusions were the more frequently observed cerebral lesions. 3 of our patients presented with a skull base fracture. Anti-epileptic therapy was applied to 4 out of 6 patients, to 2 for prevention and to the other 2 for late post-traumatic seizures (difficult to manage in one). The majority of deaths (4 out of 6) occurred during sleep.
Conclusion: Mortality aetiology in brain-injury patients is not widely studied, least of all late sudden death. Recent data have pointed out a higher risk of sudden death in young adults with epilepsy, especially those with nocturnal convulsions. Death mechanism is not well clarified, though a correlation with a neuro-vegetative dysfunction of cardio-pulmonary origin can be considered. We discuss the possibility of establishing a direct connection between epilepsy and the occurrence of unexpected death following brain injury, in order to evaluate and modify our clinical and therapeutic approach to late post-traumatic seizures.

p921
Influence of Aetiology on Seizures Frequency in Localisation-related Refractory Epilepsy: A Study of Adult Epilepsy Patients.
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Purpose: To study the influence of aetiology in localisation-related refractory epilepsy, use of AEDs (antiepileptic drugs) and duration of epilepsy and seizure frequency.
Methods: The study took place in the outpatient clinic of the Department of Neurology in Tampere University Hospital that treats the majority of refractory patients in the area (population of 440,000 inhabitants). 131 consecutive adult localisation-related refractory epilepsy patients followed up in our centre were retrospectively evaluated on the basis of clinical and brain imaging data. Refractoriness was defined as having seizures after two years adequate therapy with at least two AEDs. The cause of epilepsy was classified as: HS (hippocampal sclerosis), dual pathology (HS associated with another brain lesion), trauma, CD (cortical dysplasia), tumour, vascular malformation, other hippocampal pathology, CNS (central nervous system) infection, other cause and cryptogenic. Seizure frequency was classified into groups: 0/year, 1-11/year, 1-15/month and >15/month in a two-year follow-up. Duration of epilepsy was recorded.
Results: 106 patients had persistent seizures, the majority of them frequent. 25 achieved six months remission. The most common aetiologies included HS, trauma, tumour and CD. All patients with vascular malformation, dual pathology and CD and most HS- and trauma patients were difficult-to-control. Most patients had undergone many earlier AEDs and were still on at least dual therapy. The median duration of epilepsy was long.
Conclusion: There was no specific aetiology with good outcome and no difference in the outcome of remote symptomatic and cryptogenic aetiologies, but in symptomatic patients seizures were more frequent. Duration of epilepsy did not influence the outcome. There was a small group of patients achieving remission after multiple AED regimens. The most refractory patients were MRI-positive.

p922
Aetiology of Symptomatic Focal Seizures in a Semi-urban Centre in South India
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Purpose: To study the aetiological spectrum of symptomatic focal seizures encountered in a semi-urban centre in a developing country.
Methods: 58 patients with focal seizures and abnormal neuroimaging scans seen between April 2003 and December 2004 were analysed for the identification of aetiological factors for symptomatic seizures.
Results: Focal motor seizure with secondary generalisation was the most common seizure type, seen in 80% of cases. Status epilepticus was encountered in 10 cases (17.2%). Solitary computer tomography enhancing lesion (SCTEL) and focal cerebral calcification (FCC) were the distinct aetiological factors in 40% of cases. The other aetiological entities included ischemic stroke (33%), cerebral sinovenous thrombosis (12%), eclamptic encephalopathy (7%), haemorrhagic stroke (3%), posterior leucoencephalopathy (3%) and acute disseminated encephalomyelitis (2%). Seizure recurrence was observed in 13% of patients followed up over 1 to 20 months (mean: 4 months)
Conclusion: The aetiological spectrum of seizures in a developing country reflects the geographically distinct pathological entities. SCTEL, FCC, cerebral sinovenous thrombosis and eclamptic encephalopathy were important causes of seizures, apart from ischaemic stroke. Identification of these aetiologies would help to avoid categorising these cases as epilepsy and thereby minimise the

attendant social stigma and the need for long term antiepileptic medication.

p923
Adult-onset Rasmussen's Encephalitis: Clinical Features and Non-surgical Therapeutic Options
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Purpose: Rasmussen's encephalitis (RE) is characterised by intractable focal seizures, EPC, and progressive hemispheric dysfunction, rarely described in adulthood. We describe the clinical features and therapeutic options in adult-onset RE (a-RE).
Methods: The study group comprises 7 female patients (mean age 34.1 yrs). All patients underwent to an extensive non-invasive clinical work up comprising repeat EEGs, neuropsychological assessment, high-resolution anatomical MRI, and FDG-PET. CSF was examined in all patients.
Results: Epilepsy was the onset symptom in all patients (mean age at onset 16.5 yrs), anticipating by several years neurological deficits (mean age 22.8 yrs). Typical MRI features included atrophy of the frontal-insular cortex and nucleus caudatus, and white matter hyperintensity in T2-w.i.; FDG-PET showed regional hypometabolism congruent with the MRI findings. Neurological and neuroradiological progression was observed in all patients. Severely drug-refractory focal motor seizures were reported in all patients and EPC in 6/7 subjects. Scalp EEG showed interictal slow and epileptic activity, involving mainly the frontal-central regions. CSF anti-GluR3 antibodies were detected in 1/7 patients, whereas oligoclonal bands were observed in 5/7 patients. 6/7 patients progressed to high dose IVIg, and (4/7) subsequently to selective adsorption of circulating IgGs. All received steroids, chronically. None of the patients were submitted to surgery.
Conclusion: a-RE is an exceedingly rare progressive condition with a variable course; accurate clinical, neurophysiological and neuroimaging features allowed non-invasive early diagnosis. In a-RE, high dose IVIg and immunoabsorption treatments may warrant long term benefits before planning surgical treatment.

p924
Seizures Associated with Cerebrovascular Diseases: An Indian Experience.
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Purpose: Cerebrovascular diseases are the commonest cause of seizures in an elderly population. Seizures can occur either during an acute stroke or as sequelae. The prevalence of seizures associated with cerebrovascular diseases is uncertain in developing countries where there are no stroke registers. The present study was carried out to find the prevalence of seizures in stroke patients and to identify any associated risk factors.
Methods: 181 consecutive patients who were admitted with CT proven stroke in our hospital were evaluated. The occurrence of seizures was studied during their hospital stay and on follow up visits. The patients were studied for type of stroke as well as for predisposing factors for developing seizures, and for the impact of seizures on morbidity and mortality.
Results: Mean age of patients was 53.91 years (16-85 years). 102 patients were males and 79 were females. Cerebral infarction was present in 127 patients; 49 had cerebral haemorrhage and 5 patients had subarachnoid haemorrhage. 19 patients (9 males and 10 females) developed seizures thereby giving a prevalence of 9.5%. The occurrence of the seizures was seen more in ischaemic strokes and the majority of these were cortical lesions. 16% of these patients with seizures experienced puerperium related strokes. 10.5% patients with seizures had recurrent strokes. Seizures were mostly focal or focal onset generalised.
Conclusion: Seizures associated with strokes are prevalent in 9.5% of patients. Puerperium related and recurrent strokes are more likely to cause the development of seizures. These patients had significant morbidity and residual disability.

p925
Inflammatory Granuloma: Most Common Cause of Focal Seizures in North India
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Purpose: To evaluate the aetiological factor in epilepsy patients attending neurology OPD in a tertiary care referral hospital under University of Delhi.
Methods: We evaluated the cause of epilepsy in 212 patients with CT or MRI being the most important investigation, and with additional investigations wherever necessary.
Results: Out of the total 212 patients GTCS were seen in 142 patients (67%) and focal seizures in 70 patients (33%). The CT or MRI was abnormal in 43.4% of total cases. Among patients with GTCS, CT or MRI, abnormality was observed in 35.2% of cases as compared to 60% of patients with focal seizures. The most common abnormality in CT or MRI was multiple ring enhancing or calcified lesions consistent with inflammatory granulomas, seen in 51.4% of cases of focal seizures compared to only 28.4% cases of GTCS. Neurocysticercosis was the leading cause as compared to multiple tuberculomas. Normal imaging was seen in 40.8% of cases with GTCS in contrast to only 15.7% of cases of focal seizures. In 20% of cases with GTCS and focal seizures, imaging was either being done or the report was not available during the study.
Conclusion: Inflammatory granulomas are the most common identifiable cause of epilepsy in focal seizures though this may not reflect the general population because only difficult or complicated cases may have been referred to our hospital.

p926
Spontaneous Resolution of Intractable Epileptic Seizures following Probable HHV-7 Infection
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Purpose: We report a 3 year-old female with intractable epilepsy post West syndrome whose seizures disappeared following an acute viral infection, without changes to anti-epileptic therapy. Questionnaires were also sent to characterise this phenomenon through a clinical survey.
Methods: The female infant was born at term to a healthy mother after an uneventful pregnancy and delivery. At the age of 5 months, intractable brief tonic spasm and a series of infantile spasms developed, and an electroencephalogram indicated hypsarrhythmia. She was diagnosed with West syndrome. The seizures were uncontrollable with conventional therapy, such as ACTH, vigabatrin, sodium valproate, clonazepam, zonisamide, and ketogenic diet. Multiple daily generalised tonic seizures and brief tonic spasms were observed before this infectious episode. Questionnaires were sent to Paediatric neurologists in 73 institutions in Japan.
Results: At the age of 3 years, the intractable seizures disappeared after a febrile rash illness probably due to human herpes virus 7(HHV-7) infection without changes to anti-epileptic drugs. Completed surveys were received from 11 institutions, and 21 cases similar to this case were selected.
Conclusion: The disappearance of intractable epileptic seizures following acute viral infections might be related to the associated inflammatory or immunologic processes.

p927
Acute Onset Mutism and Epilepsy Partialis Continua as First Symptom in Multiple Sclerosis (MS)
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Purpose: The overwhelming appearance of epileptic crises with mutism represents an extremely intense diagnostic and therapeutic problem, especially when it comes to young people with no medical record. In this research we analyse this case in one young patient.
Methods: A young woman, 26 years of age, married with one child, who has never been ill in previous years. After a cold and respiratory inflammation, she presented conscience disturbances, sensory tensions and mutism. After her hospitalisation, she was diagnosed with possible depression and sent home with an anti-depression therapy.
Results: The next day her condition became much worse, causing the intensification of the mutism symptoms. Simultaneously, her right arm presented continuous myoclonies of the first three fingers.
Conclusion: The extended neurophysiological control (EEG, 24-hour EEG recording, EMG, SSEP and MRI) demonstrated clear sign of focus disturbances and showed the diagnosis of partialis continua in case of MS.

p928
Neurosyphilis
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Purpose: A 64-year old male patient with neurosyphilis is reported.
Methods: The complaints began 9 years ago with an episode of vertigo and 'loss of consciousness'. Other symptoms were gait disturbance, headache, hearing loss, forgetfulness, mood changes, ulceration on the right leg. The patient reported several episodes of epileptic seizures. He did not mention a history of syphilis.
Results: The clinical examination revealed pupillary changes, anisocoria, positive Argyll-Robertson's pupil sign, deafness, cerebral ataxia, positive Romberg's sign, hypesthesia for light touch of the under extremities, loss of deep sensitivity, loss of the patellar and Achilles tendon reflexes, neuropathic arthropathy, trophic ulcer on the right heel. Neuroimaging - X-ray computerised tomography and magnetic resonance showed leucoencephalomalacia in the basal ganglia of the brain, cerebrovasculitis, low-grade ventricular dilatation and degenerative changes of the spinal cord. The EEG noted slowing bioelectrical activity. Serological tests for syphilis (VDRL, TPHA, FTA-ABS) were positive in serum and CTSF.
Conclusion: Central nervous system invasion by treponema pallidum may occur in more patients than are usually diagnosed with syphilis. Neurosyphilis is a significant medical problem and should be considered in differential diagnosis. Clinicians must approach this important condition using a combination of clinical and laboratory findings and good understanding of the disease.

p929
Antibodies against Glutamic Acid Decarboxylase, Temporal Lobe Epilepsy and Hippocampal Sclerosis: A New Syndrome?
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Purpose: Epilepsy with antibodies against glutamic acid decarboxylase (GAD) has been reported either in isolation or in association with stiff person syndrome. Importantly no clear epilepsy syndrome is recognised. Our aim was to define a syndrome of epilepsy associated with anti-GAD antibodies. We noted that temporal lobe epilepsy (TLE) is associated with auto-antibodies against voltage-gated potassium channels (VGKC) and so we hypothesised that auto-antibodies against synaptic proteins may be responsible for otherwise unexplained TLE.
Methods: 22 well-characterised cases of TLE were stratified into four groups according to age of onset and initial presentation. Antibodies against GAD and VGKC were measured by radio-binding assays.
Results: No cases of elevated levels of auto-antibodies against VGKC were found but 3 cases of very high titers of anti-GAD antibodies were detected, all from the same clinical group (adult onset encephalitis with epilepsy: total 5 cases). Analysis of our cases and those previously described in the literature allowed us to propose a syndrome for epilepsy associated with anti-GAD antibodies, namely acute severe onset TLE associated with MRI abnormalities of the hippocampi, typically hippocampal sclerosis, and chronic medically intractable seizures. This syndrome was seen predominantly in females with onset in the second and third decades, a peak demographic for onset of autoimmune disease.
Conclusion: We have defined a putative epilepsy syndrome associated with autoantibodies against GAD. Improved recognition and detection of this syndrome of immune-mediated epilepsy would allow early treatment with immune-modulators such as steroids, plasma exchange or intravenous immunoglobulin, thereby hopefully preventing the development of medically intractable epilepsy.

p930
The Expression of Tau Protein in Patients with Intractable Epilepsy
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Purpose: To investigate the expression of Tau protein in lesions of those who had undergone surgical treatment for intractable epilepsy, and to estimate the role of Tau protein in the pathogenesis of epilepsy.
Methods: 48 patients with intractable epilepsy underwent surgical therapy (32 cases with temporal lobectomy and 16 cases with hippocampus resection). We examined the expression of Tau protein in resective brain tissue by immunohistochemistry, and meanwhile, we observed the mossy fibre sprouting in the hippocampus and compared it with that of the control group.
Results: We discovered that the photo density of phosphorylation Tau protein in the CA3 areas and the molecular layers of dentate gyrus increases compared with the control group ($p<0.05$). Simultaneously, the mossy fibre in the dentate gyrus as well as in the hippocampus increased.
Conclusion: Synaptic reorganization plays an important role in the pathogenesis of epilepsy. Using experimental animals, it was discovered that excessive Tau protein could activate axon growth. This study shows excessive expression of Tau protein of dentate gyrus and hippocampus in patients with intractable epilepsy. We deduced this is perhaps the important mechanism of synaptic reorganization, and therefore, regulating the expression of Tau protein may improve the prognoses of patients with intractable epilepsy.

p931
Clinical and Neuroimaging Features of Malformations of Cortical Development in a Large Population with Epilepsy
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Purpose: Malformations of Cortical Development (MCD) represent heterogenous disorders of neuronal proliferation, migration and organization commonly associated with intractable epilepsy. The aim of the study was to evaluate clinical and neuroimaging features of MCD in a large epilepsy out-patient clinic.

Methods: All patients with MRI verified MCD underwent clinical, neuroimaging and electrophysiological assessment.
Results: We reviewed 83 patients, 39 females (47%) and 44 males (53%); median age was 38 years (range 18 - 72). Epilepsies were classified as generalised (GE) in 9 (11%) and partial (PE) in 74 (89%). Among GE were Lennox-Gastaut Syndrome (3) and West Syndrome (2). PE included extra-temporal [ETE (51)] and temporal lobe [TLE (23)] epilepsies. In ETE group vs. TLE group: 18 vs. 3 had simple partial seizures, 20 vs. 2 had complex partial seizures and 13 vs. 18 had both types of seizures. 46 patients with PE had secondary generalised seizures. The following MCD categories were identified in ETE vs. TLE: focal cortical dysplasia (FCD) 7 vs. 8, malformations of neuronal proliferation 13 vs. 5, malformations of migration 7 vs. 7, malformations of organisation 10 vs. 1, combined malformations 14 vs. 2. In GE group: FCD (2), malformations of neuronal proliferation (3), malformations of migration (3), malformations of organisation (1).
Conclusion: The majority of patients had PE (89%), of which the largest group was ETE (69%) displaying an increased tendency of matching with combined malformations (27.5%) and malformations of proliferation (25.5%). In TLE group FCD (34.8%) was most frequently encountered. All MCD types were almost equally distributed in the GE group.

p932
First Unverricht-Lundborg Case in Balkan Region
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Purpose: Unverricht-Lundborg disease is a form of progressive myoclonic epilepsy (PME), characterised by clinical trials: stimulus sensitive myoclonus, generalised epileptic seizures (GTC) and progressive neurological and cognitive deterioration. This disease has been reported predominantly in Scandinavian and Mediterranean regions, with only a few sporadic cases elsewhere. Until now, there were no genetically confirmed cases in the Balkan region.
Methods: In order to confirm a suspected Unverricht-Lundborg case, apart from neurophysiological, neuroradiological, immunological, and histopathological and biochemical analysis, molecular diagnostics (PCR amplification and Southern blot hybridisation) were used.
Results: Our patient (male, 28 years) had the first symptoms of PME at the age of 15, with predominant stimulus sensitive myoclonus, slowly progressive cerebella symptoms (dysarthria, dysmetria, ataxia), rare GTC and low concentration as the only cognitive symptom. He was treated with mono- and polytherapy (carbamazepine, dyphetoine, phenobarbital, valproic acid), and inadequately responded to therapy. At the age of 26 he was hospitalised with the symptoms of myoclonic epileptic status, when the therapy was changed (carbamazepine was excluded and dosage of valproic acid was increased, with slow introduction of piracetam). He responded to the new therapy (frequency and intensity of stimulus sensitive myoclonic seizures were decreased), so after two months he became self-functional. During hospitalisation all biochemical tests were normal and immunological and virological negative, evoked potentials showed giant SEP, CT and MRI showed no pathological changes. EEG before the introduction of new therapy showed SW and PSW (3-4 Hz) discharges, which were no longer present during the control EEG examination. Neuropsychological examination showed only discreet reduction of attention, with no elements of cognitive deterioration. Biopsy of m. triceps surae showed no 'ragged red fibres'.
Conclusion: Molecular diagnostics confirmed suspected Unverricht-Lundborg disease, which is the first case of this form of PME in this region.

p933
Pure Sleep Seizures: Risk of Seizures While Awake
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Purpose: To estimate the risk of seizures while awake in pure sleep epilepsies in a long follow-up study.
Methods: Patients who have had pure sleep epilepsy for at least ten years were followed at a Neurology department. Patients younger than 18 years were excluded. The primary endpoint was the occurrence of seizures while awake, after 10 years or longer having pure sleep seizures.
Results: 96 patients were identified with sleep seizures, and 55 of them who fulfilled the inclusion criteria were enrolled in the study. The evolution of pure sleep seizures ranged from 10 to 67 years (median 22). Patient's age ranged from 18 to 88 years (median 50). 44% patients suffered from apparently generalised seizures. Epilepsy was considered undetermined in 38.2%, focal cryptogenic in 38.2%, and focal symptomatic in 21.8%. There was a single case of idiopathic generalised epilepsy. At the end of follow-up 35 patients were on monotherapy and 2 were not receiving treatment. Seizure frequency was <1/year in 65.5%, 1-10/year in 14.5%, >1/month in 9.1%. 17 patients (30.9%) presented one or more seizures while awake. Multivariate analysis showed that sudden withdrawal of treatment ($p<0.032$) and a polytherapy ($p<0.18$) were associated with an increased risk of seizures while awake.
Conclusion: This long follow-up study of pure sleep epilepsy demonstrated that in spite of the small number of seizures and good response to monotherapy, a third of our patients suffered seizures while awake. The significant risk factors are sudden withdrawal of treatment and polytherapy.

p934
Outcome of Epilepsy Surgery in Patients with Normal MRI
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Purpose: The advent of high quality MRI provides identification of likely underlying substrate preoperatively. Nevertheless, patients with medically intractable seizures undergo several expensive investigations as part of their assessment for suitability for surgery. The purpose of this study was to ascertain whether patients, in whom high resolution MRI showed no definite lesion, were likely to benefit from surgical treatment.
Methods: Between January 1998 and January 2004, 171 patients with refractory epilepsy were treated surgically. Procedures performed included 118 temporal lobectomies (69%), 9 temporal lesionectomies (5%), 19 frontal lesionectomies (11%), 8 hemispherectomies (5%), 7 parietal lesionectomies (4%), 5 parietal and frontal resections (3%) and other (4%). The majority of the patients had a focal lesion on the MRI. 6 patients who underwent a surgical procedure had a normal MRI of the brain. The surgical decision was based on clinical semiology, video-EEG telemetry and PET scan. 3 of these patients needed subdural recording of the suspected epileptic focus; 3 had a temporal lobectomy, 2 were treated with multiple subpial transection and 1 patient underwent perirolandic cortical resection.
Results: 2 patients (temporal lobectomy) became seizure free. 1 patient (multiple subpial transection) had more than 90% reduction in seizure frequency. The other 3 patients (multiple subpial transection, temporal lobectomy, perirolandic resection) had no significant benefit.
Conclusion: Successful epilepsy surgery is a possible outcome in MRI negative cases.

p935
Clinical-epidemiological Characteristics of a Series of 93 Cases of Janz Syndrome (Epilepsy Mioclónica Juvenil) in the Service of Neurology of the General Hospital of Mexico, O.D.
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Purpose: Describes the clinical and epidemiological characteristics of a population of 93 patients diagnosed with myoclonic juvenile epilepsy.
Methods: The records of 93 patients diagnosed with Janz Syndrome from 1998 to 2004, were retrospectively analysed in the Service of Neurology of the General Hospital of Mexico, O.D.
Results: 93 files of patients with a diagnosis of Janz were reviewed; 59 were women and 34 men, aged 5 to 34 years, average age 19 years. Patients were divided by age group; the most frequent being 15-19 years (39.78%) and 20 to 24 years (30.10%). 33 patients (35.48%) of the sample presented/displayed family antecedents of epilepsy. Three types of crisis were analysed: crisis of absences 59/93 patients (63.44 %), average age at presentation 11 years; myoclonias with a sample of 79/93 patients (84.94%), average age at presentation 13 years; and generalised clonic tonic seizures with a sample of 78/93 patients (83.87%), middle ages of presentation 13 years. The middle age with Janz diagnosis was 18 years, with a delay in the diagnosis from 1 to 24 years, with an average of 6 years. Of these patients 40.86% (38 patients) were without treatment to the moment of the first valuation; the rest were taking anti-epileptic drugs alone or in combination. Only 11.8% were taking the anti-epileptic drug of choice (election), valproic acid.
Conclusion: The JEM in our survey presents behaviour similar to that reported in the literature; diagnosis is based on the clinical picture, nevertheless ignorance of this type of epilepsy determines an important delay in diagnosis and consequently in treatment. The EEG is typical in this type of epilepsy; previously it was discarded or one doubted the diagnosis if focal activity existed. Nowadays it is well known that this result should not be excluded if the rest of the electroencephalographical elements are clinically present. It is reported in the literature that there is a delay in diagnosis of an average of 14.5 years from the beginning of the crises. In addition, as also reported in other studies, more than half of the incorrectly diagnosed patients have been using inappropriate anti-epileptic drugs. In JME the way of inheritance is complex; several studies have found 2 locus, in the chromosome 6p21 (the most described) and the chromosome 15. The treatment of choice is valproic acid. 15% of patients do not achieve control with VPA as a single drug; in these cases the addition of lamotrigine or clonazepam are useful for control.

p936
Clinical Factors that Contribute to Diagnostic Delay of Juvenile Myoclonic Epilepsy
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Purpose: The aim of this study was to evaluate the clinical features of juvenile myoclonic epilepsy (JME) that could be associated with diagnostic delay of this syndrome.
Methods: We performed a retrospective study of 97 patients (41 men and 56 women, aged 14-52 years) with JME. The diagnosis of JME was established in all patients according to clinical and EEG findings. We found 37 patients with a delay in diagnosis from 1 to 20 years (average 5.8). Most of the patients (27) were initially misdiagnosed as having partial seizures and 10 were previously diagnosed as having nonepileptic events. Analysing history, clinical picture, EEG findings and early medical reports we tried to identify factors like normal or asymmetrical EEG findings, unilateral jerks, versive onset of generalised tonic-clonic seizures and misinterpreted absences that could lead to diagnostic delay of JME.
Results: Among the patients previously misdiagnosed as having partial seizures, 18 (67%) had focal or asymmetrical EEG findings, 7 (26%) had asymmetries in myoclonic jerks or motor seizures and 2 (7%) had absences treated as partial complex seizures. Initial diagnoses of nonepileptic events was established according to the normal EEG finding in 7 cases and in 3 cases myoclonic jerks were misinterpreted as behavioural disturbances.
Conclusion: We found EEG results (normal or asymmetrical) as the most common clinical feature that contribute to diagnostic delay among misdiagnosed patients with JME.

p937
Lack of Cognitive Impairment in Juvenile Myoclonic Epilepsy (JME)
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Purpose: JME is one of the most common forms of idiopathic generalised epilepsy. Recently, cognitive impairment has been described in patients with JME. The cognitive anomaly predominated over frontal functions. The patients included were not recently diagnosed. The purpose of this study is to determinate if there is cognitive impairment in newly diagnosed Juvenile Myoclonic Epilepsy (JME) patients.
Methods: 5 patients (2/3: F/M; mean age, 21.3 years; mean estimated IQ 103) that met clinical and EEG criteria of JME were studied. The patients were recently diagnosed with JME (mean time to diagnosis: 1.2 years). All of them performed a wide battery of tests, including those that tested frontal functions. The number of patients with impaired test performance and the frequency of impairment per test were calculated.
Results: Mean test punctuation scores of the patients were compared to the population score medium. No cognitive impairment was found in JME patients on tests of frontal localisation as: concept formation, abstract reasoning and mental flexibility, cognitive speed, and planning and organisation. The patients did not show any anomaly in other cognitive performance tests.
Conclusion: The patients studied did not show a clear cognitive impairment with respect to the median cognitive performance in the general population. These results do not support previous findings. We conclude that in this population of recent diagnosed JME there is no cognitive decline.

p938
Bilateral Mesial Temporal Lobe Sclerosis
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Purpose: Mesial temporal lobe sclerosis (MTLS) is the most common form of partial epilepsy, and the seizures are refractory in the majority of cases. Bilateral MTLS is rare, less than 15% of all MTLS; it is characterised by neuronal loss and gliosis with atrophy and sclerosis in both mesial temporal lobes; the neuronal systems responsible for these seizures are not yet understood. The authors analyse clinical, paraclinical and underline their good prognosis under medical treatment, in a paradoxical way versus what is described in the literature.
Methods: The authors report 4 cases with bilateral hippocampal sclerosis.
Results: The patients were females, aged respectively 45, 28, 14 and 22 years; the three first cases had a past history of febrile convulsions; the fourth case had not. The seizures were simple partial (vegetative) then complex; the clinical examination was abnormal in the last case (paraparesis). The brain MRI for 4 patients showed a bilateral hippocampal sclerosis, EEG found anterior temporal or parieto temporal foci. The use of monotherapy was surprisingly enough to control seizures in all cases. The follow-up period was between 4 and 13 months; the clinical evolution was very good especially in the first

case, this is also the case of unilateral MTLS in the majority of our patients.
Conclusion: In the literature, the rarity of bilateral MTLS is underlined, but not such a good prognosis is found either in unilateral or bilateral MTLS. The authors suggest a genetic explanation that should be confirmed by histopathological and experimental studies due to the therapeutical implications.

p939
Encephalopathy Related Seizures
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Purpose: Encephalopathy term is used for mental changes due to diffuse dysfunction of brain structures. The most frequent causes for encephalopathies are metabolic disorders like electrolyte imbalance, hypoxic-ischemic insults, toxic agents, and inflammatory and degenerative processes. Addition to cognitive impairment and alteration of consciousness, reflex changes, paresis, involuntary movements, myoclonus, convulsions can be seen. Seizures can be frequent or rare, depending on aetiologic factors. EEG changes are usually non-specific, but may vary depending on the clinical picture. In this study, we evaluated 23 inpatients diagnosed with encephalopathy retrospectively to determine the frequency of encephalopathy related seizures, aetiologic factors, seizure types and therapeutic approaches.
Methods: We evaluated the medical records of 23 patients who were diagnosed with encephalopathy with various aetiological factors. The clinical presentation, aetiological factors, seizure frequency, laboratory, neuroimaging, EEG results, and therapeutic approaches were reviewed.
Results: The study group consisted of 14 females and 9 males with an age range of 13-87. The aetiologic factors were hypoxic-ishemic insults, hypoglycaemia, hyponatremia, hyperuricemia, hepatic insufficiency, hyperammonemia, and hyperthyroidism. Of the patients, 8 had seizures. The EEG findings were non-specific, and the most frequent finding was slowness of background activity. Only 2 patients had antiepileptic therapy. The seizures in the other patients were controlled by symptomatic therapy.
Conclusion: In this paper we evaluated the encephalopathy-related seizures, seizure types, and management of the seizures.

p940
Non-convulsive Status in Elderly Patients in Clinical Practice
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Purpose: Non-convulsive status epilepticus (NCSE) is a clinical condition of difficult diagnosis, more even in the elderly population. The aim of this study is to define the features of elderly patients diagnosed in a university hospital.
Methods: For this purpose, the medical records of all patients older than 60 years diagnosed with NCSE between 1995 – 2004 were reviewed.
Results: We found 5 elderly patients diagnosed with NCSE at discharge. The age ranged from 60 to 72 (median 66). Only 1 patient had a previous diagnosis of epilepsy. Of the other 4 patients: the first patient was suffering from a herpetic encephalitis, the second probably a meningeal carcinomatosis, the third a cerebrovascular and/or febrile acute disease, and the fourth a nervous system disease which was not clarified in the follow-up. The diagnosis delay ranged from 40 minutes to 24 hours. 2 patients have had previous episodes compatible with NCSE which weren't diagnosed. The duration of NCSE ranged from ten hours to ten days. 3 patients required admission in ICU. The patient with herpetic encephalitis died. In the follow-up (range 9 to 81 months), 2 patients presented with several status, and the other two needed a change of antiepileptic drugs because of adverse events or incomplete seizure control.
Conclusion: We found few cases of NCSE in older patients; one reason can be because it is misdiagnosed. NCSE in the elderly population is a treatable condition, but often under-recognised. This study suggests that it is frequently associated with systemic and mainly neurologic morbidity in the short and long term.

p941
Pregabalin Shows Positive Effects on Sleep Disturbance in Patients with Epilepsy: An Exploratory Polysomnographic Evaluation
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Purpose: Pregabalin is an effective add-on treatment for partial seizures with or without generalisation. We evaluated the effects of adjunctive pregabalin 300mg/day versus placebo on polysomnographic (PSG) variables in patients with well controlled partial seizures and subjectively reported sleep disturbance.
Methods: An exploratory, 4-week, double-blind study with patients on AED monotherapy and with objectively reported sleep disturbance (as per Sleep Diagnosis Questionnaire evaluating sleep in prior 6 months). Mean changes from baseline (BL) to endpoint (EP) in PSG and subjective-sleep variables in patients on adjunctive pregabalin 300mg/day (n=8) were compared with patients on placebo (n=7). PSG-sleep efficiency was the primary efficacy measure. Secondary efficacy parameters included other PSG variables and subjective assessments (MOS Sleep Scale).
Results: BL PSGs indicated clinically relevant sleep disturbances due to sleep fragmentation. Mean (SE) sleep efficiency improved significantly in the pregabalin group from 73.7% (6.16) at BL to 80.8% (3.27) at EP ($p<0.05$) and did not significantly change in the placebo group. Differences between BL-EP changes were not statistically significant between groups. However, pregabalin was associated with a significant reduction in the number of awakenings ($p<0.05$), and improvement in waketime-after-sleep-onset approached significance ($p=0.055$). Pregabalin yielded significantly statistical improvements on sleep disturbance (MOS subscales; 16.9) and sleep duration (1.5h). The AEs seen in this study were within the known AEs of pregabalin.
Conclusion: This exploratory study indicates that pregabalin was well tolerated and improved sleep continuity in patients with clinically relevant sleep disturbance. The effect appeared to be independent of seizure control. Funded by Pfizer.

p942
Comorbidity in Epilepsy: Aetiology, Complications or a Concomitant Disease?
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Purpose: To establish possible reciprocal relations of comorbid conditions with epilepsy.
Methods: We studied data of neurological and somatic examination; psychological profile obtained with adequate methods of investigations in 186 patients with epilepsy aged 17-67 (males-96, females-90).
Results: There were 14 (7.5%) patients with idiopathic, 76 (40.9%) symptomatic, 89 (47.9%) cryptogenic, and 7 (3.7%) unclassified forms of epilepsy. Localisation-related epilepsy was established in 115 patients (61.8%). Among the verified causes of symptomatic epilepsies the commonest were posttraumatic, postinfectious disorders, cerebro-vascular, hereditary diseases. They have determined development of epilepsy and remained present. In these cases a combination of epilepsy with above-mentioned disorders was

estimated as aetiological comorbidity. In 52 (27.9%) patients with a duration of epilepsy of more than 5 years, psychiatric comorbidity was present. As far as it is supposed that psychiatric comorbidity and epilepsy are of common pathogenetical mechanisms, we defined such disorders as pathogenetical comorbidity disorders of various organs and systems (e.g. endocrine, digestive) stipulated by usage of AEDs may be estimated as complicated comorbidity. In a number of predominantly elderly patients a combination of two and more diseases were found. Aetiologically and pathogenetically they were not connected with each other, more often being diagnosed after epilepsy. Such comorbidity was determined as casual (second disease).
Conclusion: Evaluation of epilepsy comorbidity (aetiological, pathogenetical, complicated, casual) isn't an easy task because of overlapping symptoms and mutual impact. Nevertheless, the search for appropriate management of epilepsy depending on comorbid disorders may have a great significance for favourable epilepsy prognosis and outcome.

p943
Personality Disorders among People with Epilepsy (PWE) in Djidja, Benin
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Purpose: This study was aimed at looking for a possible existence of specific personality disorders among people with epilepsy (PWE) in the rural area of Djidja in Benin, like those reported in previous data in developed countries.
Methods: This cross-sectional descriptive study was undertaken from 15 April to 14 May 2004. In order to diagnose epilepsy cases in the community, a multi source and door to door inquiry, coupled with a neurological consultation, was conducted with 1079 persons, mainly from the Fon ethnic group (80%). Two neurologists and four residents interviewed 30 persons with epilepsy, using the Cloninger's Temperament and Character Inventory (TCI) in its French version, after having it translated into Fon, tested and adapted. Mean results were compared using a student t test.
Results: The sex ratio M/F was 1.5. The mean age was 37 +/- 14 years (15-70). Among the 30 people with epilepsy, 16 over 30 (53%) were suffering from personality disorders: passive-aggressive (13%), borderline (10%), cyclothymic (10%), schizoid (7%), histrionic (7%), passive-active (3%), obsessional (3%). From a nosological viewpoint, personality disorders of the C group (neurosis) were more frequent (20%).
Conclusion: These high rates of personality disorders corroborate the results previously observed in Togo with the TCI and existence of psychiatric disorders in PWE in these two countries. Keywords: epilepsy, personality disorders, questionnaire, Benin, West Africa.

p944
Refractory Epilepsy: Reviewing the Diagnosis, Treatment and Goals
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Purpose: The study was performed in order to evaluate and reconsider diagnosis, treatment trials and expectations for patients referred to our specialized epilepsy department because of the intractability of their seizures.
Methods: 37 patients, mean aged 25.7 years, mean duration of epilepsy of 12.3 years entered this open, prospective study. 61.1% had CPS with or without generalisation, 13.9% had simple partial seizures and 24% primary generalised seizures.
Results: Reassessment of diagnosis showed the presence of nonepileptic psychogenic seizures together with epileptic ones in 5 patients, and in 1 of them exclusively pseudoseizures occurred. Failure in syndromic classification was found in 3 cases (unrecognized JME). Careful aetiological investigations elicited cerebral sarcoidosis in 1 and encephalopathies in 2, previously classified as cryptogenic epilepsies. Treatment evaluations showed that 69.4% of patients have tried at least two of three classic AED (CBZ, VPA, PHT), but in 2/3 of them not at maximal doses. 66.6% have tried at least one of the newer AED; 62.5% benefited from them. 80.5% received two, 11.1% three drugs and 8.3% were on monotherapy. Noncompliance was found in 8.3% of patients, excess alcohol intake in 1. In 4 patients administration of already tried drugs, but now in maximal doses and different combinations, resulted in improved control, while in 5 a trial with a new agent resulted in worsening of seizures.
Conclusion: Reassessment of refractory cases sometimes reveals diagnostic errors and treatment failures, so should be done periodically. On the other side, reasonable goals should be set in really intractable epilepsies.

p945
Pharmacological Outcomes in Elderly People with Newly Diagnosed Epilepsy
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Purpose: Old age is the commonest time in life to develop epilepsy. We analysed outcome data in elderly patients aged 65 and over in whom a new diagnosis of epilepsy was made at a single centre over a 20 year period.
Methods: Diagnosis was made by obtaining a witnessed account of events. A structured case sheet was developed for each individual allowing longitudinal assessment. Patients were reviewed every 6-8 weeks until seizure free for at least 12 months or until 'optimally' controlled.
Results: 90 elderly patients (53 men, 37 women; aged 65-93 [median 73 years]) were given a diagnosis of epilepsy and started on antiepileptic (AED) drug therapy. Median duration of pre-treatment seizures was 4 months (range 1-780 months). 68 patients had routine EEGs, 26% of which showed epileptiform discharges. 84 patients underwent brain imaging, 54% of which were abnormal. 58 (64%) patients became seizure-free for at least 12 months on their first AED with 22 (24%) failing to respond. The drug was withdrawn due to side effects in the remaining 10 (12%) patients. Following further pharmacological manipulation, 76 (84%) patients eventually achieved seizure freedom for at least 12 months, 73 of whom were controlled on monotherapy. The remaining 3 patients took 2 AEDs. There was no correlation between seizure control and number of pre-treatment seizures, epileptiform activity on the EEG or abnormal imaging.
Conclusion: Over 80% of elderly people with newly diagnosed epilepsy became seizure free on AED therapy, mostly with the first or second drug.

p946
Seizure Treatment Issues with HIV-positive Patients for Clinician
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Purpose: It's usually recommended that HIV patients suffering from a first seizure without a reversible cause should be treated. Individuals with a pre-existing seizure disorder may be infected by HIV. Current management guidelines for HIV infection advocate the use of three-drug antiretroviral regimens. Antiretroviral and many of the antiepileptic drugs (AEDs) are metabolized by cytochrome P450. Levetiracetam is not significantly metabolized by this enzyme.
Methods: There are few clinical or trial data published about the use of AEDs within this population. We reviewed clinical data of two HIV

patients with seizures admitted in our hospital and treated with levetiracetam (1000 bid).
Results: The first patient was a 35 year old male suffering from epilepsy since he was 19 years old, treated with phenytoin that was withdrawn by his own decision. He was admitted in hospital diagnosed with cryptococcus neoformans infection and started treatment with levetiracetam and antiretroviral therapy; in the follow-up viral load has decreased and CD4 lymphocyte count has increased. The second patient was a 60 year old male admitted presenting an intracerebral haemorrhage and thrombocytopenia, being diagnosed seropositive for HIV. He presented seizures that were treated with phenytoin while he received other drugs for medical complications. Phenytoin serum concentration was low and didn't reach therapeutic levels, so levetiracetam was introduced and phenytoin was removed without adverse events.
Conclusion: Anticonvulsant and antiretroviral drugs may interact throughout multiple mechanisms. It is difficult to select an AED in clinical practice. We need clinical trials to know efficacy and safety of new AEDs, as levetiracetam, in HIV-seropositive individuals.

p947
Anxiety and Depression: A Psychological Point of View
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Purpose: This study was aimed at identifying depression and anxiety and their relationship to different epileptic syndromes and perception of seizure control. We also looked for the understanding of subjective aspects that surround the patients' psychological reactions.
Methods: 60 patients (G1) and 60 healthy subjects (G2) were selected at the outpatient clinic of epilepsy at the University Hospital of Campinas, Brazil. A semi-structured interview aimed at identifying the patients' perceptions, their cognitive perception of the disease, personal strategies and their perception of social support. Beck protocol of depression and the State-Trait anxiety questionnaire were used.
Results: Anxiety and depression showed a significant difference between the G1 and G2 ($p=0.01$; $p=0$ respectively) and a strong relationship between the perception of seizure control, depression and anxiety (Fisher test). Epilepsy was considered to be a disease (63.5%), mental problem (11.6), feelings of shame, fear, worry, low self-esteem, anxiety (56.4%), perception of stigma (26.6%), social support (40.2%). The adaptability strategies were looking for medical treatment, withdrawal, spiritual support and denying.
Conclusion: The perception of seizure control showed the importance of subjective aspects involved in epilepsy. Disease representation, self-esteem, interpersonal difficulties and social support perception indicate essential contingents within adaptive behaviour and temper control.

p948
Juvenile Myoclonic Epilepsy and its Pattern in Kanpur, India.
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Purpose: Juvenile Myoclonic Epilepsy (JME) is a type of idiopathic generalised epilepsy (IGE). It has variable presentations and specific treatment for a long time. We tried to study its presenting features along with the course of the condition.
Methods: Neurology Unit at G S V M Medical College, Kanpur, caters for about 5 million population with only 2 neurologists. It was established in 1989 and about 10,000 cases of neurology are seen every year. During the last 6 years around 2800 cases of epilepsy were registered. Out of 2800 cases of epilepsy, JME was diagnosed in 282 cases on the basis of clinical features and EEG pattern. Other factors like drug response, family history and tendency to recur were also considered. All cases of epilepsy were classified into epilepsy syndromes and JME was studied in detail.
Results: JME was observed in females in 68%. The diagnosis of JME was finally made after a median gap of 6 months to as long as 12 years after onset. 256 cases were diagnosed by us for the first time in the hospital OPD while only 26 cases were diagnosed as generalised epilepsy and not as JME elsewhere before their registration in our OPD. 63% of patients had early morning jerks or seizures. Patients promptly recognised their jerks when they were shown by us how they occur. 32% cases had unilateral seizures like partial seizures. The most common drug prescribed to them earlier was phenobarbitone or carbamazepine. 80% patients had EEG findings on sleep deprived EEG.
Conclusion: JME was observed in about 10% cases of all epilepsy in OPD. The syndromic diagnosis is still not made in clinical practice by physicians. Most epilepsy patients first go to their family doctors and continue their treatment. Myoclonic jerks are often not recognised in clinical practice and patients consult a specialist only when they have a recurrence of seizures. The presence of focal jerks and lack of awareness lead to delay in diagnosis. Early morning sleep deprived EEG yields more information than the routine EEG. About 20% patients were given 2 drugs including sodium valproate to control their seizures.

p949
Does the Seizure Frequency Increase in Ramadan?
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Purpose: During Ramadan, the ninth month of the Islamic lunar calendar, adult Muslims are required to refrain from taking any food, beverages, or oral drugs, as well as from sexual intercourse between dawn and sunset. In this study we aimed at discovering alterations in drug regimens and seizure frequency of epilepsy patients during Ramadan.
Methods: In the three months following Ramadan in the year 2004 (15.10.2004- 13.11.2004) 196 patients with epilepsy who came to be examined at the Department of Neurology, Ministry of Health Ankara Training and Research Hospital Epilepsy, were evaluated. 114 patients who were followed by our department for at least 1 year, and who were fasting Ramadan, were included in our study. 62 patients were female, the other 52 were male. Mean age of patients was 31.6 (age range:16-77)
Results: Of the 114 patients who were included in the study, 38 patients had a seizure and one of these patients developed status epilepticus during Ramadan. When the seizure frequency of these patients during Ramadan was compared to that in the previous year, a statistically significant increase was observed ($p<0.001$). Moreover, there was an important increase in the risk of having a seizure in the patients who changed their drug regimens compared with those who did not change ($p<0.05$).
Conclusion: During Ramadan there is an increase in seizure frequency patients with epilepsy. The most important reason for this situation was the alteration in the pharmacokinetics and pharmacodynamics of drugs and consequently in their efficacy. We believe that in the patients who received monotherapy and who did not change their drug regimes, the increase in seizure frequency may be related to the changes in their daily rhythms and their day-long starvation.

p950
Potential Efficacy of Zonisamide in Refractory Juvenile Myoclonic Epilepsy
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Purpose: To evaluate the efficacy of zonisamide (ZNS) as adjunctive therapy in treatment of refractory juvenile myoclonic epilepsy (JME).
Methods: We performed a retrospective, open-label, uncontrolled, observational study of 7 patients with refractory JME commenced on ZNS between 2001 and 2004.

Results: We retrospectively reviewed the records of 7 patients (all female, age 18-32) with refractory JME, commenced on a compassionate use basis on ZNS as adjunctive treatment between October 2001 and September 2004. All patients had refractory epilepsy despite previous or current therapy with all appropriate broad-spectrum anti-epileptic drugs. The ZNS dose range was 200-600mg/day. Follow-up range was 4-38 months (mean 17 months). 5 of 7 patients had a significant reduction in frequency of generalised tonic-clonic seizures. 2 of 7 patients had a reduction in myoclonus. 3 patients initially had side-effects (fatigue, tremor, paraesthesia) which resolved. 1 patient noted worsening of myoclonus at higher doses of ZNS which improved on dose reduction.
Conclusion: In this retrospective study, ZNS was effective and well-tolerated as adjunctive therapy in patients with refractory JME.

p951
Pharmacoeconomic Comparison of Monotherapy with Carbamazepine, Valproate and Oxcarbazepine in Bulgarian Patients with Focal and Generalised Epilepsy
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Purpose: To compare by means of pharmacoeconomic analysis the monotherapy with two Carbamazepine, one Valproate and one Oxcarbazepine products.
Methods: We researched 162 men and women, with generalised and focal epilepsy, treated on monotherapy with: Group 1: Carbamazepine (Tegretol-Novartis), Group 2: Carbamazepine (Finlepsin-Ecopharm), Group 3: Valproate (Depakine chrono – Sanofi) and Group 4: Oxcarbazepine (Trileptal-Novartis). Using methods of pharmacoeconomic analysis we assessed the effectiveness, costs and quality of life (QOL) of the patients in each group. Seizure reduction, type and number of adverse events (AEs) and time to new seizure (in weeks) were recorded as indexes of effectiveness. Costs were measured according to the official pricelist of the University Hospital, Plovdiv. QOL was assessed with the use of a questionnaire developed on the basis of QOLIE 31.
Results: The seizure control in all groups was good. The patients in Groups 2 and 3 showed significantly ($p<0.001$) higher seizure reduction (mean=90.23% and 88.45%) than those in groups 1 and 4. Group 4 patients had the lowest incidence of adverse events (average=0.875 per patient). There were no significant differences in the QOL of the patients of the four groups. Costs were significantly lower in patients of Group 2 and 3 when compared to those in Group 1 and 4.
Conclusion: All four drugs show high efficacy and safety and have a good effect on the QOL. Oxcarbazepine has the best safety profile of the four and Carbamazepine (Finlepsin) tends to be the most cost-effective providing lowest cost, good control and high quality of life

p952
Cost Effective Analysis of Antiepileptic Drugs as Monotherapy in Adults with Localisation-Related Epilepsy in a Developing Country
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Purpose: The study aims to determine the clinical profile of localisation-related epilepsy among adults in a developing country and to identify the most cost-effective anti-epileptic drug (AED) used as monotherapy in this group of patients.
Methods: Patients with localisation-related epilepsy based on the ILAE classification, that was being managed for at least one year and regularly follows-up with the Adult Neurology and Epilepsy Clinics of the Philippine General Hospital were identified. Those who were 18 years old and above, on monotherapy with the same AED for at least one year and compliant to medications were included in the study. Their past and most recent medical records were reviewed. The primary outcome was seizure freedom for at least one year. Event rates (ER), relative risk (RR), absolute risk reduction (ARR) and number needed to treat (NNT) were calculated using each AED as a treatment group. Computation in Philippine peso was done for direct and total medication cost for one year.
Results: A total of 236 patients were included in the study (mean age = 35 +/- 9.89, 68% male, 48% symptomatic). The most common aetiology was meningitis (18%) and cerebral infarction (17%). Seizure control for all AED was 42%. Phenobarbital (PB) was the most commonly used with 44% followed by Phenytoin (PHT), 24%; Carbamazepine (CBZ), 21%; Valproic acid (VPA), 5%; Topiramate (TOP), 3%; and Oxcarbazepine (OXC), 2%. Significant seizure control was noted on TOP at 100 mg/day (ER = 37%, RR = 0.65, ARR = 0.2035, NNT = 5) and PB at 180 mg/day (ER = 56%, RR = 0.96, ARR = 0.0249, NNT = 40). Direct medication cost for one year treatment with TOP was 26,280 while PB was 1,733. Total cost to prevent one seizure in a year with TOP was 131,400 while PB was 69,320.
Conclusion: Topiramate and Phenobarbital significantly controlled seizures in adults with localisation-related epilepsy. Topiramate had better control than Phenobarbital but the latter was more cost-effective.

p953
Levetiracetam Treatment Alters Sex Steroid Hormones in Female Wistar Rats
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Purpose: We have recently shown that levetiracetam in rats affect ovary morphology, giving an increase in ovary weight, a lower number of cysts, and a higher number of corpora lutea and secondary follicles. The aim of this study was to investigate the effect of long-term levetiracetam treatment on peripheral sex steroid hormones.
Methods: 50 female Wistar rats were fed per-orally through a gastric tube with levetiracetam 50 mg/kg (n=15), 150 mg/kg (n=15) or control (n=20) solution twice daily for 90-95 days. They were killed in diestrous/early proestrous phase. Serum levels of testosterone and 17β-estradiol were analysed by using radioimmunoassay kits.
Results: Serum testosterone was significantly increased in both low and high dose treated animals (0.48 nmol/l, 0.52 nmol/l), compared to the control group (0.16nmol/l, $p<0.05$). Serum estradiol was significantly reduced in the treated animals (55.8 pmol/l, 145.3 pmol/l) compared to the controls (257.5 pmol/l, $p<0.05$). Mean levetiracetam concentration 3-4 h after the last meal was 122 umol/l in the low-dose and 277 umol/l in the high dose group.
Conclusion: The study shows an effect of levetiracetam on female sex steroid hormones. The increase in testosterone and decrease in estradiol indicate a reduced transformation from testosterone to estradiol. Further studies should be encouraged to study a possible effect related to levetiracetam binding properties to the SV2A protein, which is located both in the brain and in endocrine tissue. Human studies are needed to figure out the possible clinical relevance of the findings from the present study.

p954
Temporal Pole Abnormalities in Patients with Temporal Lobe Epilepsy due to Mesial Temporal Sclerosis: Correlation to Ictal Patterns
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Purpose: The temporal poles may play a role in the physiopathology of mesial temporal lobe epilepsy (MTLE). In this study we analysed alterations in the temporal poles of patients with TLE and mesial

temporal sclerosis (MTS) and correlated them to ictal patterns observed during prolonged video-EEG monitoring.
Methods: 147 seizures of 35 patients with TLE and unilateral MTS were analysed. Ictal patterns were correlated to signal abnormalities and volumetric measures of the poles. Differences in volume over 10% were considered significant.
Results: The most frequent ictal pattern was rhythmic theta activity (RTA), in 65.5% of seizures. Rhythmic beta activity was observed in 11% of the seizures, localised attenuation in 8%, interruption of epileptiform discharges in 6%, repetitive discharges in 5.5%, and rhythmic delta activity in 4%. 66% of the patients presented signal abnormalities in the temporal pole, always ipsilateral to the MTS. 60% presented significant asymmetry of the temporal poles; in all cases, the reduced pole was ipsilateral to MTS. Patients with RTA as the predominant ictal pattern more often presented significant asymmetry of temporal poles (p=0.214). However, no association was observed between the predominant ictal pattern and signal abnormalities in the temporal poles.
Conclusion: Temporal pole signal abnormalities and volumetric reduction are common in patients with TLE and MTS, seem to be always ipsilateral to the MTS, and may have a correlation to the predominant ictal pattern, revealing a potential role of temporal poles in the origin of seizures in these patients. This work was supported by FAPESP (Fundação de Amparo à Pesquisa do Estado de São Paulo) and CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior)/CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico).

p955
Benefit of Video EEG Method in Differential Diagnosis of Seizures
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Purpose: The establishment of the benefit of video EEG method in differential diagnosis of seizures.
Methods: Retrospective analysis of a group of 124 patients was explored in the Faculty Hospital, Ostrava, between January 2003 and June 2004. All patients were investigated for 2 days by video EEG monitoring. This was performed 30 minutes provocation test - application 2ml saline solution as eliciting injection and 2ml saline solution at the final stage of the seizure in 63 cases.
Results: From January 2003 until June 2004 we investigated 124 patients. 51 men, 73 women. Entry diagnosis of epilepsy was present in 107 cases; there was no former unconsciousness closely specified in 14 cases; 3 patients had sleep disorders. The test with an eliciting injection was positive in 21 patients with a diagnosis of non epileptic seizures, there was a negative result in 33 patients, and in 9 cases the result was not evident. Of 107 cases of entry diagnosis epilepsy there was no change in 81 patients. 23 had an epileptic seizure with specific changes in the EEG, 22 patients did not have an epileptic seizure but had a positive history of seizures and had epileptic abnormality in the EEG. 36 patients had no abnormality in the EEG and no seizure during investigation but have a positive seizure medical history. The diagnosis was changed in 21 patients on the strength of a provocation test using a saline solution. 17 patients with no closely specified seizures in their history, were given a diagnosis of syncope 3x, migraine 2x, freezing somatoform disorder performing pulse of the arm 1x, recent dementia status with memory changes 2x, dismay 1x, vertigo 1x, neurogenic tetany 2x, sleep disorders 2x, epilepsy 2x. The diagnosis in 5 cases was not specified .
Conclusion: Diagnosis of epilepsy was specified in 65% patients. In 17% of cases the diagnosis was changed from epilepsy to non-epileptic seizures. In 2% of cases a non-epileptic seizure diagnosis was changed to epileptic. In 4% of patients a diagnosis was not closely specified,12%patients did not perform epileptic or non-epileptic seizures.

p956
Lateralising Value of Auditory Aura: An EEG and Clinical Study of 123 Cases
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Purpose: To describe the clinical features of auditory symptoms in partial seizures and establish a possible localising and lateralising value.
Methods: 123 patients with epilepsy and auditory aura were enrolled out of 8000. Clinical, neurophysiological and neuroradiological data were collected in a database.
Results: 55 patients (48.2%) referred auditory symptoms in both ears, 38 (33.4%) in one ear; the side was not definable in 21 (18.4%). The possible side of the epileptic zone (EZ) (i.e. the side of EEG and/or neuroradiological abnormalities or ictal focal neurological deficit like aphasia) was clearly defined in 30 out of 38 patients with lateralised aura and was controlateral to the side of aura in 55.3% of cases and ipsilateral in 44.7%. According to predominant features of the auditory sensation, we defined four subgroups: simple (1A-60pts, 48.8%) or complex (1B-38pts, 30.9%) hallucination, positive (2A-10pts, 8.1%) or negative (2B-15pts, 12.2%) illusion. Eight 1B patients had a musical aura: EZ was not definable in 4, EZ was in the non-dominant hemisphere in 3, and in the dominant hemisphere in 1. The definable EZ was in the dominant hemisphere in 17/22 patients with verbal auditory features. When definable, EZ was in the dominant hemisphere in 83% of 2B patients.
Conclusion: Auditory aura is rare in partial epilepsy. The side of aura is scarcely useful in lateralising the EZ. Complex hallucinations with musical aura seem to refer to the non-dominant hemisphere; those with verbal content to the dominant hemisphere. Negative illusions may be more frequent in dominant hemisphere foci.

p957
Analysis of Prodromal Symptoms in 100 Epilepsy Patients
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Purpose: Prodromes of epileptic seizures, understood as those pre-ictal symptoms occurring several hours before a seizure, have not been extensively investigated. The aim of this study was to identify and describe prodromic symptoms in adult epilepsy patients, as well as to determine their prevalence and analyse the association between them and several variables.
Methods: This is a pilot study, with a retrospective design including 100 epilepsy patients from systematic sampling, who met the inclusion/exclusion criteria. A semi-structured protocol was applied seeking prodromes appearing up to 24 hs preceding the seizures. Auras were specifically excluded. Validation of referred prodromes was made through x2, a=0.05.
Results: 100 patients (60 females, 40 males) with a mean age of 32+13 years, were included. In 39% of patients at least one prodromal symptom (PS) was found. The most frequently evoked PS were behavioural changes (17%), mainly in complex partial seizures. Other frequently elicited PS were mood changes and cognitive disturbances (12% each) preceding generalised tonic-clonic seizures. 90% of PS that could be submitted to the validation analysis were found to have a strong association with occurrence of seizures. Although all individual PS showed a high validation rate, it was slightly weaker (70%) for behavioural changes. PS evoked by patients with co-morbid psychiatric disturbances were less frequently validated (x2, p=0.06).
Conclusion: Prodromes appear to occur in a significant number of patients, with high consistency. A better knowledge of these pre-ictal

manifestations, could allow therapeutic intervention or protective measures, potentially increasing treatment efficacy.

p958

Lateralizing Significance of Quantitative Analysis of Versive Head Movements during Seizures of Patients with Temporal Lobe Epilepsy

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Purpose: To evaluate quantitatively the lateralising significance of ictal versive head movements of patients with temporal lobe epilepsy (TLE).
Methods: We investigated EEG-video recorded seizures of patients with TLE, in which the camera position was perpendicular to the head facing the camera in an upright position and bilateral head movement was recorded. Thirty-eight seizures (31 patients) with head movement in both directions were investigated. Ipsilateral and contralateral head movement were defined according to ictal EEG. Head movements were quantified by selecting the movement of the nose in relation to a defined point on the thorax (25/s) in the inner 90 angle facing the camera. The duration of the head version was determined independently of the camera angle. The angle, duration and angular speed of head movements were computed and inter- and intrasubject analyses were performed (Wilcoxon rank sum).
Results: Ipsilateral movement always preceded contralateral movement. The positive predictive value (PPV) was 100% for movement in both directions. The duration of contralateral head version was significantly longer than ipsilateral head movement (6.4s ± 4.1s vs. 3.9s ± 3.1s, $p<0.001$). The angular speed of both movements was similar (15.5deg/s ± 12.1 deg/s vs. 17.3 deg/s ± 13.0 deg/s). Movements with higher speeds, regardless of direction, had a shorter duration than slower movements.
Conclusion: The quantitative analysis shows the importance of sequence in the seizure's evolution and duration for correct lateralisation of versive head movement. This interobserver independent method shows the high lateralising value of ictal versive head movements in TLE.

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Ictal Ipsilateral Head Deviation in Frontal Lobe Seizures

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Purpose: The lateralising value of ictal head deviation (HD) in frontal lobe epilepsy (FLE) has been a matter of debate. Indeed, although FLE is typically associated with tonic or clonic HD contralateral to seizure onset, ipsilateral HD has been noted in numerous reports. Whether both types of HD can be distinguished according to their clinical pattern, have not yet been specifically investigated.
Methods: We studied the clinical pattern and time of occurrence of HD in 20 consecutive patients, including 19 investigated by an intracerebral stereotactic EEG procedure, who underwent surgery for FLE.
Results: 186 seizures were analysed. Ictal HD was ipsilateral to the epileptogenic zone (EZ) in five patients (25%) and 37 seizures (19.9 %) and contralateral in eight patients (40%) and 40 seizures (21.6 %). Ipsilateral HD was rarely tonic and never associated with clonic manifestation. Contralateral HD was always tonic, unnatural and associated with hemifacial clonic movements in 60% of seizures. Ipsilateral HD occurred earlier than contraversion ($p<0.004$), with a mean delay of 0.8 +/- 1.8 seconds after the first detectable ictal sign, as compared to a delay of 14.25 seconds +/- 9.17 seconds for contraversion. Moreover, ipsilateral HD always occurred prior to contraversion when both signs coexisted in the same seizure (n=12, 6.5%). Our patients with ipsilateral HD either demonstrated an anterior or dorsolateral frontal EZ.
Conclusion: Ipsilateral HD is a frequent ictal sign during FLE which can be distinguished from contraversion by its time of occurrence at or immediately after seizure onset and its non-clonic pattern.

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Transient Cognitive Impairment During Generalised or Diffuse Epileptiform EEG Discharges

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Purpose: Epileptiform EEG discharges are a frequent finding in people with epilepsy, and may occur in other clinical conditions. Formal testing during electroencephalographic (EEG) recording may demonstrate transitory cognitive impairment. We studied the occurrence of transitory cognitive impairment with different tests during epileptiform EEG discharges in patients with or without epilepsy.
Methods: 30 patients ranging in age from 2 to 13 years with frequent generalised or diffuse epileptiform EEG discharges on a previous examination were studied. 27 patients had epilepsy (17 symptomatic, 10 idiopathic) and 3 had no epileptic seizures. In a subsequent examination, a 21-channel EEG was synchronized with a computerised cognitive test system (Mindtracer). Tests of animal/thing categorisation, colour discrimination, verbal and auditory memory, pattern recognition and time evaluation were applied during the EEG. The numbers of correct or incorrect answers were statistically compared for each EEG condition; epileptiform discharge, no discharge.
Results: Transitory cognitive impairment was characterised in 43.3% of the patients (11 patients with epilepsy, 2 without epilepsy). In 7 cases epileptiform EEG discharges were rare and it was not possible to evaluate the occurrence of transitory cognitive impairment. It was possible to observe transitory impairment even in short discharges (0.5-1s duration). One child had an absence.
Conclusion: Our findings confirm that otherwise subclinical epileptiform discharges may be accompanied by transitory cognitive impairment in epilepsy and non-epilepsy patients. There is a need for research to evaluate the relevance of transitory cognitive impairment, and to determine when epileptiform EEG discharges should be treated.

p961

Localising and Lateralising Value of Language Manifestations During Partial Seizures

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Purpose: To evaluate the localising and lateralising value of ictal and postictal language manifestations observed during partial seizures.
Methods: Ictal video-EEG recordings obtained between October 2001 and October 2004 have been reviewed. Language manifestations observed during seizures were classified as: ictal vocalisation without speech quality (IV), normal ictal speech (NIS), abnormal ictal speech (AIS), and abnormal postictal speech (APS). According to the site of origin, seizures were classified in temporal seizures (TS), and in extra-temporal seizures (EXS); and according to the side of onset, in right and left seizures. We analysed ictal and postictal language manifestations and their relationship with the site (TS or EXS) and side (right or left hemisphere) seizure origin, to establish their

localising and lateralising value. Logistic regression was used for statistical analysis.
Results: Language manifestations were observed in 135 seizures, corresponding to 54 consecutive right handed patients. Ictal vocalisation (IV) was observed in 48.1% seizures: 72.5% belonged to EXS group (p=0.000), without lateralising value; NIS occurred in 28.1% seizures: 84.2% corresponded to TS group (p=0.000), and when considering the side of onset, 84.2% corresponded to seizures of the right hemisphere (p=0.000); AIS was observed in 16.3% seizures, without localising or lateralising value; APS occurred in 37% seizures: 78% corresponded to TS group (p=0.004), and 82% corresponded to seizures of the left hemisphere (p=0.000).
Conclusion: Language manifestations are a frequent symptom in partial seizures and are a useful tool that contributes to the identification of the epileptogenic zone (EZ). Ictal vocalisation, NIS and APS were significantly associated with EXS, right TS and left TS, respectively.

p962
Magnetoencephalographic (MEG) Localisation of Slow-wave Activity Compared to Epileptiform Potentials in Patients with Focal Epilepsy
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Purpose: Magnetoencephalographic localisation of interictal epileptiform activity is clinically used to search for the epileptogenic focus. In epilepsy diagnostic routine, it is known that the occurrence of slow wave activity can be a hint for local functional disturbance or a lesion (Binnie CD, Stefan H, Clin Neurophysiology 1999 Oct;110(10):1671-97). The aim of the study is to examine whether in patients with mono focal epilepsy localisation results based on slow wave (2 to 6 Hz) dipole density calculations are correlated to the spike localisation results.
Methods: Spontaneous MEG was recorded using a Magnes II System, in 7 patients with focal epilepsy and 4 healthy subjects. Spike source localisation was performed in accordance to the protocol of our lab. Analysis of slow-wave activity consisted of filtering, principal component analysis, single dipole fit and dipole density calculation. Voxels of 1 millilitre with clearly increased number of dipoles are displayed in MR-images together with spike localizations.
Results: In 5 of 7 cases of patients, a local increase of slow wave density was obtained. Spike area and regions of increased slow wave density showed a small partial overlap, but were close to each other. The distances between the centre of mass of spike activity and dipole density maxima were in the range from 1 to 4 cm. 4 healthy subjects didn't show a significant increase in slow wave dipole density.
Conclusion: This study indicates that the evaluation of dipole density might be helpful to give an additional hint leading to the epileptogenic zone in patients with focal epilepsy.

p963
A Rare Video-polygraphic Demonstration of a Syncope Provoked by a Temporal Lobe Seizure
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Purpose: Bradycardia and asystole are rare during partial seizures. We report a video-polygraphic recording of cardiac asystole occurring during a temporal lobe (TL) seizure.
Methods: A 35-year-old right-handed woman had TL epilepsy and sudden falls. At age 6 she had febrile convulsions associated with bacterial meningitis. Since age 7 she has had sporadic falls with traumatic injuries associated with loss of consciousness and confusion. Since age 11 she has had nocturnal seizures characterised by fear, oroalimentary-automatisms and post-ictal confusion; diurnal seizures characterised by a warm feeling in the head, déjà veçu, facial pallor, nausea, oroalimentary-automatisms and post-ictal confusion. AED were ineffective. Cardiac investigation with long-term EKG and echocardiography were normal. The patient underwent video-polygraphic recording including EEG, ECG, plethysmogram, blood pressure, oronasal and abdominal breathing.
Results: Several seizures were recorded. At the end of one seizure, characterised by ictal paroxysmal discharges over the right temporal regions, cardiac rhythm slowed down followed by sinus arrest lasting 5.5 s.
Conclusion: Sudden falls are not typical of TLE. In our observation autonomic modifications may result from sympathetic inhibition or a parasympathetic activation probably due to the ictal discharge arising from or spreading to the central autonomic network. To our knowledge, this is the first video-polygraphic recording of syncope following a TL seizure. Because the disorder was refractory to antiepileptic medications our patient was referred for surgery. Implantation of a cardiac demand stimulator should be considered in non surgical cases.

p964
Diagnostic Value, Adverse Events and Outcomes of 419 Patients Undergoing Intensive Video-EEG Monitoring
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Purpose: Video-EEG monitoring is mandatory in presurgical evaluation of medically refractory epilepsies and in diagnosis of unclear seizure disorders. The aim of this study was to analyse the diagnostic value of video-EEG monitoring in a large university hospital.
Methods: We investigated retrospectively all patients (pts) referred to our video-EEG monitoring unit between 1999 and 2004. We examined duration of monitoring, number of seizures, adverse events and outcomes (i.e. change in AED, as well as operative consequences) and follow-up after monitoring.
Results: 419 pts. (192 m, mean age 37±14, range 9-80) were analysed in 490 sessions. 56 were monitored 2 to 6 times. Average monitoring duration was 5 d (range 1-37). We recorded 3981 (90%) epileptic and 452 (10%) non-epileptic seizures. Adverse events were: status epilepticus (8 pts), mild head injuries (14 pts), severe head trauma with epidural haematoma (1 pt) and post-ictal psychosis (11 pts). In 295 pts, the AED regimen was changed: 16 were previously not on AED and for 29 pts inappropriate AEDs were discontinued. 21 pts were invasively recorded (9 FO, 13 subdurals). 103 (25%) pts were subsequently operated. Post-op, 78% of them were seizure free (i.e. Wieser class 1, 1% 2, 4% 3, 16% 4, 1% 5). In 11 pts, a VNS was implanted. Mean follow-up was 21 months.
Conclusion: Video-EEG monitoring is a safe and reliable procedure in classifying seizure disorders and localising the seizure onset zone. Status epilepticus, head injuries and postictal psychosis are the most frequent adverse events.

p965
Variation of Epileptic Spike Source Localisations in MEG and EEG due to Different Volume Conductors
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Purpose: Epilepsy surgery must rely on precise information about the area eliciting the seizure. This study compares the relative position of epileptic spikes recorded with magnetoencephalography (MEG) and electroencephalography (EEG) using two volume conductor models.
Methods: MEG/EEG was recorded simultaneously during presurgical epilepsy evaluation in 100 patients, using a 74 channel dual unit

biomagnetometer (Magnes II, 4D-Neuroimaging) and 31 scalp electrodes (international 10/20 system). Source localisations from 1353 MEG and 493 EEG interictal spikes were calculated with the single equivalent dipole model. A 3 spherical shell model (3SS) and boundary element method volume conductor (BEM) segmented from MRI were used. Distances between centroids of clusters of source localisations are given as mean +/- sem ($p<0.05$).
Results: Appling similar selection criteria MEG yielded more spikes than EEG. In a 3SS model MEG source localisations were 5.6 +/-1.5 mm inferior to those obtained with EEG, while in a BEM model MEG source localisations were 6.3 +/-1.9 mm anterior and 4.8 +/-1.8mm superior. The mean distance of centroids of source localisations between both volume conductor models was 19.5 +/-0.9mm for EEG and 9.6 +/-0.9 mm for MEG. MEG analysis showed no systematic difference between BEM and 3SS source localisations. For EEG, source localisations with BEM were 5.9 +/-1.3 mm posterior and 11.7 +/-1.1 mm inferior when compared to 3SS.
Conclusion: Influence of the volume conductor or source signal for a large number of patients with measured epileptic spikes yields systematic differences, which should be considered when only one source signal is recorded or volume conductor calculated.

p966
Management and Outcome of Three Cases of Prolonged Refractory Status Epilepticus
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Purpose: Refractory status epilepticus (RSE) is associated with a high mortality and high incidence of neurological sequelae. We report the management and successful outcome of three cases.
Methods: 3 female patients ages 17, 29 and 33 yrs were admitted to the ICU in status epilepticus refractory to standard treatment. 2 were new onset seizures secondary to viral encephalitis and the third was an exacerbation of seizure activity secondary to a mitochondrial disorder. Prolonged iatrogenic coma was induced for up to 54, 59 and 81 days respectively. Prolonged propofol drip was required to successfully break the status in 2 cases. The third patient was initially treated with pentobarbital but was then changed to midazolam due to complications. All 3 required high doses of antiepileptic medications, in polypharmacy. In 1 patient, the VNS was implanted to control the seizures. Serial EEGs in addition to intermittent EEG monitoring were obtained in each case.
Results: 2 patients remain seizure-free on medication and are cognitively functional. 1 requires a leg brace for mild monoparesis. The third patient has a greater than 90% reduction in seizure frequency and increased cognition compared to the pre-status state. Subsequently, the antiepileptic drug regimens have been simplified with reduction of dosage or number of medications for each.
Conclusion: The management of RSE remains a challenge. Each of the patients required prolonged iatrogenic coma. Each responded to different agents and to polypharmacy. Despite the perception that RSE carries a poor prognosis, close supervision and aggressive treatment can result in a favourable outcome.

p967
Access Time Influence to Antiepileptic Treatment in the Evolution of Status Epilepticus
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Purpose: The natural history of status epilepticus (SE) influences the speed of therapy initiation, which will affect changes in mortality and morbidity. In our environment, unknown factors include the history of patients with SE, the aetiology of the SE, how access time influences the treatment of SE, and the most frequent electroencephalogram findings (EEG) of the SE. We therefore tried to study these factors through this investigation.
Methods: An observational and descriptive investigation of patients with SE was carried out from May to December 2004.
Results: The delay time from the beginning of SE to the arrival of paramedics (Time I), was up to 30 minutes for 41% of cases. Time of transfer to the hospital centre (Time II) was up to 10 minutes in 20.83% of cases and antiepileptic treatment administration in the hospital centre (Time III) was achieved in less than 30 minutes in 66.6% of the population. An economic limit was observed for the accomplishment of the imagenologic study, and of immunology tests of LCR. In relation to the EEG, periodic lateral epileptiform discharges (PLEDs) were observed, highly correlated with deaths.
Conclusion: The prognosis of our patients was severely affected by the time that passed from the beginning of the SE to the beginning of effective therapy, which indicates a necessity to educate medical and paramedical personnel to provide urgent attention to patients with SE.

p968
Memory Disturbance as a Manifestation of Non-Convulsive Status Epilepticus: A Case Report
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Purpose: Non-convulsive status epilepticus is a condition of status epilepticus where a seizure is not the main manifestation, but delirium, memory disturbance, aphasia, clonic and myoclonic movement and mutism can be present. The incidence is quite frequent, 19%-25% of all status epilepticus.
Methods: We report a 25 year old woman, whose chief complaint was loss of memory after repetitive general seizures 3 times in 7 days. Seizures began with simultaneous shaking of her arms and legs, loss of consciousness, eyes fixed on one point, and confusion after the seizure. One day after the last seizure, there was short and long term memory disturbance, including her activity, her friend's name and her family, without any focal of neurology deficits. All examinations (blood, urine, brain CT scan, MRI) were normal, except the EEG which showed an abnormal pattern with general slow waves and epileptic discharge at bitemporal especially in the right hemisphere.
Results: We administered phenytoin 300 mg, piracetam 3600 mg, folic acid, and roborantia. After 2 weeks daycare, we made an EEG evaluation and the result was normal.
Conclusion: Today, she still takes her treatment, and when she takes the treatment regularly, she has no attacks (memory disturbance).
Keywords: memory disturbance, non-convulsive status epilepticus.

p969
Refractory Status Epilepticus (RSE): Retrospective Analysis
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Purpose: Refractory status epilepticus (RSE) is life-threatening condition (high morbidity and mortality), with seizures lasting over one hour and not responding to first and second-line anticonvulsant drug therapy. We describe 10 cases with refractory status epilepticus (RSE) treated in our hospital (before transfer to intensive care unit) during last year (2004).
Methods: We treated 10 hospitalised adult pts (6M-4F: medium age 48 ys) with prolonged SE (over 60'). All patients were submitted to EEG registration that showed focal or generalised continuous epileptic or slow activity. 6/10 pts had partial motor (unilateral) SE, 2 had myoclonic SE and 2 subtle SE (electric SE). The causes of SE were: idiopathic in 4 pts, cerebrovascular in 3 pts and brain neoplasia in 3; 2 pts had a symptomatic form of partial E. All pts didn't respond to the first (diazepam, lorazepam) and second line (i.v. charge with phenytoin) therapy. We used iv sodium-valproate (20-30 mg/kg, in 6

cases), iv piracetam high doses (30 g in all 10 cases) and levetiracetam per os (2000 mg in 2 cases).
Results: 2 of the pt treated with iv-VPA and 1 with levetiracetam stopped SE, the others were transferred in ICU (among these 2 died).
Conclusion: Our results, although the exiguity of sample didn't allow statistic inferences, seem to encourage the use other AEDs before the introduction of general anaesthetics, and underline the importance of EEG monitoring.

p970
Complex Partial Status Epilepticus (CPSE) as a Paraneoplastic Syndrome in a Patient with Breast Cancer
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Purpose: CPSE, a relatively rare form of non-convulsive status epilepticus is usually seen in patients with underlying structural, vascular, metabolic or infective pathologies. Previously thought to be benign, CPSE is presently associated with significant neurological morbidity. CPSE as a cause of altered mental status in patients without the above-mentioned pathologies presents a diagnostic challenge. Our case reports the unusual occurrence of CPSE as a possible paraneoplastic syndrome.
Methods: A 58-year-old female with no prior neurological illness including seizures was diagnosed as having carcinoma of the left breast. She underwent mastectomy and received adjuvant chemotherapy. While on chemotherapy, she was admitted for treatment of neutropenia. In hospital, she had multiple stereotyped episodes of altered behaviour including unresponsiveness and muscular twitching of the face. These episodes were preceded by visual aura. She had brief post-ictal confusion followed by recurrence of the episodes. Neuro-imaging was negative. Toxic, metabolic, infective screens and CSF were unremarkable. Video EEG monitoring during the spells revealed diffusely distributed, predominantly left hemispherical epileptiform discharges. These discharges correlated with and were related to the spells. Inter-ictal EEG revealed diffuse bursts of epileptiform discharges. Anti-epileptic medications brought a significant improvement to the clinical and EEG picture.
Results: Our patient meets the Treiman-Delgado criteria for CPSE. New onset seizures not ascribable to metastatic, hormonal, metabolic or infective processes due to underlying tumour qualify for a paraneoplastic syndrome.
Conclusion: CPSE occurring as a paraneoplastic syndrome is very uncommon. It requires a high degree of suspicion, appropriate neuro-imaging and continuous EEG monitoring for accurate diagnosis.

p971
Appearance of Epileptic Seizures in Pregnant Women without a Previous History of Epilepsy
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Purpose: Epileptic seizures are always a special problem because of the particular physiological condition of patients and the choice of medication. We present two woman patients without a previous history of any kind of epileptic seizure, who experienced their first seizures during pregnancy, due to hormonal-metabolic disturbances and increased brain excitability.
Methods: The first patient, age 23 years (first pregnancy), had her first generalised tonic clonic seizure during sleep in the seventh month of her pregnancy, and the second patient had the same type seizure (during wakening) in the eight month of her pregnancy. In both patients the seizures were repeated; in the first patient after a period of three weeks, and in the second patient after a period of two weeks. We gave mild doses of natrium valproate (apilepsin 300 mg divided in two daily doses, which successfully and completely diminished the seizures.
Results: Our results: EEG,CT-scan, MRI were within physiological limits. AED showed value under therapeutic level of natrium valproate in the serum. Very important is the fact that we found a mild fall of the progesterone hormone in the blood. The dosage of the drug was not increased because the epileptic seizures were successfully controlled with low dosages of apilepsin. The pregnancies and postpartum period were successfully finished. After the pregnancies, therapy was discontinued and by the follow up period 10 months later, neither patient had experienced seizures.
Conclusion: In the discussion and as a conclusion we will point out that molecular mechanisms involved in the pathophysiology of epilepsy in pregnant women is not well known, although it is well known that estrogen hormones are proconvulsive, and progesterone has anticonvulsive effects. In our first patient there was a slight decrease of progesterone in the blood in the 7, 8 and 9 month of pregnancy, and in 8 and 9 month in the second patient.

p972
Menstrual Disorders and Hyperandrogenism in Adolescent Girls with Epilepsy Manifested at Puberty
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P Purpose: Menstrual disorders (MD) are often associated with anovulatory cycles and are main symptoms of several types of reproductive endocrine disorders, such as hyperandrogenism (HA). About 10% of all adolescent girls have MD and HA which are often found in women with epilepsy, especially in women with epilepsy manifested at puberty (EMP). Early correction of MD and HA may favour in treatment of epilepsy. The goal of research is to investigate occurrence of MD and HA among treated and nontreated EMP girls.
Methods: 111 consecutive girls with epilepsy, age 12-18 with EMP were recruited. Menstrual cycle (MC) intervals (by individual calendars during 3 months) and levels of luteinizing, follicle stimulating, prolactin, progesterone and free testosterone were measured on the days 11-14th with shorter (<24 days) MC, on the days 21-22nd with normal MC (24-34 days) or oligomenorrhoea (34 day<3 month) and randomly in girls with amenorrhoea (no MC during 3 months). At admittance 47 had never taken AED, 64 had taken different AED therapy. Statistical analyzes held by SPSS(12).
Results: 15 patients (13.5%) had amenorrhea, 41 (36.9%) oligomenorrhea, 4(3.6%) shorter MC and 51(45.9%) normal MC. HA revealed in 38 (34.2%) cases and anovulatory cycles in 52 (46.8%) cases. Anovulatory cycles with HA was revealed in 21 (18.9%) cases, and of them 8 girls had normal MC intervals ($p<.000$). Treated and non-treated EMP girls did not significantly differ by the occurrence of MD ($p<0.1$) and HA ($p<0.3$).
Conclusion: Regardless of AED treatment, occurrence of MD and HA is higher among EMP girls than in the same age non-epileptic population.

p973
Prospective Follow-up of Pregnant Patients with Epilepsy in an Epilepsy Centre
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Purpose: Treating and counselling women with epilepsy at childbearing age is a specific challenge, especially with many new AEDs becoming available. We report prospectively collected data from pregnant epilepsy patients who are followed-up at Ghent University Hospital.
Methods: Since 2002, prospective data on seizure type, seizure frequency, AEDs before, during and following delivery are being collected from pregnant epilepsy patients.
Results: 13 patients have been included. At conception, 9 patients were on monotherapy, 2 patients had 2 AEDs, 2 patients had 3 or

more. 2 patients were also treated with VNS. 7 patients were treated with new AEDs (LTG: 6, LEV:1). 8 patients had CPS (seizure-free: n=5), 5 patients had PGE (seizure free: n=4). 3 patients showed an increase in seizure frequency during pregnancy, 1 patient had a decrease. In 7 patients, AEDs were changed during pregnancy with an increase of LTG dosage in 6 patients and interruption of VPA in one. 5/13 patients are currently pregnant. 8/13 patients have delivered a baby. 2/8 had a caesarean section. One patient had a GTC seizure during delivery. None of the offspring have major malformations, one baby had a postoperative intracranial haemorrhage that fully resolved, one baby has 2 small VSD. One baby was showing sedation signs during breastfeeding.
Conclusion: In the majority of the patients included in this study, pregnancy and delivery were uneventful. However, increased seizure frequency during pregnancy may occur and necessitate appropriate adjustment of AED treatment. K. Vonck, V. De Herdt and P. Boon are supported by the FWO-Flanders.

p974
Focus Laterality and Psychic Phenomena in Catamenial Epilepsy
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Purpose: Although catamenial epilepsy is a well recognised disorder, little is known about the possible relationship between focus laterality and psychopathological phenomena in women with catamenial epilepsy. The current study was carried out in order to find the mentioned possible relationship.
Methods: 23 females with catamenial form with simple and complex partial and secondary generalised seizures in temporal lobe epilepsy (TLE) with comorbid psychiatric disorders were evaluated by using the Hopkins Symptom Checklist (SCL-90 Revised). The side of foci also was defined and comparison between patients with left-sided and right-sided foci was performed.
Results: Among all groups of patients 17 (74%) females had left-sided and 6 (26%) right-sided foci. In 8 patients the organic affective disorder was diagnosed, while in 15 patients, diagnosis of personality changes due to epilepsy was set. Comparison between left- and right-sided foci patients revealed the more exaggerate rate of all SCL-90 constructions except the 'interpersonal sensitivity' in patients with right-sided foci. All differences reached a high level of statistical significance (p= 0,00001- 0,04).
Conclusion: The right-sided foci females with catamenial epilepsy seem to exaggerate, while the women with the left-sided foci seem to underestimate the severity of such SCL-90 clusters, as 'somatisation', 'obsessive-compulsive behaviour', 'depression', 'anxiety', 'hostility', 'phobic anxiety', 'paranoid ideation' and 'psychoticism'. Due to subjective assessment of psychiatric phenomena in the current study the final interpretation of obtained results should be viewed cautiously. Probably, the obtained findings point to demonstrative features in females with right-sided foci.

p975
Sex Hormone, Cortisol, and Dehydroepiandrosterone Sulphate (DHEAS) Changes in Epilepsy Women on Treatment: Variable Role of Antiepileptic Drugs and Seizure Frequency
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Purpose: Hormonal changes occur in epilepsy (E) because of seizures themselves and antiepileptic drug (AED) effects on steroid setup. Steroids may influence neuron activity and excitability. This study was aimed at evaluating estradiol (E2), progesterone (Pg), cortisol (C) and dehydroepiandrosterone sulphate (DHEAS) levels in female patients with differing E severity.
Methods: Morning serum levels of E2, Pg, C, DHEAS and sex hormone binding globulin (SHBG) were assayed during the mid-luteal phase in 113 consecutive female E patients of fertile age, on treatment with enzyme-inducing (EIAEDs) and/or non-inducing AEDs (NEIAEDs). Hormonal data were correlated with clinical parameters including seizure frequency over the six months before the study (seizure frequency score SFS: 1- absent; 2-one seizure monthly or less; 3-four seizures monthly or less; 4- over one seizure weekly up to one or more seizure daily) and compared with those of 30 age matched healthy women.
Results: In E patients E2, Pg, and DHEAS levels were significantly lower (student's t test: p = 0.001, 0.011, 0.001), while SHBG (p=0.001), C (p=0.001) and C to DHEAS ratios (C/Dr; p=0.001) were significantly higher than in controls. Both E2 and DHEAS were significantly higher (General Linear Model GLM procedure: p= 0.04 and 0.0001) in patients on NEIAED monotherapy than in other groups. No significant changes in C and C/Dr values were found between patients on various AED treatments. Patients with various SFSs did not show significant differences in sex hormone and SHBG levels. C and C/Dr were significantly heightened (GLM: p= 0.002 and 0.001) and DHEAS significantly lowered (p=0.001) in patients with SFS 2 and 3-4 versus SFS 1 and healthy subjects. CORR statistical procedure showed that SFS mainly explained C and C/Dr increase in patients with more active disease, while changes in DHEAS levels correlated with SFS and epilepsy syndrome, as well as with AED treatments and ages.
Conclusion: AEDs, seizure frequency and other parameters variably affect hormonal changes in female epilepsy patients. Women with more frequent seizures show steroid alterations which might be relevant to seizure control and patient health.

p976
Comparison of Catamenial and Noncatamenial Epilepsy in Females
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Purpose: To find any possible discrepancies in symptoms between catamenial and noncatamenial forms of epilepsy in females.
Methods: 26 women with catamenial and 107 with noncatamenial forms within temporal lobe epilepsy (TLE) were analysed for any discrepancies in basic epileptic variables, including the history of epilepsy and concomitant endocrine pathology, type and frequency of seizures and type and mean daily dose of AED.
Results: The catamenial group was characterised by a longer duration of concomitant endocrine pathology in years (9.76+-7.03 vs. 5.,82+-3.84; p=0.001); had more frequent primary generalised seizures (PGS) per half year (3.22+-7.1 vs.0.58+-1.55; p=0.0006); had higher prolactin (PRL) level (468.44+-252.4 vs.268.3+-160.62, p=0.05) and less reduction of simple partial seizures (SPS) (0.12+-0.27 vs. 0.3+-0.44, p=0.008) compared with the noncatamenial group. All the other variables showed no significant differences between the two groups.
Conclusion: The catamenial group seems to be distinguished from noncatamenial epilepsy on the duration of concomitant endocrine pathology and PRL level. Obviously, the hormonal profile of catamenial epilepsy should be regarded as a main pathogenic mechanism in seizure genesis and propagation. The higher PRL level may be considered as one of the causes in delayed response of SPS to AED treatment in females with catamenial epilepsy.

Wednesday 31st August and Thursday 1st September 2005
13:15 – 14:15
Poster Session
Neuropsychology

p977
Impaired Recognition of Facial Emotions in Children with Temporal Epilepsy
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Purpose: Impairments in recognising facial emotions, especially fearful faces, are reported in adults with early-onset right mesial temporal lobe epilepsy and after right temporal lobectomy. Thus, we hypothesize that children with temporal epilepsy can also be impaired in recognising emotional facial expressions, before and after surgery.
Methods: We tested 17 children with epilepsy (mean age=11.8; sd=2.8 years; mean IQ=87, sd=25.8) with a new paradigm of recognition of facial expressions which contains 5 emotions (happiness, sadness, fear, disgust and anger) and neutral faces. Performances of 6 children with right temporal epilepsy (3 unresected), 6 children with left temporal epilepsy (one unresected) and 5 children with extratemporal focal resection were compared with those of 161 healthy children of 7 to 15 years (mean age=10, sd=2.2 years).
Results: On our test of recognition of emotional facial expressions, children with epilepsy had performances that differed significantly from controls ($p < 0.01$). Children with temporal lobe epilepsy had lower performances than children with extratemporal resection ($p < 0.01$) and controls ($p < 0.01$). No difference was observed between children with left and right temporal epilepsy.
Conclusion: Our preliminary results show that children with temporal lobe epilepsy are impaired in recognition of emotional facial expressions whereas children with extratemporal resection performed as well as healthy children. Early temporal lobe epilepsy compromised the development of recognition of emotional facial expressions but further data are needed to better understand the influence of hemispheric specialisation.

p978
Primary and Secondary Emotional Disturbances in Children and Adolescents with Epilepsy
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Purpose: Epilepsy as a long term condition is one of the risk factors appearing in emotional disturbances and disturbances in socio-emotional development. These problems are connected with brain pathology, side effects of pharmacotherapy or psychosocial aspects of the condition (labelling, mistakes in parenting etc.). The aim of the study was to evaluate the structure of emotions. The character of emotions, ability of control and reactivity were evaluated.
Methods: 30 children and adolescents aged 7-18 years with epilepsy treated with novel and conventional AEDs participated in the study. The mean age for first epilepsy seizure was 4.5 years. Neuropsychological experiments on recognising emotions, reactivity, control of emotions, recognising social 'emotional' situations and, additionally, tests of thinking, memory and intelligence were used in the study.
Results: The results showed a higher incidence of emotional dysfunction in children and adolescents with epilepsy than is found in a healthy population. Problems in controlling emotions were observed. Disturbances were connected with the duration of the condition. Patients with newly diagnosed epilepsy showed minor problems with reactivity and control of emotions.
Conclusion: Emotional disturbances in patients with epilepsy appear more often than in the general population. These problems are connected with inefficient control of emotions. The data analysis showed that the prime reason of dysfunction is epilepsy. Secondary factors connected with social influence overlap these disturbances

p979
Memory in Children with Temporal Lobe Epilepsy
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Purpose: In adults, temporal lobe epilepsy (TLE) is usually associated with memory and language impairments. In childhood it is not well established whether neuropsychological deficits are the same. The purpose of this study was to evaluate if children with TLE present the same type of neuropsychological deficits presented by adults.
Methods: This study was conducted at the paediatric outpatient epilepsy clinics of our university hospitals. We performed neuropsychological assessment in 20 children with clinico-electroencephalographic and MRI findings of TLE. The tests used were: WISC III, colour and shape perception, Boston Naming Test, Dichotic Listening and Wide Range Assessment of Memory and Learning (WRAML). Assessment aimed to evaluate attention, visual perception, intellectual level, handedness, language and memory (verbal, visual, global and learning). Control group was formed by 20 normal children with comparable age and socio-economic level (mean +/- 1SD).
Results: Global cognitive performance was normal in all patients. Abnormal results were found in Boston Naming Test (9 patients), verbal memory (10 patients), visual memory (9 patients), and global memory (7 patients).
Conclusion: Specific memory and language neuropsychological deficits may be found in children with TLE, with normal global cognitive performance. These findings are in keeping with those found in adults.

p980
Acquisition of New Concepts in Childhood Amnesic Syndrome due to Hippocampal Injury after Status Epilepticus: A Case Report
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Purpose: Epileptic activity may impair the slow consolidation and storage of episodic and semantic memories (Mayes et al., 2003). However, no study has investigated the acquisition of novel concepts in children with hippocampal injury due to status epilepticus followed by recurrent temporal lobe seizures. The aim of this study was to demonstrate lasting and flexible semantic acquisition in KF, a 7 year old girl who became amnesic after a prolonged status epilepticus and who developed intractable bitemporal epilepsy.
Methods: Our protocol concerned the acquisition of labels and features of 8 novel concepts using relevant techniques described in the literature as errorless learning and vanishing cues methods. It included several assessments of episodic memory using original tasks both during and after the learning phase.
Results: Despite profound anterograde amnesia, we observed significant semantic acquisition (comparable percentage as her control) and long-term retention (one year) in KF. On episodic memory tasks, she mainly performed recognition tasks on the basis of a feeling of familiarity that was dependent on semantic, not episodic,

memory and could not produce spatiotemporal evidence to justify her choices.
Conclusion: Firstly, these results, recorded in the context of intractable mesio-temporal lobe epilepsy, challenge the theories of consolidation. Secondly, this work supports earlier studies demonstrating semantic learning in amnesia and specifies that episodic memory is not necessary for long-term acquisition. Moreover, this study argues the case for memory rehabilitation in young patients suffering epilepsy using the original methodology applied here.

p981
Neuropsychological Dysfunctions in Absence Epilepsy
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Purpose: Absence epilepsy (EA) is the commonest form of idiopathic generalised epilepsies of childhood. Usually is not associated with global cognitive impairment. Some authors found a mild low cognitive level and selective psychological disabilities in EA patients (Echenne e coll., 2001; Ronen e coll., 2001; Pavone e coll., 2001). The aim of this work is to examine neuropsychological profiles of a sample of subjects affected by EA.
Methods: The patients group included 16 children (9 males and 7 females, mean age 8 years and 6 moths) diagnosed as having EA. All patients were seizure-free from 12 to 24 months. 50% of patients did not show any EEG abnormalities. All patients were on antiepileptic medications. They were examined with a set of tests investigating neuropsychological functions: memory, attention, perceptive, motor, linguistic and academic (reading, writing and arithmetic) abilities. The same instruments have been given to a control group homogeneous as regards sex, age, level of education and socio-economic background.
Results: None of the subjects affected by AE showed intellectual deficit (mean IQ in Wechsler 90.09; DS 7.9). Neuropsychological evaluations showed statistically significant differences of some parameters. Total IQ score was lower in epilepsy patients compared to controls ($p<0.01$). We also found selective dysfunctions relating to all linguistic tasks ($p<0.01$): naming, phonological and metaphonological tasks, phonological and semantic verbal fluency. A selective deficit was also found in perceptive visual-spatial tasks ($p<0.05$), manual dexterity ($p<0.01$), reading, writing and a arithmetic abilities ($p<0.01$).
Conclusion: This study further confirms that EA patients may present selective neuropsychological dysfunctions in some areas of cognitive organization. The presence of learning selective disturbances is the major finding of our study. We can argue that linguistic and visual-perceptive difficulties compromised numeric and graphic code learning. The presence of neuropsychological difficulties in EA struggle with the concept of benignity classically attributed to this syndrome and support the hypothesis that these patients may have a neurocognitive impairment.

p982
Effects of Psychoeducational Therapy for Patients with Epilepsy with Continuous Slow Waves during Slow Wave Sleep and Landau-Kleffner Syndrome
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Purpose: To evaluate the effects of psychoeducational therapy for patients with continuous slow waves during slow wave sleep (CSWS) and Landau-Kleffner syndrome (LKS).
Methods: 5 patients with CSWS and 3 patients with LKS were neuropsychologically examined twice with the interval of mean 26 months. The profiles and the change of the results were analysed comparing those of 3 CSWS and 1 LKS who were under drug therapy only (Group A) with those of 2 CSWS and 2 LKS who underwent psychoeducational therapy (cognitive learning and behavioural adjustment) for mean 16 months in addition to drug therapy (Group B).
Results: In Group A, 2 CSWS patients showed improvement in learning and behaviour with increasing IQ, and one LKS patient had a slight improvement in learning despite unchanged IQ. Seizures and EEG got better in these patients. In another CSWS patient who still had seizures and EEG abnormality, IQ was decreased and hyperactivity and distracted attention remained unchanged. In Group B, 2 patients (CSWS and LKS) with EEG and seizure betterment showed an increase of IQ and learning function resulting in cognitive and behaviour improvement. Of the other 2 patients who still had seizures and/or EEG abnormality, 1 with CSWS showed an increase of IQ and learning function, and another with LKS learned communication skills using sign language. Their hyperactivity and distracted attention changed for the better.
Conclusion: The psychoeducational therapy for patients with CSWS and LKS proved to be effective in improving their cognition and behaviour when combined with drug therapy.

p983
Neurophysiological and Neuropsychological Assessment of Children with Epilepsy with Syndromes of Attention Deficit and Hyperactivity
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Purpose: Epilepsy is a common neurological disorder in general populations. In infancy, far from being a condition in which only convulsive phenomena occur, epilepsy also has important cognitive and behavioural components. The psychological repercussions of epilepsy are the sum of various factors due to the epilepsy itself: the treatment given, the side-effects of drugs given and the manner in which the patient copes with the condition. The relationship between epilepsy and SADH is highest, and that is why we set out to identify the major psychological and neurophysiological manifestations in a group of children with epilepsy and with SADH and to determine in which manner they are related.
Methods: A descriptive and retrospective study was made of 33 children with epilepsy who attended the Special School 'Frank País' of Santiago, Cuba. They were characterised by demographic and clinical variables. Observation and interview were the methods used to determined the psychological manifestation. The absolute numbers and percent were used for statistical analysis.
Results: Our patients were predominantly male. The most significant psychological manifestations were: hyperactivity, attention disorder, problems with social relationships, learning difficulties, and behavioural problems. The EEG between the seizures was abnormal in 40% of the patients in frontal and parietal regions. The neuroimaging studies were made only with patient who had a positive physical examination results.
Conclusion: The integral neurological assessment in all children with epilepsy should be directed towards the detection and surveillance of the most common neuropsychological problems.

p984
Cognitive Functions and Quality of Life in Untreated Patients with Localisation-related Epilepsy
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Purpose: To investigate the pattern of cognitive disturbances and quality of life in a homogeneous group of adult patients with recent onset localisation-related epilepsy prior to onset of drug therapy.
Methods: We investigated 30 patients with new onset, complex partial or secondarily generalised seizures (MMSE = 28.9) as compared with 25 normal controls (MMSE = 29.4). The study groups were closely matched in terms of age and education. All subjects were assessed by means of a comprehensive neuropsychological battery designed to

measure reaction time, memory, language, praxis and executive functions. We also applied a subjective self-assessment scale of neurotoxicity and life quality (Side Effect and Life Satisfaction Scale, SEALS), including 5 sub-scales (cognition, dysphoria, temper, tiredness, worry).
Results: Patients with epilepsy had significantly worse scores on simple reaction time (p=0.03), verbal fluency (p=0.0005), digit symbol test (p=0.025), trail making test A and B (p=0.003 and 0.04, respectively) and SEALS (especially worry sub-scale p=0.05).
Conclusion: Despite the comparable global cognitive functioning, patients with localisation-related epilepsy show activation/alertness impairment and executive function deficits relative to normal controls. Executive function deficits appear predominantly in tasks requiring response inhibition, switching, cognitive flexibility and self-monitoring. With the advent and widespread use of new antiepileptic drug therapies, future clinical trials will undoubtedly test their effect on executive functions. Moreover, the results of this study will be useful in the counselling of patients on their educational, social and vocational needs.

p985
Cognitive Effects of Topiramate and Depakine for Frontal Lobe Epilepsy
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Purpose: The aim of the study was to analyse the cognitive effects of topiramate (TPM) in patients with symptomatic frontal lobe epilepsy as compared with depakine (VPA) effects and control.
Methods: Two groups of patients and control (healthy subjects, without drug intake) were administrated neuropsychological and cognitive tests for attention, memory, psychomotor speed, language, and for frontal lobe functions (Wisconsin Card Sorting Test, etc). The first group included patients with symptomatic partial frontal lobe epilepsy with secondarily generalised seizures (9 women, mean age 24 years, sd 4.5). They were tested twice (before VPA was withdrawn and one year after TPM therapy). They were free from seizures and had medium TPM dosage of 275 mg/day, on average. The second group had the same form of epilepsy and long-term VPA therapy, mean VPA dosage of 25 mg/kg/day (8 women, mean age of 25.5 years, sd 3.5). The statistical intergroup comparisons were analysed for all tests in double-blind study.
Results: The statistically significant differences on measures of attention, digit backwards, speed performance, and frontal lobe associated functions (on WCST, etc) were obtained for all groups. In performance of these tests, the higher scores in cognitive performance were observed in the TPM group as compared with the results before VPA withdrawal and with the second group. The findings also demonstrate also qualitative features of patients in the second group as compared with the first and with control groups (a slight decline in synthesis, lowering of flexibility, temporal ordering impairment, etc).
Conclusion: In symptomatic partial epilepsy with secondarily generalised seizures, VPA therapy displayed slight adverse cognitive effects in the majority of cognitive tests, while the TPM group demonstrated mild positive alterations in frontal lobe associated functions and minimal negative effects in other neuropsychological parameters (compared with the control group).

p986
Add-on Treatment with LEV and its Influence on Cognition
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Purpose: Levetiracetam (LEV) is one of the novel antiepileptic drugs effective in the treatment of focal and primary generalised epilepsies (Ben-Menachem et al., 2003). There have been reports on psychiatric side effects of LEV as well as reports on quality of life of patients taking LEV (Cramer et al., 2003). Less is known about the influence of LEV on cognitive function.
Methods: In this open observational study effects of LEV on attention, verbal and figural memory, executive functions, and on visuospatial abilities were evaluated in 24 patients (13 male, mean age 36 years, sd=10 years). Cognitive functions were assessed prior to titration (T1) and after reaching steady state of the individual target dosage (mean=2239 mg, sd=764 mg; T2) of LEV. Both patients with idiopathic (n=4) and focal epilepsies (n=20) were assessed. Statistical analysis was performed via multiple ANOVA's with repeated measurement and Bonferroni correction.
Results: 50% of the patients achieved seizure freedom at T2. Statistically significant improvements under LEV medication regardless of the seizure situation at T2 were seen in selective attention, verbal fluency and visuoconstruction. The performance in the remaining neuropsychological tests did not change significantly under the therapy of LEV.
Conclusion: No negative side effects of LEV were observed in any of the cognitive domains investigated. The observed improvements in some cognitive functions need further exploration in a larger number of patients. The lack of side effects of treatment with LEV with regard to cognitive functions may be a major advantage of this drug.
Acknowledgement: The evaluation of neuropsychological data was financially supported by UCB (Kerpen, FRG).

p987
Cognitive Disturbances in Extratemporal Epilepsies
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Purpose: To investigate and document cognitive and memory impairment in patients with extratemporal epilepsies with different aetiological factors.
Methods: The patients (n=28) were grouped into frontal, parietal and occipital lobe epilepsies according to ictal and interictal EEG, MRI, and in some patients with SPECT and PET. The patients were assessed with a comprehensive neuropsychological battery. Test performances were adjusted for age, gender and education. Analyses included group comparisons and correlations of duration of epilepsy with cognitive and memory impairment.
Results: In frontal lobe epilepsy patients (n=15), attention, abstraction, verbal fluency, response inhibition and working memory were affected. In patients with parietal lobe epilepsy (n=7), apraxia was a prominent finding and on the right side visuospatial disturbances were frequent. Visual memory, visuospatial functions, face recognition and judgment of line orientation were affected in patients with occipital lobe epilepsy (n=6). The worst cognitive disturbances were detected in patients with frontotemporal and temporoparietooccipital junction localisation.
Conclusion: Neuropsychological tests can help us to confirm the lateralisation and localisation of the epileptic focus. If the epileptogenic area is widespread and more than one lobe or junction areas are affected, cognitive disturbances are the worst outcome.

p988
Refractory Mesial Temporal Lobe Epilepsy: Cognitive Function Assessment in a Pre-surgical Series
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Purpose: Neuropsychological testing is routinely used in pre-surgical evaluations of patients. Cognitive dysfunction has some degree of correlation with lateralisation and localisation of epileptic activity, thus helping to determine a surgical strategy. The aims of this study were to assess the cognitive function status before surgery in patients with refractory temporal lobe epilepsy, to determine their cognitive function profile and to correlate cognitive dysfunction with the

lateralisation and the localisation of seizure origin (mesial or lateral temporal lobe).
Methods: After pre-surgical evaluation, our series of 29 patients was found to have seizures of unilateral left (n=16) or right (n=13) and mesial (n=22) or lateral (n=7) temporal lobe origin. Patients were assessed before surgery, with a neuropsychological protocol that included measures of intelligence, attention, executive functions, language, visuospatial functions, verbal memory and visual memory. $\chi 2$ and correlation tests were used.
Results: One or more cognitive dysfunctions were found in 26 patients (90%). There is no correlation between selected cognitive impairment and lateralisation or localisation of epileptic activity. However neuropsychological testing detected lateralised deficits (language and verbal memory for the dominant hemisphere and visuospatial functions and visual memory for the non-dominant hemisphere) in 14 patients (48%). This lateralisation was concordant with the side of seizure origin in 13 patients ($p<0.05$, incorrect lateralisation in 7%).
Conclusion: Generalised and non specific cognitive impairments are associated with refractory temporal lobe epilepsy. When lateralised cognitive deficit is present, it is correlated with the lateralisation of seizure origin.

p989
Right Temporal Interictal Epileptiform EEG Discharges Decrease Delayed Face Recognition in MRI Negative Temporal Lobe Epilepsy (TLE)
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Purpose: There is conflicting evidence whether temporal interictal epileptiform EEG discharges (IED) may suppress memory functions. We wanted to test whether in patients with TLE without pathological MRI findings delayed face recognition is influenced by the presence of right temporal IED.
Methods: Patients with TLE (according to seizure semiology) and normal MRI undergoing diagnostic workup with 24-72h video EEG monitoring were investigated. Recent MRIs including thin-sliced coronal sequences were normal. EEG recorded by scalp electrodes was classified as showing left or right temporal IED according to the appearance of spike-slow-waves in the electrodes T1/2, F7/8, T5/6. Eleven TLE-patients with right IED, 11 with left IED, 11 without IED, and, in addition, 12 generalised epilepsy patients were included (mean age=39 (sd=15), verbal IQ=99 (sd=7)). Results were compared with 38 healthy controls (mean age=34 (sd=15), verbal IQ=100 (sd=11)). Twenty unfamiliar faces were shown for 5 seconds each, and had to be recognised from 40 faces immediately and after 24 hours. Percentage of recognition was corrected for false positives. RANCOVA (groups*immediate/delayed) was performed.
Results: Only right IED patients performed worse than healthy controls (right IED: immediate 65% (sd=21), delayed 47% (sd=19); controls: immediate 76% (sd=12), delayed 74% (sd=14); $p=0.002$). Right IED patients showed an impaired delayed recognition ($p=0.002$), but did not differ from the other groups in immediate recognition ($p>0.20$).
Conclusion: Our results demonstrate that in TLE patients without hippocampal atrophy/sclerosis only right temporal IEDs are correlated with impaired facial memory functions. A 24h delay raises the sensitivity of detecting these deficits. Our study helps to explain conflicting results in studies of hemispheric face memory dominance.

p990
Wechsler Intelligence Scale to Evaluate Cognitive Deterioration in Epilepsy: Analysis of Neurobiological Factors
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Purpose: Our purpose is identify cognitive deterioration in a group of subjects who have epilepsy, using the Wechsler intelligence scale, in order to analyse the neurobiological factors that can cause deterioration.
Methods: Wechsler deterioration scale was applied to a group of 100 patients who have epilepsy. We studied a set of biological variables such as family record of epilepsy, past history of cerebral lesion, age at the beginning of seizures (younger and older than 15 years), time of evolution of the seizures (more than 15 years) high frequency of seizures (more than one in a mouth), type of epilepsy and type of seizures.
Results: 43% of the group presented cognitive deterioration (31% with severe deterioration and the other 12% with only minimum deterioration). Also, 20% of the group had experienced a high frequency of seizures since the onset of epilepsy (more than 1 in a month). In this group, 80% suffered cognitive deterioration ($X2= 12.664$ $p = 3.7286\text{-}04$ $DF = 1$).
Conclusion: The most important biological factors related to neurological deterioration of these patients is the frequency of the seizures.

p991
Investigation of Cognitive Function in Epilepsy and Exploration of the Independent Risk Factors
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Purpose: To evaluate the cognitive functioning of patients with epilepsy and to explore the effect of factors related to epilepsy on cognition in China.
Methods: 60 registered patients, newly diagnosed with cryptogenic epilepsy and who met the criteria of the study, were arranged for the Wechsler intelligence scale and registered their clinical manifestation including age at seizure onset, seizure type, frequency, duration of seizure disorder, family history and the localisation of the epileptic lesion before the treatment. The patients were paired with 60 healthy volunteer controls.
Results: Epilepsy patients had lower FIQ, VIQ and PIQ than the healthy controls (99.96±18.03 vs 116.80±12.53, 103.92±19.63 vs 120.68±13.62, 95.32±16.60 vs 108.85±11.76, separately), with significant differences. Similar results were also reported in the adult and child subgroups. The results of the risk factors on cognition showed that FIQ, VIQ and PIQ had a negative correlation with duration of seizure disorders (-0.478, -0.487, -0.406, separately, $p<0.001$), and seizure frequency (correlation coefficient: -0.493, -0.474, -0.443 separately, $p<0.001$); similar results were seen in the adult and child subgroup. No statistical difference in FIQ, VIQ and PIQ existed in analysis of other risk factors. Suggesting duration as a covariant, correlation index of FIQ and seizure frequency was 0.243, $p<0.01$, while suggesting seizure frequency as a covariant, the counterpart was -0.092, $p>0.05$.
Conclusion: These findings indicate that IQs of patients with epilepsy are lower than those of the healthy population and that seizure frequency is the independent risk factor of impaired cognition in epilepsy.

p992

Effect of Chemically-induced Seizures on Learning, Memory and Behaviour in Rats

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Purpose: The study was conducted to see the effect of acute administration of a 100% convulsant dose of pentylenetetrazole (PTZ) and chronic administration of subconvulsant dose of PTZ (kindled seizures) on learning, memory and behaviour in rats.
Methods: PTZ was dissolved in normal saline (0.9% NaCl) and administered intraperitoneally in a single dose of 60mg/kg for acute administration in a volume not exceeding 1ml/100gm to three groups of rats (n=8). Rats were observed for a period of 30 min. post PTZ injection and the behavioural tests were carried out on the day after PTZ administration, 7th Day, 15th day in separate groups. Another group (n=8) was administered PTZ 30mg/kg, i.p. for two weeks on alternate days (chronic administration). Learning and memory were tested by using elevated plus maze and the behavioural responses to a novel environment was assessed through the open field test and photoactometer. For each group, control experiments were run simultaneously.
Results: In the elevated plus maze test, while the transfer latencies tended to decline from day 1 to day 3 in all groups, they were not significantly different in any of the groups vs their controls. Similarly, the total number of open arm and closed arm entries were not altered. However, with 7th day animals there was no change. Both kindled and day 1 animals spent more time in open arm and the day15 group spent less time in open arm. In the open field test, there was no change in any parameter studied in the chronically treated (kindled animals) experiments. However, a clear-cut pattern based on the number of entries could not be defined clearly in any of the groups. For locomotor activity, there was no significant difference between control and drug treated on the day after PTZ administration but on the whole the activity counts tended to decline in both 7th day and 15th day animals vs controls. In the chronic administration the counts per se in both saline treated and PTZ treated animals were less than when compared to acute treatment.
Conclusion: There are subtle differences in the response to various behavioural tests between acute and chronically PTZ treated animals and in the case of acute administration, day post PTZ exposure also matters.

p993

Memory Analysis in Temporal Lobe Epilepsy Patients, With and Without Hippocampal Sclerosis

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Purpose: Mesial temporal lobe epilepsy and hippocampal sclerosis syndrome (MTLE+HE) presents material-specific episodic memory deficits, due to hippocampal system damage produced by the lesion. This damage is associated with different variables like epilepsy years of evolution, age of onset and seizure frequency. The aim of this study is to analyse hippocampal sclerosis involvement as the probable cause of memory deficit, comparing results of neuropsychological evaluation in MTLE+HE patients and temporal lobe epilepsy patients with a lesion non HE.
Methods: We selected 123 patients with temporal lobe epilepsy, divided into 2 groups: 101 patients with MTLE+HE and 22 patients with temporal lesion non HE. We used the following neuropsychological protocol: WAIS-R (IQ), Edinburgh questionnaire, Rey Auditory Verbal Learning Test, List Learning Test, Rey complex figure. Boston Naming Test, Wisconsin Card Sorting Test, Trail Making Test (A y B) and verbal fluency. Statistical analysis: an ANOVA test was used to analyse data and with significance variables we applied a chi square test.
Results: The MTLE+HE group presented a significantly more epilepsy years of evolution (p=0.04), a lower age of onset (p=0.01) and more memory deficit (p=0.004), than the temporal lesion non HS group of patients.
Conclusion: Our findings indicate that memory deficits on MTLE+HE patients would be directly related with HE as was reported by other authors.

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Cognitive Study in Epilepsy: Analysis of Amnestic Features

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Purpose: Recent surveys show that nearly 50% of epilepsy patients are likely to be aware of problems with cognitive function (International Bureau for Epilepsy Patients in Mind Survey of Cognitive Function, 2004). The current contribution is part of a study aimed at investigating the correspondence between objective psychological and electrophysiological features characterising such impairments.
Methods: Two different test batteries of diagnostic methods were designed: a combination of neuropsychological tests and a combination of electrophysiological cognitive stimulation paradigms. Both were applied in a group of patients with focal, and focal secondary generalised epilepsy (n=10, age 39.9±11.7) and a group of neurologically healthy controls (n=15, age 37.3±11.4). Here, focus is on the statistical parametric (t-Test, (TT)) and nonparametric (Wilcoxon-Test, (WT)) analysis of selected amnestic features from the Berlin Amnesia Test (BAT) and the Diagnostic Cerebral Damage Test (DCS).
Results: The comparison between the groups shows that firstly, there is no difference between the features 'recall unstructured' (RU) and 'recall associative pattern' (RA); secondly, the feature 'recall semantic structure' (RS) (alpha=0.05,TT), 'recall and destructor' (RD) (alpha=0.10,TT), 'short time memory–span' (SM) (alpha=0.05,WT), 'semantic interference' (SI) (alpha=0.05,TT) are significantly different and the DCS 'index of lability' (LI) (alpha=0.05,WT) is significantly higher in the patient group.
Conclusion: The results entail that there are no differences between verbal and figural working memory. The conspicuousness in the RD, ST and SI as well as the higher LI, point out a presumably weak memory trace. The lower value of RS indicates possible deficits in strategies of the storage process.

p995

Memory Deficits Related to Hippocampal Volume and Neuronal Loss in a Series of Patients with Mesial Temporal Sclerosis

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Purpose: Memory functions are impaired in temporal lobe epilepsy (TLE) associated with mesial temporal sclerosis (MTS). The aim of this study is to correlate memory data with volumetric evaluation of mesial temporal structures and hippocampal cell counting in patients submitted to corticoamygdalohippocampectomy.
Methods: 14 patients (7 left and 7 right MTS) had volumetric measurement of the mesial temporal structures on MRI exams and neuropsychological evaluation applying tests of logical memory (LM) I and II and visual reproduction (VR) I and II (WMS-R). Hippocampal specimens were obtained and neuronal counting was done in 5 µm sections stained with cresyl violet.

Results: The group of right MTS presented normal mean scores in verbal tests (LM I 48; LM II 45) and poorer scores in spatial recall tasks (VR I 40.5; VR II 21.7). Hippocampal volume measured varied from 740.3 to 2103.1 (mean 1445.6 mean AI 21.3%). Mean neuronal cell counting was CA1 18; CA3 14.2; CA4 17.2 and CA2 27.5. Left MTS patients showed both verbal and spatial memory impairment (LM I 20.4; LM II 12.8; VR I 40.8; VR II 37.8). Volumetry of the hippocampus varied from 712.1 to 2165.3 (mean 1.135,5 mean AI 30.8%). Mean neuronal cell counting was CA1 6.1; CA3 4.2; CA4 10.5 and CA2 25.
Conclusion: In this series, left MTS was associated with global memory impairment and hippocampal volume and neuronal loss greater than right MTS. More severe pathological substrate on left MTS might be responsible for more important memory deficits classically described in these patients.

p996
Cognitive and Memory Impairment in Temporal Lobe Epilepsies with Different Pathologies
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Purpose: To investigate and document cognitive and memory impairment in patients with temporal lobe epilepsies with different aetiological factors.
Methods: Temporal lobe epilepsy patients (n=63) were grouped into mesial, lateral and bilateral temporal lobe epilepsy and were assessed with a comprehensive neuropsychological battery. Test performances were adjusted for age, gender and education. Analyses included group comparisons and correlations of duration of epilepsy with cognitive and memory impairment. Aetiologic factors and laterality were determined by ictal and interictal EEG, MRI, and in some patients with SPECT and PET.
Results: Global cognitive impairment was detected in patients with bilateral temporal lobe epilepsy (n=5). While verbal memory impairment was prominent in left mesial temporal lobe epilepsy patients (n=22), visual memory decline and visuospatial dysfunction were frequents in right patients (n=15). Frontal lobe functions were affected in both groups to some extent. Patients with other pathologies than hippocampal sclerosis like tumours, arteriovenous malformations and gliosis (n=21) were better than mesial temporal lobe epilepsies with hippocampal sclerosis.
Conclusion: In temporal lobe epilepsies, laterality and subgroups (mesial or lateral) may determine cognitive impairment and memory dysfunction. Mesial temporal lobe epilepsies with hippocampal sclerosis and bilateral lesions have the worst cognitive disturbances.

p997
Cognitive Analysis Before and After Surgery in Spanish-speaking Temporal Lobe Epilepsy Patients
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Purpose: The aim of this study is to analyse neuropsychological evaluation results in temporal lobe refractory epilepsy patients, before and after anterior temporal lobectomy.
Methods: We selected 35 patients (p.) with refractory temporal lobe epilepsy. All patients were evaluated with a neuropsychological protocol that includes the assessment of intelligence, attention, handedness, verbal memory, visual memory, language and executive function. A z-score was applied to raw values for each patient. The results were compared with those from a normal population. According to this, patients were classified as 'normal' when test results presented values above z-2. We also compared raw values for each test, before surgery, 6 months, and one year after surgery.
Results: We have 17 patients with left anterior temporal lobectomy (LATL) and 18 patients with right anterior temporal lobectomy (RATL). From the total population evaluated, 83% have memory deficits. From the analysis of raw test values, we found after surgery, p. with visual memory deficits (delay recall) (p=0.03), executive function, specially Wisconsin card sorting test (p=0.03), and word generation test (FAS) (p=0.02), improved significantly after a year from the surgery. On verbal memory, language and attention test, there were no significant changes after surgery. From the analysis of each patient, after surgery, we found a variable outcome with a better prognosis on RATL group.
Conclusion: On the studied patients the neuropsychological profile was characterised by material-specific (verbal/visual) memory deficits. We found a better prognosis after surgery when they had visual memory deficits and a RATL as was described by other authors.

p998
Verbal and Spatial Learning after Temporal Resection in Children
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Purpose: Selective memory deficits are found in adults after temporal resection but more conflicting results have been reported in children. We assess verbal and spatial learning in children after antero-mesial temporal resection (AMTR): 1) to evaluate material-specific effect, 2) to differentiate an encoding, a storage or a retrieval deficit.
Methods: 15 right handed patients, 8 left AMTR, 7 right AMTR, (IQ > 80), aged 8 to 15 years (mean=13.2, sd=2.5) and 15 matched controls were evaluated with a French Grober and Buschke's adaptation using the same design for verbal and visuo-spatial material: controlled encoding, 3 trials, free and cued recall, delayed recall and recognition.
Results: The right AMTR group had poorer scores than controls on the 3d trial of spatial cued recall ($p < 0.05$) and in recognition tasks ($p < 0.05$). The left AMTR group had verbal memory that differed from controls (total recall, $p < 0.001$; free delayed recall, $p < 0.001$; recognition, $p < 0.05$), except for initial encoding. No difference was observed between children with left AMTR and controls in spatial tasks. Children with left AMTR had poorer total free and cued verbal recall ($p < 0.001$ and $p < 0.05$) and delayed free verbal recall ($p < 0.05$) than children with right AMTR.
Conclusion: Using Grober and Buschke's adaptation, we found verbal learning impairment in the left temporal group contrasting with material-specificity more often found in children for visual information. Poor recognition in children with epilepsy also suggests disturbance in consolidation after temporal resection.

p999
Functional MRI (fMRI) and Neuropsychological Evaluation after Right Frontal Corticectomy in Two Drug-resistant Epilepsy Patients
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Purpose: To compare fMRI and neuropsychological assessment before and after right frontal corticectomy in 2 epilepsy patients.
Methods: 2 patients (1 female and 1 male, mean age 30 years) suffering from right frontal drug-resistant epilepsy, (1 post-abscess porencephaly, 1 cortical dysplasia) were submitted for presurgical evaluation, including neuropsychological assessment and functional MRI (naming test and phonological verbal fluency). Right frontal

corticectomy was performed in both patients. Four months later, morphological and functional MRI were carried out. One year after surgery, they were submitted for neuropsychological evaluation. Seizure outcome: Class Ia.
Results: In both patients, presurgical fMRI demonstrated left dominance for language while neuropsychological evaluation showed a moderate impairment in verbal and non-verbal tests. In 1 of them (patient 1) fMRI demonstrated a slight activation of both the left and right dorsolateral frontal cortex. Post-surgical fMRI showed greater percentual variation of BOLD signal of left activated areas in both subjects. Moreover, in patient 1, the number of activated areas increased. Neuropsychological verbal and non verbal tests improved in both patients. However, in patient 1, verbal performances showed a greater improvement than nonverbal ones while the opposite pattern was observed in patient 2.
Conclusion: These data confirmed the role of fMRI in the presurgical evaluation of epilepsy. Furthermore, even in the case of large resections, epilepsy surgery when effective, seems to induce an improvement of neuropsychological performances. The fMRI evidence of reallocation of linguistic abilities in the dominant hemisphere after right frontal surgery, might be explained by a phenomenon of neuronal plasticity.

p1000
Neuropsychological and Quality of Life Outcome after Anterior Temporal Lobectomy for Medically Refractory Temporal lobe Epilepsy
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Purpose: To assess the cognitive and long term quality of life (QOL) outcome after anterior temporal lobectomy with amygdalohippocampectomy (ATL).
Methods: A detailed neuropsychological evaluation of 450 patients was carried out over a period of 1995-2003. The patients underwent ATL (right-175, left-275) and completed ≥ 2 years of follow up using various tests like Wechsler Adult Intelligence Scale, subtests of Wechsler Memory scale (WMS), word list learning, Trail making tests, Rey Complex figure and faces test. Postoperative seizure outcome was determined by Engel's seizure scoring system. QOL was assessed using QOLIE-31-scale up to 8 years.
Results: Patients who underwent left ATL had significantly more impairment in verbal subtests of WMS (4.2 ± 5.5 versus 7.4 ± 6.8, p=0.01). Average verbal IQ was 83.1 in right and 84.3 in left ATL patients (p=0.596). Rey complex delayed score was 6.8 in right and 6.0 in left patients respectively (p=0.39). Paired associate learning test scored was 8.9 in right as compared to 6.8 in left (p=0.001). QOL also showed improvement, which was positively correlated to seizure outcome.
Conclusion: Patients who underwent left ATL had impaired verbal memory and word list recall, which had a negative impact on their daily living. Counselling had to be given to them to reinforce their memory skills. On the contrary, non-verbal memory tests showed mild, insignificant impairment in patients with right ATL. Complete seizure freedom is the most important determinant of post-operative QOL outcome. More important is the long term follow up and monitoring their QOL on a long-term basis, which is seldom done.

p1001
Relation Between Epileptic Seizures and Periodic Dysthymic Disorders: Pro or Contra?
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Purpose: It is known that the second clinical component of epilepsy after seizures are psychical disorders: periodic or chronic. But the relation between this main clinical manifestation, in particular seizures and dysthymic, is not sufficiently clear. The usual appearance and increase in dysthymic disorders is connected with epileptic seizures, but the alternative relation between them sometimes occurs. The aim of this investigation is to study the relationship between epileptic seizures and periodic dysthymic disorders in patients with mesial temporal and prefrontal epilepsy.
Methods: Patients aged 6-40 years were studied. Clinical, psychological, MRI, EEG including, if needed, video EEG sleep monitoring and method of dipole localisation of spike activity scores were used.
Results: Among 127 patients with mesial temporal epilepsy, in 33 (24.0%) periodic dysthymic disorders were revealed; among 53 patients with prefrontal epilepsy, in 8 (14.4%), ($p<0.05$). The main risk factor was pharmacoresistance and its predictors: severe organic brain disturbances, high rate and asynchronous seizures, as well as inadequate therapy in past and family psychic disorders. 10 patients with mesial temporal epilepsy with alternative relations between seizures and dysthymic events were discovered. All these patients had approximately a month cyclic generalised seizures. Dysthymic disorder appeared in the second time of rhythmic interictal period and gradually increased, evoked social disadaptation and completed by GTCS. Then in the periods after a seizure, a good mood was recovered and social communication was restored. These events repeated in the following cycles. Patients therefore longed for a seizure as a rescue.
Conclusion: In patients with mesial temporal lobe epilepsy there are two types of relationship between epileptic seizures and dysthymic disorders: epileptic seizures can promote dysthymic disorders; more often a variant or opposite play protective role - more rare variant.

p1002
Emotional Profile Patients with Well-controlled Epilepsy
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Purpose: The purpose of this study was to explore and compare emotional profile patients with well-controlled epilepsy to the emotional profile of a healthy population. We also compared the emotional profile between men and women suffering from epilepsy.
Methods: To detect the emotional profile we used Plutchik index of emotion. We studied 33 patients (22 women and 11 men) suffering from well-controlled uncomplicated epilepsy who experienced from none to three seizures per year.
Results: Contrasting analysis of emotional profiles between the healthy population and patients with well-controlled epilepsy did not reveal any significant differences for any of the profile dimensions examined. Relating to sex, very small differences were registered. Women were a little more aggressive and less self-protective then men. Results confirm a very similar emotional profile between the healthy population and patients with well controlled epilepsy.
Conclusion: Despite the fact that we studied a relatively small sample of patients with well-controlled epilepsy, our results showed that their emotional health remained almost unaffected.

p1003
Higher Scores on Clinical MMPI-2 Scales in Patients with Left than in Patients with Right Temporal Epileptic Foci
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Purpose: Minnesota Multiphasic Personality Inventory (MMPI) has been widely used to measure psychopathology in patients with epilepsy. Some studies have shown higher scores on clinical scales in patients with left than in patients with right temporal foci, but this has not been a consistent finding. This study investigated whether such lateralisation effects could be found in patients with temporal lobe epilepsy using the revised version of the inventory (MMPI-2).

Methods: Patients at a regional epilepsy unit with right-sided (N=17, 10 women) and left-sided (N=27, 12 women) temporal epileptic foci were administered the MMPI-2 as part of a comprehensive neuropsychological assessment. The groups were matched according to age.
Results: Patients with left-sided foci scored significantly ($p<0.05$) higher than patients with right-sided foci on one validation scale (F), three clinical scales (D, Pa and Sc), and four content scales (OBS, DEP, LSE and TRT). The only scales where patients with right-sided foci had higher scores were on validation scales measuring defensiveness (L, K and S), but group differences were not significant in those scales.
Conclusion: Patients with left-sided temporal epileptic foci, as a group, showed higher scores than patients with right-sided foci on a number of clinical and content MMPI-2 scales. The results support the idea that there are hemispheric differences in emotional processing. Having a left-sided temporal focus may increase the probability of admitting psychopathology.

p1004
The 'Sensed Presence': An Epileptic Aura with Religious Overtones
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Purpose: To describe and demonstrate the experience of a 'sensed presence' as an epileptic aura. 'Sensed presence' is a person's perception that a person or a 'power' is present in the room, often accompanied by a religious sensation of clarity or happiness. It has been focused on in recent neuropsychological research as it is reported to be inducible in healthy objects by weak complex electromagnetic fields applied to the temporal lobes.
Methods: The documentation regards a 22 year old male with onset of complex partial seizures at the age of three. MRI of the brain was normal, interictal EEGs showed epileptiform waves over the left temporal lobe. The aura is identical in all seizures, described by the patient like "a feeling that someone stands behind me, someone with a distinct wish to comfort me". The sensation is nice, but it transforms into a state of altered consciousness and an urge to urinate. There was no religious interpretation by our patient.
Results: The phenomenon 'sensed presence' as defined in recent neuropsychological research and the experiences of our patient are strikingly similar; 'sensed presence' can thus without doubt correspond to an epileptic aura. Potential religious interpretations will probably depend on the specific ethnocultural background of the individual.
Conclusion: The demonstration of 'sensed presence' as an epileptic aura has a bearing on present neurotheological discussions, and is furthermore interesting as an unusual sign of complex psychological symptoms in epilepsy.

Wednesday 31st August and Thursday 1st September 2005
13:15 – 14:15
Poster Session
Epilepsy Surgery

p1005
Brain Maturation and Epilepsy Onset in Mesial Temporal Lobe Epilepsy: A New Look in an Old Taylor's Hypothesis
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Purpose: Brain development might affect the clinical course of several neurological diseases during childhood. In this study we test Taylor's hypothesis (Lancet 1969;2:140-2) of possible interactions of brain maturation and age of epilepsy onset in mesial temporal sclerosis associated to hippocampal sclerosis (MTLE-HS) in our series of patients.
Methods: In a retrospective hospital-based hypothesis-driven cohort study, we analysed the age at epilepsy onset in MTLE-HS, split by side of hippocampal sclerosis for 156 male and for 162 female surgically treated patients.
Results: For males, right mesial temporal sclerosis (MTS) was observed to occur at a higher frequency if epilepsy onset occurred in an age-frame ranging from the end of the third year to the end of the eighth year of life ($p<0.005$; O.R.=2.8; C.I.=1.39-5.59). For females, right MTS was observed at a significantly higher frequency if epilepsy onset occurred in an age-frame ranging from the beginning of the second year to the end of the fourth year of life ($p<0.001$; O.R.=4.6; C.I.=1.88-11.28). When epilepsy started out of these ranges, left MTS was more commonly found for most ages.
Conclusion: Age at epilepsy onset in MTLE-HS is associated with the side of hippocampal sclerosis in patterns that are different for each gender, possibly reflecting influences of brain maturation in MTLE-HS epilepsy onset. Our study supports an old, but still influential Taylor's exploratory analysis which proposed that differential rates of cerebral maturation between sexes and between hemispheres seem to be associated with differences in epilepsy onset in MTLE-HS.
Supported by FAPESP (02/03743-0).

p1006
Laughter, but no Mirth, Induced by Electrical Stimulation
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Purpose: The study for the neurobiological basis of laughter has attracted researchers for centuries given that it is an essential part of our daily life contributing significantly to our well-being. It is hypothesized that the cortical representation of laughter is dissociated. While the emotional aspects seemed to be processed in the basal temporal lobe, the motor aspects associated to laughter (e.g. diaphragm, facial musculature movements) supposedly rely on the mesial frontal cortex. However, there are only a few studies of patients in whom laughter was elicited by cortical electrical stimulation (ES) and so far none have been described where laughter was not associated to a feeling of mirth.
Methods: Here we report the case of a 21 year old patient suffering from intractable left temporo-parietal epilepsy. High resolution MRI did not reveal any focal abnormalities. He underwent implantation with depth electrodes covering bilaterally the cingulate, orbito-frontal and lateral frontal structures as well as the left temporal and left parietal cortex providing a total of 110 recording sites.
Results: Smile and, with increasing stimulus intensity, also laughter was induced by ES of the right anterior cingulate cortex. However, no feeling of mirth or any other emotional change was reported. No interference with other movements was observed.
Conclusion: This is the first case in which only the motor aspects of laughter were induced, thus completing previous reports and supporting the concept of the dissociated cortical representation of laughter.

p1007
Ictal Clinical Symptoms Differentiating Temporal Lobe from Temporal
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Purpose: To assess whether it is possible to identify patients suffering from temporal 'plus' seizures (T+) on the basis of ictal clinical features.

Methods: We included in this study 82 patients who underwent, on the basis of stereotactic intracerebral EEG recordings (SEEG), either a standard temporal lobectomy (TL patients, n=59) or a temporal lobe resection extending outside the borders of a standard temporal lobectomy (T+ patients, n=23). This latter group included 3 subgroups depending on the extratemporal areas that were removed: T-perisylvian (TS, n=6), T-frontal (TF, n=9) and T-posterior (TPost, n=8). The most representative seizure recorded during SEEG was analysed in each patient, according to a working definition of ictal symptoms. In that respect, 130 clinical signs, grouped into 31 main categories, were defined. Absolute and relatives frequency symptom distributions and contingency tables were computed for ictal events between the groups. Finally, cluster analysis was performed.
Results: Abdominal aura, mimicry changes, language deficits and ability to advice at seizure onset was found significant for TL patients, while gustatory aura, vestibular aura, and versive manifestations were found significant for T+ patients. In the T+ group, vestibular aura and gustatory aura were significantly associated with TPost seizures and TS seizures, respectively. Versive movements were found to occur more frequently during TF seizures, but this finding did not reach statistical significance.
Conclusion: Our results seem to suggest that ictal clinical symptomatology may help to differentiate TL from T+ patients.

p1008
Ictal Repetitive Grasping: A Motor Sign Characterising 'Frontal Hyperkinetic' Seizures
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Purpose: To investigate ictal grasping (IG) behaviour and to evaluate whether it characterises specific seizure types.
Methods: We analysed the video recordings of 694 seizures in 109 consecutive patients, all candidates for epilepsy surgery. Seizures with motor manifestations (n=511) were selected and divided into four semiological groups: (a) nocturnal frontal 'hyperkinetic' (Blume et al., Epilepsia 2001;42:1212-8) seizures (NFHS): 30 seizures, 12 patients, (b) frontal lobe seizures (FLS) other than NFHS: 228 seizures, 26 patients, (c) temporal lobe seizures (TLS): 194 seizures, 55 patients, (d) extra-frontal/extra-temporal seizures (EF/ETS): 59 seizures, 16 patients. We evaluated IG features by means of video-analysis.
Results: IG was observed in 96.7% NFHS (100% of patients), with a mean latency of 3 seconds, and a mean prevalence of 7.9 IG per seizure, directed to a limited number of surrounding objects or body parts. During NFHS, grasping usually was preceded by a reaching movement and followed by holding or pulling and was performed with both arms in an alternating fashion. In 22.4% FLS (11.5% of patients) 1-3 prolonged IGs were present, mainly directed to a fixed external point. Not repeated IG was occasionally present in TLS (10.3%, in 20% of patients) and EF/ETS (5.1%, in 12.5% of patients), with longer latency. We did not find a consistent relationship between side of hand grasping and side of ictal EEG discharge or MRI lesion.
Conclusion: Early, forced and repetitive IG was a typical manifestation of NFHS. It had constant semiological features, similar to voluntary prehension, suggesting an ictal release of physiological grasping behaviour.

p1009
Pathological Findings of Mesial Temporal Lobe Epilepsy
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Purpose: To investigate the surgical outcomes and pathological findings of mesial temporal lobe epilepsy (MTLE).
Methods: Subjects comprised 57 patients (32 women, 25 men) who underwent anterior temporal lobectomy and amygdalo-hippocampectomy. Pathological findings in the hippocampus, amygdaloid body and temporal lobe were investigated.
Results: Postoperative results according to Engel class were as follows: class 1, 44 (77.2%); class 2, 8 (14.0%); and class 3, 5 (8.8%). Pathological findings of the hippocampus were classified by Watson grading: grade 0-2, 13; grade 3, 13; grade 3-4, 13; grade 4-5, 15; and unclassifiable, 3. Age at seizure onset was significantly lower in patients with high-degree hippocampal sclerosis (HS) than in patients with no or mild HS. All 5 cases of Engel class 3 were included in the group of Watson grade 0-2. Examination of the temporal lobe revealed: CD (microdysgenesis) in 52 cases; increased number of heterotopic neurons in subcortical white matter in 33 cases; abnormal cortical lamination in 31 cases; and astrocytosis in all cases to a greater or lesser degree. In all 6 cases classified as Watson grade 0-1, granule cell layer dispersion in the hippocampus and CD in the temporal lobe was observed.
Conclusion: Age at seizure onset was significantly lower in patients with advanced HS than in patients with mild HS, and CD (microdysgenesis) was common (91%) in the lateral temporal cortex of MTLE patients. Some sort of developmental abnormality is thus presumably involved in the epileptogenesis of MTLE.

p1010
Oxidative Stress and Antioxidative Activity in Human Epilepsy
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Purpose: Epilepsy is a neurological disorder characterised by spontaneous, recurrent and paroxysmal cerebral discharges. Recently, oxidative stress in the brain is increasingly recognised as a cause of cellular injury in many neurological insults. However, the role of oxidative stress in the epileptogenecity is still unknown. Therefore, the main purpose of this study is to investigate the oxidative stress and antioxidative activity in human epilepsy. The epileptogenic foci was identified using electrocorticography during surgery in 15 epilepsy patients with and/or without brain lesion that include spike, non-spike or hippocampus.
Methods: Lipid peroxidation was measured as thiobarbituric acid reactive substances expressed in MDA equivalents. ROS generation was monitored with a luminometer using luminal as the probe. Hcy levels were assayed based on HPLC of the fluorescent 7-Fluorobenzo-2-oxa-1,3-diazole-4-sulfonic acid derivative. Activities of antioxidative enzymes were measured by kinetics of enzymes using UV spectrophotometer. Glutathione and glutathione disulfide were quantified by fluorescence spectrophotometer after derivation with O-Phthalaldehyde.
Results: The results showed that the spike region and hippocampus had higher oxidative stress and antioxidative activity than the non-spike region. Mitochondrial function exhibited a higher percentage of high MMP cells, mit[Ca2+]i and ddDNA in the non-spike region compared to that in spike and hippocampus regions.

Conclusion: This study indicates that oxidative stress and antioxidative activity which is compensatory induced by oxidative stress are involved in the occurrence of spikes in human epilepsy.

p1011
Tertiary Epilepsy Care in Belgium: The Practice at Ghent University Hospital Reference Centre for Refractory Epilepsy
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Purpose: In Belgium, presurgical evaluation for epilepsy is reimbursed only in Reference Centres for Refractory Epilepsy (RCRE). Criteria for recognition by the health authorities include adequate infrastructure (video-EEG monitoring, FDG-PET, optimum MRI-fMRI, neuropsychological assessment, WADA-test); a multidisciplinary team (epileptologists, neurosurgeons, neuroradiologists and neuropsychologists); regular multidisciplinary discussions to select patients for resective and disconnective surgery, VNS and DBS and standardised assessment of outcome. Performance parameters are assessed yearly. We report on presurgical assessment and outcome during a 12-month period at Ghent University Hospital, one of the first RCRE recognised in Belgium, where epilepsy surgery started in 1991.
Methods: During the study period, 134 patients were admitted in the video-EEG monitoring unit. 84 received a reimbursement agreement and consequently underwent a full presurgical evaluation. All patients were discussed at monthly multidisciplinary meetings.
Results: 7/84 patients underwent invasive video-EEG monitoring; 21/84 underwent resective surgery: temporal lobectomy (TL): 20/21, frontal lobectomy (FL): 1/21; 3/84 underwent MST; 20 VNS; 2 DBS; 38/84 patients continued only antiepileptic drug treatment. 17/20 patients with TL have Engel class I outcome (FU: 6-23 months), 1 patient had class Ia, 1 patient class II, 1 patient was lost in FU. The patient with FL has class Ia after 16 months, 3 patients with MST have Engel class III (FU: 9-12 months), 1 DBS patient had a >50% seizure reduction, 1 patient is a non-responder. 17/20 VNS patients had a 36% seizure frequency reduction (FU>3 months).
Conclusion: Results of presurgical evaluation at Ghent University Hospital RCRE compare favourably with other published series.

p1012
Ten-year Experience of a Public Epilepsy Surgery Program in Brazil: A Viable Model for Developing Countries
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Purpose: To present the results of the first ten years of the Brazilian government epilepsy surgery program in one of the eight participating centres. To suggest that similar programs should be encouraged in developing countries.
Methods: A specific protocol defines clinical intractability. Patients are then referred to a national database of surgical candidates, which assigns a centre for pre-operative investigation and surgery. A fixed amount is paid for the investigation, as well as for the surgery. Basic investigation includes 32-channel video-EEG, MRI, neuropsychological testing and neuropsychiatric evaluation. Advanced MRI techniques, invasive 64-channel video-EEG, Wada test and SPECT are also available, when indicated. After surgery, patients return for 3, 6, 12 and 24 months follow-up.
Results: A total of 1067 surgeries were performed. 69% were temporal resections for mesial temporal epilepsy; 12.2% were corticectomies and/or lesionectomies; 9.6% were callosotomies; 1.8% hemispherectomies; and 6.8% were re-operations. Overall results for seizure control were: class I 63.8%; class II 11.9%; class III 14.6%; and class IV 9.7%. For mesial temporal lobe epilepsies only, there were 78% class I, 9% class II, 9% class III and 4% class IV.
Conclusion: The Brazilian epilepsy surgery program has completed ten years of activities, offering high quality treatment to the population, with minimal costs and results comparable to traditional worldwide centres. We believe similar programs should be encouraged in developing countries. A complete compilation of the national results is being prepared by the Brazilian chapter of the ILAE.

p1013
Temporal Lobe Epilepsy Surgery: Experience at a Single Centre over 14 Years
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Purpose: To analyse the outcome following temporal lobe epilepsy surgery with respect to pathology and type of surgical procedure performed over a 14 year period. Secondly, to ascertain if a surgical learning curve was observed.
Methods: A total of 483 patients (33.3□10.4 years; M: F 250:233) with refractory seizures were treated surgically from 1990 to 2003. Engel's classification was used to record seizure outcome 1 year following surgery. Seizure outcome was assessed in relation to pathology and surgical procedure. The results were analysed for two time frames 1990-1996 (n=209) and 1997-2003 (n=274) to assess the effect of the surgical learning curve.
Results: There were 372 anterior temporal lobe resections (ATLR), 77 lesionectomies, 15 extratemporal resections, 7 hemispherectomies, 7 multiple subpial transections, and 5 corpus callosotomies performed during the study period. In the first 7 years of the study (1990-1996) more lesionectomies were performed (21.1% vs 11.4%). However, in the last 7 years (1997-2003) more ATLRs were performed (80.5% vs 71.3%). Overall good (Engel I) surgical outcome at 1 year following surgery was noted in 80.4%. Subgroup analysis for seizure freedom (Engel I) at 1 year revealed: ATLR for hippocampal sclerosis (HS) – 85.4%, ATLR with dual pathology – 80%, ATLR without HS – 74.5% and temporal lobe lesionectomy – 69.7%. The outcome was significantly different in above subgroups ($p = 0.047$). In patients who underwent ATLR for HS, the Engel I outcome increased from 82.8% to 87.3% between the two time periods ($p=0.3$).
Conclusion: Temporal lobe surgery for epilepsy can produce seizure freedom in excess of 80% of carefully selected patients. The surgical outcome in cases of pure HS is better than for other temporal lobe pathologies. The extent of temporal lobe resection did not affect seizure freedom in purely lesional cases. Experience improves seizure freedom in surgery for HS.

p1014
Psychosocial Status after Surgical Treatment of Temporal Lobe Epilepsy
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Purpose: The aim of this study is to accept or reject the hypothesis that the psychosocial status of successfully operated patients with refractory temporal lobe epilepsy (TLE) differs from that of non-operated patients.
Methods: 110 patients were investigated. 60 were operated seizure free patients and 50 non-operated controls. Structured interviews of patients included Emotional Profile Index, Pluckic (PIE) and Beck Depression Inventory Scale, Questionnaire of psychosocial problems and examination of medical case-notes.
Results: Compared with the non-operated patients, operated patients showed an increase in employment in 6.7%, improvement of financial status in 18% and 10% gained a driving licence without any traffic accidents. Family overprotection in operated patients declined by 27%, social isolation by 55% and surrounding dependence by 45%. The non-operated patients were twice as likely to be depressed and

were four times more aggressive and anxious. Mood changes were not a problem in 42% of operated patients, with improvement of sexual function noted in over 10%. Signs of insecurity, disorganisation of actions and mind, impulsiveness and passive aggression were seen in both groups. In the operated group these disturbances were compensated by improvement in function as a result of feeling stronger emotionally and feeling more socially accepted.
Conclusion: In conclusion these results confirm the hypothesis that surgical treatment may not solve all the psychosocial problems of epilepsy but does achieve a significant improvement in psychosocial well-being.

p1015
Surgery in Children with Intractable Epilepsy: The Malaysian Experience
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Purpose: The paediatric epilepsy surgery programme started in 2002 in Malaysia. We would like to review the outcome of surgery in children with intractable epilepsy under this programme.
Methods: A retrospective case note review undertaken in the only tertiary paediatrics centre performing epilepsy surgery in Malaysia. From January 2002 to December 2004, 8 children underwent surgery for intractable epilepsy. Their ages at surgery ranged from 4.1 to 16 years.
Results: Mean duration of epilepsy was 8.3 years (range 0.5 to 15 years). All children had learning difficulties, suffered many seizures each week and were receiving at least two antiepileptic agents (AEDs) at surgery. All patients had EEG and MRI brain scans, 6 had video EEG telemetry, 5 had neuropsychological testing. Mean follow-up duration was 2.2 years (range 1.1 to 2.9 years). Resections: temporal lobe resection was performed on 3 children and parietal lesionectomy on 2. Three patients were seizure-free and AED-free, 1 had more than 75% reduction in seizures. 1 patient had no improvement. Callosotomies: 2 children had anterior two-thirds callosotomy for drop attacks. Both had transient improvement but underwent posterior callosotomy subsequently. Both had more than 50% reduction in drop attacks. Functional hemispherectomy was performed on 1 patient with Rasmussen encephalitis. Except for an aura of fear, the patient was seizure-free. In all but 1 patient, AEDs were either discontinued or reduced. No major complications were encountered. 1 patient had mild hemiparesis following parietal lesionectomy.
Conclusion: In a setting with limited resources, surgery is a feasible option for children with intractable epilepsy.

p1016
Results of Surgery for Refractory Epilepsy: Highlights from a Series of 919 Patients Submitted to Surgery
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Purpose: This paper reviewed a large series of epilepsy patients submitted to surgery in the MR era.
Methods: 919 patients submitted to epilepsy surgery from 1996 to 2004 were studied. Mean age at surgery was 24 years. Mean postoperative follow-up period was 3.8 years). 568 patients were submitted to temporal lobe, 95 to frontal, 55 to rolandic, 27 to posterior quadrant, 19 to parietal, 11 to occipital and 5 to insular cortical resection. 38 patients were submitted to hemispherectomy and 101 patients to callosotomy. Additionally, 16 patients were submitted to vagus nerve stimulation .
Results: The outcome of patients with temporal lobe epilepsy was studied in 4 groups according to their MRI findings: group I with unilateral mesial temporal sclerosis (86% seizure-free and 14% Engel II), group II with bilateral mesial temporal sclerosis (83% seizure-free and 17% Engel II), group III with temporal lobe lesions (91% seizure-free and 9% Engel II) and group IV with normal MRI. Group IV was further divided into those patients with unilateral neurophysiological findings (90% seizure-free and 10% Engel II) and those with nonlateralising neurophysiology (66% seizure-free and 34% Engel II). 82% of patients submitted to hemispherectomy have been rendered seizure-free. 91% of patients with MRI-positive frontal lobe have been rendered seizure-free; 64% of patients with MRI-negative frontal lobe epilepsy have been rendered seizure-free. All patients submitted to occipital, parietal and insular resections were MRI-positive; 87%, 78% and 100% of them, respectively, have been rendered seizure-free after surgery. 61% of patients submitted to posterior quadrant resections were MRI-positive; 87% of them have been seizure-free after surgery. MRI-negative patients submitted to posterior quadrant resection did somewhat worse (71% seizure-free). There has been an 89% reduction in generalised seizure frequency in those patients with Lennox-Gastaut and Lennox-Like syndromes submitted to maximized (90%) callosotomy; surprisingly, 5% of the patients submitted to callosal section have been unexpectedly rendered seizure-free.
Conclusion: Compared to pre-MRI series, the present series showed an improvement in surgical outcome, especially in patients with MRI-defined lesions. MRI negative patients still represent a challenge.

p1017
Results of Selective Transsylvian Amygdalohippocampectomy in the Innsbruck Epilepsy Surgery Program (INES)
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Purpose: Pro and cons of selective amygdalohippocampectomy (SAH) and optimal route of access to the mesial temporal region are not clear due to lack of outcome data. We present surgical and epileptological results after two years in a consecutive series of 40 adult patients with mesial temporal lobe epilepsy and hippocampal sclerosis (MTLE-HS).
Methods: All patients underwent presurgical evaluation within the Comprehensive Epilepsy Surgery Program of the Innsbruck Medical University. All were subjected to selective subpial removal of laterobasal amygdala, hippocampus and parahippocampal gyrus via a transsylvian route. Outcome was classified using the modified Engel classification and the new ILAE classification. To delineate learning effects, patients were divided in two cohorts of 20.
Results: All patients improved (Engel Classes I –III) with good seizure control (Engel Classes I and II) in 37/40 (92.5%). 22 patients (55%) are completely seizure-free (Engel Class IA) since surgery. At last follow-up, 3 patients (7.5%) had one to three and 4 patients had more than three seizure-days, respectively. 3 patients (7.5%) no longer need anticonvulsive medication. No differences in seizure outcome were noted between the first and the second cohort. Mortality was zero. New neurological deficits were noted in 12 patients (30%) after surgery, but only 1 patient with dysphasia was slightly impaired at last follow-up. Cranial nerve deficits and motor hemisyndromes were seen more often in the first cohort. Language deficits occurred independently from the position of the patient within the series.
Conclusion: SAH offers a high chance for improvement to patients with MTLE-HS. Morbidity is related to the learning curve and is not trivial. Long term prognosis of complications is good.

p1018
Temporal Lobe Resection for Epilepsy in Mentally Retarded Patients: Data from the Swedish National Epilepsy Surgery Register 1990-1999
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Purpose: Epilepsy surgery has been questioned for patients with mental retardation (MR) since MR may indicate a widespread disturbance of cerebral function with unsatisfactory prognosis following resective surgery. However, there are few studies of the outcome of epilepsy surgery in relation to IQ.
Methods: The Swedish National Epilepsy Surgery Register, which includes data on all epilepsy surgery procedures in Sweden since 1990, was analysed with respect to outcome of temporal lobe resections (TLR) in relation to IQ. The endpoint was seizure outcome at the two-year follow-up.
Results: 308 patients underwent TLR in Sweden 1990-99. 38 of these (12%) had MR, which was moderate in 30 (IQ 50-70) and severe in 8 (IQ<50), while 270 patients had IQ>70. Two years after surgery 65% in the IQ>70 group were seizure free, while 40% of those with IQ 50-70 and only 12% (n=1) of those with IQ<50 were seizure free. The total group was analysed for worthwhile outcome defined as seizure freedom or >75% reduction of seizure frequency: 80% in the IQ>70 group, 70% of those with IQ 50-70 and 50% of those with IQ<50 had a worthwhile outcome.
Conclusion: In the Swedish series seizure outcome after TLR for epilepsy varies in relation to IQ with the lowest degree of seizure freedom among patients with severe MR. However, a substantial number of patients with MR benefit from TLR and MR should not be an exclusion criterion for resective epilepsy surgery.

p1019
Failed Surgery for Temporal Lobe Epilepsy: Predictors of Long-term Seizure-free Course
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Purpose: To identify prognostic factors which predict the outcome 2 years after TLE surgery in those patients who were not seizure-free at the 6-month postoperative examination.
Methods: We included 86 postoperative TLE patients who had undergone presurgical evaluation, including video-EEG and high-resolution MRI, and who had seizures between the second and sixth postoperative months.
Results: 32% of patients were seizure-free in the second postoperative year. We found that normal MRI findings and secondarily generalised seizures (SGTCS) preoperatively were associated with a non-seizure-free outcome, while rare postoperative seizures and ipsilateral temporal IED were associated with a seizure-free outcome. Newly administered levetiracetam showed a significant positive effect on the postoperative outcome independent of other prognostic factors. 5 of 7 patients who received levetiracetam became seizure-free (p=0.006).
Conclusion: One-third of patients who did not become seizure-free immediately after surgery, eventually achieved long-term seizure freedom. We suggest watching for long-term seizure freedom after failed epilepsy surgery especially in patients who had rare postoperative seizures, focal MRI abnormality, ipsilateral temporal spikes, or no SGTCS preoperatively. Levetiracetam may have a positive effect on postsurgical seizures.

p1020
Postoperative Seizure Outcome in Mesial Temporal Lobe Epilepsy with Secondarily Generalised Tonic-Clonic Seizures
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Purpose: We attempt to determine if complex partial seizures progressing to secondarily generalised tonic clonic seizures portend a poor prognosis for seizure control after anteromesial temporal lobectomy. A large ongoing epilepsy surgery trial design (ERSET or Early Randomized Surgical Epilepsy Trial) excludes cases with over 4 generalised seizures per year for more than 3 years because of a perception that these cases have a poorer postoperative outcome.
Methods: Patients with video EEG monitoring evaluated from 1998 to 2004 were included. Patients with documented complex partial seizures evolving to secondarily generalised tonic-clonic seizures and where the clinician concluded they had mesial temporal epilepsy based on MRI, interictal and ictal EEG, PET, SPECT, neuropsychology and Wada test, were cross referenced with a database of anteromesial temporal lobe surgical outcomes according to the classification of Engel (1993). Follow-up exceeded one year.
Results: 16 patients met inclusion criteria. Anteromesial temporal resections were left sided in 10 and right sided in 6. Postoperative seizure outcomes were 13 (81.25%) Engel Class IA (completely seizure-free since surgery), one (6.25%) Class IB (nondisabling simple partial seizures only since surgery), and two (12.5%) Class IIB cases (rare disabling seizures since surgery). One of the Class IIB cases was remonitored several times and recurrent seizures and nonepileptic events were documented off medications.
Conclusion: In this highly selected epilepsy surgery patient population meeting preoperative evaluation criteria for a diagnosis of mesial temporal lobe epilepsy, excellent postoperative seizure reductions occurred despite the history and documentation of secondarily generalised tonic clonic seizures.

p1021
Results of Surgery in Patients with Refractory Temporal Lobe Epilepsy and Norman MRI
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Purpose: This paper reports on the surgical outcome of a series of patients with refractory temporal lobe epilepsy and normal MRI.
Methods: 31 consecutive adult patients extracted from a series of 297 submitted to temporal lobe resections between 1996 and 2002 at Hospital Brigadeiro and Clinica de Epilepsia were studied. Mean follow-up time was 49 months. Patients were divided into two groups: Group I (n=8) included patients with normal MRI and unilateral video-EEG findings and Group II (n=23) included patients with normal MRI and bilateral or non-localising surface video-EEG findings. All Group I patients have been submitted to surgery at the side suggested by video-EEG findings. All Group II patients have been additionally submitted to invasive recordings by means of bilaterally implanted subdural grids.
Results: 7 out of the 8 Group I patients have been rendered seizure-free after surgery and 66% of Group II patients were also. The rest of Group I and II patients were in Engel II outcome scale postoperatively. Invasive recording findings in Group II patients were as follows: unilateral seizure onset in 18 out of 23 patients; 18 patients with focal and 5 patients with regional seizures onset; 17 patients with initial ipsilateral spread of epileptic discharges and 6 with early contralateral spread. 4 of the 31 patients studied in this series proved to have mesial temporal sclerosis after pathological examination of the resected tissue; in 11, microdysgenesis was disclosed and 16 patients had no identifiable lesion.
Conclusion: Patients with refractory temporal lobe epilepsy and normal MRI represent a challenge but a good surgical outcome could

be achieved although a more extensive workup is generally needed, often including invasive studies.

p1022
Mesial Temporal Lobe Epilepsy: A Prospective Short-term Study Comparing Surgical and Clinical Treatments
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Purpose: To study the efficacy of surgical and medical treatments for refractory mesial temporal lobe epilepsy (MTLE).
Methods: We prospectively studied 101 patients with refractory MTLE associated with hippocampal sclerosis between the period of August 2002 and October 2004. All patients failed to achieve seizure control with at least two first line antiepileptic drugs (AED) for partial seizures before entering the study. 26 patients underwent surgical treatment and 75 patients underwent clinical treatment with further AED trials. We used Kaplan-Meier survival analyses as a function of time of seizure recurrence to obtain estimates of 95% confidence interval of seizure freedom and log-rank test to compare the status of seizure control between the two groups.
Results: The mean follow up was 12.7 (range 3-24) months for the surgical group and 12.7 (range 2-24) months for the clinical group (p=0.96). The cumulative proportion of patients free of all seizures (Engel's class IA) was higher in the surgical group (73.1%) compared to the clinical group (12%) (p<0.0001). The overall improvement in the surgical group (92.3% in Engel I+II) was also higher than in the clinical (21.3% of patients with at least 50% reduction in seizure frequency) (p<0.0001). In the clinical group 7 patients (9.3%) presented adverse events during the follow up, including burns and status epilepticus. In the surgical group 2 patients (7.6%) had transient adverse effects and another 2 patients (7.6%) had permanent deficits related to the surgery.
Conclusion: Surgical treatment for patients with refractory MTLE was more efficient than medical treatment with further trials with AED.

p1023
Relationship Between a Resection Volume and Outcomes in Surgical Treatment of Temporal Lobe Epilepsy
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Purpose: Analysis of the results of neurosurgical treatment of temporal lobe epilepsy.
Methods: The results for 30 patients with medically intractable lesional temporal lobe epilepsy. There were 'low-grade' gliomas in 18 patients, cavernomas in 2, cortical dysplasias in 4, residual lesions in 6. 2 patients had the 'focal' type of seizure onset; the others had 'regional' onset. Lesionectomy was performed in 16 cases, medial resections in 5, 'standard' temporal lobectomy in 6 and temporal lobectomy with extended medial resections in 8 cases. Electrocorticography was used for extending medial and lateral resections during medial removals and lobectomies. Engel classification of outcomes was used.
Results: The relationship between a resection volume and outcomes was noted: in cases of partial lesion removal I, II, III and IV classes outcomes accordingly in 1, 1, 4 and 3 patients were noted, in cases of complete removal in 1, 9, 2 and 2, in cases of more extended resections all 6 patients achieved I class. Outcomes I, II, III and IV classes noted accordingly in 0, 6, 5 and 3 cases if less than 1/2 hippocampal volume was removed, in 8, 3, 2 and 1 cases if hippocampal resections were more extensive. There was no significant association between the duration of epilepsy or presence of contralateral epileptic activity and the outcomes. Slight verbal memory disturbances were noted in 2 patients over 40 age old.
Conclusion: Extended resections with removal of more than the lesion volume ensure better seizure control than lesionectomy only, in cases of temporal lobe epilepsy.

p1024
Electroencephalographic Changes During Two Years of Follow-up of Epilepsy Patients Submitted to Temporal Lobectomy
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Purpose: To analyse visual and quantitative resting electroencephalography during the first two years of postsurgical evolution in patients with intractable medical temporal lobe epilepsy (TLE) subjected to temporal lobectomy.
Methods: Thirty-two visual and quantitative EEGs from TLE patients were analysed in order to evaluate the evolution of interictal epileptiform discharges (IED) and base activity. The postsurgical outcome was assessed by our team, one month, six months, one year and two years after the surgery.
Results: Though we were able to prove a tendency to a stable electroencephalographic frequency, until the six months postsurgical evolution, there are some differences related to the surgery side. After two years of evolution, the patients submitted to left temporal lobectomy showed a slow global electroencephalographic activity. On the other hand, the patients with right temporal lobectomy showed a slowness in the ipsilateral temporal surgery side. The number of IED tabulated at different moments is also greater in the left temporal lobectomy group. Patients in Engel's class I showed a persistency in bilateral independent temporal IDE after two years of evolution. We have seen a growing tendency in relation to the number of them with unilateral IED. There is also a positive correlation between the duration of time of epilepsy and the presence of counterlateral IED after two years of postsurgical evolution.
Conclusion: There is a differentiated behaviour in the evolution of IED occurrence according to the laterality of the temporal lobectomy carried out in patients with MTLE. Despite the persistency of independent bilateral IED, after two years of evolution in patients with TLE submitted to successful temporal lobectomy, we have seen a growing tendency in relation to the number of them with unilateral IED ipsilateral to the temporal surgery side.

p1025
Natural History of Seizures after Temporal Lobectomy: An Actuarial Approach
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Purpose: Patterns and outcome of post-temporal lobectomy seizures require clarification for patient counselling and treatment decisions. With this perspective we studied the natural history of seizures after temporal lobectomy.
Methods: A cohort of patients operated for temporal lobe epilepsy between 1995-2002 were followed until 16 October 2004. Patients lost to follow-up were contacted by questionnaires and a personal visit. Kaplan-Meier survival curves were plotted for long-term seizure outcome for the relapsed patients.
Results: 357 temporal lobectomy patients (205 male:152 female) with mean age 26.7±9.3 (range 2.5-57) years had median follow-up of 5 (range2-9) years. Of 167 (47%) postoperatively seizure-free patients, 101 (28.3%) were off antiepileptic drugs (AED). 17 (8.9%) relapsed after AED reduction, 155 (78.3%) without discontinuation and 18 (9.5%) after AED discontinuation 0.16-59 months prior to relapse. 10 (43.5%) became seizure-free after AED reinstitution. At last follow-up, 265 (74.2%) were seizure-free, 120 (33.6%) off AEDs. Patients with histologically proven mesial temporal sclerosis had poorer long-

term seizure-freedom than tumours (p 0.045) though significantly better than normal histology. After 8 years, seizure-free probability was 18.8% after immediate postoperative, 36.5% after provoked and 27.1% after nocturnal seizures. Patients with seizure relapse <2 years (p0.005), higher seizure frequency during the first year of recurrence (p<0.001), relapse after AED discontinuation (p 0.002) and auras as initial seizure relapse (p 0.047) had poorer long-term seizure-freedom.
Conclusion: Temporal lobectomy offers a relative cure in only one-third of patients; the majority with histopathologically defined lesions. Early seizure relapse, higher seizure frequency at relapse, relapse after AED discontinuation and auras predict lower probability to long-term seizure freedom. Immediate postoperative, provoked and nocturnal seizures had outcomes similar to those without.

p1026
Long-term Seizure Outcome Following Selective Amygdalohippocampectomy in Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis
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Purpose: Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) is one of the most common medically refractory epilepsies which may be remedied by surgery. In this study, surgical cohort data was analysed, and examined the year-by-year seizure outcome following selective amygdalohippocampectomy for patients with MTLE-HS.
Methods: Data from 148 patients who were operated after a noninvasive protocol since 1995 were analysed and 136 patients (51.5% male, 53.7% right) with at least 1 year follow up after surgery were included. Age of seizure onset, duration, febrile seizures, risk factors, status epilepticus and age at surgery were accounted as independent variables and analysed using nonparametric tests, McNemar test, and linear regression analysis, as appropriate. Seizure outcome after surgery was assessed according to Engel's classification.
Results: The mean age at surgery 26.02+8.53 yrs, follow-up period 3.4+2.2 yrs (1-10 yrs). AEDs were stopped in 25.0%; all remained seizure-free for at least 2 years, and were accepted as 'cured'. Overall, AED were reduced in 65.3% of patients. When evaluated year-by-year, 74.3% were in Engel I, 8.9% in Engel II, 9.5% in Engel III, and 7.3% in Engel IV at the end of first year. 68.8% and 66.7% were in Engel I, 15.5% and 18% in Engel II, 11.7% and 10.2% in Engel III, 4% and 5.1% in Engel IV at 3rd and 5th year correspondingly. None of the variables showed a significant effect on outcome.
Conclusion: Although our results are comparable with previous reports applying similar or other types of surgery, we believe that tailored resections according to different subgroups which emerged due to semiological and EEG findings will enable better outcomes for MTLE-HS patients.

p1027
Long-term Outcome of Patients after Surgery for Frontal Partial Seizures
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Purpose: In a retrospective study, long-term seizure outcome was analysed in 53 patients who underwent surgery for frontal lobe epilepsy (FLE) in two different centres between 1990-2000.
Methods: All 53 adult patients (35 males, 18 females) with drug-resistant frontal seizures underwent the same presurgical evaluation procedure (scalp EEG video monitoring, magnetic resonance imaging, stereoelectroencephalography with depth electrodes) to define the epileptogenic zone to be resected at surgery. Seizure control outcome was assessed separately for each post-operative year using Engel's classification.
Results: Although some patients were later lost to follow-up, our results indicate that: 1) At term, 50% of patients were seizure-free (class I), 25% improved with seizure reduction (class IVA) and 25% not cured (Class IVB). Analysis of the 18 patients followed regularly for 5 or more years after surgery showed that the long-term 50% success and 50% failure rates (class IVA or IVB) were definitively established in the third post-operative year. 2) Seizure control was better for lesional than for non-lesional epilepsy: of the 38 patients with structural lesions, 71% were seizure-free, 5% improved and 24% not cured whereas of the 12 patients with no detectable structural lesion only 50% were seizure-free. 3) Better outcome was obtained when a neurodevelopmental lesion could be identified and the resection included both the lesion and the epileptogenic zone.
Conclusion: Although surgery is already generally a safe and effective treatment for FLE, new studies investigating the causes for its failure in certain cases will aid epileptologists and neurosurgeons in further improving prognosis after surgery.

p1028
Surgery for Intractable Post-Traumatic Epilepsy
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Purpose: Despite early beginnings by Penfield and Foerster in the surgical treatment of intractable post-traumatic-epilepsy (PTE) caused by encephalomalacias, there are very few studies detailing the results of surgery for this entity which is what we sought to achieve here.
Methods: We conducted a review of 9 patients who had undergone resections of encephalomalacias as treatment of intractable PTE. Presurgical evaluation included EEG/video-EEG/SPECT and an MRI employing FLAIR sequences. Focus excision was done using intraoperative electrocorticography.
Results: The mean interval between trauma and the onset of intractable epilepsy was 4 years. The median duration of suffering from epilepsy before surgery was 8 years (3-29 years), reflecting a tendency to persist with medical treatment, probably because surgical treatment for intractable PTE is not a very popular notion. The median seizure frequency was 10/month. Frontal encephalomalacia was most common with 6 patients having a unilateral-frontal foci on MR, 1 having a parietal focus and 2 having a bilateral-frontal foci. Among 7 patients with a single focus on MRI, VEEG revealed discordant foci in 2 and EEG revealed discordant foci in 4. All patients with discordant foci on VEEG/EEG ultimately underwent resection of the MR-identified-focus with Class-I seizure-outcome. Therefore with clear-cut MRI-localisation, EEG/VEEG has a mainly adjunctive value and discordance with MRI should not provoke fears. SPECT/VEEG/EEG played a greater role in the 2 patients with a bilateral-frontal foci on MRI. Both had more MR changes on the right which was confirmed to be the seizure focus with VEEG/SPECT. All 9 patients had Engel's Class I seizure outcome at a mean follow-up period of 24 months (12-63 months). Intra-operative ECoG was helpful in deciding the extent of resection in that all patients had no post-op spikes and had Class-I outcome. Functional MRI had been carried out on 2 patients and awake-craniotomy in 1, in view of the close proximity of the eloquent cortex to the surgical focus. Only 1 patient with a parietal focus had transient hemiparesis postoperatively.
Conclusion: The excellent results demonstrated following encephalomalacia resections for intractable PTE should prompt search with an MRI using FLAIR sequences for resectable foci among these patients. Surgical treatment should not be delayed. Intraoperative ECoG helps in determining the extent of resection required.

p1029
Surgical Treatment of Non-lesional Intractable Focal Epilepsy
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Purpose: To discuss the presurgical evaluation and surgical treatment of intractable epilepsy with no lesion on both MRI and CT.
Methods: We studied 38 patients with intractable non-lesional focal epilepsy (NLFE). They all underwent surgeries of epileptogenic cortex resection in our institute from 2001 to 2004. The patients were divided into a satisfactory and an unsatisfactory group according to Engel's classification of postoperative outcomes. Some factors related to pre-and intra-operative neurophysiological characteristic. Pre-surgical interictal SPECT and operation methods were compared between the two groups and the possible underlying reasons were discussed.
Results: A favourable outcome was obtained for 17 patients (45%). Significant differences were seen between the two groups when compared by either the scalp EEG with restricted interictal epileptiform discharges (IEDs) within one lobe or the intracranial EEG with focal ictal onset. Furthermore, a good outcome was significantly associated with one lobar resection rather than multilobar resections. No significant difference was found regarding the consistency of SPECT reports with the location where the operation was done and whether the cortex with IEDs detected by EcoG was completely resected.
Conclusion: For a patient with intractable NLFE, the surgery outcome is less favourable than that for lesional cases. During presurgical evaluation, invasive recording is often mandatory. The cases with widespread scalp IEDs should be evaluated with great caution. So far, the interictal SPECT and ECoG are not playing key roles in identifying the epileptogenic zones in NLFE. Multilobar resections are not superior to single lobar resections.

p1030
Focal Cortex Disconnection for the Treatment of Intractable Epilepsy
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Purpose: A wide range resection of brain cortex with epileptogenic zone may cause more insults to the brain. Focal brain disconnection may lessen such insults to the brain. We managed a wide range seizure onset zone with focal brain disconnection but not resection. Our purpose is to figure out seizure control and side effects of focal brain disconnection.
Methods: 6 surgical cases with intractable epilepsy, 5 male, 1 female, are analysed. Age range 4 to 16 years, 9.33±4.08 years. The preoperative evaluations included magnetic resonance imaging (MRI), electroencephalography, positron emission tomography (PET), and single-photon emission computed tomography (SPECT). 4 cases showed MRI lesions, whereas 2 cases were non-lesional on MRI. There were 5 cases with frontal lobe epilepsy and 1 case with occipital lobe epilepsy. No epileptogenic cortex regions were resected, but were disconnected and isolated from other brain regions.
Results: 6 patients with surgical treatments were followed up for 9 to 15 months. 5 of 6 patients became seizure free (Engel's I) after surgical treatment and 1 patient got Engel's class □ seizure control. 1 patient developed subcutaneous cerebrospinal fluid (CSF) accumulation and was relieved 2 months later. No patients developed neurological or neuropsychological deficits.
Conclusion: With certain indications and careful multiple preoperative evaluations, the focal brain disconnection for seizure control is safe and effective.

p1031
Maximised Callosotomy for Patients with Lennox-Gastaut and Lennox-like Syndrome: Technical Guidelines
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Purpose: This paper describes technical guidelines useful while performing maximized (90%) single-staged callosal sections for refractory secondary generalised seizures.
Methods: 101 patients were submitted to callosal section between 1996 and 2004 at Hospital Brigadeiro and Clinica de Epilepsia. The basic technical guidelines were: 1) position the patient's head in order to leave the callosal body in a vertical position, perpendicular to the floor; 2) perform a parasagittal craniotomy centred at the coronal suture; 3) be aware of parasagittal veins while opening the dura; 4) do not coagulate parasagittal veins, even if you feel you would need space; 5) if after all needed, never coagulate veins posterior to the coronal suture; 6) use no retraction while dissecting the interhemispheric fissure; 7) note adhesions between the cingulated gyri and holes in the falx, that could make exposure of the corpus callosum more difficult; 8) expose the anterior circulation entirely and bilaterally; 9) perform callosal section in between the anterior cerebral arteries or branches (never section lateral to the artery between it and the cortex; 10) perform the anterior portion (~50%) of the section under direct microscopic vision; 11) always keep a clean operating field, especially if you have entered the ependyma; 12) perform the posterior portion of the section by endo-callosal aspiration following the direction of the callosal body; 13) finish the procedure when you notice the posterior cingulate cortex, just anterior to the splenium.
Results: Maximized (90%) section was achieved in all but one patient. This patient had microcephaly and a very curved corpus callosum. There has been no surgical morbidity or mortality.
Conclusion: Maximized callosotomy is a single-staged and safe procedure if strict surgical guidelines are followed.

p1032
Usefulness of Corpus Callosotomy in Patients with Generalised Epilepsies associated with West Syndrome
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Purpose: To evaluate the usefulness of corpus callosotomy in patients with symptomatic generalised epilepsies associated with West syndrome, we assessed seizure control, appropriate extent of the callosal section, and appropriate timing of surgery. We also discuss patients' daily function, assessed using a Japanese infant development scale (KIDS), before and after surgery.
Methods: Between 1998 and 2004, 15 children younger than 6 years with medically refractory symptomatic generalised epilepsy associated with West syndrome were evaluated. Classification of seizure outcome was as follows: free, seizure free; excellent, greater than 80% reduction in seizure frequency; good, greater than 50% reduction; poor, no significant change; and worse, exacerbation of seizure frequency.
Results: Overall outcome was as follows: free, n=2; excellent, n=6; good, n=4; and poor, n=3. Concerning outcome with respect to seizure type, all patients with head drop attacks (3) and 3 of 4 (75%) of those with atypical absence became seizure free. Outcome was classified as better than good in 5 of 6 (84%) with tonic spasms and 7 of 9 (77%) with tonic seizures. In terms of postoperative EEG findings, 6 of multiple spike foci was altered spike reduction in 3, localisation/lateralisation in 2, and no change in 1. Moreover, of 4 patients with diffuse spikes and waves, spikes were reduced in 2 and localised/lateralised in 2. As for developmental evaluation, we generally observed improvement of developmental age after surgery
Conclusion: Total callosotomy yielded a favourable outcome in terms of seizure control, particularly for head drop attacks and tonic spasm,

with no complications. It is recommended that this procedure is performed as early as possible when seizure frequency increases.

p1033
Surgical Treatment of a Symptomatic Epilepsy in Children with Intracranial Arachnoid Cyst
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Purpose: The purpose of the research was to estimate the efficiency of surgical treatment of a symptomatic epilepsy in children with intracranial arachnoid cysts (ÀÑ).
Methods: We analysed surgical treatment of AC in 25 children, aged 1-17 years. In 18 patients the AC were localised in the area of lateral sulcus, in 4 in the convexital surface of frontal and parietal lobes, in 2 in longitudinal cerebral fissure, in 1 the cyst was localised in the suprasellar area. The duration of seizures was from 1-15 years. Cyst-hunting operations were carried out on 16 patients; the open trepanation with a fenestration of walls of a cyst was found in 6 patients; the combination of an open trepanation with cyst-hunting occurred in 3 patients.
Results: Surgical treatment has resulted in freedom of seizures for 5 patients (Class I on J. Engel), rare seizures were noted in 9 patients (Class II), lowering of frequency of seizures occurred for 8 patients (Class III), the character of seizure remained unchanged for 3 patients (Class IV).
Conclusion: Fixed, that the decrease of sizes of AC in the postoperative period was correlated with decrease of frequency of seizures. The best results are achieved for patients with a smaller interval from the beginning of seizures to surgical treatment. The treatment of epilepsy was more effective for patients with AC of convexital localisation.

p1034
Is Seizure Recording Necessary for the Presurgical Assessment of Patients with Unilaterally Predominant Temporal Lobe Interictal Spike Foci and Concordant MRI Lesions?
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Purpose: The yield of seizure recording for presurgical pharmacoresistant temporal lobe epilepsy patients is debatable in the presence of unilaterally predominant temporal interictal EEG spike foci and concordant MRI lesions. We looked for evidence of discordant or bitemporal epileptogenicity, as suggested by surface-ictal EEG recordings, in such a group, of presumably 'unitemporal' by interictal EEG and MRI patients.
Methods: Retrospective analysis of surface ictal EEG data from 30 drug-resistant presurgical temporal lobe epilepsy patients, presenting with a unilaterally predominant (>70% lateralised predominance) temporal interictal EEG spike focus and a concordant MRI lesion. Surface ictal EEG data were evaluated for the presence of a) discordant and/or bitemporal independent ictal EEG onsets, and b) lateralisation switch of ictal EEG.
Results: 110 seizures were analysed (mean: 3.7 seizures/patient, range 1-12). MRI findings were consistent with mesiotemporal sclerosis in 17 and foreign tissue lesions in 13 patients. 26/30 had localised/lateralised concordant ictal EEG discharges. 4/30 patients (3 with mesiotemporal sclerosis and 1 with a tumour) had bitemporal independent ictal onsets (1/4) or lateralisation switch of ictal EEG (3/4). 18 patients were subjected to temporal lobe surgery. Only 1/4 with bitemporal ictal onsets and lateralisation switch is seizure free postoperatively, the other 3, although improved, still experience seizures. In contrast, 13/14 operated-on patients with concordant ictal EEG are seizure free.
Conclusion: Surface-ictal EEG may reveal evidence of bitemporal epileptogenicity in 'unitemporal' patients. Such evidence may be associated with a less-than-optimal postsurgical outcome, thus supporting seizure recording even in this patient group.

p1035
Can Early Post-ictal Activities Help to Better Localise and Lateralise the Epileptogenic Zone ?
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Purpose: To evaluate the contribution of post-ictal EEG abnormalities to defining the localisation and lateralisation of the epileptogenic zone.
Methods: Post-ictal activity patterns characterised as rhythmic (theta, delta) slow activity, attenuation and/or suppression of background activity and post-ictal spikes (PIS), their duration and their distribution (focal, regional, diffuse or bilateral) over 2 minutes were analysed in 18 patients with temporal lobe seizures (TLs) and 12 patients with frontal lobe seizures (FLs) in a series of surgical candidates (between 1996-2003). Only patients with a spontaneous partial seizure recorded on both scalp-EEG and stereoelectroencephalography (SEEG) with depth electrodes and a post-surgery follow-up of at least 2 years were included.
Results: On SEEG recordings, activity suppression was observed in 17 patients with TLs versus 10 with FLs. It was more prolonged after TLs (35sec) than after frontal (4sec) seizures, widespread in TLs involving areas of onset and propagation, but restricted to the seizure onset region in FLs. PIS were recorded after TLs (17/18) and FLs (9/12) but rarely coincided with inter-ictal spikes. Slow activity was constant after TLs and rare after FLs. On scalp EEG, activity attenuation of short duration (5sec) was observed after 10 TLs and 7 FLs. PIS were exceptional, seen only after 4 FLs. Slow activity was constant after TLs and rare after FLs.
Conclusion: Some post-ictal patterns are highly accurate in lateralising/localising the epileptogenic lobe (EEG activity attenuation) and/or the epileptogenic zone (SEEG activity suppression).

p1036
Can REM Sleep Predict the Side and the Prognosis of Medial Temporal Lobe Epilepsy?
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Purpose: REM sleep is known to focus interictal epileptiform abnormalities. To determine the value of REM sleep recordings in presurgical evaluation of medial temporal lobe epilepsy (MTLE), we analysed REM sleep in 10 patients with undetermined lateralisation of MTLE.
Methods: 10 patients (5 men and 5 women, aged 22 to 54 years) with cryptogenic drug-resistant MTLE benefited from intracranial electrodes because of non conclusive surface monitoring video-EEG. All patients had had right and left occipito-hippocampal depth electrodes. All had been operated with a follow-up ranging from 4 to 11 years after surgery. Patients with bitemporal lobe epilepsy determined by depth electrodes have been excluded from this study.
Results: REM sleep indicated the side of epilepsy in 8 patients. In 4 of them, interictal epileptic abnormalities were strictly unilateral, and bilateral but with a marked predominance on one side in 4 patients. In 2 patients, interictal abnormalities were bilateral without predominance. Two years after surgery, all patients were seizure-free leading to progressive withdrawal of antiepileptic drugs. In patients with controlateral interictal abnormalities during REM sleep, seizures were observed after they completely ceased their treatment. A reintroduction of a light dose of treatment has been necessary to obtain full control of epilepsy in these patients.
Conclusion: REM sleep is a good marker for the lateralisation of the epileptic focus in MTLE. Patients with bilateral interictal epileptic abnormalities in REM sleep have a higher risk of developing seizures

after epilepsy surgery when drugs are stopped. In these patients, it is necessary to maintain antiepileptic drugs after epilepsy surgery.

p1037
Intra-individual Variability of Ictal EEG and Post-surgical Prognosis in Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis
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Purpose: The proportion of patients becoming seizure-free after surgery for mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) has been estimated to be 70%. We investigated ictal EEG seizure patterns and their prognostic value for surgical outcome in patients with MTLE-HS.
Methods: All patients with MTLE-HS operated on in Coimbra University Hospitals with a postsurgical follow-up longer than 1 year were included. Patients were grouped according to Engel score (1 and ≥2). Pre and postsurgical MRI were reviewed. All ictal EEG recorded during presurgical non-invasive EEG-video monitoring were reviewed. Ictal EEG onset and ictal sequence patterns were described based on visual analysis. Intraindividual variability was defined if more than 50% of a patient's seizures were different. Demographic, clinical, MRI characteristics and intraindividual variability of the ictal EEG were compared.
Results: 23 patients were included, 11 (47.8%) male. Mean (±SD) patient age was 37.5 (±9.6) years. Mean (±SD) duration of epilepsy before surgery was 24.7 (±11.8) years. Mean (±SD) age at surgery was 34.5 (±9.6) years. 10 (43.5%) patients had right MTLE-HS. Mean (±SD) postoperative follow-up time was 3.1(±1.6) years. 18 (78.3%) patients are in Engel 1 class, 5 (21.7%) in Engel 2 or plus. 150 ictal EEG were analysed. Theta rhythmic activity was the most frequent seizure onset pattern. Ictal EEG variability was lower in Engel 1 group, but that was not statistically significant.
Conclusion: We found no evidence to support intra-individual variability of ictal EEG as a prognostic factor of surgical outcome in MTLE-HS patients.

p1038
Interictal Electrophysiological Data in a Population of Children who Underwent Hemispherotomy
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Purpose: To evaluate interictal electrophysiological data in a population of 69 children who underwent therapeutic functional hemispherotomy (FH).
Methods: Charts of 69 children undergoing FH were retrospectively reviewed. All patients had a global pre and post operative clinical evaluation. Multiple EEG examinations before and after surgery were performed. Clinical or electrographic seizures were recorded by video-EEG monitoring of all patients before surgery.
Results: 25 children had FH for Rasmussen syndrome, 21 for multilobar cortical dysplasia, 15 for vascular congenital hemiparesis, and 8 for Sturge-Weber syndrome. Age at epilepsy onset ranged from 1 day to 13 years, and age at FH ranged from 2 months to 26 years. In the affected hemisphere (AH), interictal EEG data before surgery showed focal abnormalities (FA) in 11 cases, multifocal (MA) in 38 cases, and diffuse (DA) in 17 cases. In the 'unaffected' hemisphere (UH), 17 patients presented FA, 5 patients had MA and 8 patients showed DA. After surgery, FA persisted in 10 AH cases and in 17 UH cases. MA were observed in 38 AH patients and in 5 UH patients. DA were present in 17 AH cases and in 8 UH cases. Post-surgical outcome showed: 77% patients in class I of Engel's classification, 10.5% in class II, 8.5 % in class III, and 2% in class IV.
Conclusion: Persistence of FA, MA, and DA in the AH did not influence post-surgical follow-up. On the contrary, subjects with persistence of MA or DA in the UH showed a worse post-surgical outcome.

p1039
Safety and Utility of Insular Depth Recording Electrodes Implanted in Stereotactic Conditions Using an Oblique, Trans-frontal or Trans-parietal Approach
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Purpose: The aim of this study was to investigate the feasibility, the safety and the utility of chronic depth electrodes stereotactically implanted in the insula cortex of patients suffering from drug refractory focal temporal and/or frontal epilepsy
Methods: 29 patients, 18 males and 11 females, aged from 9 to 53 years were included in this study. The mean duration of epilepsy was 20 ± 11 years. 2 patients were left handed. All the patients underwent, in addition to prior video scalp EEG, MRI, and psychological testing, a comprehensive presurgical evaluation using stereo-EEG (SEEG) because of a discrepancy between clinical, imaging and scalp EEG data. In addition to the insula, the sampling of the cortex included in all cases the hippocampus, the lateral temporal neocortex, the perisylvian cortex, the orbito frontal region and the anterior cingulum. The targeting of the insula was planned on the basis of a pre-surgical T1-MRI scan done in stereotactic conditions in addition to a stereotactic digital cerebral angiography (Bioscan system) performed under general anaesthesia. The implantation of electrodes was performed in a second surgical step in stereotactic conditions using a robotized harm (Neuromate, ISS, France) driven by Voxim software (VoximR, IVS solution, Germany). The electrodes had a diameter of 0.8 mm and had 10 or 15 leads of 2 mm length, 1.5 mm apart (Dixi, Besançon, France). The anterior insula was investigated using an oblique trajectory with an entry point located at the frontal region level. The posterior insula was explored using a more posterior trajectory with an entry point located at the parietal level. All the contacts located in the insula were used to record EEG activity and to stimulate the insular cortex in order to replicate the patient's seizure. For each patient, the position of each electrode contact was anatomically plotted onto the corresponding slice of Talairach's stereotaxic atlas (Talairach and Tournoux, 1988). Image fusion of post-operative CT scan and axial brain T1-MRI was also systematically performed showing the co-planar localisations of each contact within the insula (VoximR, IVS solution, Germany)
Results: 32 electrodes were implanted in the insula, 25 in the right side, 7 in the left side. 220 contacts were available to sample the EEG activity of the insula cortex. No clinical morbidity was noted during the surgical procedure or the recording and stimulation steps. No haematoma was found in post-operative scans. The SEEG evaluation permitted us to conclude that the epileptogenic zone was located in the insula in 5 cases. From the latter, 3 patients underwent anterior insular resection in addition to frontal or anterior temporal lobectomy, while the remaining 2 patients did not undergo any resective surgery. In 11 cases, the insula was involved later during the seizure and for this reason, the patients underwent a resective surgery with preservation of the insula (temporal or frontal lobectomy). In the remaining 13 cases, SEEG analysis did not reveal any insular involvement at the onset of the seizure .
Conclusion: This study confirms that it is possible to explore routinely the insula using an oblique, trans frontal or trans parietal approach performed in stereotactic conditions. This technique is safe and useful for delineating the EZ when an insular involvement is clinically suspected.

p1040
Intrinsic Epileptogenicity of an Isolated Periventricular Nodular Heterotopia
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Purpose: Intrinsic epileptogenicity of a periventricular nodular heterotopia (PNH) and seizure free outcome after selective resection has not been demonstrated.
Methods: We present a patient with psychomotor seizures and a unifocal PNH adjacent to the posterior horn of the left lateral ventricle. The patient underwent surface video-EEG monitoring, stereotactic video-EEG exploration and functional MRI using a language paradigm.
Results: Surface EEG showed interictal slowing and ictal onset over the left temporal region. Stereotactic EEG evaluation demonstrated interictal activity and ictal onset confined to the intralesional electrode contact. F MRI showed activation of the PNH during the language task; however, no language impairment was noted during runs of paroxysmal fast localised over the lesional electrode contact. The patient underwent selective resection of the heterotopia and remained seizure free for two years of follow-up without deficit.
Conclusion: This case demonstrates the intrinsic epileptogenicity of a PNH and the possibility for an excellent outcome after selective surgical resection. Although nodular heterotopia might be involved in task-specific neuronal networks, resection appears feasible without functional deficit.

p1041
Outcome of Temporal Lobe Epilepsy Surgery Predicted by Peroperative Intraventricular Strips on the Amygdala-Hippocampus-Complex
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Purpose: Epilepsy surgery should be limited to the epileptogenic zone. Balancing seizure reduction and verbal memory impairment is essential during resection of the amygdala-hippocampus-complex (AH). We developed a diagnostic method and have evaluated whether it predicts surgery outcome.
Methods: Since 1993 all Danish candidates for epilepsy surgery have been referred to the Copenhagen Epilepsy Surgery Centre. 89 patients with medically refractory temporal lobe epilepsy were operated from 1993 to 2003 (age 5-59 yrs, median 31 yrs, 53 females). Most had mesial temporal sclerosis, while some had no structural abnormalities or structural abnormalities like DNET which would not have been resected had it not been due to the epilepsy. A strip was introduced into the temporal horn of the lateral ventricle and placed over the AH. A subdural grid was placed on the temporal neocortex. We recorded the occurrence of neocortical and AH spikes, and whether one or more foci were present. Outcome was 12 months Engel score.
Results: Group 1: 31 patients presenting only one spike focus which was located at AH. Group 2: the remaining 58 patients. Group 1 had a significantly better outcome (Chi-square likelihood ratio, p=0.03), with none of the 8 Engel-4 patients, and 77% Engel-1 compared to 57% in group 2.
Conclusion: Placement of an electrode strip in the temporal horn is an elegant, fast and safe way to obtain knowledge of AH spike foci. We present a novel diagnostic approach and show that identification of a single spike focus on a temporal horn strip without independent neocortical foci indicates a good prognosis. A randomised trial is needed to evaluate whether the balance between seizure freedom and verbal memory benefits from this approach.

p1042
Subdural Electrode Implantation for Invasive Neurophysiological Recordings in Patients with Refractory Epilepsy: Technical Guidelines
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Purpose: This paper describes technical issues related to subdural electrode implantations in epilepsy patients which have been used to lower the incidence of surgical morbidity such as infections, subdural collection and CSF leaks.
Methods: 77 patients were submitted to subdural grid implantations from 1996 to 2004 at the Hospital Brigadeiro and Clinica de Epilepsia. The main technical guidelines were: 1) perform a large craniotomy to accommodate the entire grid(s); 2) keep an extremely clean operating field; 3) do not allow grids to overlap; 4) do not damage or displace veins; 5) document electrode type and position; 6) attach the grid to the dura with stitches before closing it; 7) close the dura as usual and secure dural defects and electrode exit points with fibrin glue; 8) exit the electrode's tail through a burr hole; 9) exit the electrode's tail using a tailored tunnelling device avoiding the primary incision; 10) attach a subgaleal stitch around the electrode's internal skin exit point; 11) leave a subgaleal drain with no vacuum; if the craniotomy is extensive, insert two; 12) firmly attach the electrode's cable to the skin; 13) forward a clear summary to neurophysiology; 14) avoid implanting children with microcephaly and no brain atrophy. All patients received prophylactic antibiotics. No patient received steroids.
Results: One patient presented with a CSF leak through the electrode's exit point, treated with additional skin suturing. One patient had meningitis and monitoring had to be interrupted. There were no symptomatic subdural/subplate/interplate fluid collections.
Conclusion: Many complications occurring after/during subdural electrode implantations have been described in the literature. These complications might be avoided if careful technical guidelines are followed during the procedures.

p1043
Magnetic Brain Source Imaging and Ictal Spect as Pre-surgical Evaluation for Extratemporal Epilepsy Patients
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Purpose: To determine whether magnetoencephalography (MEG) and ictal single photon emission computed tomography (SPECT) can be useful in presurgical evaluation of extratemporal lobe epilepsy patients.
Methods: We analysed 19 extratemporal lobe epilepsy patients who underwent epilepsy surgery (12 males and 7 females, age range 2 to 41 years). Preoperative MEG spike localisations were displayed in patients' individual MR imaging (magnetic source imaging: MSI). SPECT images were analysed by subtraction of the ictal and interictal images co-registered to MR imaging. The localisations of dipoles on MSI and hyperperfusion areas on subtraction SPECT images were compared to the extent of surgical resection and postoperative outcome.
Results: The resection areas on postoperative MR imaging were concordant with both localisations of MSI and SPECT in 8 (Class A), with only MSI in 5 (Class B), with only SPECT in 4 (Class C) and with neither localisations of MSI nor SPECT in 2 (Class D). 7 of 8 patients (87.5%) in Class A, 3 of 5 in Class B, 0 of 4 in Class C and 1 of 2 in Class D had successful seizure outcomes after surgery (Engel class I or II). Postoperative outcomes were significantly different among these groups ($p < 0.05$).

Conclusion: MEG can determine location of the irritative zone whereas ictal SPECT can determine location of the seizure onset zone in some cases. Combining the results of refined imaging techniques of MEG and ictal SPECT holds great promise in predicting postoperative good outcome in extratemporal epilepsy patients.

p1044
Language Lateralisation in Children with Epilepsy due to Left Hemispheral Lesion: An fMRI Study
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Purpose: It is widely assumed that following early damage to the left hemisphere language functions are likely to reorganise, especially if the lesion affects classical language areas. However, few data are available about the correlation of language lateralisation and localisation with age at the onset of epilepsy, seizure frequency and semiology, and duration of epilepsy.
Methods: We studied 24 patients (11 male, 13 female, age range 7 to 18 years, mean age 12.8). All except 2 were right-handed. They suffered from focal epilepsy with onset between 1-15 years of age (mean 6.9) due to left hemispheral lesions - 6 cortical dysplasias, 6 congenital or benign tumours, 4 mesiotemporal sclerosis, 3 low grade gliomas, 2 cavernomas and 3 post-traumatic or post-inflammatory gliosis. All patients underwent MRI, EEG and neuropsychological study. Hemispheric language dominance was evaluated by fMRI using a silent word generation paradigm.
Results: During the fMRI study 9 right-handed patients showed significant co-activation of the right hemisphere, in another 3 right-handed persons a complete shift to the right hemisphere was detected. Both left-handed patients exhibited left-hemispheric language dominance. The probability of language dominance shift or significant co-activation of the non-dominant hemisphere correlated with the age at epilepsy onset and aetiology (early brain injury before the age of 6 years), and increased inversely with the distance of the lesion from supposed language centres.
Conclusion: Language dominance shift in children appears to correlate closely with the localisation of the lesion, aetiology and age at epilepsy onset.

p1045
Usefulness of Subcortical Monitoring using MEP Following Cortical or Transcranial Electrical Stimulation in the Operation of Cerebral Lesions near the Pyramidal Tract or the Central Sulcus
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Purpose: Surgery for resection of the lesions around the central sulcus or pyramidal tracts carries an associated risk of causing significant motor deficits. The use of motor evoked potential (MEP) monitoring following cortical or transcranial electrical stimulation allows these lesions to be removed with maximal safety and efficacy.
Methods: Surgical resection was performed on 40 patients with cerebral lesions adjacent to central lesions. In 8 cases with a deep-seated tumour, we oriented the scalp stimulation site just over the primary motor area using neuronavigation. Stimulation at the condition (200-250V, 500Hz, 0.2ms,3-5trains) was transcranially applied. In 32 cases with the lesion around the central sulcus, after craniotomy, central sulcus was determined by N20 phase reversal on sensory evoked potential (SEP) recording following median nerve stimulation. Cortical motor mapping was performed by monopolar anodal stimulation with a train of 500Hz (3-5 pulses) (stimulation intensity 8-25 mA). Action potentials were recorded from facial, thenar, biceps arm and quadriceps femoralis muscles. MEP recording continued for the intra-operative monitoring of the motor system until radical lesion resection was macroscopically achieved.
Results: No new postoperative motor deficits were seen in 95% of the patients in this series.
Conclusion: Subcortical MEP monitoring enhanced the safety of the operation of lesion resection near the pyramidal tract or the central sulcus.

p1046
Language Function of Mesial Temporal Epilepsy Patients: Evaluated by Wada Test
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Purpose: To evaluate the language function of patients with mesial temporal lobe epilepsy (mTLE) using the Wada test.
Methods: 55 patients (27 men and 28 women, aged, 14-58 years, mean 35.3 years) with mTLE, who underwent epilepsy surgery and had good surgical outcomes after more than a year follow-up period. Seizure onset ages ranged from 1 to 18 years old. Intervals between the onset and the surgery were 25 to 43 years. We performed the Wada test to evaluate their language function.
Results: 52 of 55 patients (95%) were right-handed. 47 of 52 patients (90%) had left language dominancy, only 1 (2%) had right language dominancy. 2 of 3 left-handed patients had right language dominancy. 5 of 55 patients (9%) had bilateral language function. 4 had contralateral Wernicke's speech area and ipsilateral Broca's speech area to the epileptic focus. Magnetoencephalography of these 3 patients showed interictal spike discharges in the left superior temporal gyrus. The other one had bilateral Broca's area and Wernicke's area.
Conclusion: Long term history of patients with mTLE possibly affects language function. It is suggested that spike discharges can shift temporal language function to the opposite side to the focus.

p1047
Wada Rest with Propofol in Temporal Lobe Epilepsy
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Purpose: To describe the use of Propofol as an anaesthetic substance used during a Wada test as a substitute for amytal.
Methods: We studied 2 women and 3 men, older than 14 years who presented with epilepsy seizures not controlled by pharmacological treatment, and who were presented for epilepsy surgery having already received medical, neurological , neuropsychological, video monitoring investigation and EEG and MRI, and showing a diagnosis of mesial temporal epilepsy (2 left and 3 right, after undergoing the Wada test with propofol). Language functions and memory were tested after injection of 20 mg of propofol in the carotid intern artery. The test was subdivided into three procedures: to name objects, to read sentences, to remember objects they were exposed to during the effect of the drug: the Seattle procedure, to remember objects seen after the drug effect; the Montreal procedure, to remember events which happened during the period of the drug effect; and the Interview procedure.
Results: After the injections of propofol the average time of duration of the drug effect was 6 minutes for the first injection and 11 minutes for the second. The procedures proved satisfactory. One patient presented a speech block of approximately 2 minutes and during the second injection we could verify the intense drug effect.
Conclusion: Propofol showed to be a good option when it is not possible to use amytal. More tests should be carried out to determine the correct dose of propofol, so that the results of the test are similar to those using amytal.

p1048
Effect of Mesial Pathology and Extent of Resection on Seizure and Memory Outcome after Selective Amygdala-Hippocampectomy (SAH)
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Purpose: Recent developments in epilepsy surgery indicate a trend of increasingly more restrictive and selective surgery to control pharmacoresistant epilepsy. The aim of this study was to evaluate whether the outcome of super selective surgery in mesial temporal lobe epilepsy depends on the extent of the mesial pathology.
Methods: In a prospective randomised study 46 patients with mesial TLE and hippocampal sclerosis underwent SAH with a short (S<=2,5cm) or long (L>=3,5cm) hippocampal resection. Resection length was evaluated intraoperatively. Using visual MRI inspection, patients were subdivided into a group with more anterior (A) versus posterior (P) pathology. Four study-groups resulted (AS; AL; PS; PL). Three months postoperative seizure outcome was available for all 46 patients; a 12 months follow-up including neuropsychology for 29 patients.
Results: In the 3 and 12 months follow-up group only the location of pathology appeared to have some effect on seizure outcome. However, this effect was observed at 3 months and disappeared 12 months after surgery. Finally, 3/8 PS (37%), 6/13 PL (46%) and 2/3 AS (67%), 3/5 AL (60%) were continuously seizure-free. Pre- and postoperative memory outcome was determined only by the lateralisation of the resection/epilepsy.
Conclusion: Preliminary findings in this prospective randomised trial on super selective surgical strategies in SAH provide mild evidence that a more posterior pathology carries a generally higher risk of continuing seizures, and that, although this did not yet become significant, a longer resection should be considered. Shorter resection in patients with anterior pathology appears to be an option, but long-term outcome must be considered as well, and from a neuropsychological view no different outcome was indicated.
Supported by DFG(SFB/TR3)

p1049
Cognitive Impairment in Premotor Drug-resistant Epilepsies
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Purpose: The specific cognitive features of neuropsychological impairment in frontal lobe epilepsy are still difficult to define and remain overwhelmed by the temporal lobe epilepsy data. The purpose of this study is to outline the neuropsychologically distinct features of premotor epilepsies.
Methods: The evaluation is based on 10 patients with drug-resistant epilepsy who were successively explored with depth electrodes in Rennes and were given a complete neuropsychological assessment (mean age at evaluation 25 years, range 14 to 39).
Results: The epileptogenic zone included lateral premotor, supplementary motor area or/and central areas (3 in dominant, 7 in non-dominant hemisphere). All patients had a lesion, 8 were operated and the pathological examination revealed a focal cortical dysplasia in 7. In 3 patients we were able to prove their progressive intellectual impairment by reference to previous neuropsychological tests while in the other 7 this was only suspected by the academic history. In all patients we emphasised the IQ to be inferior to the MQ as a strikingly constant feature of their neuropsychological profile. Concomitantly, by depth electrode recordings, the interictal anomalies proved to be always localised and there was no evidence of interictal dysfunction of the whole frontal lobe.
Conclusion: This suggests that these areas might have a more important cognitive function than previously thought, which might be related to the recently described mirror neurons.

p1050
Does Early Epilepsy Surgery Improve Neurodevelopmental Status in Children?
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Purpose: Young children with refractory symptomatic epilepsy are at risk of developing neurological and cognitive disabilities. Epilepsy surgery can provide relief from seizures, but only a few data are available about neurodevelopmental outcome in this group of patients.
Methods: We report 15 children under 5 years of age (mean 34.4 months) who underwent frontal (n= 3), temporal (n= 2), multilobar (n=6) resection or functional hemispherectomy (n=4). All suffered from catastrophic epilepsy due to focal cortical dysplasia (n= 5) , ganglioglioma (n=3), hemimegalencephaly (n=3), Sturge-Weber syndrome (n=2) or Rasmussen's encephalitis (n=2). Neurodevelopmental status before surgery was assessed as normal in 4 children, developmental delay was stated in 11 patients – in 3 of mild degree, in 5 of moderate and 2 of severe degree. Except for the standard preoperative examination all children underwent neuropsychological evaluation before and one year after surgery.
Results: At follow-up period of 12-58 months (mean 27 months) 6 patients were seizure-free (Engel I), 4 had rare seizures (Engel II), 4 exhibited worthwhile improvement (Engel III). One year after surgery 13 patients showed no improvement in their development. Only 1 child achieved marked developmental progress. We observed some worsening in the neurodevelopmental status in 1 child, who suffered from ischemic perioperative complications.
Conclusion: We conclude that early epilepsy surgery usually brings seizure relief to young children with intractable epilepsy, but doesn't guarantee enhanced development.

p1051
AED Withdrawal Analysis during Video EEG Monitoring Before and After Epilepsy Surgery
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Purpose: From our previous data, we showed the benefits of AED withdrawal (abrupt) in candidates for epilepsy surgery, reducing the number of days in the long term monitoring unit. The aim of this protocol is to establish the safety of a withdrawal protocol and the correlation with the epilepsy surgery outcome.
Methods: Patients who were candidates for epilepsy surgery Phase I, II and III admitted in our video EEG unit (LTM) from 2001 to February 2005 were analysed. AED's were withdrawn suddenly from all patients before admission. 82 patients were included. 26 patients underwent epilepsy surgery.
Results: Video EEG monitoring lasted 3.7 days. Complex partial seizures were more frequent in comparison with simple and partial generalised tonic-clonic seizures. The seizure average was 6.2 per patient. The epilepsy surgery group spent more time in the LTM unit. 15 patients had temporal lobectomy, 2 had hemispherectomy for Rasmussen's Encephalitis and 9 patients had frontal resection including 2 cases with tuberous sclerosis and Sturge-weber. The vast majority of patients in the surgical group had a good outcome. There was a good correlation between epileptic focus localisation during the video EEG monitoring in all the patients, and the rapid AED withdrawal which increased the seizure frequency and severity.
Conclusion: AED withdrawal is safe in our experience. There was early seizure detection, with good surgical outcome for all patients who underwent epilepsy surgery. The small sample size of the current investigation is a limitation, and caution should be taken when generalising these findings. Further and multicentred studies are necessary to define a safe protocol.

p1052
Vagus Nerve Stimulation in Paediatric Patients with Refractory Epilepsy
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Purpose: Long-term vagus nerve stimulation (VNS) is a therapeutic option for patients with pharmacoresistant seizures. The patients with refractory seizures should be considered for VNS therapy if their seizures have not responded to antiepileptic drugs (AEDs) and if they are not good candidates for resective epilepsy surgery.
Methods: Our cohort consisted of 14 paediatric patients age 6-18 years with refractory seizures. 5 of the patients suffer from Lennox–Gastaut syndrome. The efficacy of VNS treatment was evaluated after 6 months, 1, 2 and more years. Seizure frequency, neuropsychological parameters and adverse effects of the treatment were evaluated.
Results: One patient is seizure free on VNS. One patient had more than 75% seizure frequency reduction; 50% to 75% reduction of seizure frequency was seen in 3 patients; 5 patients had less than 50% improvement. Concomitant AEDs were reduced in 3 patients. Adverse effects in our group comprised voice alteration, cough and mild dysphagia.
Conclusion: VNS therapy system is safe and effective. We confirmed improvement in both seizure frequency and quality of life parameters in our group of patients. Supported by Research Project No. 00000064203.

p1053
Outcome of Vagus Nerve Stimulation (VNS) in 59 Patients with Intractable Epilepsy more than Six Years after Implantation.
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Purpose: To determine the retention rate and the effect of long term VNS on seizure frequency and quality of life in patients with intractable epilepsy.
Methods: 62 patients with a mean age of 28.7 years (range 6 to 59 years) at time of implantation of VNS were retrospectively studied. The average duration of epilepsy at implantation was 20.4 years (4 to 56), the mean age at seizure onset was 8.8 years (0 to 50), mean follow-up was 76 months (51 to 114), and 3 patients died of SUDEP. We questioned patients on differences in memory, achievements, mood, verbal skills, alertness, cluster seizures, and post-ictal confusion.
Results: The median pre- and post-implantation monthly seizure frequency in the 35 patients who continue to use the device are 24 (3 to 1800) and 4.5 (0 to 1000) respectively (mean improvement 59.1%, median follow-up 71 months). Retention rate is 59.3%. Corresponding median monthly seizure frequency in all patients was 22 (1 to 1800), and 9.5 (0 to 1000). 26 patients (44%) had no improvement, 5 (8%) had less than 50% improvement, 26 (44%) had greater than 50% improvement in seizure frequency (including 4 seizure-free), and 2 (3.4%) were worse. 24 patients who no longer use the device have undergone explanation (median 71 months follow-up; one infection, 23 non-efficacy). Mean quality of life measures showed an improvement in all domains.
Conclusion: VNS shows a long term retention rate and efficacy which is highly favourable when compared to medical treatments for intractable epilepsy.

Wednesday 31st August and Thursday 1st September 2005
13:15 – 14:15
Poster Session
Neuroimaging

p1054
Epilepsy and Tumours: Unusual Imaging Findings
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Purpose: To illustrate pitfalls in neuroimaging of primary brain tumours.
Methods: We recently encountered 2 patients with tumours in our epilepsy surgery program who exhibited paradoxical findings on both MRI and FDG-PET scans. Both patients presented with medically intractable epilepsy. Both patients underwent MRI brain, FDG-PET scans, EEG-video monitoring, and neuropsychological evaluations.
Results: Patient #1 presented with a 2 year history of temporal lobe epilepsy. MRI scan revealed a right medial temporal homogenous, nonenhancing lesion involving the right amygdala and uncus. FDG-PET showed hypometabolism in the right medial as well as neocortical temporal lobe structures. The patient underwent a right temporal lobectomy including amygdalohippocampectomy. Postoperative histopathology showed a glioblastoma (grade IV). Patient #2 presented with a 7 year history of left sided sensory seizures. MRI scan revealed a 4cm diameter intraaxial mass involving the right posterior parietal region adjacent to the falx cerebri. This tumour had minimal mass effect, heterogeneous signal on T1 and T2-weighted images, cyst formation, a large area of surrounding edema, and moderate enhancement with contrast. FDG-PET revealed increased glucose uptake in the region of the lesion, and simultaneous EEG tracing was normal. Subsequently, the patient underwent intracranial subdural grid placement, motor/sensory mapping, and resection of the lesion as well as the surrounding epileptogenic cortex. Postoperative histopathology showed an oligodendroglioma (grade II) without anaplastic features.
Conclusion: The combination of MRI and FDG-PET is a useful tool for noninvasive grading of gliomas, but rare exceptions do occur. Caution should be taken when interpreting and discussing these studies with patients.

p1055
Volumetric MRI Study of the Hippocampus and the Parahippocampal Region after Unilateral Temporal Lobe Resection
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Purpose: This anatomical study presents MRI-based volumetric analysis of the hippocampus, the temporopolar cortex and the parahippocampal gyrus (perirhinal, entorhinal and parahippocampal cortices) spared after unilateral medial temporal-lobe (MTL) removal carried out for the treatment of drug-refractory temporal-lobe epilepsy. Such methods already applied to epilepsy patients before surgery, have not been used after surgical treatment.
Methods: Based on the location of the remaining anatomical landmarks, we quantified the volume of all these regions in 24 patients after unilateral MTL resection (right: n=12; left: n=12) and in 16 control participants using MRI-based volumetric analysis.
Results: The results confirmed that (1) the mean volumes of these regions contralateral to the epileptic focus were similar to those measured from normal subjects (2) the volumetric measures obtained from the resected side were obviously much smaller than those from

the non-resected side or from normal values and (3) the extent of MTL resection was comparable in right or left MTL surgery. Individual differences noted across the patient samples were also analysed and showed that the parahippocampal cortex, as opposed to the other regions, was not systematically removed.
Conclusion: The segmentation guidelines presented here should provide a useful tool to study the involvement of different anatomical regions of the MTL in surgical outcomes and in human cognition and memory.

p1056
MRI Findings Associated with Non-convulsive Status Epilepticus
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Purpose: We investigated brain MRI changes associated with non convulsive status epilepticus (NCSE), and evaluated whether changes were transient or permanent.
Methods: Retrospective MRI review in patients who were treated for NCSE in an inner city teaching hospital. Brain MRI's were collected over a three year period, and obtained up to three days after NCSE . MRI was performed using T1, T2, FLAIR and diffusion weighted images (DWI). Patients with acute focal or progressive brain lesions including stroke, brain tumour, traumatic brain injury and encephalitis were excluded. DWI and ADC maps excluded patients with acute infarction. EEG localisation was obtained in all patients.
Results: 11 patients were identified with MRI changes presumed secondary to NCSE. Scans may show more than one abnormality. In 3, MRI showed progressive focal cortical atrophy, and 2 were receiving tacrolimus. Three patients had MRI evidence of diffuse multilobar cortical thickening, which normalised on subsequent scans, and 2 had transient meningeal enhancement. 2 patients had ipsilateral thalamic changes, and MRI demonstrated hippocampal signal changes ipsilateral to an extratemporal focus in 3. Focal hyperintense signal changes were present on FLAIR sequences in 3 additional patients.
Conclusion: MRI changes associated with NCSE were both permanent and reversible. The most severe finding was focal cortical atrophy accompanied by significant clinical deficits. Transient and reversible findings included regional meningeal enhancement, focal cortical thickening, and signal changes. FLAIR sequences were most sensitive. Radiological finding suggest that NCSE may result in a permanent focal cortical injury, justifying aggressive treatment.

p1057
Evaluation of the Hypothalami of Menopausal Women with Epilepsy Compared to Menopausal Women without Epilepsy using 1H-MRS
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Purpose: The aim of this study was to determine if women with epilepsy and early onset menopause have abnormal neuronal integrity of the hypothalamus as measured by proton-magnetic resonance spectroscopy (1H-MRS). It is known that frequent interictal seizure disruption of the hypothalamus may lead to reproductive endocrine disorders in women (1). The hypothalamus is an integral part in the regulation, production and secretion of reproductive hormones. MRS may confirm hypothalamic abnormalities that are manifested through early onset menopause in women with epileptic seizures in comparison to age matched controls.
Methods: 5 women (ages 52.6±2.7 years) presenting a history of epilepsy and early menopause were studied along with a set of age matched controls (n=5, ages 52.4±2.4 years). The age of last menses was also matched to within a year between the patient and control groups. All data were acquired on a 3.0 Tesla eclipse GE MRI scanner (Milwaukee, WI) using a transmit/receive head coil. A 512x512 T1 weighted coronal series was prescribed along the anterior/posterior commissure line to localise the base of the third ventricle and place the axial MRS slices. A multi-slice 2D-CSI sequence from the NIH (J. Duyn, J.W. van der Veen) was used to prescribe 3 slices having a 32x32 grid size and a 7.5x7.5x15 mm voxel size. The PRESS based sequence used a sweep width of 1000 Hz, 256 points, a TR of 2300 ms and a TE of 280 ms for a scan time of 30 minutes. Outer volume suppression, optimised water suppression and shimming algorithms were employed to obtain optimal quality spectra. Spectra were transferred to an SGI octane workstation for analysis using XsOsNMR software (X. Mao, D.C. Shungu). Low-pass Hamming and Fermi k-space filters removed high frequency noise components prior to FFT. A low-frequency Gaussian function was convolved with and subtracted from the data to remove the residual water signal. Data were zero-filled in time, to 512 points, and space to yield a 64x64 grid. Voxel shifting was performed prior to FFT in order to place a single CSI voxel on the centre of each side of the hypothalamus. A representative spectrum referenced NAA at 2.02 ppm and this spectrum was then used as a reference for susceptibility corrections applied to the entire grid. The correlation coefficient between each spectrum and that of the reference spectrum was minimised to eliminate spectral shifts between voxels. Peak areas were integrated between fixed ranges to obtain NAA, CRE and CHO values in ratio to RMS noise.
Results: Metabolic ratios of NAA/CRE, NAA/CHO and CHO/CRE were calculated for the hypothalamus comparing values from the right side against the left as well as between the patient and control populations. In addition, ratios for the total hypothalamus were calculated and compared with normal grey matter within the same slice as shown in the table below. No significant variations in metabolic ratios between patient and control populations were observed. NAA/CRE NAA/CHO CHO/CRE controls – right hypothalamus 1.87±0.20 1.34±0.13 1.40±0.15 patients – right hypothalamus 2.08±0.38 1.53±0.28 1.37±0.13 controls – left hypothalamus 1.85±0.25 1.31±0.26 1.43±0.21 patients – left hypothalamus 2.01±0.44 1.48±0.43 1.38±0.17 controls – total hypothalamus 1.86±0.21 1.33±0.20 1.42±0.17 patients – total hypothalamus 2.04±0.39 1.50±0.34 1.38±0.14 controls – grey matter 2.10±0.26 1.54±0.27 1.38±0.13 patients – grey matter 1.75±0.30 1.54±0.21 1.16±0.29
Conclusion: Spectroscopic studies have not focused specifically on the hypothalamus primarily due to the small structural size and resulting lack of signal to noise ratio. No published studies at 3.0 Tesla could be found that examined the normal hypothalamus or that of patients with epilepsy. Several studies examined hypothalamic hamartomas but were at 1.5T using different acquisition parameters making direct comparison of metabolic ratios difficult. The resulting lack of significant MRS detectable metabolic variations between the patient and control populations may be due to the additional localisation of reproductive dysfunction in the pituitary and peripheral glands in addition to the hypothalamus.(1) Spectral quality at 3.0 Tesla in this small structure was more than adequate to provide accurate measures of metabolic ratios. Additional studies may provide more information on the location of metabolic abnormalities in patients with epilepsy that affect reproductive dysfunction. It is the goal of this study to pursue 1H-MRS as a non-invasive complementary technique to standard clinical screening in patients with epilepsy. Ref: 1) Ann Neurol 2003;54(5):625-37.

p1058
Increased Thalamus Levels of Glx in Patients with Primarily Generalised Epilepsy
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Purpose: Impaired thalamo-cortical oscillations constitute an important pathophysiological mechanism behind idiopathic generalised epilepsy (IGE). While thalamic involvement has long been indicated by electrophysiological data, it has recently become possible to analyse with independent methods. In this magnetic resonance spectroscopy (MRS) study we investigated metabolic and structural integrity of this structure. Of particular interest were

possible changes of glutamine+glutamate (Glx) concentrations and signs of neuronal damage.
Methods: 43 IGE patients and 38 age and sex matched healthy controls were investigated with a 1.5 Tesla MR system. Quantitative single volume MRS was used to measure the concentrations of Glx and N-acetyl-aspartate (NAA) in the thalamus and occipital cortex. Thalamic volumes were measured on high-resolution gradient echo images and thalamic grey and white matter fractions assessed with voxel-based morphometry (VBM), SPM99.
Results: IGE patients showed elevated Glx and reduced NAA concentrations in the thalamus when compared with controls (12.1±2.6mM vs 8.9±4.2 mM, p=0.0026 for Glx, and 9.9±1.1 mM vs10.8±0.9 mM, p=0.012 for NAA). The thalamus grey matter fraction was reduced, and white matter fraction increased, maximally in the dorso-medial thalamus. The thalamus volume (cm3) was reduced in patients (6.7±0.7 vs 7.2±0.6 in controls; p=0.0001), as was the total cerebral volume (1163±128 vs 1250±102; p=0.0003), leaving the thalamus/brain ratios unaltered.
Conclusion: Quantitative MRS and VBM provide additional evidence for thalamus involvement in IGE. The observed elevation of Glx levels along with the reductions in NAA levels and grey matter fractions suggest epilepsy related excitotoxicity as a possible underlying mechanism.

p1059
Proton In-vivo MR-Spectroscopy (1H MRS) in Children with Seizure Disorders
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Purpose: We propose quantitative indicators for the characteristics of regional and age peculiarities of brain metabolism in normally developing children and in children with seizure disorders using primary spectral parameters of three main metabolites: N-acetylaspartic acid (NAA), total creatine (Cr) and choline (Cho).
Methods: 82 children were examined by 1H MRS using 1.5T magnetom vision (SIEMENS). All subjects were divided into two groups. The first group (NG) consisted of 10 healthy children (aged 1 month to 16 years). The second group (PG) included 72 developmentally delayed children with seizure disorders (aged 2 weeks to 16 years). The subjects of both groups were divided into 5 age groups: less than 1 month, from 1 month – to 1 year, from 1 year to 3 years, from 3 years to 8 years, and older than 8 years. For some children the monitoring of brain maturation in uterus and then in early newborn age was provided. Spectral matrixes in the supraventricular region parallel to the canthomeatal line were obtained. 2DCSI 1H spectra were recorded with TR/TE = 1500/135, 175, 215 ms; NS = 1.
Results: In each voxel of the spectral matrix we introduced two indicators: the metabolite content AM as the peak area and the metabolite concentration CM as the ratio of the peak area to the sum of all the peak areas S: CM=AM/S. We describe the metabolic state in each voxel by the triad T* ={ACho, ACr, ANAA}, where ACho, ACr, and ANAA are the peak areas of the signals from Cho, Cr and NAA. For each of the areas we assigned three values: 1, 2 and 3, to obtain six symbolic spectral configurations:1* ={1,2,3}, 2* = {2,1,3}, 3* ={1,3,2}, 4* ={3,2,1}, 5* ={3,1,2} and 6* ={2,3,1}. We analysed the temporal alterations of triad distributions during neurodevelopment. In the NG aged 1 to 3 months spectral configuration 1* was absent, configurations 2* and 6* were frequently observed, and the main configurations were 4* and 5*. In the NG aged 6 to 10 months all spectral configurations (1*, 2*, 3*, 4*, 5* and 6*) were present. The large enough dispersion is characteristic for the values of NAA-, Cr- and Cho-concentrations of configurations 1* and 2*. In the NG and PG in the age group older than 10 months the most frequent configurations were 1* and 2*, and dispersion of the main metabolite concentrations decreased with age. Configuration 3* was the most frequent in children with neurological disorders (PG). In the PG configurations 5* and 6* electrically defined seizure foci were observed. Signal of lactate was elevated only in children of PG, who had seizures immediately before MRS-examination.
Conclusion: MRS investigation of the foetal, neonatal and adolescent human brain gives us a unique possibility for monitoring neurodevelopment and providing a baseline for age related differences in the normal human brain and in the brain under pathology. The quantitative classification of the brain state according to the trident configurations and the regional triad maps essentially amplify MRI examinations of patients with brain pathologies.

p1060
Diffusion Weighted Imaging and Volumetric Measurements Show Abnormalities in the Thalamus in Patients with Refractory Temporal Lobe Epilepsy
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Purpose: The thalamus is an important relay station in the limbic circuitry and has a modulating influence on seizure propagation. We hypothesised that volumetric and diffusion measurements of the thalamus will be abnormal in patients with intractable temporal lobe epilepsy (TLE) compared to a control group and may provide lateralising information.
Methods: 31 patients (17 left, 14 right TLE) who had undergone temporal lobectomy and 16 controls were included. We performed volumetric measurements of the thalamus on high resolution T1 scans (in cm3) using in house developed software. T1 volumetric acquisition and apparent diffusion coefficient (ADC, values in x10 -5 mm2/s) maps were coregistered to measure thalamic ADCs. Unpaired U-test was used for comparisons between groups, paired U-test between ipsilateral to contralateral values (mean+/-SD).
Results: ADC values were significantly increased in the thalamus in patients with left and right TLE compared to controls (all P<0.001); (left TLE: ADC left: 97.99+/-8.2, right: 99.84+/-7.5, right TLE: ADC left: 96.08+/-6.31, right 99.67+/-6.9; controls: ADC left: 87.2+/-4.9; right: 88.39+/-4.79). The ADC values however provided no lateralising value. Thalamic volumes (TV) were smaller ipsilateral to the epileptogenic zone in our patients with TLE compared to controls. In patients with left TLE, left TVs were significantly smaller compared to controls (left TV: 4.99+/-0.84, control 5.59+/-0.73 (P<0.01), right TV: 5.25+/-0.93, controls 5.75+/-0.9, ns). In patients with right TLE, right TVs were marginally smaller compared to controls (right TV: 5.08+/-1.07, controls: 5.75+/-0.9, P<0.058); left TV: 5.26+/-0.84, controls: 5.58+/-0.73, ns). Even though TVs were smaller ipsilateral to the epileptogenic focus compared to contralateral, this was not significant.
Conclusion: Thalamic atrophy predominantly ipsilateral to the epileptogenic zone and bilateral diffusion abnormalities in patients with intractable TLE provide evidence for widespread damage within the limbic circuitry.

p1061
Reversible MR Signal Changes Associated with Epilepsy: Periictal Diffusion-weighted Imaging
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Purpose: To investigate reversible MR signal changes on perictal images of patients with epilepsy and to evaluate the clinical manifestation of these findings for differential diagnosis considering the pathophysiology of transient brain changes during seizures.
Methods: Four patients showing seizure-related MR signal changes had their records retrospectively reviewed. Two of the patients presented with status epilepticus (SE), one with complex partial seizures (CPS), and the other with partial seizures (PS). T2*-weighted images (T2*WI) and diffusion-weighted images (DWI) were performed for all patients. We evaluated the signal changes and location of the lesions, and compared the signal changes of the initial MR images to those of the follow up MR images.

Results: Case 1 was diagnosed as having NCSE with suggested origin in the right occipital and temporal structures, corresponding with the reversible hyperintensity in DWI and T2*WI. In Case 2, who experienced metamorphopsia during his CPS, only DWI showed transient cortical hyperintensity over the right occipital lobe. In Case 3, a pregnant woman who complained of visual hallucination during her PS, DWI and T2*WI showed involvement transiently in the brain stem. Another patient with SE experienced convulsive seizures with electrical changes suggesting an origin in the right frontal cortex, whereas the transient DWI changes appeared in distant temporal and occipital cortex.
Conclusion: Our cases suggest that the transient periictal imaging changes may occur in the region of the epileptic discharge or in distant structures, and especially tend to localise in the posterior portion of the brain related to vertebrobasilar circulation.

p1062
Uncinate Fasciculus Fibre Tracking in Temporal Lobe Epilepsy
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Purpose: The aim was to find a structural correlate linked with temporo-insulo-perisylvian PET hypometabolism in mesial temporal sclerosis (MTS). Uncinate fasciculus (UF) connecting frontobasal and temporal pole may be involved in ictal spread. We compared diffusion tensor imaging (DTI) measurements along UF in patients with epilepsy due to right MTS (MTLE) and controls, expecting structural changes prominently along UF ipsilateral to MTS.
Methods: 6 right handed patients referred for MTLE presurgical work-up (1 female and 5 males, mean age 26.5 years) were investigated on a 1.5-T MR scanner including T1-weighted and DTI sequences (56 slices, 2.4 mm thick, 36 directions, b=700). Patients had interictal [18F] PET showing right temporo-insulo-perisylvian hypometabolism. Control group consisted of 6 right-handed subjects (age/gender match). Both side UF segmentation was performed using fibre tracking, its fractional anisotropy (FA) values were compared inside and between groups using the Mann-Whitney U test.
Results: FA asymmetry was found in the control group: right-greater-than-left for FA ($p<0.04$). This asymmetrical pattern was lost in the patient group; FA decreased bilaterally and more prominently ipsilateral to MTS ($p<0.002$). Left minus right FA values significantly differed between groups ($p<0.02$).
Conclusion: Because of FA drop prominently ipsilateral to MTS, patients had no evidence of the right-greater-than-left FA asymmetry found in controls. This preliminary finding, probably reflecting loss of UF integrity, is of interest to further investigate interictal MTS PET hypometabolism.

p1063
Diffusion Tensor White Matter Abnormalities in Temporal Lobe Epilepsy with Mesial Temporal Sclerosis
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Purpose: Diffusion tensor magnetic resonance imaging (DTI) provides indirect information on axonal integrity by measuring the diffusion properties of water. We recently reported bilateral symmetrical DTI abnormalities (reduced fractional anisotropy, FA) of the fornix and cingulum in patients with temporal lobe epilepsy (TLE) with unilateral mesial temporal sclerosis (MTS) (Concha, et al. Ann Neurol 2005;57:188-196). The objective of this project was to study other white matter tracts in the same patient population in order to determine whether white matter abnormalities in patients with TLE and MTS are global or limbic system specific.
Methods: DTI was performed on a series of 8 patients with TLE and unilateral MTS and 9 age-matched controls. A blinded investigator manually delineated regions of interest for the corpus callosum (genu and splenium), the internal capsule (anterior and posterior limbs) and the external capsule with between group differences in FA being compared.
Results: A significant reduction in FA of patients was observed in the genu of the corpus callosum ($p= 0.009$) and the posterior limb of the internal capsule ipsilateral to MTS ($p=0.045$) with no difference seen in the splenium, anterior limb of internal capsule and external capsule.
Conclusion: While the corpus callosum and internal capsule are not conventionally considered part of the limbic system, the demonstration of limbic specific surface antigens, in both structures in foetal rats strongly suggests the presence of significant limbic connections (Horton and Levitt. J Neurosci 1988;8:4653-4661). The current observations suggest that patients with TLE and unilateral MTS have limbic specific (as opposed to global) white matter pathology.

p1064
Diffusion Tensor Imaging Demonstrates Postictal Changes in Intractable Epilepsy
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Purpose: Our objective was to examine whether diffusion tensor imaging (DTI) detects postictal diffusion abnormalities in patients with intractable epilepsy, and to determine the time course of these changes and their concurrence with the epileptic focus.
Methods: 25 patients with intractable epilepsy (23 with focal, 2 with generalised epilepsy) were scanned with DTI after 27 ictal events. Two sets of images were acquired interictally, and a median of 49 minutes postictally. 20 controls were scanned twice with repeated acquisition. Statistical parametric mapping (SPM) was used to detect changes in diffusion between acute postictal (PI1) and interictal (II1) scans and compared to the differences noted between control scans. The time course of changes was evaluated by measuring the mean diffusivity (MD) from the areas of change identified in the SPM analysis.
Results: Areas of decreased diffusion (n=24) between PI1 and II1 scans were detected in 12 (44 %) patients. 5 of the 12 patients also had areas of increased diffusion (n=10). 3 of the 12 patients had MD changes ipsilateral to the presumed seizure focus. The changes were bilateral in 2 patients. The MD values in repeated postictal scans; after 30 minutes, from the areas with significant postictal decreases (PI1 vs II1) showed a subsequent recovery towards interictal diffusivity values.
Conclusion: DTI can identify areas of diffusion changes postictally in patients with intractable epilepsy. The changes are presumed to reflect altered cell function and may have the potential to locate an epileptic focus to aid presurgical assessment. (Supported by the Academy of Finland (80592/201697), Action Medical Research (SP3772).)

p1065
Diffusion and Magnetization Transfer Imaging Demonstrate Brain Damage Associated with the Syndrome of Bilateral Occipital Calcifications, Epilepsy and Celiac Disease
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Purpose: To study by magnetic resonance (MR) with diffusion and magnetization techniques patients affected by the syndrome of bilateral occipital calcifications, epilepsy and celiac disease (BOCEC).
Methods: We performed a brain magnetic resonance (MR) study on 10 patients with BOCEC, 8 patients with celiac disease (CD) without epilepsy or neurological deficit and 17 healthy volunteers. The MR study included T1, T2 weighted images, diffusion and magnetization transfer (MT) imaging. The apparent diffusion coefficient (ADC) and MT ratio maps were analysed with histograms and the Statistical Parametric Mapping 2 (SPM2) software. In addition turbo spectroscopic imaging acquisitions were obtained at the mid and supra-ventricular levels.
Results: Focal white matter lesions were observed in 5 BOCEC patients, in 3 CD patients and in none of the controls. BOCEC ($p = 0.006$) and CD ($p=0.01$) patients showed a higher whole brain ADC as compared to healthy controls. They also showed a non-significant decrease of the whole brain MTR. SPM2 showed bilateral areas of significantly decreased MTR in the parieto-temporo-occipital white matter in the BOCEC patients which were not correlated with the extent of calcifications. The N-acetyl-aspartate/creatine and choline/creatine ratios in normal appearing white matter were not significantly different in the three groups of subjects.
Conclusion: In conclusion, diffuse increase of the apparent diffusion coefficient (ADC) and selective damage of the temporo-parieto-occipital white matter exhibiting abnormally reduced magnetization transfer (MT) ratio and possibly related to gliosis were found.

p1066
Temporal Lobe Epilepsy (TLE) and Chronic Interictal Psychosis: Evidence of Focal Structural Brain Abnormalities from Magnetisation Transfer Imaging (MTI)
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Purpose: Interictal psychosis has been reported in 4-10% of patients with epilepsy and particularly with temporal lobe epilepsy (TLE). The pathophysiological mechanisms of interictal psychosis are still not known. Magnetisation transfer imaging (MTI) has been shown to be sensitive in detecting subtle structural brain abnormalities that are undetected by conventional MRI. Widespread cortical abnormalities have been detected in patients with chronic schizophrenia using MTI (Foong et al 2001). The aim of this study was to determine whether MTI abnormalities can be detected in interictal psychosis, and whether these changes are similar to those seen in chronic schizophrenia.
Methods: 20 patients with TLE and interictal psychosis with either hippocampal sclerosis (HS) (6 left HS, 4 right HS) or no focal lesions (n=10) on conventional MRI were compared to non psychotic TLE patients who were matched with respect to age and conventional MRI findings.
Results: A voxel-based analysis of the magnetisation transfer ratio (MTR) maps revealed significant reductions of MTR in the left superior and middle temporal gyrus in the subgroup of psychotic patients with no focal lesions when compared to non-psychotic patients. The MTR reductions could not be attributed to volume reductions.
Conclusion: Left temporal MTR reductions can be detected in some patients with TLE and interictal psychosis which are not detectable on conventional MRI. These focal MTR abnormalities might reflect subtle neuropathological changes. Our findings are in contrast to the widespread MTR abnormalities reported in patients with chronic schizophrenia. This study was supported by the Big Lottery Fund (RG/1/010026026).

p1067
BOLD/fMRI Localisation in Partial Epilepsy without EEG Correlation
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Purpose: EEG/fMRI method for sources localisation of interictal and sub-clinical epileptic discharges (IEDs, SCEDs) is limited by scalp EEG. It shows partly or does not show depth discharges whereas MRI can display whole BOLD activation. For utilising MR physics we proposed BOLD/fMRI continuous acquisition with reference to benzodiazepine effect and without EEG correlation (1). Our results showed a better display of BOLD activations. However, both with and without EEG correlation, we often found multiple and confusing activations. With the purpose of a better identification of epileptogenic zone we have used temporal clustering analysis (TCA) (2,3) centred on the regions of interest (ROIs).
Methods: 10 patients (7 with temporal lobe epilepsy (TLE) due to hippocampal sclerosis, 2 with cryptogenic frontal (FLE) and 1 occipital lobe epilepsy (OLE), respectively) underwent BOLD/fMRI according to the procedure previously reported (1,4). For this study we centred EPI images on ROIs. MRI inter-slice gap was reduced to 2.5 mm. TCA was chosen because it was suitable for discriminating BOLD responses according to the peaks of activation.
Results: BOLD activations concordant with the other diagnostic tests were obtained in 8 out of 10 patients (7 TLE, 1 FLE). Multiple activations, when evident, were discriminated by TCA.
Conclusion: BOLD/fMRI method with reference to benzodiazepine effect associated with TCA may play a role in a more realistic delimitation of epileptogenic zone. References 1. Ricci GB et. al., Magn. Reson. Imaging; 2004, 22: 1487-92 2. Yee SH. et. al., Magn. Reson. Imaging; 2003, 21: 51-53 3. Morgan VL et. al., Neuroimage, 2004,21: 473-481 4, Garreffa G et. al., Magn. Reson. Imaging ; 2003, 21: 1175-89.

p1068
Mapping of Interictal Epileptic Discharges: Comparison of Results from Event-related BOLD MRI and Dipole Source Analysis
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Purpose: Simultaneous recording of blood oxygen level-dependent (BOLD) MRI data and EEG data allows for mapping of interictal epileptic discharges (IED) with high spatial and temporal resolution. In this study, we present BOLD MRI activation patterns and dipole

source analysis data related to IED recorded inside the MR scanner. Validity of results and possible clinical implications are discussed.
Methods: 3 patients suffering from focal epilepsy were investigated in the MR scanner. At the time of investigation, simultaneous surface EEG showed intermittent or discontinuous, uni- or multifocal IED. MRI: 2.9T scanner (Siemens Trio), 8-channel phased-array head coil. Gradient-echo echo-planar-imaging (EPI, 2x2x4mm), T1-weighted anatomical dataset at 1mm isotropic resolution. EEG: Continuous 32-channel MR-compatible 10/20 surface EEG (Brainproducts). Analysis: Gradient- and cardioballistic artefact were removed off-line. IED were identified in the EEG and event-related correlation analysis of BOLD MRI data was performed. Resulting activation patterns were co-registered to T1-weighted anatomical images (Brainvoyager). BOLD MRI activation patterns were taken as seed points for dipole source analysis and results were compared to dipole source analysis solutions found independently of BOLD MRI data (BESA).
Results: In selected cases, good concordance of BOLD MRI activation patterns and dipole source locations could be seen. However, contradictory findings in other cases emphasise that each method's unique set of limitations (e.g. head model in dipole source analysis, hemodynamic effects in BOLD MRI) can potentiate difficulties in the interpretation of combined approaches.
Conclusion: The combination of BOLD MRI and EEG is a methodologically challenging but promising technique to further enhance diagnostic procedures in epilepsy.

p1069
Simultaneous fMRI and EEG Recording in Epilepsy Patients with 3 T MRI Scan
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Purpose: Functional magnetic resonance imaging (fMRI) with simultaneous EEG recording in epilepsy is a useful tool to localise the interictal spikes to anatomical MRI using BOLD signal changes. These methods for epilepsy patients have been mainly applied to 1.5 T MRI. We analysed the results of the fMRI with simultaneous EEG recording inside 3 T MRI in 12 focal epilepsy patients.
Methods: EEG recording with a 32 channel magnetic compatible recording system was performed inside 3T MR scanner (ISOL technology). The EEG data was processed offline in order to filter out the scanner artefact. Filtered EEGs were reviewed and the timing of epileptiform discharges marked. The SPM99 package was used to fMRI data analysis. The quality of recording EEG was classified into 'good', 'fair', and 'bad' by visual analysis.
Results: Fourteen studies were performed on 12 patients. Numbers of spikes in patients with activation areas were 5 to 122 spikes. EEG quality was 'good' in 1, 'fair' in 8 and 'bad' in 3. Patients with 'poor' EEG quality or no spikes during recordings could not be analysed. Activation regions concordant with EEG and MRI/PET localisation were seen in 5 (41.7%) of 12 patients. In considering 7 patients with interictal spikes (+) during the recording, 5 (71%) patients had fMRI activation areas concordant with epileptic foci, which was higher than the results in 1.5 T. In 5 patients with activation, activation areas were 2 to 5 regions dependent on the patients. 3 (60%) of 5 patients with bursts of IEDs showed activation and 2 of 3 patients with isolated IEDs showed activation. This difference was not statistically significant. 3 of 5 patients (60%) with normal MRI had activation and 2 of 7 patients (28.6%) with abnormal MRIs had activation.
Conclusion: Simultaneous fMRI and EEG recording with 3 T MRI showed clear fMRI activation areas, compatible with the source of interictal spikes, in 5 of 7 focal epilepsy patients with interictal spikes (+) during the recording. This work was partly supported by MOST (Korean Ministry of Science and Technology) with grant No. M1-0107-07-0001.

p1070
Memory-related Hippocampal FMRI Activation in Presurgical Assessment of Patients with Temporal Lobe Epilepsy: A Pilot Study
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Purpose: In presurgical temporal lobe epilepsy (TLE) planning, establishing the integrity of hippocampal memory function is essential. The present pilot study explores the utility of fMRI as a non-invasive alternative to the intracarotid amobarbital test (IAT).
Methods: 6 healthy, right-handed control persons and 6 right-handed TLE patients were tested. IAT results indicated left-hemisphere language dominance for all patients. IAT indicated that 4 patients had bilateral memory representation while 2 had unilateral representation (1 in the right and 1 in the left hemisphere). Novel pictures (50%) and repeated (and prelearned) pictures were presented in a variable block length design (180 pictures in total). Imaging was performed with a 1.5 Tesla scanner. Data were analysed using SPM99. We defined a ROI including hippocampus and looked for differential activations between groups.
Results: An area in the left hippocampus showed higher activation ($p=0.005$) for control subjects than for patients. All hippocampus activation was higher for controls than for patients. Hippocampus activation (higher for novel than repeated pictures) was bilaterally stronger for controls than for patients, particularly for right lateral activation ($p=0.002$). Only a small left lateral activation ($p=0.02$) was seen in the patient group.
Conclusion: Hippocampus activations were higher for novel than repeated pictures, and higher for normal subjects than for patients. Normal control subjects showed bilateral activation. Only a small left lateral activation was found in the patient group. This may partly relate to a mixed pathology in the patient group. The chosen design seems promising for larger scale research.

p1071
Language Lateralisation is No Different Between Patients with Temporal Lobe Developmental Tumours and Hippocampal Sclerosis
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Purpose: Epilepsy patients show a higher degree of atypical language lateralisation than controls. Early onset of seizures and acquired lesions are suggested risk factors for atypical lateralisation. We investigate language lateralisation in epilepsy patients with temporal lobe developmental tumours (DNET) and with hippocampal sclerosis (HS).
Methods: From a series of patients, undergoing pre-operative language fMRI, we identified 17 patients with a temporal lobe DNET and selected 17 HS patients, matched for gender and focus side. Neuropsychological testing included IQ and verbal memory testing. Functional MRI was performed using a noun-verb generation task, performed in a block design. The fMRI data was processed using SPM2 (www.fil.ion.ucl.ac.uk/spm). A laterality index was calculated based on the number of activated voxels in left- and right-sided frontal lobe language areas. Atypical lateralisation was considered if the index was $<= 0.2$.
Results: HS patients had an earlier onset and longer duration of their epilepsy, and a higher incidence of significant antecedent events. However, language fMRI showed no difference in the amount of activation or in the laterality index between DNET (0.49 ± 0.5) and HS patients (0.46 ± 0.4, $p=0.9$), and the frequency of atypical lateralisation

was similar in both groups (18%). There was also no difference between the groups in IQ or verbal memory tests.
Conclusion: Our results imply that language reorganisation in refractory epilepsy cannot be simply attributed to effects of an early seizure onset or nature of the lesion, but may be related to a more complex interaction of the epilepsy with the language consolidation.

p1072
Cerebral Glucose Metabolism Analysis by Using 18FDG-PET and SPM in Children with Developmental Delay and Epilepsy
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Purpose: To evaluate brain regions with abnormal function in children with developmental delay and epilepsy by using 2-deoxy-2-□18F□fluoro-D-glucose (FDG) positron emission tomography (PET) and statistical parametric mapping (SPM).
Methods: Detailed psychodevelopmental assessment and FDG-PET scanning were performed on 10 children aged between 6.3 and 12.8 years (mean age 10.4 years) with developmental delay and epilepsy. We applied the objective technique of statistical parametric mapping (SPM) to define focal abnormalities of glucose metabolism, and compared with those of a group of normal adult subjects (n=7, mean age 29 years) as well as age-matched children with developmental delay but without epilepsy (n=13, mean age 9.7 years) and epilepsy without developmental delay (n=10, mean age 12.8 years).
Results: SPM analysis in the group showing developmental delay with epilepsy, revealed extensive glucose hypometabolism in the anterior cingulate, limbic lobe and frontal areas when compared with that in the normal adult control group. In children with development delay without epilepsy, hypometabolism was noted in areas of the cingulate gyrus and limbic lobe. Comparing children with both developmental delay and epilepsy and those with epilepsy only, reduced glucose metabolism showed a similar pattern but hypometabolism in the anterior cingulate, limbic lobe and frontal areas were prominent in the former group only.
Conclusion: Hypometabolism in the anterior cingulate, limbic lobe with frontal areas in children with developmental delay and epilepsy may be related to decreased cognitive function and widespread dysfunction of cortical regions.

p1073
In Vivo Positron Emission Tomography (PET) Study of the Mutated a4b2 Nicotinic Receptors using [18F]-A-85380 in Patients with Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE)
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Purpose: Mutations in the a4 or b2 nicotinic receptor subunits have now been identified in 12 families with ADNFLE. Electrophysiological studies of the receptors carrying the different mutations identified a common alteration in their properties, corresponding to a gain of function. However, the precise mechanisms leading to the frontal lobe epilepsy remain elusive. Studies of the distribution of the mutated a4b2 receptors in ADNFLE patients would constitute an important step in the understanding of ADNFLE pathogenesis.
Methods: The distribution of a4b2 nicotinic receptors was studied in ADNFLE patients carrying a nicotinic receptor mutation, by a PET-scan using [18F]-F-A-85380, a ligand with a high affinity and specificity for a4b2 nicotinic receptors. 7 epilepsy patients, from 4 different families, participated in the study. Causative mutations were: a4-S248F (4 patients), a4-S252L (1 patient) and b2-V287L (2 patients). Regional brain concentrations of the radiotracer in the ADNFLE patients were compared with those obtained in a group of 7 control subjects.
Results: The pattern of the brain distribution of the radiotracer was found different in the ADNFLE patients when compared to the control subjects. In particular the radiotracer concentration was found higher in the cerebellum and the pons. Further analyses are being undertaken.
Conclusion: ADNFLE mutations of the nicotinic receptor subunits appear to modify the level and pattern of a4b2 nicotinic receptor expression in the living human brain. This finding might bring new insights in the understanding of ADNFLE pathogenesis.
Acknowledgment : The study was partly supported by Sanofi-Aventis.

p1074
Cerebral Perfusion Changes after Lamotrigine Medication
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Purpose: To investigate the effect of lamotrigine medication on cerebral perfusion in new-onset epilepsy patients.
Methods: We enrolled 30 patients (M/F=15/15, 26.8+/-9.3 years) with new-onset epilepsy, who had no history of drug treatment. Cerebral perfusion was measured by brain single photon emission computed tomography (SPECT) using 99mTc-ethylcysteinate dimmer. Brain SPECT was performed before and after lamotrigine administration, respectively. Lamotrigine dosages were gradually increased to a therapeutic level. For statistical parametric mapping (SPM) analysis, all SPECT images were spatially normalised to the standard SPECT template and then smoothed with a 14-mm full width at half-maximum Gaussian kernel. The paired t-test was used to compare pre- and post-lamotrigine SPECTs. Concomitant EEG monitoring was conducted during SPECT to confirm interictal and waking state.
Results: Seizure types were complex partial seizures in 15 patients, secondarily generalised tonic clonic seizures in 9, and myoclonic seizures in 6. Mean seizure frequency was 3.2 (0.5~50) per month before lamotrigine administration. All patients became seizure free with lamotrigine (100~300mg/day) medication for more than 16 weeks without serious adverse events. SPM analysis of pre- and post-lamotrigine brain SPECTs showed hypoperfusion in bilateral mediodorsal thalamic nuclei, right superior/inferior frontal gyri, right precentral gyrus, bilateral uncus, right amygdala, bilateral superior/inferior temporal gyri, and brainstem at the level of false discovery rate corrected $p<0.05$ after lamotrigine medication.
Conclusion: This study first shows reduced cerebral perfusion in subcortical and cortical areas after lamotrigine treatment in epileptic brain.

p1075
Ictal Hyperperfusion Contralateral to the Seizure Focus: How Might Mirror Images Modify SPECT Analysis?
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Purpose: Ictal SPECT explores the brain perfusion modifications related to ictal activity to localise the seizure onset zone (SOZ). However, areas of propagation of the epileptic discharge, especially in

the contralateral hemisphere, also determine hyperperfusions which might perturb SPECT analysis. The occurrence, the topography and the clinical value of such contralateral ictal hyperperfusions (CIHP) was therefore examined.
Methods: A population of 36 consecutive patients with pharmacoresistant partial epilepsy of various localisations was retrospectively studied. Ictal and interictal SPECT examinations were made with 99mTc-ECD and the scans were processed for co-registration, normalisation, subtraction and merging with MRI images.
Results: CIHP were observed in 72% (26/36) of patients - 7/14 mesio-temporal epilepsy cases with hippocampal sclerosis, 6/7 other mesiotemporal epilepsies, 6/7 neocortical lateral temporal epilepsies and 7/8 extratemporal epilepsies. CIHP were usually symmetrical to the SOZ, forming a mirror image in 20/26 cases, or 57.1% of the patients. The symmetrical nature of the mirror image was taken in account in SPECT analysis. It was rarely misleading. It could confirm the location of the SOZ (11 patients) and sometimes even improve the precision of its definition (9 patients), by restraining several potential SOZ related hyperperfusions to a single one or by permitting a restricted localisation of the SOZ in a large hyperperfusion.
Conclusion: Mirror images are common. Knowledge of their spatial characteristics may help interpret SPECT examinations permitting, by reverse symmetry, an improved localisation of the seizure onset zone.

p1076
Correlation of Hypoaccumulated Areas Detected by Iomazenil Spect and Distribution Interictal and Ictal Discharge Recorded by Chronic Intracranial EEG Monitoring in Patients with Intractable Partial Epilepsy
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Purpose: 123I iomazenil (IMZ) SPECT that examines the changes of central benzodiazepine receptor (cBZR) density often shows multiple areas of hypoaccumulation in patients with intractable seizures. This phenomenon makes it difficult to decide the true epileptogenic focus. This study was performed to clarify the correlation of hypoaccumulated areas detected by IMZ SPECT and distribution of interictal and ictal discharges recorded by chronic intracranial EEG monitoring (CIEM).
Methods: IMZ SPECT was performed in 9 patients with medically intractable partial seizures. Focal abnormality on MRI was found in 5 patients. All patients underwent CIEM for 14 days to identify the epileptogenic focus. The findings of IMZ SPECT and CIEM were compared retrospectively.
Results: (1) Three patients with medial temporal origin showed bilateral mediobasal temporal hypoaccumulated areas, while CIEM demonstrated bitemporal foci in 2 and unilateral focus in 1. (2) Two patients with unilateral frontal focus identified by CIEM showed ipsilateral frontal and temporal hypoaccumulation. Interictal spike and ictal discharge distributed in the same frontotemporal region. (3) Four patients (frontal origin in 3 and posterior temporal origin in 1Å@) showed relatively localised hypoaccumulation consistent with the epileptogenic focus identified by CIEM. (4) Excluding two cases with bilateral temporal foci, the remaining 7 patients underwent surgery (frontal corticectomy in 6 and amygdalohippocampectomy in 1) and achieved a good outcome.
Conclusion: IMZ SPECT provides useful information for placing intracranial electrodes to determine the epileptogenic focus, although precise surgical implications of hypoaccumulation on IMZ SPECT need to be confirmed in further studies.

p1077
Role of Siscom in Startle-induced Seizures
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Purpose: Startle-induced seizures (SIS) are the most common type of reflex epilepsy. The pathogenic mechanism for these seizures remains to be elucidated. The aim of this study is to find cortical regions involved in the SIS generation using the substraction ictal SPECT coregistered with MRI (SISCOM).
Methods: 2 patients with SIS monitoring by video-EEG.
Results: Case 1: A 33 year old left-handed man with SIS symptomatic to post-infectious left frontotemporal porencephalic cyst. Seizures were preceded by a somatosensory right arm aura and consisted of bilateral asymmetric tonic seizures followed by right arm clonic movements. Ictal-EEG pattern was characterised by a diffuse paroxysmal fast activity. Tracer injection was performed 7 seconds after the EEG-seizure onset. SISCOM showed a left perirolandic (centro-parietal) hyperperfusion. Case 2: A 27 year old right-handed woman with SIS symptomatic to a congenital bilateral perisylvian polymicrogyria. These were preceded by a left arm somatosensory aura followed by a symmetric axial tonic seizures. Ictal-EEG was characterised by paroxysmal fast activity over the right temporo-parietal region. The tracer injection was performed 18 seconds after the beginning of the seizure. SISCOM showed a right parietal and insular hyperperfusion following the malformation of cortical development.
Conclusion: SISCOM may be a useful tool to study SIS. Ictal onset zone in these seizures usually is located in the supplementary sensorimotor area (SSMA), as generally believed. However, other cortical regions, sometimes distant from SSMA, may be involved in seizure generation depending on the underlying pathology. This seems to be especially true in the case of MCD, probably because of functional reorganisation.

p1078
SISCOM Analysis by 99MTC-ECD in Patients with Frontal Lobe Epilepsy
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Purpose: The method of subtracting interictal from ictal SPECT and co-registering to 3-dimentional MRI (SISCOM) has been recently introduced. We attempted to evaluate the accuracy of detecting the epileptogenic zone by SISCOM analysis in frontal lobe epilepsy, comparing this with the resected area and surgical outcome.
Methods: We retrospectively studied patients with frontal lobe epilepsy who underwent partial frontal lobectomy between January 1998 and February 2004. Ictal and interictal SPECT were obtained using the radiotracer 99mTc-ECD. 11 patients who had undergone ictal and interictal SPECT and preoperative MRI were analysed by the SISCOM method. The histopathological diagnoses were cortical dysplasia in 7, scar in 3, and unknown in 1. The surgical outcomes were Engel's Class I in 6, Class II in 2, and Class IV in 3.
Results: Of 8 Class I or II cases, 5 showed abnormal findings almost confined to the resected area and 3 showed abnormalities partially in the resection area, while none showed abnormality entirely outside the resection area. Of 3 Class IV patients, abnormalities were found almost within the resected area in 1, partially within the resected area in 1, and outside the resected area in 1. Excluding 1 Class IV case with an abnormal finding outside the resected area, SISCOM analysis detected the true epileptogenic focus in 8 cases and indicated a false focus in 2 cases. When using SISCOM analysis of ECD-SPECT, the focus detection rate was 80%.
Conclusion: SISCOM analysis was shown to be effective for the detection of the epileptogenic zone in frontal lobe epilepsy.

p1079
Value of SPECT in Differential Diagnosis of Psychogenic Pseudoepileptic and Epileptic Seizures
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Purpose: Progress of new neuroimaging techniques like single–photon emission tomography (SPECT) allows for estimation not only of morphological changes but changes of perfusion during epileptic seizures and psychogenic pseudoepileptic seizures (PPS). The purpose of this study was to assess the value of ictal and interictal SPECT in diagnosis of PPS.
Methods: Group of 71 patients with PPS – group I (n=33), epilepsy – group II (n=30) and with both type of seizures – group III (n=8), confirmed by video-EEG monitoring with ictal and interictal SPECT were studied. Semi-quantitative analysis of tomographic images was performed. χ^2 test and Mann-Whitney were used for statistical analysis.
Results: Interictal SPECT was analysed in all patients. Ictal SPECT was performed in 19 cases. 70% of patients from I and II group showed regional decrease of perfusion during interictal SPECT most in the left hemisphere (group I – 20 cases, in group II – 19 ones), which was statistically significant (χ^2 - $p<0.01$). Comparison of ictal and interictal SPECT in all groups showed three different patterns of perfusion: no changes in both phases, area of regional hypoperfusion in interictal phase and normalisation in ictal phase or area of regional hypoperfusion in ictal phase but in different region than in interictal SPECT. No regions of hyperperfusion (typical for epileptic seizure) in all patients with PPS during ictal SPECT were found.
Conclusion: Interictal SPECT image cannot be a differential factor in diagnosis of PPS and epileptic seizures. Ictal SPECT with decreasing perfusion can be a useful tool in differential diagnosis.

p1080
Ictal HMPAO SPECT in Epileptic Seizures due to Hypothalamic Haematoma
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Purpose: Hypothalamic haematoma with gelastic seizures (HHGS) is an uncommon, often unrecognised, epileptic syndrome with onset of symptoms during childhood. The origin of the seizures is difficult to determinate, but EEG findings might indicate a frontal onset. In order to evaluate seizure onset in a patient with hypothalamic haematoma and uncontrolled seizures an HMPAO SPECT was performed during a seizure.
Methods: A 29 year old man with a hypothalamic haematoma and persistent seizures in spite of a wide combination of different antiepileptic drugs, was studied by ictal SPECT. The patient began having seizures when he was 2 years old; the seizures were conscious myoclonic jerks of the right face that would continue with a grimacing smile, and secondarily evolved to both arms extension and a generalised seizure. At age 21 it was decided to carry out only partial removal of the tumour. Surgical therapy revealed this as a valid option in the treatment of the seizures, and the patient remained seizure free for 6 years. Afterwards, the seizures recurred and the patient was not controlled with antiepileptic drug therapy. The patient underwent VIDEO EEG monitoring and an ictal SPECT was performed.
Results: The ictal SPECT showed a generalised cortical hypoperfusion with an increase of the signal over the frontal midline, and a marked hypoperfusion deficit over temporal lobes. Besides, a cerebellar perfusion asymmetry was found. Interictal SPECT showed a normal cortical perfusion without cerebellar asymmetries.
Conclusion: These findings might indicate that in hypothalamic haematomas, seizure onset may be related to frontal lobe diffusion. Due to the short duration of seizures the ictal studies are very difficult to accomplish, and some of the changes may be due to postictal changes.

p1081
Clinical Assessment of Epileptic Spikes in Patients with Neocortical Epilepsy: A Novel Approach with Animated Gradient-magnetic Field Topography
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Purpose: Animated gradient-magnetic field topography (AGMT) with superimposed serial changes of magnetic field topography of epileptic spikes on individual magnetic resonance imaging was innovated. The purpose of this study was to investigate if the AGMT-derived spatial distribution of epileptic zones would provide reliable information for surgical strategies in patients with neocortical epilepsy.
Methods: We retrospectively studied 3 patients with neocortical epilepsy secondary to dysembryoplastic neuroepithelial tumour (DNT), polymicrogyria coincided with hippocampal sclerosis and arteriovenous malformation (AVM). We compared the AGMT-derived epileptic zones with extraoperative invasive encephaloelectrography (IVEEG).
Results: Interictal magnetoencephalographic (MEG) spike sources estimated by equivalent current dipoles (ECDs) were found in proximity to the lesions in all patients. The AGMT portrayed spatial extents of the magnetic field topography of epileptic spikes on a 3-dimensional (3D) reconstructed brain surface. These AGMT-derived epileptic zones of a lesionectomized patient and 2 with incomplete cortical resections of the epileptic foci correlated well with the ictal onset zones and/or active interictal zones on extraoperative IVEEG. In follow-up periods of 1 to 3 years, 1 patient was seizure-free (Engel class I) and 2 rarely experienced residual seizures (class II).
Conclusion: The AGMT method, which delineated epileptic zones surrounding the lesions, provides unique information on electrode localisation with spatial extents not available with the usual ECD analysis for MEG spikes. This method may be useful to guide placement of intracranial electrodes.

p1082
Detecting a Shift in Subdural Electrode Location with Fusion Computed Tomography during Extraoperative Invasive Video-encephaloelectrographic Monitoring
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Purpose: For extraoperative invasive video-EEG monitoring (IVEEG), it is important to recognise the accurate relationship between the subdural electrode position and the brain anatomy. Some patients who underwent implantation of subdural electrodes may show a shift in the electrode location by effusion and haematoma frequently encountered in secondary surgeries. The purpose of this study was to examine whether fusion computed tomography (CT) would provide accurate information on the relationship between electrode location and brain surface anatomy.
Methods: 3 patients with a history of extra-temporal lobe epilepsy underwent implantation of subdural electrodes. Plain CT was performed before and after the electrode placement. Two sets of 3-dimensional (3D) brain surface imaging with and without electrode images were constructed with 3D image analyses software (Virtual Place, Ver. 2.02, AZE, Japan). Electrode images on the brain surface were fused with preoperative 3D-CT images in order to reduce artefacts due to the electrodes. We compared the electrode locations on these 3D-CT (Fusion CT) images to the actual electrode positions in secondary surgeries.

Results: 3D brain surface images with electrodes were successfully constructed. The difference in the electrode locations between actual findings and fusion CT images was within one-gyrus displacement. There was a case where the shift in electrode location was revealed by subdural haematoma before secondary surgeries.
Conclusion: Present fusion CT imaging with IVEEG furnished accurate simulation for epileptic zone delineation on 3D brain surfaces prior to secondary resective surgeries.

p1083
Coregistration of MEG, MRT and FMZ-PET in Refractory Epilepsy
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Purpose: Magnetelectroencephalography (MEG) and 11C-Flumazenil-PET (FMZ-PET) record different aspects of the epileptogenic process. In patients with refractory epilepsy we studied the regional relationship between MEG visualised maximum of spiking and gabaergic neurotransmission
Methods: 7 patients (5 male, 2 female, 30 to 55 years of age) suffering from cryptogenic (n=4) or symptomatic (n=3) epilepsy were studied. Epileptogenic activity was recorded simultaneously by MEG/EEG (magnes II 4D neuroimaging). Benzodiazepine receptor binding was assessed by FMZ-PET (ECAT EXACT HR, Siemens CTI). Alterations of FMZ-binding compared to age matched controls (n=9) were calculated by ANCOVA (SPM99). Region of epileptogenic activity was calculated by MEG from the weighted centre of two typical interictal spikes using a one-dipol-model of realistic head-model (CURRY V 45 Neuroscan-Compumedics). These data were coregistered to FMZ- and MRT images and stereotactically normalised (SPM99).
Results: In all 7 patients MEG localised an epileptic focus. FMZ-PET identified regions of significant reduced FMZ-binding in 5 patients. In 3 of 7 patients, abnormality of FMZ-binding and spike focus showed congruent localisation. These cases revealed abnormalities in the temporal lobe. In 2 patients no close relationship between FMZ- and MEG focus was evident. In 5 of 7 patients abnormalities of FMZ-binding were observed in multiple regions.
Conclusion: These preliminary results demonstrate that changes in FMZ-binding do not always correlate with the MEG focus, which indicates the complexity of neurotransmitter activity in epileptic disturbances. However, the congruence of findings in cases with temporal lobe epilepsy suggests a potential role of multimodal coregistration for non-invasive presurgical evaluation of epilepsy patients and justifies further studies.

p1084
Intracarotid Amobarbital Procedures in a Pair of Adult Craniopagus Twins
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Purpose: Cranially conjoined twins are rare and pose unique challenges in evaluating language function. We present our experience in performing intracarotid amobarbital procedures (IAPs) on a pair of adult craniopagus twins before planned separation surgery.
Methods: A pair of 27-year old female Iranian twins with total parieto-temporo-occipital craniopagus underwent language assessment simultaneously by 2 neurologists during IAPs. Both twins were university graduates and fluent in Persian/Farsi (mother tongue) and English. The right twin (RT) was right-handed and the other left. With one neurologist standing on the right side of RT and the other on the left side of the left twin (LT), 4 IAPs were performed at half-hour intervals in the following sequence: right internal carotid artery (RICA) of LT, left ICA (LICA) of RT, LICA of LT, and RICA of RT. During transient hemiplegia in one twin, English language was simultaneously tested for both twins. With return of power/language, memory was tested simultaneously for both twins.
Results: RICA injection in LT: left hemiparesis and paraphasia in LT only. LICA injection in RT: right hemiplegia and aphasia/paraphasia in RT only. LICA injection in LT: right hemiplegia and aphasia/paraphasia in LT only. RICA injection of RT: left hemiplegia only in RT. No single injection produced language disturbance simultaneously in both twins. RT's left hemisphere was dominant for English language and LT's bilateral English language representation (L>R) were concordant with fMRI study.
Conclusion: Technically IAP could be performed in craniopagus twins with due consideration to sequence and side of injection to each twin, minimising simultaneous cross-over effects.

Wednesday 31st August and Thursday 1st September 2005
13:15 – 14:15
Poster Session
Psychiatry

p1085
Prevalence and Predictive Variables of Psychosis in Temporal Lobe Epilepsy
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Purpose: The relationship between epilepsy and psychosis is intriguing but poorly understood. The prevalence of epilepsy related psychosis varies among different reports. In temporal lobe epilepsy (TLE), it has been estimated to be 10-15%. We investigated the prevalence of psychosis in TLE and studied the predictive value of certain variables for psychosis.
Methods: Out of 452 TLE patients who underwent prolonged video EEG monitoring, we identified 46 patients with a history of postictal, interictal or bimodal (post- and interictal) psychosis. The control group consisted of 60 age- and gender matched TLE patients with no history of psychosis. Patients and controls were examined for age at seizure onset, duration of epilepsy, seizure frequency, history of an initial precipitating incident, family history of epilepsy, location of the irritative zone and the seizure onset zone, and structural abnormalities on MRI. The significance of each variable for the development of psychosis was evaluated using a stepwise binary logistic regression model.
Results: The prevalence of psychosis in TLE was 10.2% (postictal psychosis: 48%; interictal psychosis: 30%; bimodal psychosis: 22%). Three significant predictors of the occurrence of any type of psychosis were identified: age of seizure onset (OR=1.06, p=0.003), overall seizure frequency (OR=0.871, p=0.024) and the presence of bitemporal interictal spikes (OR=0.217, p=0.003).
Conclusion: Our data confirm the previously reported prevalence for psychosis in TLE of at least 10%. An early onset of epilepsy, the occurrence of bitemporal interictal spikes, and a high seizure frequency may be predictive for the development of psychosis. It has yet to be clarified whether there is a structural or functional alteration common to both conditions that, when exacerbated by seizures, kindles pathways that provoke psychotic symptoms.

p1086
Postictal Mania and Postictal Psychosis
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Purpose: To clarify the differences of clinical features between postictal mania and postictal psychosis.

Methods: Ten postictal manic episodes in 5 patients (M group) were compared with 15 postictal psychotic episodes in 15 patients (P group).
Results: Organic and functional abnormalities were located in the left temporal lobe (n=1) and in the left temporal and frontal lobes (n=3) in the M group; whereas they were located in the left mesial temporal lobe (n=4), right mesial temporal lobe (n=2), bilateral mesial temporal lobes (n=2), left temporal lobe (n=3), right temporal lobe (n=1) and right temporo-parieto-occipital lobes (n=2) in the P group. 3 patients had frontal lobe epilepsy and 2 had temporal lobe epilepsy in the M group; whereas 14 patients had temporal lobe epilepsy (6 had mesial temporal lobe epilepsy) and 1 had symptomatic localisation-related epilepsy in the P group. M group had on average 8.5 manic episodes and P group had on average 2.2 psychotic episodes. The mean duration of the mental disorder episodes was significantly longer in the M group (mean, 15.3 days) than in the P group (mean, 6.4 days).
Conclusion: Patients with postictal mania had more recurrent mental disorder episodes than patients with postictal psychosis. Postictal manic episodes lasted for a longer period than postictal psychotic episodes. Organic and functional abnormalities suggested that postictal mania was associated with the frontal and temporal lobes and postictal psychosis with the temporal lobe. Postictal mania was associated with frontal lobe epilepsy and postictal psychosis was associated with temporal, particularly mesial temporal lobe epilepsy.

p1087
Unexpected Sudden Death in Patients with Epilepsy and Associated Chronic Psychosis Deceased in Havana's Psychiatric Hospital Between 1970 and 2004
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Purpose: This research paper analyses the causes of death in epilepsy patients with psychiatric disorders, the majority of which suffered an unexpected sudden death. The mean age at the time of death in these patients was studied and compared to a group of schizophrenic patients who died in the same hospital during the same period of time, and to another with non-mental disorders, located in another hospital.
Methods: The protocols of the 268 necropsies on patients who suffered from epilepsy and associated psychosis were compared with 2203 schizophrenic patients from the same hospital and with another 540 patients that died in a general hospital between 1970 and 2004.
Results: The mean age at the time of death in patients suffering from epilepsy and associated psychiatric disorders is 51.82 years old. The mean age in the group of schizophrenic patients was 62.38 years and in the group of patients with no mental disorders it was 72.43 years old. Unexpected sudden death is one of the five main causes of death in epilepsy patients (24 deaths) being this type of death only present in this type of patients. The so-called main causes of death also include accidents during a seizure by bronchoaspiration, status epilepticus and cranium traumatism (33 patients).
Conclusion: The mean age of patients with epilepsy and mental disorders is lower than that of schizophrenic patients in the general population of the country. Unexpected sudden death and accidents during seizures lowers the life expectancy of these patients; a fact that is evidenced only within this group.

p1088
Two Cases of Biphasic Postictal Psychosis Following Frontal Lobe Seizure
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Purpose: The symptomatology of postictal psychosis (PIP) has yet to be fully evaluated. We report two patients with frontal lobe epilepsy who developed a peculiar biphasic PIP.
Methods: Case 1: A 17 year old right handed man with complex partial seizures (CPS) consisting of a brief duration of loss of consciousness. Case 2: A 30 year old right handed man whose seizures began with paresthesia of the left upper limb, later evolving into a secondarily tonic-clonic seizure (sGTC). The clinical seizure types and EEG findings for each patient supported a diagnosis of frontal lobe epilepsy.
Results: These 2 patients experienced PIP consisting of two phases: during phase one, occurring one day after a cluster of CPSs or sGTCs and continuing over a number of days, they showed psychomotor excitement and impulsive behaviour, with or without auditory hallucination; later, during phase two, they began to show viscosity and regression, complaining of ambiguous anxiety and somatic concerns. During this phase, they also exhibited an obsession with trivial daily events and excessive dependence on medical staff. These symptoms completely resolved within 3 weeks.
Conclusion: We found a number of differences between the symptoms of PIP in these two cases and those found in temporal lobe epilepsy as reported by other researchers. These differences may be due to the association here with frontal lobe dysfunction.

p1089
Analysis of Risk Factors for Postictal and Interictal Psychosis in Patients with Refractory Epilepsy
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Purpose: Epilepsy patients are at a higher risk for acute and chronic psychotic states. In this study we analysed the presence of risk factors for developing postictal psychosis (PIP) and interictal psychosis (IP).
Methods: 113 consecutive patients with refractory epilepsy were evaluated; 82% had temporal origin. All patients underwent complete neurological, neuroimaging, neuropsychological, and psychiatric assessment. Clinical, demographic, psychiatric, neuropsychological, and neuroimaging data were assessed by logistic regression.
Results: 24% of patients had a positive history for PIP and 38% had IP psychosis. 51% did not show any type of psychosis. Epilepsy time duration, presence of febrile seizure history, and the absence of experiential aura were significantly more frequent in patients with PIP ($p \leq 0.05$). 8% of patients with temporal lobe epilepsy had bilateral hippocampal sclerosis in the MRI, and 62% of them had PIP and 75% IP ($p \leq 0.05$ compared with patients with no history of psychosis). The presence of hippocampal sclerosis plus in RMN was associated with the absence of PIP history ($p \leq 0.05$).
Conclusion: Postictal psychosis was more common in patients with longer epilepsy duration, febrile seizure history, and absence of experiential auras. The presence of bilateral hippocampal sclerosis was associated with both PIP and IP. Other features associated with IP were not found. Risk factors for PIP seem to be more distinctiveness than those for IP.

p1090
Plasma Folate and Homocysteine Levels in Interictal 'Schizophrenia-like' Psychosis in Patients with Epilepsy.
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Purpose: Genetic and clinical data suggest that folate and homocysteine may play a role in the pathogenesis of psychiatric disorders. We thus investigated whether or not a functional folate deficiency and/or elevated levels of plasma homocysteine may be related to an interictal 'schizophrenia-like' psychosis.
Methods: We studied the plasma folate, vitamin B12, and homocysteine levels of 32 age- and sex-matched epilepsy patients

with or without interictal psychosis. Each group included 25 localisation-related epilepsies and 7 generalised epilepsies.
Results: The epilepsy patients with interictal psychosis had significantly lower folate levels and higher homocysteine levels than those without interictal psychosis. There were no significant differences in the vitamin B12 levels between the two groups.
Conclusion: The present study suggests that low plasma folate and high plasma homocysteine levels may be related to the pathophysiology of interictal psychosis of epilepsy. The present findings should be confirmed by prospective longitudinal studies in a larger group of patients with epilepsy.

p1091
Psychosis and Epilepsy: Clinical and Epidemiological Aspects
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Purpose: It is accepted that epilepsy predisposes certain kinds of mental disease, mainly psychosis; these findings were based on calculations in groups of selected and uncontrolled patients that epidemiological studies did not support. We wanted to know if epidemiological methods could predict this predisposition to psychosis in epilepsy patients.
Methods: We used a representative epidemiological sample of 70 epilepsy patients from the municipality of Comalcalco, Tabasco, México; population 140,000 with a prevalence of epilepsy of 20/1000. A neurological and psychiatric evaluation was performed to determine if they had a psychiatric disorder in agreement with DMS IV and CIE 10 classifications. SPSS10.0 was used for statistical and descriptive analysis.
Results: 57 epilepsy patients were evaluated, and none had psychotic symptoms. 91.3% were free of other psychiatric symptoms with only 8.7% having symptoms that were diagnosed as personality changes (DSM IV). These were associated with a certain degree of mental retardation and/or other neurological sequelae. One male patient (1.7%) had had a psychotic episode 6 years prior to this study, having been hospitalised and started on neuroleptics, that he takes to this day.
Conclusion: Our study showed that epilepsy is poorly associated with psychiatric symptoms, and in a similar number to that of the general population. It cannot be affirmed that epilepsy predisposes psychosis.

p1092
Training of Psychical Higher Functions for Rehabilitating Patients with Epilepsy and Psychosis
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Purpose: Our purpose was to train functions of orientation, memory and thought with the objective of rehabilitating in someway the psychological state of a group of patients who suffer epilepsy and psychosis of long evolution.
Methods: A group of 20 subjects suffering from epilepsy and psychosis took part in the study. Median age was 55 years, all were female and median cultural level was 8th grade. We designed a series of tasks of easy application that allowed us to train the functions of orientation memory and thought. We used the Mini-mental State Examination (MMSE), The Scale for the Assessment of Negative Symptoms (SANS), and Montgomery and Asberg Depression Rating Scale (MADRS).
Results: Through the applied techniques we got as a result significant differences in the group of patients studied before and after the process of rehabilitation.
Conclusion: In the development of this investigation we found the importance of training higher psychological functions in patients suffering from epilepsy and psychosis of long-term evolution, in aiming to contribute to the rehabilitation process.

p1093
Epilepsy and Schizophrenia: Association or Antagonism?
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Purpose: The relationship between epilepsy and schizophrenia is complex.
Methods: Review of the literature.
Results: In 1934, von Meduna proposed camphor-induced convulsions in the treatment of schizophrenia and concluded that there was a biological antagonism between epilepsy and schizophrenia. From the 1950s on, the prevalence of psychosis in epilepsy patients has been repeatedly studied. The work of Slater et al. (1969) had a profound impact. Over a few years, they collected 69 cases of inter-ictal psychosis among people with epilepsy. The onset of seizures preceded the development of mental deterioration by an interval of several years. Temporal lobe epilepsy was over-represented. Although the patients exhibited at times all the cardinal features of schizophrenia, the psychoses observed deviated from schizophrenic norms in some respects. Conversely, the occurrence of seizures and/or epilepsy in people with schizophrenia was documented many years ago and was not considered a major problem. Recently, using modern diagnostic criteria of schizophrenia and epilepsy, Gelisse et al. (1999) confirmed that the prevalence of epilepsy and acute symptomatic seizures was low in people with schizophrenia, which points to a possible relative 'resistance' to factors of epileptic seizures. Another important problem is the possibility that temporal lobe surgery for epilepsy may be associated with post-operative schizophrenia.
Conclusion: In this communication, we discuss the relationship between epilepsy and schizophrenia and hypothesize that there is an antagonism between seizures (not epilepsy) and schizophrenia. However, there is a link between longstanding and drug-resistant epilepsy and interictal psychosis, so epilepsy and schizophrenia can be associated.

p1094
Major Depression is Predicted by the Neurological Disorders Depression Inventory, but not Quality of Life or Medication Toxicity
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Purpose: To determine the predictors of major depression and quality of life in the clinical evaluation of epilepsy.
Methods: We prospectively evaluated 205 adult epilepsy outpatients from five academic medical centers using the Neurological Disorders Inventory for Epilepsy (NDDIE), the Adverse Events Profile (AEP), and the Quality of Life in Epilepsy Inventory (QOLIE)-89 summary scores. The diagnosis of major depression was determined for each subject using the Structured Clinical Interview for the DSM-IV. Person correlation evaluated the association of each clinical variable, and logistic regression modelling determined the independent correlation of each variable with the diagnosis of major depression.
Results: The NDDIE, AEP, and QOLIE-89 summary scores each correlated with the others (range of r from 0.4 to 0.8; $p < 0.05$) in the bivariate analyses. However, only the NDDIE significantly correlated with diagnosis of major depression in the logistic regression analysis. Both the NDDIE and the AEP were strongly independently associated with the QOLIE-89 when the QOLIE-9 was used as the dependent

variable in the logistic regression analysis (adjusted R2 =0.72; p<0.0001).
Conclusion: Quality of life and antiepileptic medication toxicity are not independently associated with major depression in persons with epilepsy, but appear to be confounders after controlling for the score of a reliable and valid screening instrument for depression. This finding suggests that 1) depression is not usually caused by poor quality of life or medication toxicity in epilepsy, and 2) the diagnosis of depression can be facilitated by specific screening instruments designed to identify the most important symptoms of depression in persons with epilepsy.

p1095
Does the Presence of Major Depression Alter the Morphology of Mesial Temporal Structures in Temporal Lobe Epilepsy?
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Purpose: Refractory temporal lobe epilepsy (TLE) is often associated with mood disorders. We investigate the morphology of mesial temporal structures in TLE patients with and without major depression.
Methods: We identified 47 TLE patients that had detailed psychiatric assessment and a 3T MRI as part of pre-surgical epilepsy investigations between January 2003 and October 2004. Current or past major depression, and presence or absence of hippocampal sclerosis (HS) was noted. MRI comprised of a 3D T1-weighted sequence and whole brain T2-relaxometry. Manual measurement of bilateral hippocampal and amygdaloid volumes and T2-relaxation times were performed blinded to the depression status.
Results: Major depression (current or past) was more frequent in HS (53% of 32 patients) than in other TLE (20% of 15 patients, p=0.03, Chi square). There was no difference between depressed and not depressed HS patients in the hippocampal and amygdaloid volumes. However, HS patients with current or past major depression had normal contralateral amygdaloid signal (contra 95±10 msec), whereas not depressed HS patients had bilaterally increased amygdaloid signal (contra 103 ±8, p=0.02). HS patients with current depression had relatively less signal change in the ipsilateral hippocampus, and ipsilateral and contralateral amygdala (depressed 91±11; not depressed 103±8, p=0.01).
Conclusion: Major depression is particularly frequent in HS. Volume deficit is attributed to neuron cell loss, whereas signal increase to gliosis. Our results suggest that depressed HS patients have less severe gliosis in the mesial temporal structures. The integrity of the contralateral amygdala may be important for the development of major depression.

p1096
Depression and Health-related Life Quality of Epilepsy Patients in Taiwan
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Purpose: The aim of this study was to evaluate the prevalence of depression in epilepsy patients in Taiwan and to explore the possible factors that may contribute to low quality of life in these patients.
Methods: 80 consecutive epilepsy patients (M:F= 41:39, age=37.1 ± 13.1) were recruited from the neurological OPD of Kaohsiung Medical University Hospitals for evaluation. Various demographical factors as well as health-related life quality questionnaire (SF-36) and depression scale (CESD) were used for evaluation.
Results: 38 patients (47.5%) were found to be dysthymic, and twelve (15%) had major depression. Factors related to depression were female sex and jobless. All patients were found to have at least one SF-36 subdomain below the average level. Depression was the most powerful determinant to low life quality. Female sex, low education level, single, and jobless were also related to lower SF36 scores. Epileptic syndromes, seizure types, anti-epileptic drugs, and total duration of epilepsy are not related to the degree of depression or quality of life.
Conclusion: The high prevalence of depression found in the present study may be due to the cultural attitude to epilepsy. Low quality of life is also found to be more related to degree of depression than poor seizure control. Other factors contributing to life qualities were gender, low educational level, and jobless. Therefore, treatment of depression, provision of education and a job may help to improve life quality in epilepsy patients.

p1097
Depression Severity but not Quality of Life Predicts Suicidal Ideation in Epilepsy
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Purpose: Suicidal ideation and suicide attempts are elevated in epilepsy patients. Depression may increase the risk for developing seizures, and increase the risk of suicide. We determined prevalence and predicting factors of suicidal ideation in epilepsy outpatients.
Methods: In this prospective study we evaluated 193 consecutive adult epilepsy patients for depression, using Beck Depression Inventory (BDI), seizure factors, medication toxicity with the Adverse Events Profile (AEP) and health outcome measures with QOLIE-89, and demographic data. Question 9 of the BDI was used to examine suicidal ideation during the previous two weeks. Student's t-test, chi-square and Mann-Whitney U tests were utilised for statistical analysis.
Results: The prevalence of suicidal ideation was 12% in our epilepsy clinic. 38% of the patients were depressed, and the frequency of suicidal ideas was associated with severity of depression. However, nearly one third scored in the euthymic or mild depression range. The only independent predictor of suicidal ideation was presence of depressive symptoms, but not seizure rate or duration, age, gender, medication toxicity or QOLIE-89 total score (regression analysis, for total BDI score beta= 0.177, p< 0.0001).
Conclusion: Suicidal ideation occurs in more than 10% of epilepsy outpatients, and it is associated with severity of depression. Depression screening may be required to attenuate the risk of suicide. We hypothesize that patients with suicidal ideation and increased risk of suicide have a specific aspect of brain dysfunction with implications for neurobiology of depression in epilepsy. This work was supported by NIH and Epilepsy Foundation grants.

p1098
Temporal Lobe Epilepsy (TLE) and Depression: Analysis of Patients from a Private Neurological Clinic
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Purpose: To analyse the occurrence of depression in patients with temporal lobe epilepsy with mesial temporal sclerosis from a private neurological clinic.
Methods: A total of 30 patients with temporal lobe epilepsy with mesial temporal sclerosis were analysed and all patients completed the Beck Depression Inventory (BDI).
Results: 30 patients, 19 females and 11 males, completed the form. The mean age of patients was 24.2 years, and the mean duration of epilepsy was 13.9 years. 16 patients had refractory epilepsy and 14 had well-controlled seizures. All patients had mesial temporal sclerosis: 11 right-sided and 19 left-sided. We observed abnormal BDI scores in 36% of our sample (even those with controlled seizures); 3 of whom were being treated with antidepressant medication. The mean score of patients with abnormal scores was 17 (sd 6.7). 3 patients reported suicidal thoughts.

Conclusion: The epilepsies are commonly associated with brain dysfunction, social isolation, and vocational difficulty. Depression has been a major concern in the treatment of patients with temporal lobe epilepsy. The treatment of depression in patients with temporal lobe epilepsy is crucial for improving the quality of life of many people with seizures. Identification and treatment of depression may be the most important aspect of care to improve the patient's health status.

p1099
Comorbidity of Epilepsy and Bipolar Disorder: A Clinical Case Series Analysis
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Purpose: Introduction of novel anti-epileptic drugs actualised the question of common neurobiological grounds for bipolar disorder and certain epilepsies. This study examines clinical challenges of cases in which childhood epilepsy is associated with later bipolar disorder diagnosis.
Methods: First, epilepsy-bipolar disorder (BPD) comorbidity was systematically reviewed. Second, a clinical case series (n=6) was retrospectively analysed with a developmental mapping procedure including relevant factors extracted from review (e.g. maternal/paternal family history, illness-onset ages, status epilepticus, interictal and bipolar mania characteristics, life events and medication follow-up). Patients (4 boys, 2 girls) were first diagnosed and treated for epilepsy at ages 3 to 7, and re-examined following drug therapy discontinuation (ages 12 to 18).
Results: Comorbid BPD prevalence in (mostly temporal lobe) epilepsy only recently became documented yet may amount to 8-10%. While childhood epilepsy is readily recognised, juvenile BPD remains underdiagnosed compared to prevalence estimates. All case mappings showed development of paroxistic manifestations following single/recurring epileptic episodes, presenting as fugues, theft, psychomotor agitation, or impulsive actions. One case also involved pseudoseizures sharing phenomenology with both BPD mania and epilepsy. Epilepsy treatment discontinuation in all cases was associated with expression of BPD manifestations at puberty after traumatic life events. Family histories carried BPD antecedents.
Conclusion: Early-onset bipolar disorder requires a focus of clinical investigation since it may go unnoticed in the context of overlapping symptoms with an epileptic syndrome when these benefit from similar medication modalities. Further research on BPD-epilepsy comorbidity should allow more effective discrimination between manifestations of primary mania, secondary mania and pseudoseizures.

p1100
Affective Disorders and Psychotic Episodes in Patients with Chronic Active Epilepsy
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Purpose: The aim of the study was to estimate the frequency and types of affective disorders and psychotic episodes in patients with chronic active epilepsy.
Methods: Evaluation of all patients with chronic epilepsy referred for hospitalisation to the Department of Epileptology for a period of one year, was carried out in this open, prospective, observational study. 34 patients, mean age 32.4 years, mean duration of epilepsy 19.1 years, were included. Comprehensive interviews with patients, inquiries with families and sometimes psychological testing (MMPI, PIE) were used.
Results: 19 (56%) of patients showed affective symptoms. 2 of them presented euphoric mood and 4, irritable-explosive affect. 13 experienced depressive mood changes (ranging from a major depressive episode with a suicide attempt in 1, to a low-grade disorder of dysthymia and short-term depressive and anxiety interictal dysphoric episodes). 5 patients with depressive mood changes required drug treatment. 69.2% of depressive patients had complex partial seizures (CPS), which exceeded the total number of patients with CPS in the group (55.9%). Two-thirds of these patients had left-sided temporal foci in EEG. Only 2 of our patients had psychotic episodes; one of them treatment related (with Topiramate).
Conclusion: Results showed a high percentage of affective disturbances in our group, but it must be kept in mind that these patients were admitted to a specialised clinic for severity or aggravation of their illness. On the other hand, the importance of affective disturbance recognition and treatment must be stressed, as they are inherent, and a frequent manifestation of disordered cerebral function in epilepsy patients.

p1101
Depressive Disorders in Patients with Epilepsy During Remission
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Purpose: Revealing the nature and frequency of depressive disorders in patients with epilepsy during remission (free from seizures periods).
Methods: Subjects were 150 patients of both genders between the ages of 18 and 65 years with duration of remission from 8 months to 20 years. Clinical psychopathological methods and electroencephalogram (EEG) were used.
Results: Depressive disorders were revealed in 46% of patients. 49.2% of identified depressive disorders had a psychogenic nature either related to disease awareness or not related to it. 10.1% of depressive disorders were considered to be a reflection of the epileptic process. The following characteristics of depressive disorders speak in favour of our assumption: sudden onset, short duration - from several hours to several days, sudden stopping, presence of epileptic activity on the EEG during depressive disorder, positive effect of anticonvulsant drug administration or dose increase. The nature of depressive disorders in 40.5% of patients remained unclear. Such disorders were observed in patients with both idiopathic and symptomatic (cryptogenic) epilepsy, who responded to antidepressant drug therapy and apparently had common pathogenesis.
Conclusion: The obtained results indicate the necessity to differentiate approaches towards treatment of depression in patients with epilepsy during remission according to its aetiologic and pathogenetic factors.

p1102
Morbidity of Depression in Patients with Epilepsy
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Purpose: Some multi-aetiological variables that are present in epilepsy patients were studied as to how they may be the cause of depression. The variables studied were depression in family backgrounds, epilepsy in family backgrounds, brain injury backgrounds, time of evolution of the crisis (>15 years), high frequency of crisis (>1 month), type of epilepsy, more than one type of crisis, use of more than one type of antiepileptic drug (AED) and the presence of cephalea.
Methods: A total of 100 epilepsy patients who attended between January 2002 and December 2003 were studied using the Beck inventory for depression. A group of 8 variables were developed and the patients were divided into two subgroups (the positive and the negative subgroups). In each subgroup those suffering from depression and those without depression were separated. Chi square statistical method was used.
Results: 38% of patients referred had a high frequency of crisis (more than one a month) and 50% of them had depression, while from the patients referring a frequency lower than one in a month and only 22.68% suffered from depression (X2 = 1,684E-3; DF = 1). 34% of epilepsy patients also complained of cephalea, and from this group, 47% suffered from depression, while in the rest (without suffering from cephalea) 21.21% suffered from depression (X2 = 1,544E -03 DF = 1).
Conclusion: Significant differences were found only in patients with more than one seizure a month and in those suffering from cephalea

associated to epilepsy. However, neither in epilepsy patients, nor in those using more than one AED, were significative differences found.

p1103
Differentiating Anxiety and Depression in Epilepsy Patients
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Purpose: To define differences between anxiety and depression and their differential impacts on health-related quality of life (HRQOL) domains in patients with refractory partial epilepsy.
Methods: In the USA, adult epilepsy patients (N=201) taking two or more antiepileptic drugs completed a health status survey including demographic items, Hospital Anxiety and Depression Scale (HADS) and QOLIE-10.
Results: Subjects had a high incidence of anxiety (52% none, 25% mild, 16% moderate, 7% severe) and depression (62% none, 20% mild, 14% moderate, 4% severe) based on HADS scores. All HRQOL domains worsened significantly with increasing levels of anxiety and depression: total QOLIE-10 scores decreased from 72+-18 in patients with no anxiety to 54+-13 in those with mild, 48+-18 moderate, and 40+-23 severe anxiety ($p<0.0001$). Total QOLIE-10 scores decreased from 70+-16 in patients with no depression to 50+-16 in those with mild, 45+-16 moderate, and 24+-21 severe depression ($p<0.0001$). Anxiety and depression affected subscale scores similarly (all $p<0.0001$). Patients with mild-moderate depression scores had mild-moderate levels of anxiety. However, patients with mild-moderate-severe anxiety scores had lower mean depression scores. Variance as predictors of HRQOL differed (R-squared 0.337 anxiety, 0.511 depression).
Conclusion: This study revealed anxious and depressive symptoms in half the patients, with significant effects on all HRQOL domains. Mild anxiety or depression resulted in 25-29% reductions in total QOLIE-10 scores, declining further with moderate and severe ratings. Anxiety and depression could be differentiated, though they are often associated. Patients with epilepsy may benefit from increased attention to the role of anxiety separately from depression. Pfizer funded.

p1104
Ictal Fear Versus Panic Attacks: First Results from Conversation Analysis of Clinical Interviews
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Purpose: Clinically it can be difficult to differentiate episodes of ictal fear from panic attacks. We aimed to identify differentiating features in the verbal communication of patients with ictal fear and of patients with panic disorders. We explored doctor-patient interaction using conversation analysis, an established qualitative linguistic approach.
Methods: We studied 5 patients with ictal fear and 7 patients with panic disorder, representing theoretically most different patient groups with similar symptoms. 12 in-depth open interviews were conducted with the medical doctor refraining from directive questioning. Interviews were recorded and transcribed. Transcriptions of episodes of ictal fear, of panic attacks and of common fear (in situations of everyday life) were analysed. At this stage, qualitative linguistic analysis used an iterative approach to identify features that were characteristic for the individual patient's description of his/her attacks and of common fear, respectively.
Results: Patients with panic disorder fluently described, using conversational techniques, exaggerating both their panic attacks and their common fear, but also using preformed expressions. Epilepsy patients needed more interactive elaboration to describe their ictal fear and, finally, came up with very detailed descriptions.
Conclusion: These findings suggest that patients with panic disorder describe their attacks very similarly compared to their description of common every-day-life fear. Whether these similarities are associated with a pathological cognitive style (e.g. learned helplessness) affecting patients with panic attacks but not patients with ictal fear, remains hypothetical. This kind of qualitative research might lead to hypotheses which can then be tested using quantitative approaches, like quantitative linguistic tests, psychometric tests or fMRI (see abstract by Woermann et al).

p1105
Dissociative Experiences in Epilepsy Patients with Pseudoseizures
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Purpose: To clarify the relation between psychogenic pseudoseizures (PS) and dissociation, we evaluated general dissociative symptoms in epilepsy patients with PS using a Japanese version of the Dissociative Experiences Scale (J-DES).
Methods: Subjects consisted of 29 epilepsy patients with PS (mean age 33.5, male 10 and female 19) and 29 epilepsy patients with no PS (mean age 34.4, male 10 and female 19). There were no differences in age, sex, years of education, epilepsy type, seizure frequency, or number of antiepileptic drugs between the two groups. J-DES was administered in all patients. The J-DES scores for the two groups were compared and analysed for association with other clinical features.
Results: The mean J-DES score in patients with PS (25.4) was significantly higher than that in those without PS (12.8) ($p=0.006$). High DES scores (J-DES>30) were observed more frequently in patients with PS (n=13) than in patients without PS (n=3) ($p=0.007$). Logistic regression analysis revealed that J-DES>30 was a risk factor in the development of PS. The DES score was not directly associated with PS frequency or its level of life disturbance.
Conclusion: Our findings suggest that dissociation may play a significant role in the pathophysiology of PS in patients with epilepsy. The J-DES may, therefore, be a viable screening tool for the detection of PS in patients with epilepsy. On the other hand, J-DES scores are not proportional to the severity of the symptoms of PS.

p1106
Gestalt-based Approach in Psycho-diagnostics of the Patients with Epilepsy and non-Epileptic Seizures: Identifying Dysfunctional Boundaries in Relationships within the Family
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Purpose: Evaluation of the results of psychological exploration on patients with epilepsy and pseudo-epileptic seizures hospitalised in the Clinic for Neurology and Psychiatry of Children and Youth, Belgrade, November 2003 to February 2005.
Methods: Analysed, retrospectively, data from an applied battery of psychological tests, techniques and scales: semi-standardised interview, Wechsler children and adults intelligence scales, Machover test, ego-perception and ego-ideal, MMPI. Examined 8 patients, 5 female, 3 male, age 9-24, average 18. Procedure, except in 2 cases, also included interviews with at least one parent. Psycho-diagnostic evaluation encompassed elements of the theory of Gestalt-therapy: the individual as a function of the organism-environment field, and unity of body and psyche, focusing on 'boundary' disorders in parent-child relations.
Results: Found intelligence coefficients in range IQ 55-116. 62.5% of the examinees are of average intelligence and involved in regular education (one examinee completed secondary school). One subject has limited intellectual functioning, two have light mental retardation (emotionally, socially and educationally deprived). Significant

presence of dysfunctional boundaries in relations with parents. Confluence is a dominant mechanism, while introjection, retroflection and projection are also present. In three of the family systems, boundaries between the patient and other members are mixed-up and misplaced; it is not clear where he/she 'ends' and where the others 'begin'. The case of a female patient aged 19 will be presented.
Conclusion: Psycho-diagnostic practice derived on the holistic doctrine of Gestalt-therapy is a basis in planning psychotherapy of patients with epilepsy and pseudo-seizures, as well as for parent counselling. Psychological evaluation itself includes some therapeutic interventions.

p1107
Placebo Induction Benefits and Clinical Features Assessment in Patients with Psychogenic Nonepileptic Seizures
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Purpose: Psychogenic nonepileptic seizures (PNES) are paroxysmal changes of consciousness, behaviour, perception, thinking and emotions which are time limited and may resemble epileptic seizures. Sensitivity of placebo induction of PNES was tested and analysis of the clinical features of PNES during video monitoring was performed.
Methods: Diagnosis of probable PNES was assumptive on the basis of history data, eyewitness' seizure description, normal electroencephalographic findings and unremarkable neuroimaging. Patients were told that it is necessary to record their typical seizures during EEG with video monitoring either spontaneously or by provocation. Informed consent was signed prior to seizure induction by all analysed (39 patients). Subcutaneous saline administration and simulation (pinprick) or authentic saline intravenous bolus was used. Clinical features of typical seizure were analysed on video records.
Results: We were unable to induce typical PNEN in only 2 patients (5.1%) where the psychiatric origin was Munchausen's syndrome and antisocial psychopathy. Positive placebo induction of typical (description matched) seizures in 11 patients (28.2%) with coexisting epilepsy denotes 100% specificity. In one patient PNES was induced either by the standard method or by particular music playing (history matched). Average seizure duration in the analysed group was 12.4 minutes. Bilateral convulsions, eye closure and pelvic thrusting were the most frequent clinical characteristics of induced PNES. Other registered peculiar clinical features (bark onomatopoeia, embracing, EEG cap pulling) were case specific.
Conclusion: PNES placebo induction is highly sensitive and specific. Despite objections on ethical dimensions of PNES placebo induction and significant encroachment of patient-doctor relations we consider that adequate diagnostic benefits exceed potential damage.

Wednesday 31st August and Thursday 1st September 2005
13:15 – 14:15
Poster Session
Social Issues / Nursing

p1108
Fewer Women Receive Tertiary Care for Epilepsy in Kerala State, India
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Purpose: Stigma attached to epilepsy is known to restrict early diagnosis and optimal care, particularly among the under privileged. We aimed to ascertain any gender bias in utilisation of tertiary care for epilepsy in Kerala State, India.
Methods: R. Madhavan Nair Centre for Comprehensive Epilepsy Care is a tertiary care centre attached to a large referral hospital for neurological disorders in South India. We analysed the sex ratio - SR (number of women per one thousand men) of all registrations in this centre according to year of registration, age, income and religion.
Results: The SR for the 12,352 registrations for epilepsy between 1976 and 2004 was 729. There was no significant variation in the SR among different five year time periods. Age specific SR increased up to the 3rd decade (864) and thereafter progressively declined (569 for the 6th decade and above). The SR for Christians (742) and Hindus (736) was higher than that for Muslims (690). The SR for the lower income group (635) was significantly lower than that for higher income groups (800).
Conclusion: It appears that fewer women with epilepsy receive tertiary care in this state, in spite of a higher SR in the community (907 for epilepsy and 1058 for all population). Women belonging to the lower socioeconomic group or Muslim religion appeared to be vulnerable and less likely to receive advanced care. The treatment gap is wider for women over 30 years (particularly over 50 years) when their longer life expectancy is also taken into consideration.

p1109
Epidemiology of Epilepsy in Asia
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Purpose: Epilepsy is a frequent neurological disease in Asia, as in other regions of the world. A Study of the epidemiology, aetiologies, environmental and sociocultural factors of epilepsy in Asian countries is reported.
Methods: Review of the medical literature. The few existing data allowed us to have an overview of the situation and specificities of the disease in the context.
Results: The number of people with epilepsy is estimated at 30 million in Asia. The prevalence of epilepsy varied between 3 and 15 per 1000 depending on the countries studied. It seems, however, lower than in other tropical zones, without obvious reasons. Its incidence varies widely: in Bengal (India), it was estimated at 49.3 per 100,000 inhabitants per year. Surprisingly it seems more frequent in women than in men, in particular in some studies in Thailand. Aetiologies are dominated by perinatal disorders and parasitic infections like neurocysticercosis, although these are not present in all countries. Where socioeconomic development is better, as in Singapore, head traumas and stroke take the leading role in the aetiology of epilepsy. First line antiepileptic drugs are predominant but they undergo availability and accessibility problems. These difficulties, associated with socio-cultural specificities, explain why the treatment gap is estimated between 70 to 90% in Asia.
Conclusion: It is necessary to continue the study of epilepsy in the less developed Asian countries. It is the aim of the research of the Network created between the Institutions presenting this work.

p1110
Epilepsy and Memory Problems: A Community-based Model of Education and Support for Individuals and Families
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Purpose: Develop, deliver and assess the effectiveness of a community-based education and support programme for adults with epilepsy and memory problems.
Methods: Adults with epilepsy and memory problems attended a series of 3 memory workshops with a partner, friend or carer. Based on a model previously developed by the writers, workshops provided information about memory and introduced memory support techniques. The support role of close companions was emphasised. Participants were invited to select a particular memory problem, choose a memory technique to improve the problem and identify the

support they required from companions at home. At follow up workshops, progress was reviewed and further coaching in memory techniques provided. The stress on individuals and families living with epilepsy and memory problems was demonstrated through role-play and solutions explored in discussion groups. Practical advice on diet and lifestyle was provided. Evaluation was based on facilitators' observations, individual feedback from participants and companions and from group discussion.
Results: Participants enjoyed memory workshops and commented on the value of having their memory problems acknowledged and addressed. Basic study techniques, association and practical solutions e.g. using diaries, were of benefit to participants. More complicated memory support techniques were difficult to apply in daily life.
Conclusion: The effort and commitment required to develop memory skills can be underestimated. There is a need for ongoing support to encourage participants to practice memory support techniques at home. Resources are required to develop this model and provide memory awareness training for community-based staff working with people with epilepsy.

p1111
Prevalence of Epilepsy in Workers in an Urban Area of Benin
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Purpose: The aim of this study was to analyse the characteristics of workers with epilepsy in companies in Benin.
Methods: A cross-sectional study was carried out between November 1999 and May 2000 in 5 urban volunteer companies of south Benin with 4,584 employees entering the survey. The technique of sampling used was proportional random sampling to the size for each company and the minimal subject numbers were 1,009 employees. For the selected subjects the data collected were socio-professional data and the screening of epilepsy which had been identified by the questionnaire for investigation of epilepsy in tropical areas. The epilepsy was confirmed by a neurologist.
Results: In this study, 1,232 workers were included. 46 were suspected of having epilepsy and 13 were confirmed (12 were males and 1 was female). The prevalence of epilepsy was 10.6% (95% CI: 5.9-18.5). The epilepsy was active in 9 patients and the type of epileptic seizures were continuously generalised. 7 patients with epilepsy reported seizure onset before their employment and nobody had declared this to their employer. 11 patients with epilepsy had presented seizures in their workplace. Comparisons with the other workers showed a significant difference only for the working hours.
Conclusion: Epilepsy, in Africa or in developed countries, is always believed to make one unfit for work. In Benin, many patients with epilepsy are working in urban areas. The professional characteristics of employees with epilepsy were not so different from those of the basic workforce population.

p1112
Bio-Psycho-Social Factors in Epilepsy: Gender Differences
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Purpose: To delineate gender differences in epilepsy from the perspective of work beliefs, pain, suffering and self-efficacy.
Methods: A validated questionnaire (MASQ-II) to assess work beliefs, pain, suffering and self-efficacy, scored on a Likert-type scale (1-5) where 5 was the worst response, was given to 113 persons with epilepsy [58 females (F), 55 males (M), mean age 41.56 yrs old plus-minus 11.42 sd, seizure duration 22.88 yrs plus-minus12.96 sd].
Results: There were no statistically significant gender differences for the constructs of suffering, work beliefs, pain or self-efficacy. Significant suffering item gender differences were found for: body impairments [mean 2.62 plus-minus1.46 sd (F) vs mean 1.92 plus-minus 1.24 sd (M), p=0.01], emotional feelings [mean 2.58 plus-minus 1.50 sd (F) vs mean 1.88 plus-minus 1.24 sd (M), p=0.01]. Males were more concerned that they would not be able to manage alone [mean 2.29 plus-minus 1.54 sd (M) vs mean 1.70 plus-minus 0.97 sd (F), p=0.02]. Item differences were marginal for work beliefs indicating that females believed their families did not want them to work [mean 2.32 plus-minus 1.73 sd (F) vs mean 1.7 6plus-minus 1.38 sd (M), p=0.06], they could not manage transportation alone [mean 1.91 plus-minus 1.53 sd (F) vs mean 1.40 plus 0.99 sd (M), p=0.04] while males believed that it was necessary to have a job to be 'normal' [mean 2.81 plus-minus 1.85 sd (M) vs mean 2.23 plus-minus 1.71 sd (F), p=0.09] and potential pension loss was of greater concern [mean 1.33 plus-minus 2.06 sd (F) vs mean 2.05 plus-minus 2.26 sd (M), p=0.08]. Females did more work in the home [mean 1.60 plus-minus 1.01 sd (F) vs mean 2.23 plus-minus 1.34 sd (M), p=0.007] and had marginally more pain than males [mean 3.70 plus-minus 0.92 sd (F) vs mean 3.39 plus-minus 0.92 sd (M), p=0.30]. No differences were found for pain intensity or self-efficacy items.
Conclusion: Discreet gender differences focus on emotional feelings, body impairments and coping alone.

p1113
Action in Communities Against Epilepsy in Senegal
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Purpose: In developing countries the management of epilepsy faces a lot of difficulties. Accessibility to care is the main challenge against epilepsy in the those areas, particularly in Africa. The lack of specialists, means of diagnosis (EEG, IRM, Scanner) added to lack of knowledge about the condition are the real factors of this non access to care. In the context of the international campaign against epilepsy “Out of the Shadows" organised by WHO, ILAE and the IBE, we lay down strategies to contribute to decentralisation in communities of means of diagnosis.
Methods: For two years, visits are organised to one suburban and two rural countries in Senegal (Touba 200km and Ziguinchor 480 km from Dakar) once every fifteen days or once a month during the week-end (free days for us). The team is comprised of one psychiatrist specialising in epilepsy, an EEG technician, a driver and sometimes, members of the Senegalese league against epilepsy. Opportunities are given to people to have a diagnosis of their epilepsy by a specialist and an examination, an EEG report from a mobile device and a prescription are given .
Results: The time to get care is reduced and people get medication with prime generation or second generation AE drugs. Education and information about epilepsy is given to the patients and parents during consultations and also by radio programmes. After each programme the number of patients coming to the next consultation increases. We reduce in these areas the financial and physical efforts made by the population to come to the capital (Dakar) for care, because of distance, poverty and lack of specialist and EEG devices out of Dakar. Medical staff in the visited area have a reactualisation of knowledge about epilepsy through seminars .
Conclusion: This action proves that a real involvement of specialists in link with SLAE gives access to care to rural people with limited means. Voluntary actions and participation of certain leaders in communities help to reduce the stigma of epilepsy.

p1114
Use of Seizure and Epilepsy Codes in Emergency Department and Inpatient Discharges
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Purpose: Discharge diagnoses in the United States are currently coded using ICD-9-CM. These codes are often collected into databases to

assign disease prevalence and direct disease costs. This study attempts to determine the accuracy of the use of seizure and epilepsy related codes in a state-wide population.
Methods: We used an administrative database consisting of all 2001 and 2002 emergency department and inpatient discharges from non-federal hospitals in the state of South Carolina. A sample of approximately 35% of 345.x (epilepsy) diagnoses, 5% of 780.3 (convulsions), 1% of 780.2 (syncope and collapse), and 5% of 293.0 (acute delirium) was selected for a total of 4742 charts. 3994 charts (84%) were located and abstracted for seizure-related information. Epilepsy specialists reviewed the data for appropriateness of diagnostic coding according to the International Classification of Epileptic Seizures from the International League Against Epilepsy. 3531 (88.4%) charts have been reviewed thus far.
Results: 36% of the codes were judged to be accurate, 55% to be inaccurate, and 9% with insufficient information to determine accuracy. 2293 of the charts had a 780.39 code indicating seizures not otherwise specified (NOS), yet 74% of these charts showed evidence of a past history of seizures which would suggest epilepsy. The predictive value positive was 96% for discharge codes indicating epilepsy (345.x). Sensitivity of these epilepsy codes was only 28%.
Conclusion: The use ICD-9-CM codes in an administrative database to determine prevalence of epilepsy would result in a gross underestimation. Most cases coded as seizures NOS appear to be epilepsy. Funding supported by a cooperative agreement with the Centers for Disease Control and Prevention, # U36/CCU319276

p1115
Meta-Analysis on the Epidemiology of Epilepsies in Latin America: A Neglected Public Health Problem
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1) ILAE, Latin American Epilepsy Commission

Purpose: The purpose of this study was to conduct a meta-analysis of the epidemiological studies on epilepsy performed in Latin America and to evaluate prevalence, incidence, aetiologies and risk factors in the region.
Methods: We performed a systematic review of articles on epilepsies in Latin America, with emphasis on those providing information on prevalence, incidence, aetiologies and risk factors (especially population-based studies). Data for this meta-analysis was identified in two electronic databases: MEDLINE (1966-2004) and LILACS/BIREME (1980-2004) by using the terms "epilepsy" and "Latin America", "epidemiology", "prevalence", "incidence", "aetiology", "risk factors", and the name of every country in the region. Other sources included presentations and reports at the ILAE Latin American Commission meetings. Papers published in English, Spanish and Portuguese were included.
Results: Epidemiological data from 21 Latin American countries was evaluated. Epilepsy prevalence ranges from 3x1000 (Cuba) to 57x1000 (Panama Caribbean coastal Guaymi Indians). In general, prevalence data show that epilepsies are two or three times more common in Latin America than in industrialised countries. Data on incidence, aetiology and risk factors for epilepsy are scarce, but evidence indicates that neurocysticercosis represents the main cause of epilepsy in many Latin American countries.
Conclusion: Epilepsies in Latin America are a neglected public health problem that affects at least one million of people. More epidemiological studies with improved methodology are required. This will help the establishment of interventional measures for control and prevention.

p1116
Treatment Seeking Behaviour in People with Epilepsy: A Community-based Study in South India (Comprehensive Rural Epilepsy Study, South India CRESSI)
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Purpose: To study the treatment seeking behaviour of people with epilepsy (PWE) in a rural community in South India.
Methods: PWE identified in the CRESSI prevalence study were the subjects of the study. Data collected included: 1) initial treatment and change over to other systems; 2) details of alternate systems; 3) treatment compliance and reasons for poor compliance; 4) patient's, family's assessment of treatment response. We modified defined daily dose (DDD) values assigned by the World Health Organization to suit the lower body weight of the local population. To calculate the dosage of AEDs, we used the ratio of the prescribed daily dose (PDD) to the modified DDD.
Results: Of the 462 PWE identified in the prevalence study, analysis of the data was done for 358 (77.5%). Initial treatment of choice was allopathic in 264 (74%) and traditional in 35 (10%). A total of 58 (16%) PWE were exposed to one of the forms of the traditional system, ayurveda 33 (57%); homeopathy 11 (19%); and traditional faith healers 14 (24%). None had scarification as the treatment. 59 (16%) PWE had never received any form of treatment. Of the total 281 PWE who had received allopathic drugs as the initial or subsequent medication, 151 (54%) patients were on polytherapy (mostly 2 AEDs), the PDD was in the expected DDD range only in 66 (23.5%) patients and drug compliance was poor in 172 (61%) patients. The common reason for poor drug compliance was lack of purchasing capacity to buy the drugs regularly. The treatment gap on the prevalence day was 81.5%. There was a fair correlation between treatment seeking behaviour and knowledge, attitude, and practice (KAP) of epilepsy in the community: allopathic system 64% vs 74%; alternative systems (ayurveda and homeopathy) 34% vs 12%; religious faith 35% vs 4%. In the KAP study there was more than one option when asked about efficacy of various treatment modalities.
Conclusion: Allopathic system was the initial choice of treatment in about two-thirds of PWE. But there was a poor drug compliance mainly related to lack of purchasing capacity. Traditional systems were the initial treatment in only 10% of patients. Treatment seeking behaviour fairly correlated with knowledge about epilepsy in the community.

p1117
Epidemiological, Socio-cultural and Clinical Profile of Epilepsy in Northwest India
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Purpose: To study the epidemiological characteristics of epilepsy in Northwest India.
Methods: The data on 400 epilepsy patients (200 idiopathic and 200 symptomatic) were collected for their clinical, demographic and socio-cultural characteristics. The diagnostic criteria of ILAE were used for seizure classification.
Results: In 88% cases, the age of seizure onset was < 34 years and in one-third cases (33%), it was <15 years. Sleep deprivation was reported as a major triggering factor. No difference was seen for place of residence. The male female ratio was higher in epilepsy patients (1.33:1 in idiopathic and 1.47:1 in symptomatic epilepsy patients). Epilepsy before and around 20 years of age affected marital and fertility rates. The families transmitted information about the disease

to teachers/neighbours/colleagues and others in 94% cases. The help of faith healers was taken in 7.5% cases. Families adopted various management practices to control involuntary movements during seizures. A positive family history was recorded in 11% first-degree relatives and 4% second-degree relatives. Generalised seizures were noticed in 67.5% of idiopathic epilepsy patients, while partial seizures with and without secondary generalisation (50.5%) and generalised seizures (49.5%) were equally common in symptomatic epilepsy patients. Such trends find no mention in earlier Indian studies. The types of seizures show statistically significant differences.
Conclusion: The study demonstrated differences only in the type of seizures and not in other demographic, clinical and psycho-social traits. The males have a higher risk of epilepsy than females. The epidemiological characteristics of epileptics show variations across populations and within a population.

p1118
Working Conditions among People with Epilepsy
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Purpose: To know the unemployment rate and working conditions of patients with epilepsy in Spain and to identify which clinical factors may have an influence.
Methods: Between May and October 2001, a survey was carried out in 32 Spanish medical centres. The selection criteria were to attend a routine medical visit, to be aged between 16-64 years and not having learning disabilities. Patients were asked to fill out a self-administered questionnaire that collected socio-demographic characteristics and questions related to their employment status and working conditions. Only 4% of the patients refused to answer the questionnaire. Multiple logistic regression models were fitted in order to calculate adjusted odds ratios (aOR) and their 95% confidence interval.
Results: 9,90 patients were included. The proportions of men and women were similar, mean age 38 years (sd=11.7). The unemployment rate was 12% (9% men and 13% women). About half of the unemployed epilepsy patients considered that epilepsy was related to their unemployment. Variables associated with a higher risk of unemployment were age of epilepsy onset, aOR=2.67[95%CI=1.13-6.32] and seizure frequency, aOR=2.68[95%CI=1.43-5.00]. Only 8% of the epilepsy patients had employees. 21% of the patients had precarious work. These and other variables studied were related also with age of epilepsy onset and seizure frequency.
Conclusion: The unemployment rate found in our study is similar to the Spanish rate of unemployment. Earlier age of onset and higher seizure frequency increase the risk of occupying an unskilled job and decrease the possibility of having employees; gender differences also exist.

p1119
Epilepsy Care in Rural Zimbabwe: A Global Campaign Against Epilepsy Project
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Purpose: 1) To establish the burden of epilepsy in a rural area of Zimbabwe by estimating the number of people with active epilepsy not receiving available treatment, i.e. the treatment gap. 2) To assess the impact of epilepsy on the Q.O.L of the people and their family. 3) To test interventions to improve the treatment gap with available means.
Methods: Hwedza district, a mainly communal farming area with a population of 90350, was selected and a community based prevalence survey carried out. Techniques were the same as used in a GCAE epilepsy project in China and in Senegal. (Neurology 2003;60:1544 – 1545 and Seizure 2005;14:106 – 111). Training of primary health care workers from all health facilities in the district in the diagnosis and management of epilepsy using a specially developed teaching module was carried out. Community health campaigns mounted by primary health care staff were held. Newly diagnosed people with epilepsy were followed up in the community.
Results: In the year before the project (2000), 41 PWE were under treatment (a 'pseudo-prevalence' of 0.45/1000). The prevalence study sampled 6274 persons and demonstrated an actual prevalence of 13.39/1000, and therefore a treatment gap of 93.1%. After the interventions a reduction of the treatment gap by 10% has been achieved.
Conclusion: This report is partial as a result of changes in the political and economic situation in Zimbabwe. Nevertheless the number of PWE receiving treatment after the intervention has more than doubled.

p1120
Labour and professional satisfaction in patient with epilepsy.
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Purpose: To detect possible deficits in shaping professional motivation as a special feature of personality.
Methods: 60 patients with diagnosed epilepsy were studied by means of the Washington Psychosocial Inventory (WPSI). Other techniques used were interviews and autobiographies, which aimed to determine the patients' level of professional and job satisfaction.
Results: There is job and professional dissatisfaction in most of the studied subjects. The testimony from one of the patients is presented to illustrate misunderstandings and limitations these people with epilepsy face from school days to working times.
Conclusion: Evidence was collected on the existence of prejudices and wrong ideas concerning epilepsy, which hinder a solid motivational forming in this area.

p1121
Epilepsy as a Cause of Mobbing: Study of Social Problems of Polish Epilepsy Patients in their Jobs
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Purpose: The aim of this study was to assess whether social attitude to epilepsy patients may be a factor disturbing normal professional development of the patients.
Methods: We have used an original questionnaire focusing on the issues of employment and work. Those questionnaires were sent to Polish local associations of patients with epilepsy by mail. Members of the associations were supposed to send back the completed questionnaires.
Results: We sent out 300 questionnaires and we received 118 completed questionnaires. We received questionnaires from 57 women and 61 men. The mean age of the examined group was 37.2 years. 31 patients had never worked in their lifetime, 81 patients have some job experience and 25 had a job at the time of the study. Among the patients who had worked 41 (50.6%) had to change their job because of epilepsy. 31 patients (38.3%) believe that they were laid off because of epilepsy at least once. The majority of the patients have informed their employers (80.2%) and their co-workers (70.4%) about their disease. 45 patients (55.6%) have experienced some forms of mobbing, e.g. nastiness, social isolation, lack of trust, because of being ill. 46 patients (56.8%) believe that due to epilepsy they are less worthy workers and 86 patients (72.9% of the whole examined group) believe that epilepsy makes finding a more satisfying and better paid job impossible.

Conclusion: We found that epilepsy is a significant risk factor of mobbing. It prevents the patients from satisfying professional development and makes earning their living difficult for them.

p1122
Significant Variables Associated with Epilepsy
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Purpose: To study the characteristics of people with epilepsy and the risk factors contributing to the development of epilepsy.
Methods: We report on a descriptive study conducted at the Free Epilepsy Clinic at Ahbab Hospital, Lahore from June 2002 to August 2002. Data was collected from 158 subjects, 89 males and 69 females, suffering from epilepsy. The information about socio-demographic characteristics and family history of illness, perinatal morbidity, birth place and mother's age at the time of delivery was obtained using a pre-tested questionnaire. Data was analysed on SPSS version 10.
Results: The majority of the subjects were single (77.84%), 1st born among their siblings (25.95%), belonged to a low social class (50.63%), and were unemployed (25.31%). The major risk factors were family history of illness (23.52%) and positive medical problem around birth (12.66%). The presence of family history of illness, positive medical problem around birth and advanced maternal age at birth were associated with early onset of epilepsy.
Conclusion: Although the present study has identified various risk factors, the results need to be further confirmed through case-control studies.

p1123
What Kind of Seizures Appear Just Prior To, or Closely After Termination of Long-term EEG Monitoring?
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Purpose: At our centre ictal EEG registrations in the epilepsy monitoring unit (EMU) are an important tool to diagnose, classify, and localise the epilepsies. The unit is of special importance to differentiate between epileptic and psychogenic non-epileptic seizures (PNES). Previously, we have offered patients a flexible and individualised monitoring time at EMU. Due to capacity problems we now practice a fixed duration of registrations (24-72 hours). The aim of this study was to assess 'lost seizures', i.e. how many patients suffered seizures just prior to, or soon after the termination of the registrations. We also wanted to characterise those who had seizures during EEG registrations, those who had not, and those who experienced seizures close to the registrations.
Methods: We assessed all patients admitted to the department for adolescents from 11 January 2004 to 15 February 2005. We also recorded demographic and clinical data, results from long-term EEG monitoring (LTM) and diagnoses at discharge from our centre.
Results: 57 patients were admitted once or twice during the period and 40 patients had long-term EEG registrations. 17 patients (42%) experienced seizures during the stay at EMU and 11 (65%) of these had EEG correlations. 23 patients had no seizures during LTM, 9 (41%) of those experienced seizures close to LTM. 8 of the 23 patients (35%), and 5 of the 9 patients who had seizures close to LTM, had a diagnosis of PNES at discharge.
Conclusion: By having a fixed duration of registration at EMU we achieved ictal registrations in 42% of the patients. 5 out of 9 patients who experienced seizures close prior to, or closely after the registration were diagnosed to have PNES.

p1124
Infirmary Studies of the Relationship Between Anatomic-function Alterations to the Ovaries and Old Anti-epileptic Drugs Taken by Women with Epilepsy During Their Fertile Years
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Purpose: One of the objectives of nursing consultants, specialising in epilepsy, is to know the relationship between old anti-epileptic drugs and hormonal or anatomical alterations in women who visit our clinic.
Methods: The study has been undertaken over a 2 year period on a population of women aged between 17 and 44 who belong to our health area of influence in Madrid. We also investigated a protocol of appointments and diagnostic tests, plus a review of pharma treatments during the study.
Results: From the total number of women studied from an anatomical point of view, 76.5% had ultrasound results with no alterations, 21% presented follicular alterations in both ovaries, 1.1% only in their right ovary and 1.4% in their left ovary. Functional tests showed 73.5% were normal and 26.5% with alterations.
Conclusion: Our study shows that functional alterations found in women with epilepsy seem to be related to old anti-epileptic drug intake, but are not related to new generation drugs. In order to demonstrate this, we believe that further research needs to be done.

p1125
Barriers to the Use of Diazepam Rectal Gel in Day Care and School Settings
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Purpose: Children with epilepsy are frequently prescribed diazepam rectal gel for the acute treatment of seizures outside of the hospital. Parents have reported resistance by schools and daycare providers to administer diazepam rectal gel. The purpose of this study was to identify the frequency with which parents of children with epilepsy experience barriers to the use of diazepam rectal gel in daycare or school settings, what those barriers are, and what the impact is on the child and family.
Methods: During a six-month period, parents of children under 19 years seen in an epilepsy clinic who previously were prescribed diazepam rectal gel were asked to complete an 18-item questionnaire.
Results: Of 218 parents screened for the study, 86 parents qualified, and 64 parents completed the questionnaire. Of those 64 parents, 43 (68%) had asked their school or daycare provider to administer diazepam rectal gel to their child. Of those 43 parents, 35 (81%) reported that the school agreed and 8 (19%) reported the school refused to give diazepam rectal gel. Of those 8 parents, 5 (62%) reported the reason for refusal as legal concerns and 5 (62%) reported some impact on their family as a result of the school's refusal.
Conclusion: Our study demonstrated that the majority of children prescribed diazepam rectal gel do not encounter barriers to its use in school and day care settings. When such barriers exist, however, they are most frequently related to legal concerns and the quality of life of the child and family can be significantly impacted.

p1126
Prevalence of Post-Traumatic Epilepsy Among Patients Seen in a Private Clinic
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Purpose: The aim of the present study was to find out the prevalence of seizures caused by head injury among patients with epilepsy and the various contributing factors responsible for the development of such seizures.
Methods: This study was conducted retrospectively on patients with epilepsy attending my clinic. All patients were interviewed for a detailed history with special stress on their history of head trauma. All

cases with a history of head trauma were selected for further evaluation. The medical records of the index cases were reviewed for details of head trauma; type and severity of injury. All investigations in the records were reviewed, especially radiological imaging and EEG.
Results: We screened 1470 patients with epilepsy; 101 patients had a past history of head trauma. Road traffic accidents were responsible for 80% of the head trauma, followed by falls from a height 15%. Most of the patients (90%) had their seizures within the first five years after the head trauma, The shortest time between trauma and onset of seizures was 6 months, the longest time was 8 years following severe head trauma. Partial seizures with secondary generalisation was the commonest type of seizures found in 49.5% of patients followed by generalised tonic-clonic seizures in 25.7%, while complex partial were found in 12.87% and simple partial seizures in 11.88%. EEG was positive in 85% of cases and helped in classification of the type of epilepsy.
Conclusion: Post-traumatic epilepsy represents about 7% of the epileptic population in this study. Most of the cases are caused by road traffic accidents. Improving the quality of safe driving for both drivers and pedestrians could prevent a high percentage of head injuries and subsequent epilepsy.

p1127
A Personal Account of Epilepsy and Anxiety Disorder
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Purpose: This study aims to assist people with epilepsy experiencing a form of anxiety disorder for various reasons; The diagnosis of epilepsy, anxiety as a symptom, a traumatic experience.
Methods: A self-study of a subject through consultations with neurologist, psychologist and social worker: anxiety developed after diagnosis of epilepsy; the fear of having a seizure after an 'aura' and reaction of witnesses; social phobia due to rejection; identifying other symptoms of anxiety due to traumatic experience; consultations with neurologist confirmed certain experiences were related to epilepsy and others to anxiety disorder; neurologist referred subject to psychologist with regard to anxiety disorder and prescribed anti-anxiety medication along with anti-convulsant medication; psychologist dealt with anxiety disorder through counselling and suggested physical exercise to alleviate symptoms of anxiety disorder i.e. breathing difficulty; social worker dealt with traumatic experience through counselling; medical treatment and psychotherapy determined a link between the two conditions as well as the similarities presented in the subject.
Results: This study determined that people with epilepsy could experience an anxiety disorder. It can sometimes be confused as epilepsy due to the symptoms of anxiety; i.e. intense feelings of nervousness, fear, hyperventilation, accelerated heartbeat, flushing of skin.
Conclusion: Thorough investigation of symptoms through psychotherapy and medical tests can determine whether symptoms are epilepsy or anxiety related or both. My conclusions are based on consultations with neurologist Dr. E Lee Pan, UCT Medical Centre and Diane Mallaby, Counselling Psychologist.

p1128
Access to Healthcare: United States Epilepsy Centres and the Hispanic Population
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Purpose: Statistical research and community outreach to our communities show Hispanics to be medically underserved by virtue of: location, lack of education, low income, inability to speak English and fear of healthcare and other complex systems. Dramatically growing in numbers, and facing economic, cultural and linguistic barriers to personal health services, many are left unaware of basic epilepsy education and many more are unaware of services provided at comprehensive epilepsy centres.
Methods: In order to determine if epilepsy centres throughout the US are recognising and addressing the needs of the Hispanic population, a survey was sent to the directors of every centre throughout the States. 35 directors of the 73 centres responded (47.95%).
Results: 20 (57%) report a rise in Spanish-speaking patients. 11 (41.43%) of the centre directors speak Spanish. 23 (65.71%) employ Spanish-speaking physicians. 22 (62.86%) employ Spanish-speaking support staff. 29 (82.86%) have Spanish educational materials available. 33 (94.29%) have access to an interpreter. 8 (22.86%) have their own Hispanic outreach program.
Conclusion: Our results show the great efforts of responding epilepsy centres to the needs of this population. They are creating a venue where Hispanic access to information about epilepsy and healthcare is viable, professional interest is stimulated, and the gap between what physicians know and what patients understand is closing. An increase in the use of formalised outreach programmes using local native-speaking representatives would further this trend.

p1129
Neurocysticercosis: Analysis of a Preventable Cause of Epilepsy in a Rural Sector of India
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1) Karandikar Hospital and Research Centre, Nasik, India.

Purpose: Neurocysticercosis is the most common parasitic disease of the central nervous system and is a preventable and treatable cause of epilepsy. This study was undertaken to analyse the incidence, distribution patterns, epidemiological factors, clinical presentation and socio- demographic elements influencing the cause of the illness, to formulate definitive preventive protocols.
Methods: 586 patients with epilepsy attended the institute over 7 years. Out of these, 83 patients from rural areas with neurocysticercosis were included in the study. A diagnosis was made based on the CT scan findings and haematology. A retrospective analysis was done based on age, occupation, education, sanitation facilities, water source, type of seizures and follow up pattern.
Results: 83 out of 586 patients (14.16%) of epilepsy were found to have neurocysticercosis. 65% of patients were in the age group 10-30 years, 53.12% of these were uneducated. The main occupation was farming (66.26%). Sanitation facilities were available to 68.6% of individuals. 54.21% had well water as the only source of drinking water. The commonest presentation was generalised seizures (43.37% of patients). Regular follow up after education and counselling was found only in 63.58%.
Conclusion: The subgroup between 10-30 years was found to be of significant importance. Epilepsy in these formative years of life endangers the educational, occupational, social, economic career of these individuals. Definitive protocols for education, sanitation facilities, propagation of healthy habits can improve the situation and prevent these individuals from neurocysticercosis and hence, the stigma of epilepsy.

p1130
Physical Activity in Children and Adolescents with Epilepsy
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Purpose: To study sports inclusion and the level of physical activity among children and adolescents with epilepsy, and to identify predictors of active living.
Methods: A questionnaire was given to 180 children and adolescents with epilepsy, aged from 6.5 to 22 years. Six domains were assessed: sports inclusion and participation, physical activities and their level, socio-demographics, attitudes toward sports, sociability, and epilepsy characteristics.
Results: Analysis of physical activities showed that 65-93% of children with epilepsy were periodically engaged in leisure time activities, 70% participated in school physical exercises, and nearly

38% were included in structured sporting activities. The highest level of physical activity was concluded in 35% of these children and adolescents, intermediate, but insufficient engagement was noted in 40%. A subgroup of 25% was almost inactive, reporting the lowest level of active living. Factors consistently associated with improved active living in epilepsy were male sex, living with parents, city residence, positive attitudes toward sports and epilepsy, and perceived importance of physical exercising ($p<0.01$). School experiences, environmental relations, and sociability were also identified as important parameters. However, illness severity index (comprising seizure type, seizure frequency, and antiepileptic drugs) emerged as the most important determinant for sports inclusion ($r = -0.842$, $p<0.01$).
Conclusion: Active living in youth with epilepsy is irregular, insufficient, and heterogeneous. Personal attitudes, sociability, and seizure control had the strongest influences on the levels of physical activity. Interventions to improve these variables could bring better physical activity to these children and adolescents.

p1131
Science and Prejudice: A Social History of Epilepsy in Brazilian Early Medical Academic Writings 1859 - 1906
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Purpose: The main objective is to study Brazilian medical writings on epilepsy from 1859 (first doctoral thesis about epilepsy in Rio de Janeiro Medical School) to 1906 (Golgi and Cajal Nobel Prize) in order to identify particular patterns of prejudices and stigmas towards this illness and its patients and to verify how current prejudices at the time towards epilepsy are present among Brazilian physicians and how specific stigma, peculiar of a hierarchic and slave-labour based society, appears in academic papers.
Methods: Historical analysis of medical doctoral thesis about epilepsy or related subjects and of papers published in Brazilian Medical Journals. Iconography (religious, moral and medical) and literature are considered subsidiary documents.
Results: 25 doctoral theses on epilepsy have been studied (76 identified) and are very similar, follow the same narrative protocol and show a main influence of French physicians. Prejudices towards patients with epilepsy are patent (vocabulary, aetiology, treatment procedures, moralising accent, social issues). Different approaches and public health policy are more openly discussed in Medical Journals (34 titles), where it is possible to identify a lineage of Brazilian physicians, influenced by Lombroso's theories, that directly linked epilepsy and criminal tendencies and had a great ascendance in criminology and public health policy.
Conclusion: Further research is required, but it is possible to state that gender, moral and sexual prejudices as well as social stigmas are strongly present in the early Brazilian medical writings about epilepsy, while there is a significant silence about racial issues. Sponsors: CNPq and FAPERJ (Federal and State Research Councils).

p1132
Stigma in Mexican Epilepsy Patients
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Purpose: Stigma is defined as the clue that a disease leaves in the body or the characteristics that define a person who is affected by an illness. Stigma is an embarrassing self-perception that concerns the person more than the illness itself, makes the person feel ashamed and leads to depression among other psychopathologies.
Methods: The research was carried out during the III Latin American Epilepsy Congress in Mexico City on 2 July, attended by 600 persons with epilepsy and their relatives. 185 patients older than 16 years agreed to answer the following questionnaire: I feel that people are not comfortable with me. I feel some people treat me as inferior. I feel some people prefer not to be with me. Each question was to be answered with YES or NO, and each YES scored 1 point.
Results: 63 (34%) persons answered NO to all questions, 31 (16.7%) said one YES; 37 (20%) had two YES and 54 (29.3%) answered three YES. At least one YES was considered indicative of stigma.
Conclusion: The application of a similar questionnaire in 14 European countries (5211 persons) showed stigma in 51%; in Atlanta, USA, among 314 patients 54% manifested stigma and in Stonia 51% from 90 patients had it. We did not correlate with other variables, because the aim of our study was only a screening of an open population obtained from an invitation through radio and TV to attend the congress. Our results indicate a larger population with stigma (66%) perhaps not correlated with more factors than the diagnosis of epilepsy itself.

p1133
Developing Approaches to Reducing Stigma of Epilepsy: Findings from a Rapid Appraisal of Epilepsy Care in Vietnam
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Purpose: We present findings from a rapid assessment conducted in two provinces in Vietnam, as part of an international collaborative research project which aims to inform development of culturally appropriate approaches to reducing epilepsy stigma and discrimination in the developing world.
Methods: Hand searching and collation of secondary data from accessible sources, and 24 key informant interviews.
Results: Available data provided variable prevalence figures, ranging from 3-10 per thousand. The discrepancy between the number of people estimated to have epilepsy from these figures and the number of people with epilepsy (PWEs) registered in the vertical health care programme suggests a significant treatment gap. There is also limited choice of antiepileptic drugs. Epilepsy denotes a disease characterised by weak nerves, seizures, loss of control and mental retardation. The most popular health seeking behaviour is 'having illness, pray in four direction'. People seek treatment from providers operating at different levels and sectors, using both traditional and western medicines. Stigma was not explicitly stated, but observed in the form of barriers to employment opportunity, education and health care and reduced social interactions. Low expectations about the learning abilities of PWEs together with the abruptness of seizures acted as major barriers to employment. In addition, inability to obtain a driving licence, and 'gentle treatment' from family members were forms of 'enacted stigma'. The level of stigma differed between urban and rural, North and the South Vietnamese communities.
Conclusion: The results of the rapid appraisal were used to inform a more detailed ethnographic study currently underway in two provinces. Presented on behalf of the CREST (Collaborative Research on Epilepsy Stigma) Study Group: Professor Charles Begley, Professor Gus A Baker, Ms Hanneke de Boer, Professor David Chadwick, Dr Dang Vu Trung, Ms Nguyen Thanh Huong, Professor Ann Jacoby, Dr Leonid Prilipko, Dr Ria Reis, Ms Dee Snape, Professor Wenzhi Wang, Professor Jian-zhong Wu. CREST is funded by the US National Institutes of Health.

p1134
Stigma Scale of Epilepsy: Epidemiological Study in Campinas
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Purpose: To estimate epilepsy stigma in an urban society in a country with limited resources.
Methods: This is a cross-sectional population-based study in Campinas, a large city with 1 million inhabitants in the southeast of Brazil. We applied Stigma Scale of Epilepsy (SSE) in 1,850 people from all the regions within the city following a sampling selection methodology (95% confidence interval and error of 2.3%). SSE consists of 10 questions that provide a total score ranging from 0 (no stigma) to 100 (highest level of stigma). SSE was developed and validated by our group and showed high internal consistency (α Cronbach's coefficient = 0.81).
Results: The mean age of subjects was 39 (range from 12 to 90 years) and 53% were woman. The general score of epilepsy stigma was 42 (range from 3 to 98; sd=14). Women had a higher SSE score (43) than men (40) (t-test [1848]=5.42; $p<0.001$). In regard to religion, spiritualism had the lowest level of SSE score (35); (ANOVA [4,1845]=4.4; p=0.0015, Tukey's: spiritism < catholic = evangelic = others = no religion). Level of education showed an inverse relation to SSE scores; illiterate people had a higher level of SSE score (45) than people with a university degree (37) (ANOVA [4,1845]=16.3; $p<0.0001$).
Conclusion: Our study showed that the magnitude of stigma is different within segments of our society, highlighting that sociocultural factors, such as gender, religion, and level of education are important predictors of stigma. Mass media campaigns should target these social segments to fight prejudice and improve social acceptance of people with epilepsy.

p1135
Cultural Attitudes and Beliefs Concerning Epilepsy in East Timor: A Pilot Study
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Purpose: The East Timor National Mental Health Project was established to set up a mental health service in East Timor, the world's newest democracy and one of the poorest nations in Asia. As a result of successful treatment of individuals with psychiatric disorders, people with epilepsy sought treatment from Specialist Mental Health Services. Attitudes and beliefs regarding mental health disorders and epilepsy appeared similar. A pilot survey of cultural attitudes and beliefs about epilepsy was carried out.
Methods: A door-to-door survey of 200 households in the Mascarenhas area of Dili (capital of East Timor) was carried out in March 2003. If the informant stated that a member of the household suffered epilepsy, a questionnaire was completed. Identified patients were examined by a neurologist to verify the diagnosis.
Results: The 200 households represented 1252 people, of whom 27 (approx 2.5%) were believed by the informant to have epilepsy. 74% believed that epilepsy was caused by a curse. 67% believed it resulted from their having done something wrong and 17% believed they were being punished by God. However, almost half considered it a medical problem. Despite this, only 9% had seen a medical doctor and none were receiving appropriate treatment. 55% had received treatment from traditional healers.
Conclusion: Superstitions in the East Timorese community concerning epilepsy are widely held. Although many people feel that epilepsy is also a medical problem, few seek medical treatment.

p1136
Recommendations for Regulations: The Development of Guidelines for Driving and Epilepsy in the European Union
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Purpose: To give an overview of the data on which recommendations concerning epilepsy and driving can be based and the line of thought that was followed by the Working Group on Epilepsy and Driving, an advisory commission to the Driving Licence Committee of the European Union in giving recommendations for implementation in European Law.
Methods: A literature search was performed for the different clinical situations (first seizure; epilepsy; seizures only in sleep etc) to determine the level of risk, expressed as the Chance of an Occurrence of a Seizure in the next Year (COSY) for each of these situations and after different seizure-free periods. An acceptable level of risk for the individual patient on the one hand and for society on the other hand was proposed. These data were compared to each other to arrive at a corresponding required period of freedom for each clinical situation. Some other factors were considered.
Results: Recommendations were given that are intended to be liberal, simple, clear and consistent.
Conclusion: A relative risk for the individual driver of 2 to 3, implying a two- to threefold increase in risk of an accident, dependent on the clinical situation, seems a fair choice for the patient, since it is in accordance with a number of accepted risks in society and will keep the 'attributable risk' (the risk for the population) under 0.5 to 1%.

p1137
Assessing the Disease Burden due to Epilepsy by Disability Adjusted Life Year in China
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Purpose: To demonstrate the application of Disability Adjusted Life Year (DALY) as an aid in health outcome measures to evaluate the epilepsy disease burden in China. To provide a Chinese data to achieve a better understanding of the disease burden due to epilepsy.
Methods: The DALY is the sum of the number of years of survival with disability (Years Lived with Disability, YLD) and the number of years lost due to premature mortality (Years of Life lost, YLL). We calculated the YLD based on the prevalence survey of epilepsy among 66,393 people sampled in 6 provinces in 2000. The epilepsy mortality data from the Global Burden of Disease study provided the YLL due to epilepsy. We applied sensitivity analysis based on the Chinese literature estimates of mortality range to calculate the plausible range of epilepsy DALY.
Results: In 2000, the trend of DALY lost was similar to that of the prevalence of epilepsy in 6 provinces in China. Epilepsy caused 0.73 and 1.29 DALY lost per 1000 population in Shanxi and Ningxia province, which had the lowest and the highest DALY lost among the 6 provinces. The mean DALY lost due to epilepsy was 0.93 per 1000 population in China. Sensitivity analysis showed that the disease burden due to epilepsy was between 1.37 and 2.31 DALY lost per 1000 population based on the plausible range of epilepsy mortality.
Conclusion: The DALY measure, which includes the extent of disability from epilepsy, provides a useful tool for the epilepsy disease burden assessment.

p1138
Cost of Epilepsy in Turkey
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Purpose: Epilepsy poses a considerable economic burden on society. However, especially in Turkey, information about the cost of epilepsy is insufficient against the comparative costs of different diseases. The aim of this study was to compare the cost of epilepsy with diseases of different severity.
Methods: 141 patients were evaluated in this study. Mean age was 29.6. 66 (46.8%) of these patients were male and 75 (53.2%) were female. Patients were divided into four groups according to the severity of disease: A) newly diagnosed patients; B) patients with epilepsy in remission; C) patients with well controlled epilepsy (seizure reduction was greater than 50% with antiepileptic drug treatment); D) patients with poorly controlled epilepsy (seizure reduction was smaller than 50% antiepileptic drug treatment). All data (including blood tests, consultations, drugs and hospital admission) was collected for each patient in Ministry of Health Ankara Training and Research Hospital during one year and the annual cost was calculated.
Results: The mean annual cost for each patient with epilepsy was 871 Euros. Group D was the most expensive group (1820 Euros), followed by Group C (743 Euros), A (533 Euros) and B (388 Euros). Drugs were the major cost in Group B, C and D, while the cost of EEG and neuroradiological imaging was more prominent in Group A.
Conclusion: The cost of epilepsy in Turkey was varied especially depending on the severity of the condition and the response to treatment. Drugs played a significant role in the cost.

p1139
Cost-Effective Analysis of Epilepsy in 'WHO Epilepsy Demonstration Project in China'
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Purpose: In order to know the economic burden of epilepsy, the cost-effectiveness of epilepsy was analysed in the Ningxia area of the WHO demonstration project of epilepsy.
Methods: 106 patients with convulsive epilepsy were randomly selected from Ningxia 'demonstration project' areas. These patients were asked their seizure history, diagnosis, post treatment and last one-year cost, and situation of work or labour before entering the project. Patients received treatment with phenobarbital according to the technical norms of 'demonstration project'. Patients were followed-up once every three-months.100 cases finished the one-year cost-effectiveness survey. It included seizure numbers, phenobarbital dosage, side effects, compliance, work or manual labour ability, seeing doctor times, and costs in the past three months.
Results: Most patients have taken anti-epileptic drugs (AEDs) irregularly. Except for AEDs taken, 61 cases accepted other treatment, such as traditional Chinese medicine (46 cases), acupuncture (26 cases), folk prescription (35 cases), and so on. 45 cases remembered their cost average 1,355 ± 2,195 yuan (20 to 10,000 yuan). Before entry to phenobarbital treatment, they had seizures on average 19 ± 23 times/year (2 to 180 times). After one-year phenobarbital treatment, their seizures decreased to 12 ± 28 times/year (0 to 169 times). There were 44 cases seizure free, 29 cases with a seizure decrease >50%. Work or manual labour ability of patients was improved. Patients with full time work increased from 12 cases to 32. Patients with part time work increased to 8 cases. Patients with lost ability or staying at home obviously decreased. The cost of treatment of 1 patient is about 150 yuan per year (including phenobarbital 30 yuan and physician allowance 120 yuan). The patient would spend a minimum of 690 yuan and max 5,928 yuan per year, if receiving regular anti-epilepsy drug treatment in a general hospital in the same area.
Conclusion: Most patients with epilepsy in rural areas received irregular anti-epilepsy treatment and spent a lot of money. 'WHO Epilepsy Demonstration Project in China' has proved that phenobarbital is a cheap, safe and effective anti-epilepsy drug. This project has value to popularise, especially in developing countries, the poverty area.

p1140
Cost-effectiveness Study of Phenobarbital Treatment for Epilepsy in Rural China
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Purpose: As an additional resource utilisation component to the assessment package of the Global Campaign Against Epilepsy primary care demonstration project in rural China, this study evaluated the cost-effectiveness of phenobarbital treatment for epilepsy in rural Chinese patients.
Methods: In Ningxia and Shanghai rural areas, 150 involved epilepsy patients were randomly selected and asked for their medical expenses one year before and after the standardised phenobarbital treatment. The effectiveness of phenobarbital treatment came from the results of the demonstration project.
Results: The standardised phenobarbital treatment was cost saving compared to the baseline with non-standardised treatment. In Ningxia, the net cost saving was 1043.40 yuan per seizure free case and 1583.09 yuan per effective case (seizure decrease >=50%). 66.73 yuan was spent to prevent one epileptic seizure by phenobarbital treatment. These three indices were 2433.42, 2901.39 and 53.58 yuan in Shanghai, respectively.
Conclusion: The demonstration project of phenobarbital treatment resulted in high cost savings in Ningxia and Shanghai rural areas compared to non-standardised treatment. The good results of the cost-effectiveness suggest that standardised phenobarbital treatment may be economically justifiable and worth the expenditure.

p1141
Knowledge and Economic Impact of Epilepsy in a Rural Population near Chennai, India: A Pilot Study
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Purpose: Awareness of epilepsy among patients and care givers forms an integral part of management of epilepsy in order to achieve total compliance and to prevent recurrences. The study aims to address various social aspects of epilepsy.
Methods: 70 people with epilepsy who were labourers on daily wages of £ Rs 200 (US$4-5) were selected from 83 epilepsy patients attending the outpatient neurology clinic at Sri Kanchi Kamakoti Sankara Hospital. All patients were subjected to a Proforma based questionnaire filled in by a trained health worker and evaluated by a neurologist.
Results: The age group ranged from 6- 67 yrs (46 males, 24 females respectively). Mean duration of epilepsy was 5.70 ± 5.54 yrs. 82.85% of patients had no education about epilepsy; only 17.14% knew that epilepsy was related to the brain and needs regular reviews and long term treatment. 28.75% had myths that epilepsy was caused by ghosts or evil spirits. 62.8% were unaware that epilepsy was of different types. 48.75% said that they would use a piece of leather or metal, e.g. a key, during an acute attack. Only 34.3% of patients felt that people with epilepsy could lead a normal life. A large percentage of patients 71.42% were unaware of first aid for an epileptic fit.
Conclusion: This study reveals that there is ignorance regarding various aspects of epilepsy. The treating physician therefore has the responsibility to educate the patients and the public and involve social and governmental organisations to a larger extent.

p1142
Epilepsy Treatment Costs in a Chilean Population
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Purpose: Epilepsy is one of the most frequent chronic neurological diseases, with a Chilean prevalence of 17-21/1.000 inhabitants. In past years, there is concern for the high costs involved in its handling. The objective of this study is to estimate the direct costs of treatment and handling in a specific population with epilepsy.
Methods: Retrospective work, with 6 groups of people with epilepsy: a) recent diagnosis (RD); b) Remission ®; c) occasional seizures (OS); d) active without resistance to drugs (AWRD); e) resistance to pharmacological treatment (RPT); f) epilepsy surgery (ES). Data and characteristics tabulation and an economical study of each group were carried out, considering 1 year of treatment. A comparison was made between them and their average in relation to international data.
Results: 293 patients; 52% male, 76% adults, 25% students, 55% focal seizures. Costs per group: (US$/patient/year): RD 450; R 318; OS 418; AWRD 722; RPT 949; ES 4304. Direct average cost of treatment for epilepsy in this population: US$1194/patient/year.
Conclusion: When differentiating groups of individuals with epilepsy, the highest average annual cost is in surgery and the lowest in remission. In all groups, except for surgery, the highest expense is in medicines (average 77%). In relation to other countries, our direct costs are 2.3 times lower than in some developed countries and 5 times higher than in other developing countries. This data is of interest to influence governmental and financial spheres, so as to provide a better quality of life for people with epilepsy, specially lowering the costs and fees for their treatment. Epilepsy and surgery national programs are necessary.

p1143
Priority Issues for People Living with Epilepsy: A Pan Canadian Survey
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Purpose: To determine the national issues of greatest concern to people living with epilepsy in Canada.
Methods: A survey questionnaire was sent out to people living with epilepsy, their parents, their partners, medical personnel and the general public throughout Canada. Respondent were asked to indicate their top 3 choices from a list and briefly describe their statement and articulate any other concern not listed.
Results: 810 surveys were completed Canada-wide. Stigma 20.5%, driving regulations 14.5% and cost of medications 13% were the top 3 issues chosen. The results are analysed nationally and provincially and comparisons between subgroups of respondents were made.
Conclusion: Although the overall sample cannot be construed as random, it is representative of the population of interest. To our knowledge this is the only Canada-wide survey on this subject. In response to this survey, the CEA took steps that are briefly described to address these issues.

p1144
Establishment of Aims of the Associação Brasileira de Epilepsia Using a Questionnaire for People with Epilepsy in the City of São Paulo, Brazil
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1) Associação Brasileira de Epilepsia, São Paulo, Brazil

Purpose: Getting to know the profile of people with epilepsy (PWE) in the city of São Paulo, Brazil, an under developed country. To understand their expectations and necessities in order to establish guidelines to be followed by the Associação Brasileira de Epilepsia.
Methods: A person with epilepsy from the Associação applied a basic questionnaire to PWE in a tertiary epilepsy centre. This questionnaire was very simple, so as to be applied to people of any social class in the community.
Results: 411 (214 female) PWE and their families were interviewed. The ages varied between 2 and 66 yr. (69 were up to 6 yr; 111, 7-20; 231, 21-66). Among the adults, 117 were single, 96 married; 10 separated or divorced and 8 widows and widowers. Regarding schooling 53 were at school; 10 illiterate; 40 completed primary school and 81 incomplete; 57 completed secondary school and 22 incomplete; 10 completed university level while 11 incomplete. The most important factors that affected these PWE were: first, lack of medication (0-6:36; 7-20:64 and 21-66:112; this was independent of the schooling); second, lack of free transportation; third schooling; and fourth, unemployment.
Conclusion: In developed countries driving is one of the main aims; yet it was never mentioned by anyone. Among our PWE the burden of medication was a primary concern. It is almost impossible for them to deal with and the authorities do not support this basic need of PWE. Therefore, a close relationship with Governmental Health Assistance is the first step to be taken by the Associação in order to improve quality of life of PWE.

Wednesday 31st August and Thursday 1st September 2005
13:15 – 14:15
Poster Session
Alternative Therapies

p1145
Effect of Yoga on Autonomic Dysfunction Associated with Refractory Epilepsy
T.N. Sathyaprabha[1], P. Satishchandra[1], K. Netravati[1], S. Kaveri Bhat[1], S. Sinha[1], K. Thennarasu[1], T.R. Raju[1]

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Purpose: Patients with refractory epilepsy can have autonomic dysfunction (AD), which might play an important role in SUDEP. Yoga is a traditional Indian psycho-philosophical-cultural method that has multiple health benefits. The role of yoga as an intervention to manage autonomic dysfunction has been evaluated in this study.
Methods: A prospective randomised single-blinded study with 25 subjects (32.2±10.2years; M:F:15:10) with uncontrolled epilepsy (GTCS:6, Partial:19) attending the 'refractory epilepsy' clinic at a tertiary centre, with AD was conducted. Heart rate (HR) and blood pressure (BP) responses at rest and after deep breathing, valsalva manoeuvre, postural change and isometric work were recorded. AD was graded as early if either of the HR or BP test was abnormal, definite if two or more HR and severe if HR with BP based tests were abnormal. Hatha yoga, which includes meditation and yogasana, were administered as an adjuvant therapy for eight weeks, after which autonomic functions were re evaluated.
Results: The mean age at onset and duration of epilepsy was 13.5 and 18.7 years respectively. Their autonomic dysfunctions were classified as early-12, definite-9, and severe-4. The severity in terms of involvement, pre and post intervention was analysed using McNamara's test. There was a significant improvement in autonomic dysfunction–normalised in 9, early-10, definite-4, severe-2 from baseline to intervention of yoga (p=0.039).
Conclusion: Yoga has a definite role in the management of autonomic dysfunction associated with refractory epilepsy. As autonomic dysfunction is an important in pathogenesis of SUDEP, yoga could be used as an adjuvant therapy to possibly prevent SUDEP.

p1146
Refractory Epilepsy Management through Reflexology: A Non-pharmacological Method
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Purpose: Reflexology, a health science of studying human body and mind through reflex areas, was employed to manage patients who were suffering from refractory epilepsy and were surgical failures. For this purpose, the reflex regions of the vagus nerve were determined and indirect vagus nerve stimulation (indirect VNS) was applied to achieve the goal.
Methods: Sample age group is 5 yrs to 45 yrs. Duration of disease (D) is 3yrs≥ D ≥20yrs. Reflexology was employed in addition to the ongoing pharmacological drugs. Accurate pressure on the specified regions of hands and feet was applied to stimulate the reflex areas of the vagus nerve, body organs and glands. For a duration of one month, each patient was given stimulation on the reflex areas of the digestive system, urinary system, liver, adrenal glands and brain stem. In addition to these, from the second month onwards indirect VNS were applied at least 10 sessions per day with a minimum of 10 stimulations per session.
Results: The response of a sample size of 22 was monitored during a period of 6 months to 1 year. It was observed that there was an average reduction of 80% in seizure frequency, 60% reduction in duration of ictal phase, 75% prevention of seizure during aura and 75% of change in urinary-habit, sleep patterns and general behaviour.
Conclusion: The unique response of this sample group to indirect VNS reveals the effectiveness of this technique in managing refractory epilepsy patients with the least side effects and least cost, applicable at any place and any time in a nonpharmacological way, but with similar results to those obtained in an expensive procedure of VNS.

p1147
Effect of Elevated Blood-acetone Levels on Seizure Threshold in Kindled Rats: Implications for the Role of Acetone in the Anticonvulsant Mechanism of the Ketogenic Diet
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Purpose: The present study explored the relationship between blood-acetone levels and afterdischarge thresholds in well-kindled rats consuming a ketogenic diet (KD). We have hypothesised that acetone is responsible for the anticonvulsant actions of the KD. We have shown that acetone has a broad spectrum of anticonvulsant action, similar to the KD (Likhodii et al., 2003). We have also shown that blood-acetone is significantly elevated in children on the KD (Likhodii and Burnham, 2004). The purpose of this experiment was to determine whether elevations in acetone correlate with elevations in seizure threshold in well kindled rats fed a 4:1 KD.
Methods: 40 adult male Sprague-Dawley rats were surgically implanted with a chronic stimulating/recording electrode aimed at the amygdala. All animals were kindled to 30 stage-five seizures. Subjects were then divided randomly into one of four treatment groups: G1) KD + DAS; G2) KD + corn oil; G3) control diet + DAS; G4) control diet + corn oil. DAS and corn oil were administered intragastrically. Afterdischarge thresholds were determined every second day while subjects consumed experimental diets ad libitum. A blood sample (0.5mL) was drawn from the tail-vein before initiation of experimental diets and every second day (non-kindling day) during the remainder of the experiment. Blood was analysed to determine glucose levels (glucometer), β-hydroxybutyrate levels (ketometer), acetone and acetoacetate levels (high performance liquid chromatography). Levels of blood-glucose, β-hydroxybutyrate, acetoacetate and acetone were correlated with changes in afterdischarge thresholds.
Results: Blood-acetone concentrations were significantly higher in the KD+DAS group compared to other groups. However, none of the treatments elevated ADTs. Redetermination of ADTs showed that KD- and DAS-treatments prevented an otherwise significant drop in ADT seen in the CD+vehicle group.
Conclusion: The KD was unable to elevate ADTs in fully-kindled rats. KD+DAS subjects achieved blood-acetone levels of ~0.2mM. Previous research has shown that ~10mM concentrations are required to suppress 50% of generalised amygdala-kindled seizures in rats. Humans on the KD may develop blood-acetone concentrations between 1-10mM, however, rats can not achieve such levels. The present study does not discount the possibility that acetone may play a role in the KD's anticonvulsant activity in humans. It does, however, suggest that adult rats are not ideal subjects for modelling the KD.

p1148
Effects of Seizures on Quality of Life
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Purpose: Our main goal was to evaluate whether epilepsy affects quality of life (QoL), including its effects on the patient's emotion, physical and psychosocial functioning, and employment.
Methods: We studied 140 outpatients with epilepsy who were routinely examined in the outpatient clinic of epilepsy in the University Hospital of Campinas, SP, Brazil. The quality of life questionnaire (QQV-65) was individually applied to all patients.
Results: The total score of QoL ranged from 28 to 93.24 (M=61,17, SD=15.66). Among all variables investigated using the QQV-65, the most negatively affected was the sense of good health (M=52.28), followed by emotional (M=56.28) and social (M=57.77) aspects, self-concept (M=62.74), locus of control (M=63.02), and physical and cognitive (Mean=68.03) aspects. No evidence of significant correlations between QoL and age, sex, educational level, marital status, or religious beliefs were found. In contrast, there was a significant association between unemployment and epilepsy. There was a strong and positive association between those patients who perceived their seizures as controlled and all aspects of quality of life.
Conclusion: Our results indicate that the stigma of epilepsy still profoundly affects the patients' self-esteem and limits job opportunities, whereas treatment and good seizure control positively contributes to a better quality of life.

p1149
Low Power Laser Irradiation can Increase the Threshold of Paroxysmal Discharge in the Rabbit Hippocampus CA1
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Purpose: An Ih blocker, ZD7288 has a potential of antiepileptic effects: it significantly increased the threshold of electrically-induced paroxysmal discharge (PADT) in the rabbit hippocampus CA1. Ar+ laser irradiation blocked the generation of anode break excitation in frog sciatic nerves, and such an effect was similar to that of ZD7288 application. We examined effects of low power laser irradiation on PADT in the rabbit hippocampus CA1.
Methods: 26 adult male rabbits were anaesthetised with pentobarbital sodium and immobilized with D-tubocurarine. A pair of concentric electrodes was implanted into each hippocampal CA1 region: the right anterior electrode was used for stimulating as well as laser irradiation. The stimulus train was 1-ms biphasic pulses of 50 Hz for 1 s. Low power diode laser (Nd:YVO4; 532 nm; 0-200 mW) was introduced with an optical fibre (125 μm). We measured PADTs before and after the laser irradiation.
Results: The averaged PADT was 3.8±0.4 V (mean ±SE; n=18) before laser irradiation, whereas after 10 min laser irradiation of 50 mW, 75 mW, or 100 mW, it changed to 4.6±0.7 V (n=11), 4.6±0.8 V (n=11) or 5.4±0.6 V (n=14), respectively. The PADT increment in the case of 100 mW was statistically significant ($p<0.05$). The effects showed a power-dependency and a radiation time-dependency. The histological damage was ranged over 0.5-1.0 mm from the irradiation spot.

Conclusion: Based on the PADT increment, it is concluded that laser irradiation with a specific wavelength and an average power has a potential to suppress the generation of paroxysmal discharge.

p1150
Effects of Neurofeedback Training on Quality of Life in Patients with Refractory Epilepsy
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Purpose: To evaluate the effects of neurofeedback on quality of life in patients with refractory epilepsy.
Methods: A prospective controlled single-blind trial was conducted with EEG biofeedback training. Subjects (n=34) were randomly allocated to training with either a SMR (sensorimotor rhythm, 12-15Hz) protocol or to a non-neurofeedback control group. Subjects were assessed prior and subsequent to the training process on test of QOLIE-31, Hamilton Depression Scale (HDS), QEEG and seizure outcome. Subjects (both group were refractory patients with epilepsy) continued to take their primary anti-epileptic drugs (AEDs) and neurofeedback training was as an add-on therapy.
Results: 30 patients finished the 30 sessions training, 17 in the neurofeedback group, 13 in the control group and the other 4 patients discontinued the training after 5-10 sessions. In the neurofeedback training group, 3 patients were seizure free, 10 reduced the seizure onset frequency less than 70%, 4 had no change; in the control group, no patients were seizure-free, 3 decreased seizure frequency less than 50%, the others had no change. The overall scale of QOLIE-31 was significantly increased after training in the neurofeedback group, and the HDS scale was reduced significantly in the control group. The significantly improved aspects of QOL were seizure worry, energy fatigue, emotional well-being.
Conclusion: Neurofeedback training of SMR band led to significant improvement of QOLIE-31. The long effects of neurofeedback training in epilepsy patients are the next focus.

p1151
Protective Effects of Mild Hypothermia on Seizure-induced Brain Injury in Rats
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Purpose: To assess the neuroprotective effects of mild hypothermia on seizure-induced brain damage in rats.
Methods: All experimental animals (18-21 days postnatal male Wistar rats, weighing 45-50g) were provided by Laboratory Animal Department of Fudan University. The rats were given 150-180mg/kg pilocarpine (i.p.) to set the status epilepticus (SE) model. The SE rats were put into the cold box (6-8 oC), to maintain the rats' rectal temperature to 33-35oC for 72h. Pathological changes of the hippocampus were observed.
Results: In the SE model, seizure-induced damage can be found: neuronal necrosis , apoptosis and reactive gliosis in the hippocampus. After 72h mild hypothermia, the percentage of neuronal necrosis in the CA3 region was significantly reduced from 72.1±13.4% to 17.0±6.8%; apoptosis of the CA1 region was significantly reduced from 9.4±6.2 to 1.0±0.7/unit area caspase-3 positive area per unit was significantly reduced from 1.49±0.25 to 0.60±0.12 and glial cells were significantly reduced from 47.3±2.6 to 14.3±4.4/unit area.
Conclusion: Mild hypothermia may have the neuroprotective effects on seizure-induced hippocampus neuronal degeneration in rats.

p1152
Nutrition Status of Medically Refractory Patients Compared with Seizure-free Patients
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Purpose: To our Knowledge, the nutrition status of patients with epilepsy has not yet been thoroughly investigated, therefore both overweight (Body Mass Index - BMI >25) or underweight (BMI <20) status are medical problems to be considered. Objective: To evaluate the nutrition profile of patients with difficult to control epilepsy.
Methods: The authors performed a prospective study of the patients consecutively seen in a 3-month period in our outpatient department. 74 patients were included (42 women, 32 men; mean age 35.2 years): 39 refractory epilepsy patients (REP) and 35 seizure-free patients (SFP). The following parameters were analysed: type of epilepsy syndrome, seizure frequency, antiepileptic medications, BMI (kg/m2), lipid profile.
Results: 50 patients were found to have inadequate weight (65.5%): 29 were underweight (mean BMI=17.21) and 21 patients were overweight (BMI=30.03). Only 24 patients presented an adequate weight (BMI between 20 and 25). REP (14 underweight, 12 overweight) were similar to SFP (15 underweight, 9 overweight), also in terms of BMI and lipid profile (even including the AED monotherapy vs polytherapy comparative analysis).
Conclusion: In this patient sample, REP did not differ from SFP in terms of BMI. On the other hand, patients with epilepsy as a whole were found in a large proportion (more than 50%) to have nutrition problems (obesity and malnutrition), independently of other possible influences in the nutrition status (type of epileptic syndrome and antiepileptic drug therapy). Therefore, a nutritional perspective in the global management of a patient with epilepsy, with appropriate dietary guidance, seems to be mandatory.

p1153
Towards a Cell Therapy for Temporal Lobe Epilepsy (TLE)?
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Purpose: TLE is associated with damage to specific temporal lobe structures. Adult neuropotent stem cells would be an alternative cell source for cell therapy. Adult neuronal stem cells (NSC) and multipotent adult progenitor cells (MAPC) from bone marrow are evaluated for their potency to differentiate towards neuroectodermal cell types.
Methods: MAPC and NSC have been isolated and differentiated according to the protocol described by the authors (Jiang et al., 2003; Gobbel et al., 2003). Immunocytochemical staining and RT-PCR techniques were used to evaluate the expression of adult neuronal markers (tau, MAP2); an astrocytic marker (GFAP) and an oligodendrocytic marker (GalC).
Results: Immunocytochemistry showed that NSC are able to differentiate to cells, positive for neuronal, astrocytic and oligodendrocytic markers. MAPC could only be differentiated towards a few GFAP+ cells. RT-PCR also showed that the relative expression of MAP2, tau, GFAP and GalC in differentiated NSC was respectively 124 ± 6.55; 3098.46 ± 655.45; 45.35 ± 2.98; 3.02 ± 1.4 times higher than in differentiated MAPC.
Conclusion: Comparing the in vitro neuroectodermal differentiation of MAPC and NSC, using immunocytochemistry and RT-PCR, we demonstrated that the potential of MAPC to differentiate towards neuronal subtypes is considerably lower than that of NSC. In the future, genetically engineered NSC will be implanted in an animal model for TLE.

p1154
Removal of Vagal Nerve Stimulator in Children: Surgical Complications
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Purpose: The aim of this study was to analyse the incidence of surgical complications related to VNS explant/reimplant procedure in a series of children.
Methods: Operative database of 42 consecutive children submitted to VNS implantation using a single cervical incision was revised. Patients who had undergone removal or revision of the device were identified.
Results: 3 patients had a complication necessitating device removal (2 cases) or device revision (1 case). In the first 2 children the devices were revised because lead fracture occurred more than 3 years after implantation. The electrodes and the generator were removed using microsurgical techniques and then replaced. In the first patient, 45 days after surgery, voice alteration was noticed, associated with cough, hoarseness, tonsillar pain and snoring. Flexible laryngoscopy showed a left vocal cord paresis. The patient regained normal voice within three months and the other side effects also improved. The third patient experienced a loss of perceived stimulation three weeks after implant. A bad contact between one connector pin and the generator was found at the surgical revision. Finally, the generator was removed, on demand, in an 18 year old boy because of lack of efficacy and subjective intolerance.
Conclusion: Single cervical incision reduces cosmetic side effects but can determine some difficulties in the removal of the pulse generator. Our experience confirms that stimulation electrodes may be removed and repositioned even after a prolonged period without significant consequence in most cases. The unusual appearance of a delayed vocal cord paresis is discussed.

p1155
Vagus Nerve Stimulation in Very Young Children with Catastrophic Epilepsy
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Purpose: The experience with vagal nerve stimulation (VNS) in very young children is limited, mainly for those younger than 3 years. We report our experience about the effectiveness of VNS in 3 very young children.
Methods: We reviewed our paediatric case series (42 patients implanted) and we selected 3 very young patients (16 months, 17 months and 27 months) suffering from catastrophic epilepsy treated with VNS.
Results: All patients suffering from severe cognitive impairment and catastrophic epilepsy with underlying diagnosis of hemimegalencephaly, anosso-ischemia lesion and migrating partial seizure epilepsy. Surgical procedures of VNS implants were uncomplicated with single cervical incision. Follow up time averaged 3 years (range 7 months-4 years). All children have shown significant improvement in seizure control (range <75%-<90%) in seizure frequency, QOL and for 2 of them there were milestone evolutions.
Conclusion: Most authors believe that late epilepsy onset and a mild neuropsychiatric impairment could be a good prognostic factor for VNS patients. Our children, on the contrary, suffered from catastrophic epilepsy and severe cognitive impairment and they showed a good clinical response to VNS. We believe that VNS is a feasible, well tolerated and effective procedure even in toddler age children affected by severe epilepsy and multiple developmental disabilities. Therefore, VNS can be considered a surgical option even in encephalopathic children with epilepsy who were younger than 3 years.

p1156
Context of Crisis, Sociocultural Factors and Treatment of Epilepsy at Kinshasa, Democratic Republic of Congo
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Purpose: Antiepileptic treatment (AET) is generally a long and closed treatment which pre-supposes adherence to treatment involving both economic and socio-cultural factors. Because of a long and difficult political transition and war with such consequences as poverty and decreased medical systems… this treatment is most of time stopped early and patients refer to other practitioners for their treatment. The general objective is to understand the underlying reasons behind this choice and the specific objectives are to identify other caregivers involved in the treatment of epilepsy, and the socio-cultural factors which influence the adherence to medical antiepileptic drug therapy.
Methods: A prospective study of 234 patients followed in the university neuro-psychiatric hospital (CNPP) during the last five years (1999-2004) and who stopped treatment six months after the last consultation, have been interviewed at their homes. The questionnaire concerns the treatment received, the socio-cultural factors closed to this treatment and the other practitioners involved in treatment after stopping medical AET.
Results: 136 (58%) are male and 98 (42%) are female with 21.3 years for the mean age. 70% are less than 19 years old. 41.7% stopped treatment for lack of possibilities to access to medical services (including drug therapy); 53.4% for other reasons (long treatment, cultural considerations…). Church healers (37%), informal healers using phytotherapy (34%) , traditional healers (39%) have been identified as other practitioners involved in the treatment of epilepsy at Kinshasa.
Conclusion: In context of crisis, patients with epilepsy refer to other practitioners when the accessibility to medical therapy is not possible, for not only the economic reasons, but for underlying socio-cultural reasons too. It's important to include the identified practitioners in a program of treatment of patients with epilepsy in our country if we want to improve their follow-up.

p1157
Prospective Evaluation of Traditional Practices for Epilepsy Patients of Marrakech
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Purpose: The conception of epilepsy by the general public varies according to the community's traditions and beliefs and also to their socio-economic status. Many of our rural citizens consider epilepsy as a divine punishment, a black magic affliction or a jinni possession. The authors study reasons for consulting healers among our epilepsy patients, and the frequency and characteristics of traditional medicinal practices.
Methods: We report a prospective evaluation of a sample of 230 epilepsy patients from Neurology Out-patients of Marrakech, during the last three years.
Results: Among 230 patients, 163 patients visited traditional healers. There were 83 women and 80 men; the mean age was 24 years (4 to 60 years). The delay between visiting healers and medical consultation varied between 1 and 6 years. The cases originating from rural areas were predominant (70%), so 77% of them had a low socio-economic level. A third of them were illiterate, and another third had attended only the Koranic School. Two thirds of our patients used numerous maraboutic methods of healing (Talisman, amulet writings), incense burning, and different medicinal plants.
Conclusion: People still believe in surreal causes of epilepsy. In the literature traditional practices were frequently used especially in China and many African countries (best studied in South Africa). The knowledge and attitudes concerning epilepsy and the management of this disease need to be clarified. So, we hope to be able to propagate

some educational programs to help people change their traditional concept of this disease. We must also differentiate between real TM (use of medicinal plants) and charlatanism.

Wednesday 31st August and Thursday 1st September 2005
13:15 – 14:15
Poster Session
Basic Science

p1158
The Role of GABAB Receptor Agonism in the Treatment of Status Epilepticus
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Purpose: The role of GABAB receptor mediated inhibition in the development and maintenance of seizures remains unknown, as GABAB receptor activation can have both a pro- and anti-epileptic effect. We recently showed that functional GABAB receptors are downregulated after status epilepticus in both the perforant path stimulation model and pilocarpine model of status epilepticus (Chandler et al, J. Neurosci, 23 (36) 2003). Here, we asked whether the GABAB receptor agonist, baclofen, could terminate self-sustaining status epilepticus induced by perforant path stimulation. We also asked whether the antiepileptic effect of the GABA transporter inhibitor tiagabine in status epilepticus is mediated by GABAB receptors, as inhibiting GABA uptake increases the activation of both GABAA and GABAB receptors.
Methods: We induced status epilepticus in freely moving rats using 2 hours of perforant path stimulation. Once established, we then applied vehicle, baclofen or tiagabine in combination with the GABAB receptor antagonist SCH50911 and monitored the subsequent seizure activity electrographically.
Results: Baclofen had an antiepileptic effect in this model terminating the status epilepticus in 3 out of 6 rats; this was, however, at a dose that caused considerable sedation. Inhibiting GABAB receptor activation had no effect on the efficacy of tiagabine at stopping status epilepticus.
Conclusion: GABAB receptor activation can terminate status epilepticus, but only at the cost of considerable sedation. Tiagabine's main effect on status epilepticus is not mediated through an effect on GABAB receptors

p1159
Lamotrigine Attenuates Long-term Consequences of Acute and Chronic Hypoxia in the Developing Brain
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1) American University of Beirut, Lebanon

Purpose: Investigate the potential neuroprotective effects of lamotrigine on the long term consequences of acute and of chronic hypoxia in developing rat pups.
Methods: Five groups of rats were studied: Group 1) control; Group 2) chronic hypoxia rats placed under 10% O2 from birth till P21; Group 3) acute hypoxia rats subjected to a decrease in O2 level down to 4% at P10; Group 4) chronic hypoxia rats that received a daily ip injection of 20 mg/kg lamotrigine from birth till P21; Group 5) acute hypoxia rats that received 20 mg/kg lamotrigine from birth till P21. Rats were subjected to behavioural tests as of P81 (handling, Morris water maze and open field tests) and cell density per surface area in the CA1 hippocampal region was assessed.
Results: As adults the acute hypoxia rats were more aggressive, had memory impairment and lower cell counts as compared to controls ($p=0.0001$, $p=0.002$, $p=0.04$ respectively). The lamotrigine-acute hypoxia group was no different from control ($p=0.79$, $p=0.6$, $p=0.67$ respectively). Chronic hypoxia resulted in increased aggression as compared to controls ($p=0.0033$). The lamotrigine-chronic hypoxia group was no different from controls ($p=0.38$). Means±SE, for the five groups respectively, were: handling: 22.28±0.79, 29.57±2.51, 34.06±1.88, 24.08±1.42, 22.37±0.94; Morris water maze (seconds): 611.5±61.75, 594.48±77.07, 912.52±92.4, 621.8±119.24, 670.84±65.75; cell density (cells/mm2): 65.59±2.8, 62.95±4.08, 52.97±4.79, 74.37±3.45, 57.28±4.65.
Conclusion: Lamotrigine administration was associated with reduction of the long term behavioural and histological consequences of acute and chronic hypoxia.

p1160
Spike-and-wave Activity in the Amygdala of Rats
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Purpose: Limbic structures are not generally considered to be involved in the pathogenesis of absence epilepsy. In our previous studies we have shown that genetic absence epilepsy rats from Strasbourg (GAERS) are resistant to the amygdala kindling process. In this study we aimed to evaluate electroencephalogram (EEG) from the cortex and amygdala of GAERS before and after repeated kindling stimulations.
Methods: Experiments were carried out in GAERS (n=12) aged 4-9 months. All animals were instrumented stereotaxically with bilateral stimulation and recording electrodes into the basolateral amygdala (BLA) and recording electrodes on the cortex. After one week recovery period animals were electrically stimulated twice daily at their after-discharge thresholds and EEG was recorded.
Results: In 3 animals out of 12, spike-and-wave discharges (SWDs) with lower amplitude were observed in the amygdala recordings. One of them showed SWDs both in the cortex and BLA in the basal EEG. In two animals SWDs were noticed in BLA simultaneously with the cortex after 3-5 electrical stimulations, although they did not show SWDs in BLA in their basal EEG. In these animals amplitude of SWDs in BLA increased during the kindling process and after 15 stimulations reached to cortical SWD amplitude. In EEG of the remaining 9 animals SWDs were not observed before and after kindling stimulations.
Conclusion: Although limbic structures are not generally thought to contribute to the brain circuitry in which SWDs are generated, observation of SWDs in BLA suggest that in a subgroup of GAERS the amygdala seems to be involved in absence epilepsy.

p1161
Ischemic Hippocampal Lesion Leads to Cognitive Impairment and Epileptogenesis in Immature Rats
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Purpose: This study was conducted to find whether hippocampal ischemic lesion at different developmental stages impairs motor and cognitive functions and leads to development of epilepsy later in life.
Methods: Ischemic lesion was induced by intrahippocampal injection of endothelin-1 (20 or 40 pmol) in male rats on postnatal day 12 (P12) or 25 (P25). Control animals only received a solvent. Motor development was checked until adulthood using a battery of age-specific tests (negative geotaxis, wire mesh, bar holding, rotarod). Spatial memory was tested in Morris water maze 60 days after injection. After finishing behavioural testing, electrodes were implanted over the sensorimotor cortical areas and into the dorsal hippocampi of both hemispheres. Animals were video-EEG monitored for 5 consecutive days.
Results: Significant behavioural impairment occurred only in the P12 group. The 40-pmol dose of endothelin-1 ($p>0.001$) resulted in developmental retardation in the bar holding test. No differences were seen in other motor tests. Animals in this group also exhibited learning difficulties (longer latencies) in the Morris water maze. No motor or cognitive impairment was observed in P25 groups. The number of animals exhibiting epileptic seizures increased with the dose of endothelin-1 in both age groups. Non-convulsive seizures were

detected in 63% and 83% of animals receiving the two doses of endothelin-1 at P12. In P25 groups, seizures occurred in 88 and 100% of animals, respectively.
Conclusion: Focal ischemia induced in P12 or P25 rats by intrahippocampal injection of endothelin-1 induces epileptogenesis in both age groups. Behavioural impairment occurred only in animals with ischemic lesion at P12.

p1162
Changes in Patterns of Firing in Hippocampal Neurons In-vitro after Pilocarpine-induced Epilepsy
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Purpose: The aim of the study was to characterise different firing patterns of CA1 hippocampal neurons of control and pilocarpine treated rats. Electrophysiological studies and morphological identification of the recorded neurons in diverse cortical areas revealed at least three types of pyramidal neocortical neurons within the deep layers. These cell types were classified as 'regular spiking' (RS), 'intrinsic bursting' (IB), and 'repetitive oscillatory bursting' (ROB) neurons.
Methods: Male Wistar rats had status epilepticus induced by the pilocarpine model (PTR). Control rats (CR) were injected with saline. Brain slices were immediately prepared after decapitation. The slices were then transferred to a recording chamber continuously perfused and oxygenated at room temperature. Intracellular recordings were obtained from CA1. The current-voltage relationships and spike frequency adaptation were determined from response to rectangular current pulses (0.1-1.2nA) measured at steady state. The neurons studied were biocytin-stained.
Results: Electrophysiological properties of 61 neurons of CR and 28 neurons of PTR were recorded. The neurons were classified as: (1)RS-(63.93%RC and 53.57%PTR) when cells fired a train of spikes that began at high frequency and declined within 100-200 ms to lower frequencies (4 patterns recorded); (2)IB-(9.83%RC and 17.85%PTR) neurons that fired clusters of spikes (bursting cells), and (3)ROB-(26.22%RC and 28.57%PTR) neurons that fire both single and bursts of spikes (3 patterns recorded).
Conclusion: We found a higher percentage of bursting cells in the PTR group. We also recorded two subtypes of firing patterns only in the PTR group. Our results suggest that the development of epileptiform activity in the pilocarpine model may be related to the selection of viable intrinsic bursting neurons.

p1163
GABA-B Antagonist Potentiates Cortical Epileptic Afterdischarges in Immature Rats
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Purpose: To study a role of GABA-B inhibitory system in the generation and arrest of cortical epileptic afterdischarges (ADs) in developing rats.
Methods: Cortical stimulation and registration electrodes were implanted I in Wistar male rats 12, 18 and 25 days old. Low frequency electrical stimulation was repeated with intensity increasing from 0.2 to 15 mA. EEG and behaviour were recorded and four phenomena (movements elicited by stimulation, spike-and-wave ADs, clonic seizures and limbic type of ADs) were evaluated. GABA-B antagonist CGP 35348 (gift of Novartis AG) was injected in doses of 50, 100 or 200 mg/kg i.p. 15 min before the first stimulation. Control animals received saline.
Results: The highest dose of CGP 35348 significantly decreased the threshold current intensity for all four phenomena in all age groups. The most prominent change was observed in thresholds for the mixed (limbic) type of ADs, i.e. for transition of epileptic activity into limbic structures. It was significantly decreased by all doses of CGP 35348 in 18-day-old rats. CGP 35348 also markedly increased duration of ADs in all three age groups; all doses led to a significant prolongation of ADs in 12- and 18-day-old rats whereas only the highest dose was efficient in 25-day-old animals.
Conclusion: Suppression of GABA-B inhibitory system by a high dose of an antagonist resulted in an easier generation and substantial prolongation of cortical ADs. These results demonstrate that GABA-B system makes seizure generation more difficult and takes a part in seizure arrest in an immature brain.

p1164
Glucose Metabolism and Gabaergic Inhibition in the Human Epileptogenic Cortex
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Purpose: Maintenance of GABA currents requires that the type A receptors (GABAA-R) be phosphorylated by a specific endogenous kinase. We have shown that this endogenous kinase was identical with glyceraldehyde-3-phosphate dehydrogenase (GAPDH), a key glycolytic enzyme. This endogenous phosphorylation prevents or largely diminishes rundown of GABA induced currents in acutely dissociated rat neocortical neurons, function (J. Neurosci., 2004 24(35):7614-22.).
Methods: We show that this phosphorylation mechanism is deficient in the cortical tissue taken from epilepsy patients undergoing neurosurgery for therapeutic reasons.
Results: Phosphorylation of the alpha1 subunit of GABAA-R was significantly reduced in washed membranes from epileptogenic cortex (40%), compared to non-epileptogenic human cortex. This feature was not related to a reduced number of GABAA-R in the epileptogenic tissue since in the same preparation the number of the alpha1 subunits was unchanged. Patch-clamp experiments on acutely dissociated cells from epileptogenic human tissue revealed that run down of GABAA responses was faster in the epileptogenic tissue when compared to the non-epileptogenic human cortex. Glyceraldehyde-3-phosphate, the GAPDH specific substrate, markedly reduced rundown of the GABAA responses. Inhibition of a membrane-associated phosphatase by vanadate was also protective, by maintaining the GABAA receptor in its phosphorylated state.
Conclusion: These data show that GAPDH is the endogenous kinase phosphorylating the alpha1 subunit of the GABAA-R in humans, maintaining GABAA -R function. Phosphorylation of the alpha1 subunit is deficient in the epileptogenic tissue: this can promote initiation and propagation of seizures. In addition, this deficiency parallels the glucose hypometabolism associated with the epileptogenic zone in epilepsy patients.

p1165
Lamotrigine: Neuroprotective Effect in Rats after Kainic Acid Induced Seizures
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Purpose: Kainic acid (KA) is used as an experimental agent which produces convulsions and neurotoxic lesions. We examined the effects of KA induced convulsions on the activity of Na+, K+- ATPase, activation of JNK/c-jun axis and histological changes in rat hippocampus. Lamotrigine (LTG) is an antiepileptic drug, a glutamate release inhibitor, with action at the neuronal voltage-gated sodium channel. Therefore, this study was also designed to investigate the influence of LTG pre-treatment on the mentioned hippocampal changes.

Methods: The study was carried out on Hanover-Wistar rats. Na+, K+-ATPase activity from hippocampal tissue was determined two hours, three days and five days after a single subcutaneous KA (8 mg/kg) injection. The induction of JNK/c-jun and hippocampal histological changes were determined two hours and five days after KA application. LTG (30 mg/kg i.p.) was used two hours before KA application and for five consecutive days.
Results: After KA application, Na+, K+- ATPase activity was significantly inhibited and the induction of JNK/c-jun axis was observed. The number of hippocampal CA1 cells was significantly lower in all groups of the rats treated with KA. In the group of LTG pre-treated rats Na+, K+- ATPase inhibition, and JNK/c-jun induction were detected the fifth day after KA treatment, but the inhibition of Na+, K+- ATPase was significantly less pronounced. The number of damaged cells was significantly less in LTG pre-treated rats.
Conclusion: Systemic application of KA showed statistically significant changes in the evaluated parameters in the rats' hippocampus. LTG pre-treatment has a partially neuroprotective effect in KA-treated animals.

p1166
Cross-channel Coupling of Neuronal Activity in Parvalbumin-deficient Mice Susceptible to Epileptic Seizures
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Purpose: The synchronisation and coupling of electrophysiological activity in epileptic prone animal models characterised by alteration of their inhibitory network should reveal some important clues about the role of Ca2+-buffer proteins in controlling the fine tuning of the inhibitory/excitatory balance.
Methods: The analysis of multi-site recordings in the temporal cortex of parvalbumin-deficient mice (PV-/-) is performed. These animals are characterised by altered Ca2+-binding dynamics of cells normally expressing PV, which affects particularly the cortical GABAergic interneurons, and by an increased susceptibility to epileptic seizures. Temporal (cross-correlations) and frequency (cross-bispectral) domain interactions of spike trains and local field potentials are investigated from different sites within the same cortical area. The recordings were performed during steady spontaneous activity under Equithesin anaesthesia.
Results: Control animals showed a lesser degree of synchronicity in the time domain and mainly high frequency components (>65 Hz) compared to PV-/- subjects. Conversely, PV-/- subjects were characterised by increased synchronicity and by an abnormally high proportion of frequencies < 40 Hz. These results indicate prevailing short-range functional interactions and local processing in the control subjects vs. long-range coupling in PV-/-.
Conclusion: The observed alterations of cortical network activity in parvalbumin knockout mice support the hypothesis that impairment of normal Ca2+-binding dynamics in the subset of PV-ergic neurons may constitute one of the primary mechanisms that lead to the imbalance of inhibitory activity, hypersynchrony and ultimately to epileptic seizures. This study was partially supported by Swiss National Science Foundation grants: 3100-063448.00/1 and 3100A0-100400/1 (to B.S.).

p1167
High-frequency Oscillations Driven by Interneurones at Seizure Onset in the Immature Brain
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Purpose: High-frequency oscillations (HFOs, >40Hz) are present in a variety of physiological and epileptic network activities in the adult brain. Though a picture of the role of interneuron during network oscillations starts to emerge, their role at seizure onset is not known. This question is crucial for immature network where GABA is depolarising. This study focuses on the role of interneurons during HFOs at seizure onset, in the immature rat hippocampus during the first post-natal week.
Methods: We have used the intact cortico-hippocampal formation, in which ictal-like discharges occur spontaneously after removing Mg2+ from the perfusing medium. During seizures, patch clamp recordings of hippocampal neurons collect their firing pattern and their synaptic inputs. The behaviour of identified neurons is then mathematically processed with the field recordings.
Results: HFOs are present at seizure onset in the immature brain. They depend upon the activation of GABAA receptors, i.e. the firing of interneurons and upon gap junctions. Most interneurons fire in synchrony and are phase-locked with the field HFOs. Hippocampo-septal-projecting (HS) interneurons (targeting specifically interneurons) also fire in synchrony but before HFO occurrence. Most of the excitatory drive is provided by GABAergic activity, which always precedes glutamatergic activity.
Conclusion: Our results are consistent with the scheme that HFOs result from the synchronised firing of different types of interneurons. HS interneurons appear to play the role of leaders of HFOs. Their discharge occurring at high frequency before field HFOs suggests that they entrain the rest of the interneuron population in an excitatory GABA- and gap junction-dependent manner.

p1168
Investigation of the Hippocampal Slices Electrical Activity under the Pilocarpine Influence
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Purpose: The neuronal mechanisms of chronic epileptic activity (EpA) development and cessation continue to be still unclear. The main goal of the present work was to study the neuronal mechanisms of the chronic pilocarpin-induced EpA on hippocampal slices.
Methods: After decapitation the rats' transverse slices were prepared and incubated at 32oC in artificial cerebrospinal fluid. The other solutions used were lacking Ca2+ and Mg2+ ions. The population spikes (PS) recordings were made in response to Schafer collaterals of the hippocampal CA1 field electrical stimulation. Pilocarpine was added to the solution in the dose of 50 nmole. PS amplitude, threshold of excitation and the number of bursts were evaluated with the help of the 'LabView 5.0'.
Results: PS amplitude in response to Schaffer collaterals single electrical pulse-stimulation after pilocarpine addition to solution were 2.2±0.5 mV; this was greater (1.7 times) compared with the same data of intact slices. The additional discharges were registered in this condition. In the case of pilocarpine addition to solutions with decreased Ca2+ and Mg2+ concentration one could see spontaneous discharges originating with the average PS amplitude from 4.3 mV until the 5 mV and frequency equal to 8-15 per s.
Conclusion: The data obtained showed that Ca2+ and Mg2+ elimination from the superfusion solution lead to pilocarpine-induced seizure threshold decreasing. The described model of pilocarpine-induced seizures in vitro might be of great value for the potential antiepileptic substances efficacy investigation.

p1169
Alterations of Glutamate Transporters and Receptors in the Hippocampus of Pentylenetetrazol-kindled Rats
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Purpose: Kindling is regarded as a model of complex partial seizures. Although the specific mechanism remains unknown, the long-lasting excitatory synaptic transmission efficacy found in pentylenetetrazol (PTZ)-kindled animals that is related to extracellular glutamate concentration is of interest. To test our hypothesis, enhanced glutamatergic synapse transmission in PTZ kindling was associated with changes in glutamate transporter and receptor proteins, semiquantitative western blotting with antibodies specific to individual glutamate transporters (GLAST, GLT-1, EAAC-1) and receptors (GluR1, GluR2, NMDAR1) were performed in PTZ-kindled rats.
Methods: Male Sprague-Dawley rats were kindled by repetitive i.p. injection of PTZ (16 mg/ml in saline, 40mg/kg) at the ratio of three times a week. Animals were considered kindled after two consecutive stage 5 seizures (generalised tonic-clonic seizures). Twenty-four hours or 30 days after the last stage 5 seizure animals were killed and both hippocampi were removed and a crude membrane fraction was prepared for western immunoblotting.
Results: We found that levels of GLAST, GLT-1, EAAC-1, NMDAR1, GluR1 were elevated significantly at 24 hours after the last seizure. However, no change was found in any transporters and receptors compared with control at 30 days. Rats at 30 days after the last seizure had stage 5 seizures with PTZ.
Conclusion: Up-regulation of glutamate transporters during acute seizures supports the conclusion that enhanced glutamate turnover may be a necessary component in the activation of GluR1, and NMDAR1, during kindling development. It could not be required to up-regulation of glutamate transporters and receptors to maintain kindling phenomenon.

p1170
Long-term Changes in Hippocampal Excitability of the Human Hippocampus In-vivo
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Purpose: Intracranial evoked potentials (EPs) should reflect at least local excitability of a neuronal circuit and could therefore be used as an electrophysiological measure of excitability in the intact human hippocampus. We investigated the variability in hippocampal excitability by employing long-term monitoring of EPs and studied its relation to interictal and ictal events.
Methods: 3 patients with refractory temporal lobe epilepsy were bilaterally implanted with quadripolar depth EEG electrodes in the hippocampus for seizure onset localization purposes. Simultaneous with continuous video-EEG monitoring, a paired pulse stimulation was given on both hippocampal electrodes every 10 seconds (total durations: 70, 98 and 118 hours). Seizure activity and interictal discharges were localised in the corresponding EEG. EP measurements were performed using custom-designed algorithms.
Results: EP morphology consisted of multiple components and was patient-specific. Amplitudes and latencies of some of these components varied on a time basis. Analysis revealed that periods of higher EP amplitudes coincided with periods of increased interictal EEG discharges, probably both reflecting a more excitable state. Immediately following unilateral seizure activity, EP amplitudes in the ipsilateral hippocampus decreased, gradually recovering over a period of several minutes. Simultaneously, despite the absence of contralateral seizure spread, a similar decrease/recovery of EP amplitudes was found in the contralateral hippocampus, although relative amplitude decrease was smaller and recovery faster.
Conclusion: These results indicate that hippocampal excitability is: 1) subject to significant changes over time, 2) associated with the rate of hippocampal interictal discharges and 3) decreased post-ictally, both ipsilateral and contralateral to the epileptogenic temporal lobe.

p1171
Altered Drug Penetration, Not Lack of Neuronal Responsiveness is Responsible for AED Drug Resistance
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Purpose: Pharmacoresistance in epilepsy patients may be described by two explanations that are not necessarily mutually exclusive: a pharmacokinetic mechanism and a pharmacodynamic mechanism.
Methods: We used dual approaches to investigate the mechanism of multiple drug resistance to common antiepileptic drugs, carbamazepine and phenytoin (CBZ, PHT). In one set of experiments, serum:brain drug ratios were determined intraoperatively during lobectomies performed to alleviate drug-resistant seizures.
Results: The brain:plasma ratio of CBZ was 1.39 ± 0.40 (n = 22 patients) when therapeutic serum levels were achieved (15 - 34 □M), compared to reported therapeutic values of serum levels 8-48 □M in drug respondent patients. The resulting brain levels in our study were 11-50 □M compared to predicted levels of 12-72 □M in drug respondent patients. When concentrations of CBZ found in the multiple drug resistant brain were directly applied to human cortical slices made hyperexcitable and hypersynchronous by Mg2+-free aCSF, the frequency of bursts was not significantly affected. The overall excitability was reduced by only 40%. Similar results were obtained for PHT. At higher AED concentrations (60-200 □M) a dose dependent decrease of bursting frequency and amplitude was observed.
Conclusion: The response of slices from human multiple drug resistant brain were identical to rat or mouse cortex, suggesting that multiple drug resistance is not due to loss of pharmacodynamic mechanisms. Taken together, our results support the hypothesis that multiple drug resistance to antiepileptic drugs is due to cerebrovascular changes that impede achievement of appropriate drug levels in the central nervous system. Support Contributed by: NIH-RO1 HL 51614, NIH-RO1 NS 43284, and NIH-RO1 NS 38195.

p1172
Migration of Bone Marrow Stem Cell into the Brain after Status Epilepticus or Acute Seizures
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Purpose: The present study aimed to evaluate whether status epilepticus (SE) or acute epileptic seizures induce migration of bone marrow stem cells across the blood-brain barrier (BBB) and populate the brain parenchyma. To investigate this issue, we used maximal electroconvulsive shock (MES) to produce acute seizures and pilocarpine administration to provoke SE, in chimeric mice.
Methods: To assess stem cell migration from the bone marrow to the brain, we generated chimeric mice by transplanting bone marrow from green fluorescent protein (GFP) transgenic mice into lethally irradiated wild-type hosts. We induced SE or MES (1 MES or 5 MES) in chimeras to quantify the donor GFP+ cells and investigated their fates by immunofluorescence in six cerebral regions (neocortex, piriform cortex, hippocampus, thalamus, choroid plexus and lateral ventricle) at three times after SE or MES induction (2 hours, 24 hours and 48 hours).
Results: We found GFP+ cells throughout the brain in both epilepsy models. The quantification of GFP+ cells showed a significant difference for both SE and MES models ($p = 0.0049$; $p < 0.0001$) for all

evaluated areas except for choroid plexus as compared to controls. The peak of GFP+ cells in the pilocarpine model was at 48 hours after SE onset, while in 1 MES it was at 24 hours and after 5 MES it was at 2 hours.
Conclusion: Our data show that stem cells originating from the bone marrow have the capacity to migrate across the BBB and populate brain regions in convulsed animals in a seizure-dependent manner.

p1173
Increased High Frequency Oscillations Precede In-vitro Low Mg2+ Seizures
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Purpose: High frequency oscillations (HFOs) in the range of 80 Hz and above have been recorded in the neocortex and hippocampus in-vitro and in- vivo, and are associated with normal and epileptiform activity. Fast ripples (> 200 Hz) are believed to be exclusive to epileptiform activity. Although the presence of HFOs in interictal discharges has been well characterised, their temporal evolution in the transition to seizures has not been investigated. We studied this transition using an in-vitro rat hippocampal model of low Mg2+ spontaneous seizures.
Methods: Extracellular field recordings from CA1 and CA3 were obtained for 35 spontaneous seizures (and the preceding interictal discharges) from 7 rats. The discharges were analysed for time-dependent changes in spectral composition using a novel local multi-scale Fourier-based technique. The HFO content of the discharges was quantified into four bands spanning sub-ripple (0-100 Hz), ripple (100-200 Hz), and two supra-ripple frequencies (200-300 Hz and 300-400 Hz).
Results: A statistically significant increasing trend was observed in the amplitude of ripple (100-200 Hz) and fast ripple (200-300 Hz) activity in the interictal discharges leading up to all recorded seizures. Specifically, the high frequency composition of each interictal discharge changed significantly with a progressive increase in ripple and fast ripple (200-300 Hz) activity leading up to each seizure.
Conclusion: Significant and progressive changes in HFOs are seen during the transition to seizures. These changes are indicative of dynamic changes in neuronal synchronization and their characterization may offer insights into the pre-ictal state and pathophysiological processes underlying seizure initiation.

p1174
Febrile Seizures Modify the Tissular Content of Gaba, Glutamine and Glutamate in the Developing Rat Brain
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Purpose: The goal of the current study was to determine the tissular content of GABA, glutamate and glutamine in brain areas of pup rats using a hyperthermia-induced seizure model.
Methods: Pups of 10 days old were placed on a container, an air stream was directed 50 cm above them. Hyperthermia was maintained for 30 min, aiming for a core temperature of 41 C. Thereafter, pups were placed on a cool surface, monitored for 15 min, and hydrated by their mothers. The control group was normothermic. Animals were sacrificed by decapitation 30min, 24h and 20days after seizures and their brains were used for chromatography assay.
Results: Results showed FS-induced glutamine (1636.2%) and glutamate (1249.1%) increase in the cerebral cortex and GABA (310.2%), glutamine (206.2%) and glutamate (1245.0%) in the amygdala and reduction in glutamine levels (68.6%) in the hippocampus 30 min after induced seizures as compared with the control group. However, 24 hours after the FS the GABA (48.0%) and glutamate (64.3%) levels showed a reduction in the cerebral cortex, and glutamine (44.5%) in the hippocampus, whereas glutamate levels stay increase (667.0%) in the last one. At 20 days the GABA levels showed an increase (177.2%) in the cortex and amygdala (218.5%), while the hippocampus showed an increase in glutamate levels (180.9%) when compared with the control group.
Conclusion: FS produced transitory changes in the tissular content aminoacids in the immature rat brain. Moreover, it is possible that the enhanced inhibitory aminoacid levels 24h and 20d after FS may play a neuroprotector role to counteract the excessive glutamate levels.

p1175
Antiepileptic Effect of a Gap Junction Blocker in a Model of Absence Epilepsy
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Purpose: The role of gap junctions in thalamocortical loop synchronization and the antiepileptic action of carbenoxolone (gap junction blocker) were investigated in two animal models of epilepsy.
Methods: The effect of i.p. injections of carbenoxolone on the duration and frequency of spike and wave discharges (SWD) was measured in chronically implanted Genetic Absence Epilepsy Rats from Strasbourg (GAERS). The antiepileptic effect of carbenoxolone was further investigated on seizures induced by bath applied 4-aminoprydine (4-AP) in thalamocortical slices from GAERS, non epileptic rats (NE) and Wistar rats.
Results: Carbenoxolone (100mg/kg) decreased the cumulated duration of SWD in adult GAERS without change in the SW amplitude and frequency within the discharges. However, it affected the spectral power of a wide range of frequencies both in NE and GAERS rats. In thalamocortical slices exposed to 4-AP (50 µM) synchronous seizures were recorded in the thalamus and in the somatosensory cortex. These seizures were still generated in each structure when the thalamus and cortex were separated before 4-AP application. Bath-applied carbenoxolone (100µM) decreased the frequency and duration of the 4-AP induced seizures in thalamocortical slices in GAERS and NE and abolished them after 1 hour exposure. The antiepileptic effect of carbenoxolone was less fast-acting in GAERS than in NE.
Conclusion: Our results show that carbenoxolone, a gap junction blocker exerts an antiepileptic action in a genetic model and in a pharmacological model. Our findings suggest that gap junctions may represent an appropriate target for the development of new broad-spectrum drugs aimed at decreasing epileptiform synchronization and preventing epileptogenesis.

p1176
Nicotine Increases Inhibitory Currents through Activation of α4 NACHR in Frontal Lobe Layer II/III Pyramidal Cells of Two ADNFLE Mutant Mice
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Purpose: It is not known how mutations in nAChR α4 subunits result in autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE). To understand the alterations in neuronal excitability in ADNFLE, we made electrophysiological recordings from mice genetically engineered to express one of two known mutations (S252F or +L264) found in the nAChR α4 of ADNFLE patients.
Methods: Brain slices (350µm thick) were prepared from wild type (wt), heterozygous, or homozygous mutant male mice. Whole-cell voltage-clamp recordings were obtained at 32-34oC from visually identified frontal cortical layer II/III pyramidal cells (PCs). Spontaneous inhibitory (sIPSCs) and excitatory (sEPSCs) postsynaptic currents were recorded simultaneously or in isolation before and during the perfusion of 1µM nicotine. The average current produced by the synaptic events was measured during 10s epochs.
Results: In simultaneous recordings of inhibition and excitation in PCs of S252F heterozygous mice, the inhibitory component was increased ~34-fold by nicotine compared to a ~4-fold increase in wt. Isolated

sIPSCs were increased ~23-fold while a ~20-fold increase was observed in +L264 heterozygous mice compared to ~3-fold increase in wt. Isolated sEPSC did not change in response to nicotine. The effect on IPSCs was blocked by the nAChR α4 antagonist dihydro-β–erythroidine (10μM) but not by the α7 blocker methyllycaconitine (50nM). Similar results were found in S252F homozygous mice.
Conclusion: Our results demonstrate that activation of nAChR α4 significantly increases inhibitory activity in two types of mutant mice carrying human ADNFLE mutations. This suggests that seizures in ADNFLE arise from synchrony in the frontal cortex produced by interneuronal hyperactivity. Funding: NS02808 (IM), Gonda Fellowship (JG), NIH NIDA, the Milken Family Medical Foundation (JB), NIH Molecular and Cellular Neurobiology predoctoral training grant (AK).

p1177
Germanium Dyphosphanate Compound with Nicotinamide Influence on Different Forms of Seizure Activity
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Purpose: The aim of the present work was to investigate new germanium dyphosphanate compound with nicotinamide (MIGU-5) action on the different forms of seizure activity.
Methods: Pentylenetetrazol (PTZ, 100 mg/kg, s.c.)- and picrotoxin (PTX, 2,5 mg/kg, i.p.)- induced convulsions and maximal electroshock (MES) in mice CBA were used for efficacy of MIGU-5 estimation. Hippocampal slices with the thickness 300-600 mkm were prepared and population evoke potentials (EP) from hippocampal CA1 field were registered in control experiments (intact rats) and after MIGU-5 (500 nmole) administration after Shaffer collaterals stimulation.
Results: MIGU-5 decreased seizure intensity in MES- and PTZ-induced convulsions. Compound failed to influence PTX-induced convulsions. MIGU-5 administration into the incubation environment accompanied by somatic spike amplitude diminishment on average on 27-40%, caused by both first and second stimuli during pair stimulation.
Conclusion: The data obtained testify that new germanium dyphosphanate compound with nicotinamide induced pertinent antiepileptic affects in conditions of acute chemical and electrical seizures and in vitro. From a pharmacological point of view MIGU-5 appears to be a promising anticonvulsant.

p1178
Rapid Loss of Apurinic/Apyrimidinic Endonuclease and Subsequent Apoptosis in Kainate-induced Seizure Model
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Purpose: The DNA repair enzyme, apurinic/apyrimidinic endonuclease (APE) plays a role in base excision repair pathway involved in repairing apurinic/apyrimidinic (AP) site after oxidative stress. To reveal the relationship between APE and neuronal apoptosis associated with oxidative stress after kainic acid (KA) induced status epilepticus, the temporal change of APE expression was investigated in KA induced seizure model.
Methods: Status epilepticus was induced by unilateral intrahippocampal injection of KA. Superoxide anion radical production and DNA oxidation were evaluated by in situ detection of oxidised hydroethidine and 8-hydroxyguanine (8-OHG) immunoreactivity. APE expression was examined by Western blot and immunohistochemical analysis. DNA fragmentation was visualised with terminal deoxynucleotidyl transferase-mediated uridine 5'-triphosphate-biotin nick end labelling (TUNEL) staining.
Results: Cell loss occurred in CA1, CA2, and CA3 in the KA-injected hippocampus and CA3 in the contralateral hippocampus 24 hours after KA-injection. Oxidised hydroethidine and 8-OHG immunoreactivity were increased compared with control after KA treatment. APE immunoreactivity was decreased in the KA injected hippocampus after 4 hours (relative protein level = 0.75 ± 0.2, $p < 0.05$) and 24 hours (relative protein level = 0.23 ± 0.18, $p < 0.01$) after KA injection. TUNEL-positive cells were observed after 24 hours but not after 4 hours in KA injected hippocampus. In double labelling with APE and TUNEL, TUNEL-positive cells did not show APE immunoreactivity.
Conclusion: This study suggests that rapid loss of APE may produce the failure of DNA repair machinery and then induce neuronal apoptosis following KA induced status epilepticus.

p1179
Audiogenic Seizures Visualised with Transcranial Autofluorescence Imaging in the Sensorimotor Cortex of DBA/2 Mice
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Purpose: We have already used flavoprotein autofluorescence imaging to demonstrate brain function in the somatosensory cortex of anesthetised rats (Shibuki et al. J Physiol. 2003 Jun 15; 549:919-27). In the present study, we used this technique to investigate cortical activities in DBA/2 mice exhibiting audiogenic seizures in response to strong sound stimuli.
Methods: DBA/2 mice (4-6 weeks old) were anesthetised by urethane. The skin was incised and the skull was exposed. The surface of the skull was covered with clear acrylic resin for keeping the skull transparent. Three days after the operation, the skull of the mice recovered from the operation were fixed under an epifluorescence binocular microscope with a CCD camera, and cortical activities during sound stimuli at 13 kHz for 60 s were visualised as autofluorescence changes. Electrocorticogram (ECoG) was also recorded.
Results: Autofluorescent responses were observed in the sensorimotor areas approximately 40 s after the onset of the sound stimuli. The maximal amplitude of delta F/F was larger than 5.0% and lasted for more than 90 s. Epileptic discharges recorded in ECoG were observed only in the sensorimotor areas, in which autofluorescent responses were observed.
Conclusion: These observations suggest that flavoprotein autofluorescence imaging is coupled with seizure activity. It is possible that the epileptic focus is formed in the sensorimotor cortex by auditory stimulation in DBA/2 mice.

p1180
Seizure-like Events in Isolated Hippocampal Slices from Fragile X Mental Retardation Protein Knock-out Mice
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Purpose: Fragile X syndrome is the most common inherited form of mental retardation, affecting 1 in 1200 males and 1 in 2500 females. The condition is a result of loss of expression of the Fragile X Mental Retardation Protein (FMRP). This syndrome is characterised by variable intellectual impairment, hyperactivity, autistic-like behaviours, anxiety and seizures (in 20% of patients).
Methods: Using FMRP knock-out mice (FMRP-KO), we have explored the propensity of isolated hippocampal slices to display seizure-like-events (SLE) in response to low-Mg perfusate and recurrent tetanizations.
Results: In general, the slices from FMRP-KO mice exhibited a greater tendency to spontaneous bursting than those from their wild

type counterparts. A higher percentage of slices from FMRP-KO showed SLEs than wild type mice (75% vs. 40%), and the onset to the first SLE event induced in low-Mg perfusate in FMRP-KO mice was significantly reduced as compared to wild type mice (less than 10 minutes vs. over 25 minutes). As well, 2 or 3 bouts of 100 Hz tetanizations (2 seconds, every 10 minutes) were sufficient to induce SLEs in a majority of slices from FMRP-KO mice. In contrast, slices from wild type mice hippocampi could rarely be provoked into SLEs with up to 6 similar tetanizations, and less than half of these slices would exhibit SLE with a subsequent 30 minute exposure to low-Mg perfusate.
Conclusion: Investigations in our laboratory are ongoing into the mechanisms of heightened SLE exhibited by FMRP-KO hippocampi in vitro. This work was supported by The Fragile X Research Foundation of Canada.

p1181
The Acute Effects of Antiepileptic Agents on Thiocolchicoside-induced Status Epilepticus in Rats
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Purpose: Thiocolchicoside is able to induce a lasting, secondarily generalised convulsive status epilepticus (SGCSE) in rats with minimal lesions of dura and arachnoid membranes (Seizure 12; 508-515, 2003). The aim of this study was to evaluate, using this model, the effects of acute therapeutic doses of diazepam (DZP), clonazepam (CZP), phenobarbital (PB), phenytoin (PHT), carbamazepine (CBZ) and MK-801 on clinical and electrographic seizures induced by thiocolchicoside.
Methods: Adult, male Wistar rats (n=6 per group) were acutely treated with DZP (15 mg/kg ip), CZP (4 mg/kg ip), PB (80 mg/kg ip), PHT (60 mg/kg ip), CBZ (100 mg/kg ip) and MK-801 (0.05 mg/kg ip) one hour after the development of SGCSE induced by thiocolchicoside (6 mg/kg ip). The electroclinical pattern was continuously monitored for at least 3 hours after injection of the antiepileptic agents and compared with a control group (n=10 rats) treated with thiocolchicoside only (6 mg/kg ip). The blood levels of PB, PHT and CBZ were measured.
Results: About ten minutes after the administration of DZP, CZP and MK-801 the rats became sedated, without clinical seizures. The electrographic seizure activity did not change significantly. PB, blood levels between 25-30 µg/ml, and PHT, blood levels between 18-22 µg/ml had no significant effects on clinical and electrographic seizures. CBZ, blood levels between 13-18 µg/ml, significantly decreased ($p<0.01$) both the spike activity and the number of clinical and electrographic seizures.
Conclusion: The thiocolchicoside-model of status epilepticus shows a peculiar pharmacological response to antiepileptic agents. This model could have use in pharmacological studies with new drugs.

p1182
Erythropoietin Kinetics in Plasma and Cerebrospinal Fluid of Adult Rats Following High-dose Recombinant Erythropoietin.
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Purpose: Erythropoietin (Epo) is a promising neuroprotective agent that we and others are studying in status epilepticus and hypoxic seizure models in rodents. To lay the ground for its use, we investigated its kinetics and its ability to cross the blood brain barrier following intraperitoneal injection.
Methods: Adult Sprague-Dawley rats (N=15) received single intraperitoneal high-dose injections of recombinant Epo (1unit/g). Plasma and cerebrospinal fluid (CSF) samples were collected sequentially between 30 and 1260 minutes after the injection. Epo was measured using ELISA.
Results: Erythropoietin was detected in the plasma (222.09 mlUnits/ml) 30 minutes after the injection, peaked to 4547.93 mlUnits/ml at 5 hours, and decreased to 645 mlUnits/ml after 21 hours, with a half life of 7.5 hours (Plasma Epo levels in mlUnits/ml: 30 min: 222.09; 60 min: 992.23; 90 min: 1723.31; 100 min: 2331.57; 120 min: 3242.15; 145 min: 3357.85; 165 min: 4399.17; 300 min: 4547.93; 420 min: 3323.31; 1260 min: 645.62). CSF Epo concentrations paralleled the rise in plasma levels and peaked to 11 mlUnits/ml, 5 hours after the injection (CSF Epo levels in mlUnits/ml: 60 min: <2.5; 120 min: <2.5; 240 min: 4.52; 300 min: 11.24; 540 min: 4.41).
Conclusion: Epo penetrates into the CSF of adult rats, and peaks 5 hours following a high-dose intraperitoneal injection, paralleling plasma levels. When investigating the effects of Epo on the central nervous system in rodents, the intraperitoneal route is acceptable.

p1183
Molecular Regulation of Hippocampal Glutamate and Gaba Transporters in Rats Treated with Levetiracetam
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Purpose: To assess the action of levetiracetam (LEV) we measured hippocampal expression of transporters for glutamate and GABA and GTRAP3-18. We also evaluated the suppressive effects of LEV on hippocampal glutamate release.
Methods: Rats with recurrent seizures induced by amygdalar injection of 1.0microl of 100mM FeCl3 were compared to control animals with saline injected. Exp I: glutamate release evoked by hippocampal perfusion with high K+ (40 mM) was monitored with or without LEV co-perfusion in non-epileptic or epileptic rats. (LEV was given from UCB-Belgium). Exp II: animals were randomly divided into two groups and were treated either with daily i.p injections of 54mg/kg LEV or with i.p. saline. Following 14 days of treatment, ipsilateral hippocampus was removed for western blot.
Results: Exp I: in amygdalar saline control rats, glutamate release evoked by high K+ was significantly suppressed by both 30 and 100 micromole/L LEV perfusion. In epileptic rats, 30 micromole/L LEV was ineffective, but 100 micromole/L LEV caused statistically significant (about50% decrease, $P<0.01$) suppression. Exp.II: in non-epileptic rats treated with LEV, transporter changes were increased with EAAC1 (111%), GAT1 (152%) and GAT3 (136%) while GTRAP3-18 (91%) was decreased compared to saline treatment controls. In animals with seizures induced by FeCl3 and LEV treatment, EAAC1 (108%) and GAT3 (109%) were increased while GTRAP3-18 (89%) was decreased compared to saline control.
Conclusion: GTRAP3-18 regulates glutamate-binding affinity with EAAC1. Administration of LEV causing increased EAAC1 and GAT-3 with decreased GTRAP3-18 would enhance synthesis and reverse transport of GABA both in non-epileptic and epileptic rats that is associated with suppression of glutamate release by LEV. Supported by Grant-in-Aid for Scientific Res. (C16591146) Japan.

p1184
The Effects of Electromagnetic Waves of Different Frequencies on Pentylenetetrazol-induced Seizures in Mice
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Purpose: The purpose of this study was to measure the effects of different frequencies of electromagnetic waves (EMW) for long term exposure time on a pentylenetetrazol (PTZ) seizure model in mice.
Methods: The study included 60 male albino mice at 3 weeks of age, weighing 20 –35 grams. EMW of 100, 300, 500, 700, 900 MHz for 20 hours were exposed to mice. EMW were generated by a signal generator and transmitted via an antenna. The frequency of the waves was tested by A spectrum analyser and a frequency-meter. Intraperitoneal injections of PTZ (60 mg/kg) were administered immediately after EMW and the control groups. Seizure latency was assessed by the time to the first myoclonic jerk.

Results: There were no statistically significant differences between the groups when compared with each other (p>0.05).
Conclusion: Formerly we reported that the latency was reduced in prepubertal mice exposed to 900 MHz EMW for 20 h exposure with seizure intensity scores of 1 and 2 (Erdinc OO et al. Neurol Sci 2003; 24: 111-116). This effect might be related to the thermal effect and any other associated effects of EMW which may not be attributed to frequency of 900 MHz.

p1185
Cellular Distribution and Expression of Multidrug Resistance Proteins in Focal Cortical Dysplasia
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Purpose: Focal cortical dysplasia (FCD) is a congenital cortical developmental abnormality, which is generally characterised by drug resistant epilepsy. We aimed to investigate multidrug resistance-associated protein 1 (MRP-1) and multidrug resistance gene-1 P glycoprotein (MDR-1) in the resection material of patients with FCD who underwent surgery.
Methods: Formalin-fixed paraffin-embedded human brain tissues obtained from 20 patients and 10 autopsy controls were studied. Sections of 10 μm were cut and the tissue was stained with HE, Bielschowsky and Luxol-Fast-Blue. All cells within the lesion were examined for the expression MDR-1 and MRP-1 by immunocytochemistry.
Results: Neuron: MDR-1 and/or MRP1 was strongly positive in 80% of patients whereas MDR-1 was none, MRP-1 was weakly positive in 50% of controls. Astrocytes: MRD-1: 10%, MRP-1: 55% of patients where MDR-1 was none and MRP-1 was 20% weakly positive for controls. Capillary endothelial cell: MDR-1 in 90% of controls, 50% of patients, MRP-1 50% of patients, 10% of control were positive. In FCD tissue, MRP-1 was detected 70%0 of patients with dysmorphic neurons, 25% with giant neurons, 33% with balon cells.
Conclusion: The over-expression of MDR proteins within the dysplastic tissue is evidence for drug resistant seizures in patients with FCD

p1186
Status Epilepticus in Rat and Guinea Pig (Lithium-Pilocarpine and PTZ Models)
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Purpose: Status epilepticus (SE) is a serious complication for intensive care unit patients. EEG is helpful in further dividing SE into episodes that are generalised from onset, or have a partial onset. The investigation of time of SE duration in models is preferable because it is connected with the basic problem of GABAA receptors desensitization. The aims of the study were: 1) to compare the development of lithium-pilocarpine SE in the Wistar rat and Guinea pig; 2) to evaluate the correlation between neocortex EEG patterns of brain and behavioural manifestation of fits (video record); 3) to compare developing SE induced by repeated PTZ administrations.
Methods: Two models were studied in vivo in g.pig and rat. The animals were operated (deep farmotal narcosis) and chronic silver electrodes were implanted in the cortex and hippocampus using the atlases of rat brain (Fifkova, Marshall, 1962) and g.pig brain (Rapisarda, Bacchelli, 1977). Protocol in rat (by P. Mares, H. Kubova): 1 day before rats were injected with an aqueous solution of LiCl (3mmol/kg i.p. 'Acros') and 24 h later pilocarpine HCl (40 mg/kg i.p. 'Acros') made in saline, experimental SE was stopped by paraldehyde (0.6 mg/kg). Protocol in g.pig (by M. de Curtis): 1 day before g.pigs were injected with an aqueous solution of LiCl (127 mg/kg, i.p.) and 24 h later scopolamine 1 mg/kg, pilocarpine HCl (55 mg/kg or 100 mg/kg i.p.) made in saline, experimental SE was stopped by diazepam (10 mg/kg). PTZ ('Sigma') injected i.p. by modified test (25 mg/kg x 3) or bolus injection – 100 mg/kg. Control registration of basic EEG was done during interictal periods for evaluation of chronic epileptogenesis. Motor seizures were evaluated with a currently accepted scale of motor convulsions in rats.
Results: The g.pig was more sensitive to epileptogenes and non-survival of the animal after SE was the main problem in developing a chronic epilepsy model. In rat and in g.pig a more constant and effective model of chronic epileptic activity developed after PTZ injections. In g.pig three-fold injections of PTZ (dose 20-25 mg/kg) induced only 3th stage of convulsions. The 4-5th stage SE with latency >35min is less frequent. SWD was recorded after 50 min from the beginning of experiment. SE developed after 3-5 min in the case i.p. PTZ injection in dose 100 mg/kg (clonic-tonic convulsions virtually induced). Immediate blocking of SE by diazepam is required.
Conclusion: Optimal model of inducing of chronic epilepsy in g.pig was repeated PTZ injections (i.p.) in dose 100 mg/kg under conditions diazepam block of SE.

p1187
Effects of Hydro-alcoholic Extract of Thymus Vulgaris on Chemical Epilepsy in Rats
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Purpose: Previous findings suggested that Thymus Vulgaris (TV) may have modulatory effects on seizure crises. The present work investigated the effects of hydro-alcoholic extract of TV on chemical epilepsy in rats.
Methods: This experimental study was performed on 50 male rats (5 groups). During the kindling procedure the animals received one IP injection of pentylenetetrazole (PTZ) 50 mg/kg every 48 h for 3 times. Convulsive behaviour was observed for 20 min after PTZ injection. The seizures were classified in 0-5 stages: 0, no response, 1, ear and facial twitching; 2-3, myoclonic jerks without or with upright position; 4-5, clonic-tonic seizures alone or with loss of postural control. Besides the increase in seizure intensity, any subsequent mortalities, and frequency of stage 5 in final 3 doses PTZ injection were noted. Animals received vehicle or TV extract (50, 100, 200 and 500 mg/kg) 20 min before the PTZ IP injection respectively.
Results: In the PTZ group (vehicle) 25% of animals died, while in the TV–treated rats, mortality decreased by 0%. Overall, TV in dose dependent manner decreased the seizure mortality rate in PTZ-treated groups (P<0.01). Also 60% of animals in the PTZ group (control) showed stage 5 seizures in final 3 doses PTZ injection but in TV groups (200, and 500 mg/kg) the frequency of stage 5 decreased (14%) significance (P<0.05).
Conclusion: The above findings indicate that TV extract modulates seizure crises. Further research is needed to identify neurotransmitter roles or other factors that may affect this process.

p1188
Expression and Localisation of P-Glycoprotein in Several Limbic Brain Regions in Phenytoin Resistant Amygdala-kindled Rats
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Purpose: The expression of membrane drug transport systems in the central nervous system plays an important role in the brain disposition and efficacy of many pharmacological agents used in the treatment of neurological disorders such as epilepsy. In the present study we used

amygdala-kindled rats, a refractory model to antiepileptic drugs, to study the PGP-1 expression in several limbic brain regions.
Methods: Male Wistar rats (250-350g) were kindled by basolateral amygdala stimulation. After kindling acquisition, four independent acute phenytoin (75 mg/kg i.p.) trials were done for selection. Response to phenytoin was determined using a threshold after-discharge, the response was sensitive kindled (KSEN), variable (KVAR) or resistant rats (KRES). PGP-1-expression was analysed 24 h after the last kindled seizure by immunohistochemistry.. The hippocampus, cerebral cortex and amygdala were examined by confocal and light microscopy.
Results: In both kindled and KSEN rats PGP-1- staining was observed mainly in microvessel endothelial cells, astrocytes and some neurons of the hippocampus and cortex. In KSEN rats PGP-1 staining was observed in endothelial cells, neurons and astrocytes in all brain areas evaluated. KRES rats showed a increased PGP-1 expression of the endothelial vascular cells and the reactive glial cells mainly of the hippocampus and some neurons in the amygdale.
Conclusion: PGP-1 overexpression in KVAR and KRES rats mainly in the endothelial and glial cells of the blood brain barrier maybe reduce the penetration of AEDs into brain parenchyma, which could explain the variability of the response and phenytoin resistance in this epilepsy model.

p1189
Early DNA Double Strand Breaks after Status Epilepticus in Rats
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Purpose: Oxidative stress contributes to seizure-induced excitotoxicity by causing cellular damage including DNA damage. Double-strand breaks (DSBs) are a lethal type of DNA damage, yet DSB induction and repair in neurons following excitotoxic insults remains unexamined. This study examined DSB formation following status epilepticus and, to explore DSB repair mechanisms, following glutamate receptor activation in neuronal cultures.
Methods: DSBs were quantified using immunocytochemical detection of phosphorylated histone H2A.X (γ-H2AX) foci. DSBs were analysed in Sprague-Dawley rat brains following kainic acid-induced status epilepticus (lasting 30 or 120 min and then terminated with diazepam) and in cultured rat cortical neurons following NMDA or AMPA treatment. The significance level was $p < 0.05$ (Kruskall-Wallis).
Results: Status epilepticus resulted in an increase in DSBs immediately following seizure termination in multiple brain regions including hippocampus and rhinal cortex. In cultures, NMDA and AMPA caused a rapid increase in γ-H2AX foci in both the presence and absence of cell death. Foci levels decreased after a pharmacological wash with NMDA or AMPA receptor antagonists (MK801 and NBQX, respectively) but did not return to control levels. A subset of γ-H2AX foci co-localised with the DNA repair factor, Mre11.
Conclusion: Seizure activity in-vivo and glutamate receptor activation in-vitro rapidly induce DSBs in neurons. Moreover, Mre11 and γ-H2AX co-localisation suggests an attempt to repair this damage, but the failure of γ-H2AX foci to return to control levels indicates persistent DSBs. Although DSBs did not necessarily result in cell death, persistent damage may contribute to subsequent neurodegeneration. Supported by NIH funding NS046199 and MH02040.

p1190
Spike-and-slow-wave EEG Discharges: From the Experimental Model to Clinical Reality
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Purpose: Validation of the conceptual model of epileptic reorganisation of the cortical function based on cat penicillin model of experimental epilepsy (P. Gloor, 1979) still requires investigation for evidence directly supporting the hypothesis. In this research a comparison was made between temporal and spatial parameters characterising EEG cortical spindle activity in cats and rhythms of repetitive, short lasting (2-4 s) discharges of the 2-4/s spikes-and-slow wave complexes, encountered in patients with epilepsy or cerebrovascular disease.
Methods: The animal data were collected from a group of 5 cats with multiple, permanently implanted cortical electrodes. The data were collected during physiological sleep and after intraperitoneal application of crystalline penicillin, 300,000 units/kg b.w. The distribution of cortical potentials was evaluated by current source density mapping (CSD). The temporal parameters of sleep spindles in cats as well as epileptiform discharges: discharge durations and intervals between consecutive discharges or spindles were subjected to statistical analysis.
Results: There was a striking similarity between distributions of the parameters in the analysed samples: duration of spike-and-slow wave discharges about 1.6 s (mean) and interval about 3.5 s (median) and 1.4 s and 5.3 s, respectively, for the sleep spindles. The maximum amplitudes of epileptiform discharges were localised in frontal and central leads. Sleep spindles in cats are localised basically in premotor and motor cortical areas. Administration of penicillin in cats promoted rapid synchronisation of the cortical spindle activity recorded from widespread cortical fields.
Conclusion: The results of this investigation illustrate a similarity between temporal parameters characterising boundary conditions of the repetitive appearance of the cortical sleep spindles in cats and short lasting epileptiform discharges of the 2-4/s spikes-and-slow waves in human EEGs. The results support the hypothesis that an altered mechanism responsible for the appearance of cortical sleep spindles may participate in formation and generalisation of spike-and-slow wave complexes. Acknowledgment: This research was supported in part by the State Committee for Scientific Research, Poland, grant 4-T11E-008-22.

p1191
Medicinal Herbs and Epilepsy
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Purpose: Medicinal herbs have a broad spectrum of application in folk medicine, bur rarely anyone regards their unwanted effects, especially in chronic diseases. In our experiment we explored the potential influence of Hypericum perforatum L. and especially Ginkgo biloba on the number of epileptic seizures and their duration in rabbits with kindling epileptogenic focus in the hippocampus.
Methods: The Electroencephalographic method of registration (EEG) was used. Gingko biloba was administered orally at a dose of 2mm per BW, Hypericum perforatum L. was applied i.m. at a dose of 1mm /BW (the doses of the substances were defined after experience from our former investigations). EEG was registered immediately before and after administration of the substances for a period of at least three hours.
Results: The results obtained clearly reveal that use of the watery extract of Hypericum perforatum L. decreases the number of epileptogenic seizures. The application of Gingko biloba increased the

number as well as the duration of epileptogenic seizures in most of the experimental animals.
Conclusion: The medicinal herbs effected epileptic activity in rabbits. The question is still open regarding which active components of the analysed medicinal plants influence experimental epilepsies. The answer requires not only further neurophysiological but neurochemical investigations as well.

p1192
Synaptophysin Immunoreactivity in the Lithium-pilocarpine Model of Temporal Lobe Epilepsy in Adult and Immature Rats
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Purpose: The lithium-pilocarpine (Li-pilo) model is characterised by acute status epilepticus (SE) followed by a latent seizure free period and spontaneous recurrent seizures. In adult rats, extensive damage and neuronal loss are present in the hippocampus, thalamus, amygdala and ventral cortices while 21 day old rats (PN21) display less widespread and intense damage compared with that in a mature brain. We examined the features of neuronal reorganization following SE in adult and PN21 rats using the neuronal marker synaptophysin.
Methods: In adult and PN21 male rats, SE was induced by LiCl and pilocarpine. Expression of synaptophysin was examined at 3 and 7 days after SE on sections cut with a cryostat and stained free-floating with a specific antibody. The optical density of regions of interest was measured by means of an image processing system.
Results: In adult rats, synaptophysin expression increased in the lateral thalamus, amygdala, piriform and entorhinal cortices at 3 days after SE. This high expression was still present after 7 days in cortices. In the hippocampus, immunoreactivity of the protein was similar in control and Li-pilo rats. In PN21 rats, synaptophysin expression increased only in piriform and entorhinal cortices at 3 and 7 days.
Conclusion: The higher expression of synaptophysin indicates that Li-pilo SE produced severe and rapid damage, especially in piriform and entorhinal cortices. The transient increase of synaptophysin in the thalamus and amygdala reveals early neuronal loss but less damage. In PN21 rats, Li-pilo SE-induced damage and synaptophysin reactivity appear to be limited to basal cortices.

p1193
LGI1/Epitempin: Differential Protein Expression in Human Brain Regions
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Purpose: To characterise the LGI1/Epitempin protein product and determine its distribution in various regions of the human brain.
Methods: Whole cell protein extracts from mouse brain and selected regions of the human brain were analysed by Western blot using an anti-LGI1 antibody. Mouse brain fractions obtained by ultracentrifugation of tissue homogenates were also analysed by immunoblotting.
Results: Two protein products with apparent molecular weights of about 60 and 65 kDa were detected both in human and mouse brain homogenates by a polyclonal antibody to LGI1. The smaller polypeptide was more abundant than the larger one in the mouse brain; no expression of either protein was detected in other mouse tissue. The two proteins appeared to reside in different subcellular compartments, as they were fractionated by differential centrifugation. Several pieces of experimental evidence supported the LGI1-specificity of both polypeptides. Immunoblot analysis of LGI1 protein distribution in various zones of the human brain revealed variable amounts of both proteins. Notably, the two proteins were found to be more abundant in the lateral temporal cortex than in the hippocampus, the difference in abundance of the 65-kDa product being particularly pronounced.
Conclusion: Our data indicate that expression of the Lgi1/epitempin proteins is finely regulated in different brain regions and suggest that production of higher amounts of both proteins, or solely of the 65-kDa polypeptide, may cause neurons of the lateral temporal cortex to be susceptible to the epileptogenic effects of LGI1/Epitempin mutations.

p1194
Working and Reference Memory Changes in Male and Female Epilepsy Mice at Different Time Points after Pilocarpine Induced Status Epilepticus (APISE)
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Purpose: To show if there is a progressive change of working and reference memory at different time points APISE and correlate it to neuropathological change in epilepsy mice, and to find if there is any difference in working and reference memory between male and female epilepsy mice.
Methods: A behavioural test of Swiss Albino mice at 2 weeks, 2 and 6 months APISE was conducted using an eight-arm radial maze. The number of correct first choice (for reference memory), working memory error, corrected error number and ranking were analysed statistically. Mice were sacrificed after the behavioural test for NeuN immunostaining to show neuropathology changes. Some were subjected to long-term potentiation (LTP) induction in the dentate gyrus of the hippocampus by tetanic stimulation of the perforant pathway.
Results: Reference memory impairment was found in all epilepsy mice 2 months APISE. Male mice showed a significant loss of working memory at 2 weeks, 2 and 6 months APISE ($P<0.05$). However, such a loss occurred only at 6 months APISE in female mice. An electrophysiological study showed the lack of long-term potentiation in the dentate gyrus in male mice at 2 month APISE.
Conclusion: There may be a difference in working memory changes at an early stage after status epilepticus. Reference memory was lost in epilepsy mice 2 months APISE.

p1195
Comparing Seropositivity Rates of Toxocara and Toxoplasma Between Patients with Cryptogenic Epilepsy and Healthy Controls
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Purpose: The increased seropositivity of toxoplasma gondii and toxocara canis has been previously documented in epilepsy patients. Our aim is to demonstrate a relationship between cryptogenic epilepsy and these infectious agents.
Methods: We studied specific IgG antibody agents toxoplasma gondii and toxocara canis in 100 cryptogenic epilepsy patients and 50 healthy volunteers whose first degree relatives had no seizure history. We compared toxoplasma gondii and toxocara canis specific IgG antibody serum levels of the two groups ($p>0.05$).
Results: Toxoplasma gondii and toxocara canis serum IgG antibodies were higher in patients with cryptogenic epilepsy than in the control group. However, this difference was not statistically significant.
Conclusion: We did not find any relationship between these infectious agents and cryptogenic epilepsy. However, when we evaluated our data and similar study results, these two infectious agents can still be important as a cofactor in cryptogenic epilepsy.

p1196
Role of Gap Junctions in Human Neocortical Network Synchronization
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Purpose: The role of gap junctions in network synchronization was studied in epileptic and dysplastic human neocortex.
Methods: Field potential and intracellular recordings were obtained in neocortical slices prepared from epileptogenic tissue removed for therapeutic reasons in patients suffering from mesial temporal lobe epilepsy (MTLE) or epilepsy related to a focal cortical dysplasia (FCD). The effect of gap junction blockers was tested on spontaneous or on 4-aminopyridine-induced (4-AP, 50μM) epileptiform activities.
Results: During application of 4-AP spontaneous field potentials occurred synchronously at sites up to 5 mm apart in slices from MTLE patients. This activity, representing a network response to GABA released from interneurons, was disrupted or abolished by bath applied gap junctions blockers: carbenoxolone (0.3mM; n= 30), octanol (0.5-1mM; n= 18). In these conditions, electrical stimuli elicited field potentials resembling those occurring spontaneously under control conditions. Similar findings were also obtained with octanol (0.5-1 mM; n= 13) while recording intracellularly from regularly firing neocortical cells. In a second series of experiments we found that carbenoxolone (0.3 mM; n= 5) abolished the NMDA receptor-mediated synchronous activity occurring spontaneously in slices obtained from FCD tissue without 4-AP. Moreover, octanol (1 mM, n= 6) or carbenoxolone (0.3 mM; n= 3) blocked ictal-like discharges induced by 4-AP in FCD slices.
Conclusion: Gap junctions may play a role in synchronizing human neocortical networks. The ability of gap junction blockers to abolish spontaneous events and 4-AP-induced ictal discharges in FCD slices suggests that gap junctions can implement epileptogenesis in this tissue.

p1197
Changes in Spontaneous Inhibitory Synaptic Transmission with No Change in Spontaneous Excitatory Synaptic Transmission to Heterotopic Neurons in Hippocampus of Rats Exposed to Methylazoxymethanol in Utero
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Purpose: Epilepsy is often associated with brain malformations. These malformations lead to altered properties in cerebral neural networks, including changes in connectivity and efficacy in both excitatory and inhibitory synaptic transmission. Using an animal model for cerebral malformations, rats exposed to methylazoxymethanol (MAM) in utero, we investigated excitatory and inhibitory synaptic transmission in nodular heterotopias in rat hippocampus.
Methods: Pregnant Wistar rats were injected with MAM (25 mg/kg) at E15. Acute hippocampal slices were prepared from rat pups P21 to P28 using standard procedures. Whole-cell voltage-clamp recordings were made from visually identified neurons using IR-DIC video microscopy. Synaptic events were recorded from either heterotopic neurons in the CA1 region or "sliced-matched" normotopic CA1 pyramidal neurons.
Results: Clamping cells at either -70 mV or 0 mV, both spontaneous inhibitory (sIPSC) and excitatory synaptic transmission (sEPSC) to the same neurons could be recorded. We found a profound reduction in frequency of sIPSCs in heterotopic neurons (1.3 ±0.5 Hz, n=6) versus normotopic neurons (7.0 ±1.9Hz, n=5). Furthermore, as described previously, the decay of the sIPSCs in heterotopic neurons was prolonged. No significant differences in frequency (1,9 ±0,7Hz vs 2.5 ±0,7Hz) or kinetics of sEPSCs were found between heterotopic and normotopic neurons.
Conclusion: Our data suggest that there is a change in inhibitory synaptic transmission neurons, as measured by changes in sIPSCs, with no change in excitatory synaptic transmission to heterotopic neurons in hippocampus of rats exposed to MAM in utero. The decreased frequency of sIPSCs might be one factor involved in the epileptogenicity of cortical malformations.

p1198
Neurogenesis vs. Glinogenesis in Human Temporal Lobe Epilepsy: Inflammation is Critical
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Purpose: Hippocampal neurogenesis is increased in animal models of mesial temporal lobe epilepsy (MTLE) but the fate of newborn cells is unknown. Here we attempted to demonstrate neurogenesis in adult epileptic tissue obtained after hippocampectomy.
Methods: Human subjects: hippocampi were obtained in patients who underwent surgery for intractable TLE : 23 MTLE (mesial TLE with hippocampal sclerosis and a history of febrile seizure) and 8 TLE with other etiologies (DNET, hippocampal atrophy, encephalitis or cryptogenic) and in 4 non epileptic patients (NE), 2 with a parahippocampal tumour and 2 autopsied. Hippocampi were used for immunohistochemistry and western blotting.
Results: Compared to control hippocampi, MTLE hippocampi showed increased expression of division markers and of Musashi-1, a marker of neural progenitors. Large quantities of neural progenitors were obvious in the subgranular layer and the subventricular zone, both known neurogenic areas, and also in the fissura hippocampi. Some of them are present in the granular layer, the hilus and CA1 area, resembling the migratory pathways described in rodents. Musashi-1 was expressed by small cells that express mainly markers of immature astrocytes and rarely markers of immature neurons. They are negative for markers of mature neurons or astrocytes.
Conclusion: These findings demonstrate that abundant neural progenitors proliferate in chronic epilepsy but their phenotype corresponds to immature astrocytes which could participate in hyperexcitability. We suggest that the inflammatory environment is crucial for the neuronal or glial fate.

p1199
Investigation of the Relationships between Multiple Epileptic Foci
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Purpose: Understanding the mechanisms underlying the relationship between multiple epileptic foci has clinical importance. The main goal is to study the role of the nature and magnitude of epileptiform activity (EpA) and localisation in the neocortex of the focus EpA in the interrelationship of the multiple foci EpA.
Methods: Investigations were conducted on Wistar rats. Epileptic foci were induced by bicuculline, strychnine and acetylcholine applied to different zones of the neocortex. EEG registration followed each series of experiments.
Results: A focus of more powerful EpA enhances the activity of the relative weak foci EpA, combines them into a single functional complex and determines the character of activity of the whole complex. This focus appears to have the determinant role. Determinant focus activity being suppressed with the help of pentobarbital application can destroy this complex. The easther or narcotan narcosis as well as diazepam administration resulted in EpA suppression firstly in the dependent focus that was located more distantly from the determinant one.

Conclusion: EpA magnitude and cortico-cortical connections between zones of the foci localisation could determine quantitative differences between multiple foci of EpA. These conclusions were also proved in our experiments with EpA activation and suppression during pentylenetetrazol-induced chemical kindling.

p1200
Geminin Expression in Balloon Cells in Focal Cortical Dysplasia (FCD) Type IIB
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Purpose: Focal cortical dysplasia (FCD) type IIB is a common cause of focal epilepsy and characterised histologically by the presence of balloon cells and abnormal cortical architecture. Balloon cells may represent undifferentiated neurones and we have previously demonstrated expression of Mcm2 replication licensing protein in these cells in FCD, indicative of their proliferative potential. Geminin is a protein with twin functions. It is an inhibitor of DNA replication and also has a role in neuronal differentiation (Quinn et al, Genes and Development 2001; 15 : 2741-2754). Our aim was to study the expression of geminin in FCD lesions in comparison with Mcm2.
Methods: We studied 15 cases of FCD from a wide patient age range (1-81 years) including cases with balloon cells. Immunohistochemistry was carried out for geminin (G94 and G95), Mcm2, active caspase-3, Ki67, NeuN, nestin, neurofilament markers SMI31 and 32, GFAP and CD34 and in selected cases using confocal imaging.
Results: Mcm2 showed frequent labelling of balloon cell nuclei (between 50-70% of cells in FCD type IIB) in both the cortex and white matter. Geminin labelled a smaller proportion of balloon cells, was predominantly nuclear in distribution and with more prominent staining of cells in sub-cortical locations. Dysmorphic neurones were generally geminin negative. Caspase-3 showed strong nuclear positivity in many balloon cells, including multinucleated cells.
Conclusion: The identification of geminin in balloon cells supports completion of the cell cycle. Its expression may also be relevant to the neuronal differentiation observed in these cells.

p1201
A Morphological Study on the Hippocampus of Genetic Absence Epilepsy Rats Receiving Amygdaloid Kindling Stimulations
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Purpose: Genetic absence epilepsy rats from Strasbourg (GAERS) is a model of absence epilepsy. Although excessive GABAergic neuromediation within the thalamo-cortico-thalamic circuit is the accepted mechanism in absence epilepsy, neuronal networks of the hippocampus have recently received attention. The aim of the present study was to investigate whether or not amygdaloid kindling stimulations in GAERS caused neuronal degeneration in the hippocampal CA1, CA3 and dentate regions.
Methods: Adult Wistar rats and GAERS were instrumented stereotaxically with bilateral stimulation and recording electrodes into the basolateral amygdala and the cortex. Animals were electrically stimulated twice daily at their after discharge threshold currents. Animals were considered as fully-kindled when they experienced 3 stage 5 seizures. Twenty-four hours after the last stimulation, the animals were sacrificed. The brains were cut into slices and CA1, CA3 and dentate regions of the hippocampus were dissected. After routine electron microscopic procedures, semi-thin sections were cut on an ultramicrotome and stained with toluidine blue.
Results: Kindled Wistar rats showed neuronal morphological degeneration in CA1 and CA3 pyramidal and dentate granular layers. GAERS, which showed only stage 2 seizures, revealed no neuronal degeneration in these layers.
Conclusion: It is known that the hippocampus is involved in neural activity in absence epilepsy (1). In the kindling model of temporal lobe epilepsy, neuronal loss occurs in granule cell layer, CA1 and CA3 (2). The protection of principle cells in the hippocampus of GAERS might be related to the failure of this strain to reach stage 5 seizure state. Furthermore, GAERS may have different plasticity. References 1. Tenney JR et al. 34th Neuroscience Meeting, 2004, 227.17. 2. Cavazos JE et al. J Neurosci 1994;14:3106-3121. Key words: GAERS, kindling, hippocampus, neurodegeneration

p1202
Lamotrigine but not Valproate Blocks Sodium Currents in the Rat Hippocampal Slice
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Purpose: To study the effect of valproate (VPA) and lamotrigine (LTG) on the Na current in hippocampal slice neurons. The rationale was to demonstrate differences in the antiepileptic mechanism of LTG and VPA and conflicting results in previous reports on VPA effect on Na channels.
Methods: CA1 pyramidal cells in hippocampal slices from young rats were investigated using the patch-clamp technique. Action potentials (AP), and resting potential (Vm) were recorded with current clamp in whole-cells with VPA (1 mM, n=15) or LTG (0.1 mM, n=12) and in controls (n=16) for 10 min. Na currents were recorded with voltage-clamp in cell-attached configuration with VPA (2 mM, n=8) and in controls (n=5) for 25 min.
Results: LTG decreased AP rising slope by -13±17%, the peak amplitude by -10±7 %, the maximum firing frequency by -46±43% and increased peak amplitude difference between first and second AP by 474±251%. This differed ($p<0.005$) from the spontaneous changes in control cells. VPA had no significant effect on these parameters (-0.1±15%, -6±9%, 2.0±41% and 54±94%, respectively) or on peak Na current (-24±29%) vs controls.
Conclusion: 1) LTG affected the firing properties of the hippocampal neurons, which implied a decrease in the Na current due to block of Na channels. 2) VPA differed from LTG, and VPA does not seem to affect the Na current in the hippocampal slice. This differs from previous reports about VPA effects in cultured or dissociated neurons and is in agreement with a previous finding on the hippocampal slice.

p1203
Reorganization of Gliotic CA3 Area of the Mouse Hippocampus after Pilocarpine Induced Temporal Lobe Epilepsy (TLE)
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Purpose: To investigate reorganized neural circuit of CA3 area of the hippocampus in the mouse model of TLE 2 months after pilocarpine induced status epilepticus so to correlate it to epileptogenesis.
Methods: Anterograde (phaseolus vulgaris leucoagglutinin, PHA-L) or retrograde (cholera toxin subunit B, CtB) tracer was iontophoretically injected into CA3 area of the dorsal hippocampi of normal and epilepsy mice, and the brain samples were then processed for immunocytochemistry.
Results: We showed that in epilepsy mice, (i) PHA-L labelled axons and terminals almost disappeared in the bilateral dorsal part of lateral septum where significant neuronal loss occurred ($P<0.01$), and in the contralateral CA3 and CA1 areas; (ii) the number of CtB labelled neurons in the medial septum and diagonal band, medial raphe and lateral supramammillary nuclei increased significantly when compared to the control mice ($P<0.05$). However, they decreased drastically in the contralateral CA3 area; (iii) the proportion of CtB and choline acetyltransferase, calbindin or parvalbumin double labelled neurons in the medial septum, of CtB and calretinin in the

lateral supramammillary and medial raphe nuclei to all the CtB labelled neurons in the respective areas showed no significant change compared to the control.
Conclusion: Our results suggest that the increased afferent to gliotic CA3 area and decreased efferent from the same area to lateral septum may be involved in epileptogenesis. This study was supported by research grants (NMRC/0670/2002, NMRC/0777/2003, NMRC/0731/2003) from the National Medical Research Council of Singapore.

p1204
4-Aminopyridine-induced Increases in Intracellular Free Ca2+ in Cultured Mouse Cortical Neurons
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Purpose: 4-Aminopyridine (4-AP), the potassium channel blocker, has been used as a therapeutic agent in many neurological and neuromuscular junction disorders. It may also induce seizures in experimental animals. The present study assessed the effect of 4-aminopyridine (4-AP) on intracellular free calcium concentration [Ca2+]i in cultured mouse cortical neurons, with the aim of exploring the intrinsic mechanisms.
Methods: [Ca2+]i in cultured neurons was indicated by fluorescent probe Fluo-3-AM. Changes of calcium signal in response to the treatments of 4-AP (10mM) and L-glutamate (10mM) were observed and quantified by using time-lapse confocal microscopy.
Results: It was demonstrated that both 4-AP and glutamate can increase [Ca2+]i significantly in the absence of extracellular calcium, whereas the calcium response curve to each reagent was characterised in its own manner. 4-AP induced calcium response was more moderate and durative compared to the L-glutamate effect. The [Ca2+]i curve in response to simultaneous treatment of 4-AP and glutamate was similar to characterization of only glutamate induced response.
Conclusion: The pharmacological effects of 4-AP may be related to the complex change of calcium homeostasis, the underlying mechanism of which may be partially similar to that of glutamate-induced change.

p1205
Soman-induced Neuropathological Changes in Some Structures of the Rat Brain
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Purpose: In survivors of soman poisonings, especially those which demonstrate convulsions and seizure activity, neuropathology in the brain was identified. There are three hypotheses of the mechanism of these neuropathological changes: 1) excitotoxic, 2) hypoxic and 3) a direct neurotoxic effect. The majority of authors have now accepted the predominant role of the first hypothesis. However, some data indicate that the state of hypoxia could contribute to the mechanism of these changes. The purpose of this study was evaluation of the neuropathological changes in chosen structures of the rat brain after acute intoxication with soman.
Methods: Experiments were performed on Wistar rats with electrodes implanted to the sensory-motor cortex. Only animals which exhibited seizure activity confirmed electroencephalographically, were included in the study. Histopathological determinations were performed in frontoparietotemporal, perirhinal and piriform cortex, basomedial and basolateral amygdala, mediodorsal and laterodorsal thalamus, amygdalopiriform area and substantia nigra pars reticulata in animals, which survived 3 days after intoxication. Atropine methyl bromide and oxime HI-6 were used to allow survival after intoxication. Brain sections were performed according to Nissl and NeuN staining.
Results: More severe degenerative changes (necrosis and malacia of the neurons) were generally seen in the piriform cortex, basomedial and basolateral amygdala. Examples of histopathological pictures are demonstrated with the description of patterns.
Conclusion: Our results confirm that soman-induced convulsions may produce serious damage in brain structures, especially in the cortex and limbic system where neurons are probably the most susceptible for seizure activity. This work was supported by MoD/ 2004.

p1206
Effect of Melatonin on Cognitive Impairment and Oxidative Stress Induced by Intracortical Ferric Chloride Model of Posttraumatic Epilepsy in Rats
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Purpose: The present study was carried out to investigate the effect of melatonin, an endogenous neuromodulator with potent antioxidant property, against intracortical ferric chloride (FeCl3) induced cognitive impairment and oxidative stress.
Methods: Male Wistar rats weighing 200-250 g were injected FeCl3 (5ul, 100 mM) in the cortex intracortically. Rats were assessed for cognitive impairment (passive avoidance and elevated plus maze) on day 1 and 2 and subsequently sacrificed for the estimation of oxidative stress markers i.e. malondialdehyde (MDA) and catalase in brain tissue. Melatonin was injected at a dose of 50 mg/kg, i.p, 10 min before FeCl3 injection. Vehicle treated groups were run parallel.
Results: Administration of FeCl3 caused cognitive impairment as evident by increase in retention latency in elevated plus maze (80+18s) and decrease in step through latency (35+4.6 s) on day 2 as compared to day 1 (55 + 8.3s and 600 +3.2s respectively). A significant increase in levels of MDA and decrease in levels of catalase was seen in the vehicle treated FeCl3 group. Pretreatment of melatonin (50 mg/kg, i.p.) significantly ($p<0.05$) prevented the increase in MDA (185+10 nmol/g tissue) and prevented the decrease in catalase levels (114+40 U/mg protein) as compared to the vehicle treated FeCl3 rats (312+22 nmol/g tissue and 35+14 U/mg protein respectively). However, melatonin did not prevent cognitive impairment.
Conclusion: The preliminary findings suggest that though melatonin did not prevent cognitive impairment it reduced the oxidative stress induced by intracortical FeCl3.

p1207
Antiepileptic and Antiepileptogenic Properties of Levetiracetam in Rapid Kindling
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Purpose: This study assesses the antiepileptic and antiepileptogenic profile of levetiracetam (LEV) in rapid kindling with recurrent hippocampal seizures (RKRHS).
Methods: Rats were implanted with a stimulation electrode in the right hippocampus and several recording electrodes. One week later, rats were stimulated according to the serial or alternate day RKRHS protocol. Once fully kindled, they were randomly assigned to a control or an active group and accordingly treated with saline (0.9% NaCl, 2 ml/kg, i.p.) or LEV respectively, either in bolus injection (antiepileptic testing in serial day RKRHS, 54 mg/kg, i.p.) or through an implanted minipump (antiepileptogenic testing in alternate day RKRHS, 500 mg/ml, 2 ml). In the antiepileptic testing procedure, rats received additional kindling stimulations starting one hour post injection. In the antiepileptogenic testing procedure, rats were implanted with a minipump and retested for their kindled state after one week of treatment and a three day wash-out period.
Results: In the antiepileptic testing procedure, one hour following LEV administration, mean seizure stage and afterdischarge duration

dropped to 2.81 ± 1.15 and 29.47 s ± 18.48 s respectively, compared to 5 ± 0 and 51.48 s ± 16.65 s in controls ($p < 0.05$). Results from the antiepileptogenic testing procedure are still being processed and will be presented at the congress.
Conclusion: LEV displayed clear antiepileptic activity in RKRHS. The antiepileptogenic profile of LEV will be discussed at the congress.

p1208
Effects of Seizures During Pregnancy on Post-Natal Development of Offspring
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Purpose: The effect of seizures during pregnancy on physical development patterns (growth, weight and skull measures) of offspring was analysed. Maternal behaviour, number of litters, genders and presence of malformations were also evaluated using the pilocarpine model of epilepsy.
Methods: Experimental female and control rats were video monitored during pregnancy and the frequency of spontaneous seizures was observed. 12 h after birth, litter size was standardised to eight pups (males and females), followed by cross-fostering between controls and experimental and between control groups. Females were housed with their litters until weaning at postnatal P21 and their pups were analysed daily.
Results: There was no effect of maternal epilepsy on the number of pups at birth, sex distribution and weight at birth. No malformation has been observed. Quiescent nursing behaviours were not elicited in the experimental mothers and usually they eat their own pups. Offspring from experimental mothers reared by foster mothers presented low weight and growth until P20 ($p<0.001$). Control pups, which were submitted to cross-fostering also presented low weight and growth until P6, becoming similar to control at P13. The skull size of pups from experimental mothers was decreased when compared to the control group.
Conclusion: These data show that pups from mothers with epilepsy present physical developmental deficits when compared to pups from control mothers. Although cross fostering induced changes in the post-natal development of control animals, these changes were no longer noticed after the second week of life, while in pups from experimental mothers these differences remained for the whole period of observation.

p1209
Changes of Kv4.2 Channel and KChIP1 Expression in Lithium-pilocarpine-induced Epilepsy Rat Model
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Purpose: The A-type voltage-gated potassium (Kv) channels are evidenced to play a major role as modulators of somatodendritic excitability. Here we investigate whether the regulation of Kv4.2 channel and its major modulator Kv4 interacting protein (KChIP) expression may be involved in epileptogenesis.
Methods: We examined the expression levels of Kv4.2 and KChIP1 by immunoblot in lithium-pilocarpine-induced epilepsy rat model. Fluorescent immunolabelled Kv4.2 and KChIP1 were simultaneously observed under confocal microscope to analyse the correlation of localisation and changes of positive cell numbers in the hippocampus.
Results: Kv4.2 immunoreactive protein was elevated at 6h, 24h post-seizure, and showed no significant changes at 1h, 3h and 50d post seizure in the hippocampus and cerebral cortex of the model. KChIP1 expression showed an earlier and more remarkable elevation as compared with Kv4.2. Dual immunolabel test revealed Kv4.2 and KChIP1 were mostly colocalised in the same cells and abundantly expressed in the hippocampus. The number of KChIP1-positive cells was decreased in the late stage when a chronic spontaneous seizure was induced, while no significant change in the earlier stage was found.
Conclusion: In lithium-pilocarpine induced epilepsy rat model, the expression of Kv4.2 channel associated its main modulator KChIP1 was altered and redistributed in a time-dependent manner.

p1210
Effects of a Single Dose of Erythropoietin on Subsequent Seizure Susceptibility in Rats Exposed to Acute Hypoxia at P10
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Purpose: To determine if erythropoietin is protective against subsequent seizure susceptibility and against predisposition to seizure induced apoptosis in the P10 acute hypoxia model.
Methods: 3 groups of rats were manipulated at P10, as described below, and all received kainic acid (KA) (10mg/kg i.p.) at P29: Hypoxia-NS-KA group (n=11): subjected to acute hypoxia (down to 4%), and then immediately received saline i.p. Hypoxia-EPO-KA group (n=10): subjected to acute hypoxia and then immediately received erythropoietin (1000U/Kg) i.p. normoxia-NS-KA group (n=11): sham manipulated and injected with saline. After receiving KA all rats were monitored using videotape techniques, and were sacrificed at P31. TUNEL, Hoechst, and regular histology for hippocampal cell counts were performed.
Results: Normoxia-NS-KA and hypoxia-EPO-KA groups had similar [1] latencies to forelimb clonus (FLC) ($p=0.35$), [2] durations of FLC ($p=0.64$), [3] total and CA1 apoptosis severity scores ($p=0.62$), and [4] CA1 cell counts ($p=0.39$), which were [1] longer ($p=0.007$ and $p=0.04$ respectively), [2] shorter ($p=0.01$ and $p=0.033$ respectively), [3] lower ($p=0.02$ and $p=0.04$ respectively) and [4] higher ($p=0.01$ and $p=0.005$ respectively) than those of the hypoxia-NS-KA group. Means±SE: [1] FLC latency: 67.87±8.52, 56.7±10.29, 32.55±4.44 (minutes). [2] FLC duration: 3.27±0.85, 4.2±0.71, 8.27±2.04 (minutes). [3] TUNEL scores: Total: 0.75±0.31, 1.00±0.38, 3.00±0.74, CA1: 0.37±0.18, 0.71±0.28, 2.11±0.45. [4] Cell counts: CA1: 8.7 x 10-4±5.56 x 10-5, 9.52 x 10-4±1.2 x 10-4, 6.57 x 10-4±2.89 x 10-5 (cell count/pixel2).
Conclusion: Erythropoietin administered after an acute hypoxic insult at P10 protected against subsequent long term seizure susceptibility and predisposition to seizure related neuronal injury.

p1211
A Model of Neonatal Epileptic Seizures with an Interictal Suppression Burst Pattern by Glutamate Transporters Inhibition
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Purpose: Glutamate transporters are already expressed in both the human and rodent foetal brain. We have recently shown, in vivo in the newborn rat, that their inhibition by ICV injection of TBOA induces clinical manifestations that mimic seizures and in vitro in neocortical pyramidal neurons recurrent bursts of discharges. This suggested that the early expression of glutamate transporters is crucial to avoid pathological cortical network synchronisation. Because of the possible clinical relevance of these observations to human neonatal epileptic syndromes, we have further characterised the electrical activity induced by TBOA in vivo by, for the first time, coupling video monitoring with EEG recording on freely moving newborn rats.
Methods: Video-EEG monitoring in freely moving 5 days old rat.
Results: We demonstrate that TBOA generates partial motor and limbic seizures that are associated with an ictal discharge. Moreover, the inhibition of glutamate transporters disorganised the cortical electrogenesis to a pattern that resembles 'suppression burst', with burst phases often coinciding with erratic myoclonias. We also performed whole cell patch clamp recording from hippocampal CA1 neurons in slices and show that TBOA generates an NMDA receptor-dependent periodic synchronised currents/depolarisations that is reminiscent of those recorded in the neocortex.

Conclusion: We propose that this generalised recurrent activity, is pathological and might underlie the genesis of the suppression burst pattern. The similarities between our in vivo data and certain expressions of early infancy epileptic encephalopathy with suppression burst, suggest that a dysfunction of glutamate transporters may represent a potential cause of this severe disease.

p1212
Hippocampal Expression of Kinin B2 Receptor in Female Rats Submitted to the Pilocarpine Model of Epilepsy
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Purpose: Kinins, a class of polypeptides represented by bradykinin, kallidin, and their metabolites, acting via B1 and B2 receptors, have been related to inflammation, cytokines action, glutamate release and prostaglandin production. Several studies indicate that in the central nervous system and peripheral tissues, estrogen regulates the expression of the B2 receptor and reduces cytokine production and inflammatory responses. Accordingly, the present work aimed to investigate the expression of kinin B2 receptors in normal and neutered female rats, submitted to the pilocarpine model of epilepsy.
Methods: The brains of Wistar adult females of both groups of rats were removed 6h, 12h, 5 days and 60 days after pilocarpine-induced status epilepticus and immunohistochemistry (n=4) was performed to study the expression and distribution of kinin B2 receptor in the hippocampal formation.
Results: The results showed decreased immunoreactivity against the B2 receptor in non-neutered rats during the acute and silent periods of this epilepsy model. In contrast, the immunoreactivity against the B2 receptor in neutered rats was increased during the acute and silent periods when compared with control neutered rats.
Conclusion: This study provides evidence that the expression of kinin B2 receptor in the hippocampus is modified in female rats during epileptogenesis and that the expression of this receptor is modulated by steroid hormones. Supported by FAPESP, CNPq, CAPES.

p1213
Comparative Study of the Effects of Lamotrigine and Topiramate on Learning and Memory of Immature Rats with Sodium with Sodium Nitrate-induced Hypoxemia
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Purpose: The use of antiepileptic drugs (AED) as a possible neuroprotective strategy in brain ischemia is receiving increasing attention. Many AED have been tested in animal models of stroke induced by global or focal ischemia, providing encouraging results. This study was conducted to compare the effect of topiramate (TPR 5 mg/kg p.o.) and lamotrigine (LTG 0.5 mg/kg p.o.) on learning and memory in immature rats with reversible hypoxemia induced by sodium nitrate (SN 40 mg/kg i.c.).
Methods: 50 immature Wistar Rats (50 day old) were divided in five groups of ten: 1st gr (placebo-saline + SN); 2nd gr (TPR + SN); 3rd gr (LTG + SN); 4th gr (20 days TPR-pretreatment, then TPR + SN) and 5th gr (20 days LTG-pretreatment, then LTG + SN). Different behavioural appliances were used to compare the controls with the tested groups of rats: open field, step trough, step down and automatic shuttle box for passive and active avoidances, escapes, inter-training crosses and latency. Tissue samples were taken from the temporal cortex and hippocampus for histological impregnation and electro-microscopic investigation at the end of the study (48th day).
Results: Acute hypoxemia during the first day of the investigation with SN - 3rd and 5th gr. showed a significantly larger number of avoidances compared to the controls - 1st gr controls (x±SEM, resp. 0.024±0.007; 0.034±0.008 v/s 0.017±0.006; $p<0.05$). During the training tests of the 3rd and 5th gr a significantly larger number of active avoidances were revealed compared to the 1st gr of controls (x±SEM, resp. 0.30±0.07; 0.44±0.13 v/s 0.22±0.06; $p<0.05$). During the retention test 3rd, 4th and 5th gr showed a higher degree of differences compared to the controls (x±SEM, the number of active avoidances was resp. 0.35±0.08, 0.30±0.05 v/s 0.22±0.04; $p<0.05$). No statistically significant differences were determined between the tested groups and controls in regard to the number of passive avoidances, escape, latency time of step trough and step down.
Conclusion: LTG significantly increases the short and long-term memory of immature rats compared to the placebo. TPR improves short memory. Behavioural and histological results suggest that TPR- and LTG-pretreatment effectively protect the brain in the state of global sodium nitrate hypoxemia.

p1214
Differential Effects of Opioid Receptors Agonist and Antagonist on Hippocampal Seizure In-vitro
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Purpose: To determine the effect of selective agonist and antagonist of opioid receptors on hippocampal seizure in vitro, we designed the present study. Opiates have complex effects on seizure thresholds. Both anti and proconvulsive actions have been reported depending on the exact experimental conditions.
Methods: C57/b mice were anaesthetised with halothane and the brain was quickly removed and placed in continuously oxygenated (95% O2 –5% CO2), artificial cerebrospinal fluid (ACSF). Seizure activity was induced by continuously perfusing the hippocampus with Low Mg2+ ACSF. Extracellular recordings were performed mainly in the hippocampal CA1 area. Seizure activity was quantified by measuring the amplitude, duration and number of ictal events as well as the percentage of seizures in total recording time before and after application of the drugs.
Results: μ- opioid receptor agonist (DAMGO, 10 μM) depressed the seizure, whereas k-opioid receptor agonist (Dyn-A, 10 μM) potentiated it. Both effects were reversible by their antagonists (B-FNA and nor- BNI respectively). Delta -opioid receptor agonist (DPDPE) and antagonist (NTI) did not show any significant effects.
Conclusion: μ-opioid receptor has an inhibitory action on hippocampal epileptiform activity whereas K-opioid receptor has opposite effects. Probably the complex effects of morphine (anti and proconvulsive) are mediated through different opioid receptors. Key words: opioid receptors, whole hippocampus, epilepsy, mice.

p1215
Protective Effect of Vineatrol Against Kainic Acid Induced Seizures, Oxidative Stress and Expression of Heat Shock Proteins in Rats
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Purpose: To evaluate the effect of an antioxidant vineatrol against kainic acid (KA)-induced seizures, markers of oxidative stress and expression of heat shock protein (HSP)72 in brain.
Methods: Rats were administered KA (10 mg/kg) intraperitoneally (i.p) and observed for behavioural changes, incidence and latency of convulsions over a period of 4 hours. The rats were thereafter sacrificed for estimation of malondialdehyde (MDA) and expression of HSP72.
Results: KA induced long-lasting seizures, associated behavioural symptoms and significantly ($p<0.05$) increased level of brain MDA (295+18 nmol/g tissue) as compared to control (195+26 nmol/g tissue). Pretreatment (5 min) of vineatrol (10, 20 and 40 mg/kg i.p.) could not inhibit the convulsions though the latency was significantly increased with 20 and 40 mg/kg (117.5+11.6 and 128.2+12.2 min

respectively) as compared to KA group (47+4.9 min) ($p<0.05$). When the drug (20 and 40 mg/kg) was administrated 5 min prior, 30 and 90 min after KA there was significant reduction in incidence of convulsions (22.2% and 9% respectively) as compared to the KA group (100%). The brain MDA levels were significantly attenuated with 20 and 40 mg/kg (186.6+9.5 and 184+9.7 nmol/g tissue respectively). Expression of HSP72 was observed in the KA group as compared to control and was reduced by vineatrol.
Conclusion: The study suggests the potential use of vineatrol in status epilepticus.

p1216
Biochemical Markers of Excitotoxicity are not Detectable in Rat Brain Immediately Following Status Epilepticus
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Purpose: Excitotoxicity and mitochondrial dysfunction may contribute to the short and long term clinical sequelae of epilepsy. Reduced activity of mitochondrial enzymes and low levels of reduced glutathione (GSH) have been detected in discrete areas of rat brain as early as 4 hours following status epilepticus (SE) but it is unclear when these changes develop.
Methods: Perforant path stimulation was performed for 2 hours on adult Sprague-Dawley rats as previously described, generating self-sustaining limbic SE for 3 hours (n=3). Control rats (C; n=7, surgery but no stimulation) were studied in parallel. Immediately following SE animals were decapitated under anaesthesia, and brains dissected on ice. CA1, CA3 and dentate gyrus regions from right and left were pooled for analysis, homogenized and stored at –80 C. The activities of citrate synthase (CS), aconitase, alpha-ketoglutarate, and complexes I and II/III of the mitochondrial respiratory chain were measured using spectrophotometry, and reduced glutathione (GSH) measured using HPLC. Analysis was undertaken using Mann-Whitney U-test ($p<0.05$ significance).
Results: There were no significant differences between the activities of aconitase (SE:33.1nmols/mg/min+/-5.28(SEM); C:22.51nmols/mg/min+/-3.42; $p=0.183$), alphaketoglutarate dehydrogenase (SE:14.75nmols/mg/min+/-1.63; C:14.75nmols/mg/min+/-1.17; $p=0.929$), Complex I (SE:0.14CSRatio+/-0.01; C:0.11CSRatio+/-0.02; $p=0.67$), and Complex II/III (SE:0.07CS ratio+/-0; C:0.07CS ratio+/-0.01; $p=0.833$) immediately following SE, and levels of reduced glutathione were also unchanged (SE:15.14nmols/mg+/-2.38; C:16.29nmols/mg+/-1.42; $p=0.667$).
Conclusion: Previous studies have shown reductions in the activity of key mitochondrial enzymes and GSH levels as early as 4 hours following SE. These changes are not measurable immediately following SE, indicating that they occur early but not immediately. This supports the concept of a 'therapeutic window' for administration of neuroprotective strategies.

p1217
In Vitro Electrophysiological Study of the Hippocampal Formation of Proechimys Guyannensis: An Animal Specie Resistant to Experimental Models of Epilepsy
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Purpose: to investigate the antiepileptogenic mechanisms of the rodent Proechimys guyannensis (PG), observed in previous works, through in vitro electrophysiological techniques.
Methods: Intracellular and extracellular recordings were conducted in hippocampal slice preparation of Proechimys guyannensis and Wistar rats. Field excitatory postsynaptic potentials (fEPSPs) and population spike (PS) were obtained from CA1 area by electrical stimulation of CA1afferent fibres (Schaffer's collateral pathway). To induce LTP, tetanic stimuli were applied through the bipolar electrode and consisted in 2 trains of high-frequency stimulation (HFS) at 100 Hz separated by 25-s interval.
Results: Extracellular responses showed the same characteristics widely reported in other rodent species. However, a higher threshold for population spike (PS) appearance was observed. In agreement with this finding, invasive intracellular somata recordings showed a higher threshold to action potential firing when compared to Wistar rats. Our results also showed that PG was less susceptible to the GABAergic blockade by bicuculline (rare single recurrent spikes). In addition, no spontaneous activity could be recorded. Although the PS characteristics were similar to those observed in Wistar, no spontaneous activity was observed in the 0 Mg2+ protocol. Regarding LTP, although the protocol have induced successfully a potentiation in extracellular potential recorded in PG, the response reached an amplitude significantly less expressive than that observed in Wistar rats
Conclusion: Taken together our results suggest that PG has a hippocampal circuitry functionally different from that of the Wistar rat. This may be due to a different distribution and/or density of glutamatergic and GABAergic receptors or to differences in their current kinetics.

p1218
Lack of Ceramide Increase and of Apoptosis in Rats Subjected to Acute Hypoxic Seizures at P10
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Purpose: Acute hypoxic seizures at P10 results in long term seizure susceptibility, histologic changes and memory impairment. Ceramide is a mediator of cellular injury and apoptosis. The objective is to determine if ceramide increases and if apoptosis occurs in P10 pups following acute hypoxic seizures.
Methods: P10 pups were divided as follows: Controls: sham manipulated (n= 6/timepoint); Hypoxia group: subjected to acute hypoxic seizures (O2 down to 4%) (n=6/timepoint). Rats were sacrificed at 2hrs, 3hrs, 6hrs, 12hrs, 18hrs and 24hrs. Hippocampi were dissected and ceramide-DGK assay was performed. Other P10 rats were divided as follows: Controls: sham manipulated; Hypoxia group: subjected to acute hypoxic seizures. All rats were sacrificed at 1 day (n=10/group), 3 days (n=18/group), 7 days (n=12/group). TUNEL stains were then performed for assessment of DNA fragmentation.
Results: Ceramide levels did not differ between the Control and Hypoxia groups at any of the time points ($p>0.33$). Mean±SE of Cer/Pi ratio for the Control and Hypoxia groups (in nmoles): 2hrs: 4.89±0.21, 4.97±0.21. 3hrs: 5.72±0.45, 5.09±0.03. 6hrs: 5.4±0.28, 5.26±0.41. 12hrs: 6.11±0.005, 5.42±0.26. 18hrs: 6.03±0.51, 5.41±0.14. 24hrs: 5.16±0.05, 4.95±0.19 respectively. The apoptosis scores did not differ between the 2 groups ($p>0.05$). Mean±SE of total TUNEL scores (combined scores of all hippocampal subfields) were: P11: 0.00±0.00, 0.3±0.15; P13: 0.00±0.00, 0.27±0.11; P17: 0.00±0.00, 0.25±0.13 for the Control and Hypoxia groups respectively.
Conclusion: There were no ceramide increases and no evidence of apoptosis after acute hypoxia in P10 rats. This suggests that other mechanisms of neuronal injury such as necrosis should also be investigated.

p1219

Beta-CCM-induced Seizure Responses and Absence Epilepsy are Genetically Correlated: Three Reasons to Believe it

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Purpose: Beta-carboline compounds are inverse agonists of benzodiazepine sites of the GABAA receptor. They are convulsant and able to induce spike-and-wave-discharges (SWDs) characterising absence epilepsy.
Methods:
Results: 1) Two strains of mice, derived from a bidirectional selection for their seizuring response after an injection of the beta-carboline methyl-beta-carboline-3-carboxylate (beta-CCM), were characterised in our laboratory. The susceptible one, BS/Orl, exhibits spontaneous bilateral and synchronous SWDs. The resistant one, BR/Orl, does not exhibit any SWDs. Additional investigations have revealed that these two mouse lines represent adequate models for absence epilepsy. 2) A pseudo-replicated line BS2/Orl selected for beta-CCM induced-seizure susceptibility has been derived from BS/Orl.BR/Orl F2. EEG recordings have shown that this new line also presents SWDs. 3) It has been found in a linkage-testing-strain of mice C3XtEso, maintained with forced heterozygosity (Gli3Xt-j/Gli3+ vs. Gli3+/Gli3+) for a small chromosomal segment surrounding the Gli3 gene on chromosome 13, that the wild type mice Gli3+/Gli3+ were more susceptible to the beta-CCM than the mutated mice Gli3Xt-j/Gli3+. We have shown that the wild type mice Gli3+/Gli3+ present significantly more spontaneous SWDs than the mutated mice Gli3Xt-j/Gli3+.
Conclusion: Altogether, these results are converging to show that beta-CCM-susceptibility and absence epilepsy share a common genetic inheritance.

p1220

Ketogenic Diet Increases Neurogenesis after Kainic Acid-induced Seizures in Mice

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Purpose: Ketogenic diet (KD) remains a therapy in search of explanation although it is an established treatment for patients with intractable seizures. Epileptic seizures have been shown to stimulate the proliferation rate of granule cell progenitors in the adult brain. We investigated the effects of KD on neurogenesis after kainic acid (KA)-induced seizures in mice.
Methods: 13 male ICR mice were divided into two groups: ND (normal diet)-fed group (n=6) and KD-fed group (n=7). Seizures were chemically induced by intraperitoneal injection of KA (30 mg/kg) in both groups. Then, bromodeoxyuridine (BrdU, 50 mg/kg) was subsequently administered once a day for 6 consecutive days, starting at 24 hours after KA or saline treatment. Mice were sacrificed 7 days after KA administration. The number of BrdU-positive cells in the hippocampus were counted in every seventh section in a series of 30 ?m coronal sections.
Results: In the KD-fed group, BrdU-labelled cells increased significantly after KA administration compared to ND-fed group (107.17 ± 37.20 vs. 38.04 ± 24.35, $P<0.00001$).
Conclusion: In this study, quantitative analysis of BrdU labelling revealed a significant increase in the proliferation rate of neuronal progenitor cells after KA-induced seizures in KD-fed mice. Our results suggest that KD enhances neurogenesis and it may be related to the antiepileptic effect of KD. This work was supported by Korea Research Foundation Grant (KRF-2004-002-E00088).

p1221

Rufinamide (CGP 33101): A Broad-spectrum Anticonvulsant with Excellent Tolerability Profile in Rodents

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Purpose: The investigational antiepileptic drug (AED) rufinamide (RFA; 1-[2,6-difluoro-benzyl]-1H-1,2,3-triazole-4-carboxamide) is structurally unique. RFA has been found to have an effect on sustained high frequency repetitive firing of sodium-dependent action potentials in mouse spinal cord neurons by limiting firing over a broad range of concentrations. The purpose of the present investigation was to compare the preclinical anticonvulsant profile of RFA to that of the established AEDs phenytoin, phenobarbital, ethosuximide, and sodium valproate.
Methods: Varying doses of RFA were administered orally to CF1 mice or Sprague-Dawley rats. Efficacy against tonic extension and clonic seizures induced by maximal electroshock (MES) and s.c. pentylenetetrazol (PTZ) was established at the predetermined time to peak effect. Efficacy against clonic seizures induced by bicuculline (BIC), picrotoxin (PIC) and strychnine (STR) was also assessed following i.p. administration to mice.
Results: RFA protected mice/rats against MES-induced tonic-clonic seizures (ED50s 23.9 and 6.1 mg/kg p.o., respectively). No development of tolerance against MES-induced seizures was observed (rats). Orally-administered RFA also suppressed PTZ-induced seizures in mice (ED50: 45.8 mg/kg), but not in rats. In addition, i.p. administered RFA suppressed PTZ-, BIC- and PIC-induced clonus in mice (ED50s 50.5-76.3 mg/kg) and was partially effective in the mouse STR test. The protective index (ratio of rotarod TD50 to anticonvulsant ED50) of RFA was superior to that of the prototype AEDs. Overall, RFA was well tolerated and displayed a broad anticonvulsant profile that was most comparable to phenobarbital and sodium valproate.
Conclusion: RFA displayed a broad-spectrum anticonvulsant profile in animal seizure models predictive of efficacy against generalised and partial epilepsies.

p1222

The Pre-clinical Profile of the Novel Anticonvulsant Lacosamide

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Purpose: Lacosamide, previously called harkoseride or SPM 927, belongs to a series of functionalised amino acids which have been synthesised as a new class of anticonvulsant agents. A series of experiments in rodent models of partial and generalised epilepsy were designed to describe its anticonvulsant profile.
Methods: Lacosamide was evaluated as part of the antiepileptic drug development program by the NIH (White HS et al. Adv. Neurol. 1998; 76, 29-39.) using standard rodent models for epilepsy. In addition, lacosamide's effects on generalised tonic clonic seizures induced by cobalt/homocysteine were assessed. Finally, potential neuroprotective effects of lacosamide were measured in organotypic hippocampal slice cultures following exposure to oxygen glucose deprivation or glutamate.

Results: Lacosamide was effective against maximal electroshock induced seizures in rats (3.9 mg/kg p.o.) and mice (4.46 mg/kg i.p.); in the rat hippocampal kindling model of partial seizures (13.5 mg/kg i.p.), against sound-induced seizures in the genetically susceptible Frings mouse (0.63 mg/kg i.p.), and in the 6Hz model of psychomotor seizures in mice (9.9 mg/kg i.p.). In contrast, lacosamide was inactive against clonic seizures induced by picrotoxin, bicuculline or pentylenetetrazol. However, it did antagonise NMDA-induced seizures in mice (10-50 mg/kg i.p.) and showed full efficacy in the homocysteine model of status epilepticus (40 mg/kg i.p.). Finally, lacosamide displayed neuroprotective properties in in-vitro hippocampal slice cultures.
Conclusion: In summary, the overall anticonvulsant profile of lacosamide in animal models for epilepsy appears to be broad and unique.

p1223
Peripheral Benzodiazepine Receptors Increased in Epilepsy Patients with Focal Cortical Dysplasia
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Purpose: Peripheral benzodiazepine receptors (PBR) exist on glial cells and have been implicated to promote seizures. We conducted a quantitative analysis of PBR in resected specimens from patients with focal cortical dysplasia (FCD).
Methods: 14 resected specimens were obtained from patients with intractable localisation related epilepsy (ages at onset 0-9 years, mean 4.7 years; ages at operation 2-36 years, mean 18.4 years). The specimens were immediately frozen and used for in vitro autoradiography with 3H-PK11195 as ligand of PBR. Histopathological examinations were conducted on specimens adjacent to those used for receptor density analysis, and confirmed a diagnosis of FCD in all patients. The lesions were classified according to severity of dysplasia into 3 groups: Taylor Type 1, Type 2A, and Type 2B. We quantified the receptor densities in various areas of the lesion.
Results: The autoradiograms showed high ligand accumulation in the dysplastic areas. In all cases, the mean receptor densities (fmol/mg tissue) in individual areas were 124.6 in Type 1, 167.6 in Type 2A, and 208.3 in Type 2B areas, with a significantly higher density in Type 2B area than in Type 1 area. On the contrary, PBR densities were higher in Type 2A than in Type 2B areas in 3 cases. PBR densities showed no correlation with clinical features, age at onset, age at operation, and seizure frequency.
Conclusion: PBR densities increased especially in severe dysplastic area of FCD. These results suggest that PBR contribute to hyperexcitability of FCD in patients with epilepsy.

p1224
The Role of Nitric Oxide System in Epilepsy and Electro-acupuncture Anti-epilepsy
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Purpose: To investigate whether the anticonvulsive effect of electroacupuncture (EA) on epilepsy is via nitric oxide (NO) and nitric oxide synthase (NOS).
Methods: We measured the levels of hippocampal NO and NOS during epilepsy and after acupuncture treatment. Epilepsy model was induced by injecting penicillin into rat hippocampus and electroacupuncture treatment was performed on 'Feng Fu' (DU 16) and 'Jin Suo' (DU 8) points in Wistar rats. NO concentration was determined by NO-sensitive electrode with potentiostat and NOS mRNA level of rat hippocampus was detected by Northern Blot.
Results: Both NO and NOS mRNA levels markedly increased during epilepsy. EA inhibited the epilepsy and decreased the levels of both NO and NOS mRNA.
Conclusion: The results indicated that penicillin-induced epilepsy caused an increase in both nitric oxide and nitric oxide synthase, and EA might inhibit epilepsy through decreasing NOS transcription and/or NOS catalytic activity in hippocampus.

p1225
The Effect of Electromagnetic Fields on Chemoconvulsant - induced Seizures
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Purpose: The problems of the harmful influence of electromagnetic field radiation from various technical devices (TV set, radio-telephone, micro-wave) on epilepsy patients is not understood, and should be re-investigated using a physically correct protocol. The aim of the study was the evaluation of the predisposition of rat's brain to epilepsy after exposure to electromagnetic influence.
Methods: The modified PTZ-test (dropped imp. administration of penthelenetetrazole in dose 25+25 mg/kg - 3 times) was used for the evaluation of thresholds and scores of epileptic fits. Experimental conditions: the rats were put into boxes under the beam of display of a computer; distance 20 sm from screen, exposure during 1 week/8h daily. Measurements of density of magnetic flood: 5Hz-2kHz/ 242 nTl ; 2kHz-400kHz/23 nTl. The latency, threshold of clonic-tonic stage and severity of motor seizures were measured.
Results: The latencies of fits were shorted (from 25 min to 20 min), the threshold decreased after exposure of the rats to the display (10 animals in cages in the experimental room, n=60); the severity of seizures were high, but the duration of tonic-clonic stage of seizures in the rats were not changed. The significant decree sign of excitability of the brain was demonstrated in 66% of animals. Special experiments in vivo demonstrated the changes of the rat's lymphatic vessel activity and increased response of contractile activity of vessel muscle cells on the norepinephrine application (10-6 M) applications.
Conclusion: There are significant effects of decreasing the threshold of epileptic fits induced by a chemoconvulsant under the electromagnetic field of PC display.

p1226
Gene Expression Changes in the (Para) Hippocampal Region Reveal Specific Biological Processes Involved in the Progression of Temporal Lobe Epilepsy
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Purpose: In order to get insight into the mechanisms that may lead to progression of temporal lobe epilepsy we investigated gene expression during epileptogenesis in the rat.
Methods: RNA was obtained from three different brain regions (CA3, entorhinal cortex and cerebellum) at three different time points (1 day = acute phase; and 1 week = latent period; 5 months = chronic epileptic) after electrically induced status epilepticus (SE); a group that was stimulated but that had not developed epilepsy was also included. Gene expression analysis was performed using the Affymetrics Gene Chip System (230A). We used GENMAPP and Gene Ontology to identify global biological trends in gene expression data.
Results: The following biological processes were upregulated in rats with a progressive seizure evolution in both CA3 and entorhinal cortex but not in the cerebellum: iron ion homeostasis, defence response and neurogenesis. Downregulated processes were: GABA

signalling pathway, chloride transport and protein biosynthesis. Rats that were stimulated but that did not develop spontaneous seizures later on also had some changes in gene expression but this was not reflected in a significant change of a biological process
Conclusion: These data suggest that the targeting of specific genes that are involved in these biological processes may be a promising strategy to slow down or prevent the progression of epilepsy.

p1227
Effect of Free-radical Spin Trap N-tert-butyl-alpha-phenylnitrone on Seizures Induced in Immature Rats by Homocysteic Acid
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Purpose: To examine the effect of a free radical scavenger N-tert-butyl-alpha-phenylnitrone (PBN) on seizures induced in immature rats by DL-homocysteic acid (DL-HCA).
Methods: Seizures were induced by bilateral icv infusion of DL-HCA (600 nmol/side) in 12-day-old male Wistar rats with implanted cannulae. PBN was given i.p. in two doses (100 mg/kg each), 30 min prior and 30 min after DL-HCA infusion. Control animals received a corresponding volume of the vehicle. Energy metabolites were determined by fluorimetric enzymatic methods. Neuronal injury was evaluated using Nissl and Fluoro-Jade B staining.
Results: Severity of convulsions (according to behavioural symptoms and EEG recordings) were slightly reduced by PBN. PBN treatment led to the recovery of decreased levels of ATP in the hippocampus, to a substantial amelioration of lactate accumulation both in the cerebral cortex and hippocampus, and to a partial protection of neuronal damage associated with HCA-induced seizures in many brain regions, as observed after both 1 and 6 days of survival.
Conclusion: The present findings suggest that free radical scavengers may be considered as drugs with a potential beneficial effect in treating epilepsy and its consequences. Supported by Grant Agency of the Czech Republic, grants No. 309/02/1238 and No.309/05/2015.

p1228
Effects of Rufinamide on Sodium-Dependent Action Potential Firing and Sodium Currents of Rodent Central Neurons
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Purpose: Rufinamide (CGP-33101; RFA) is an investigational anticonvulsant with broad-spectrum efficacy against electrically- and chemically-induced seizures in animal models. Some anticonvulsant drugs are effective in the treatment of partial and generalised tonic-clonic seizures, including carbamazepine, oxcarbazepine, phenytoin and lamotrigine, limit action potential (AP) firing and block sodium currents. The present studies examined effects of RFA on these electrophysiological properties of neurons in vitro.
Methods: Intracellular electrophysiological recording techniques were used to record sustained high frequency repetitive firing of sodium-dependent APs in cultured spinal cord neurons. The recording chamber was perfused with phosphate buffered saline containing 7 millimoles/L magnesium to suppress spontaneous firing at 35-37oC. Neurons were exposed to RFA in the superfusate (>30 min) and/or culture medium (up to 48 hours) to insure equilibration. Whole-cell patch clamp recordings were used to measure effects of RFA on sodium currents of freshly dispersed rat cortical neurons.
Results: AP firing in response to intracellularly-applied depolarising current pulses up to 40 seconds in duration was limited in neurons exposed to 1-500 micromoles/litre of RFA. The respective IC50 value amounted to 3.8 (2-10) micromoles/L. The degree of limitation was mild or moderate in some neurons and severe in others exposed to 1-100 micromoles/litre of RFA. All neurons demonstrated severe limitation of firing when exposed to >200 micromoles/litre. RFA produced rest- and use-dependent block of sodium currents and slowed recovery from inactivation.
Conclusion: These findings suggest that RFA limits AP firing by sodium channel blockade over a broad range of concentrations. This mechanism of action may contribute to anticonvulsant effects of RFA.

p1229
Expression and the Clinical Significance of Five Multidrug Resistance Associated Genes in Refractory Epilepsy Brain Tissues
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Purpose: To investigate the expression and the clinical significance of five multidrug resistance associated genes in refractory epilepsy brain tissues.
Methods: 17 refractory epilepsy patients were divided into two groups: long course group (more than ten years), short course group (less than ten years). The expression levels of Pgp, MRP, GST-π, LRP, Topo-□were detected in the long course group, the short course group and the control group by the S-P immunohistochemistry method.
Results: The expression levels of Pgp in the short course group were significantly higher than those in the long course group and control group. The expression levels of MRP, GST-π in long course group was significantly higher than those in the short course group and the control group; the expression of the other two multidrug resistance associated genes show no significant difference between the three groups.
Conclusion: Pgp may play an important role in the early phase of refractory epilepsy; while MRP, GST-π may be involved in the later phase of refractory epilepsy.

p1230
Frontal Lobe Associated Cognitive Function of Newly Diagnosed Adult Partial Epilepsy and the Influence of AEDs
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Purpose: To explore cognitive function related to the frontal lobe among newly diagnosed adult partial epilepsy and the influence of AEDs.
Methods: This is a prospective, randomised and controlled study. According to diagnostic criteria for epilepsy of the ILAE in 1981 and 1989, 48 newly diagnosed patients with partial epilepsy and 35 healthy people with the same features of gender, age and education level were enrolled in the study. They were given 6 neuropsychological tests including digit span, verbal fluency, trail making test (TMT), the Stroop-test, Wisconsin card sorting test (WCST) and Tower of Hanoi. After the first test all patients were randomised into 3 groups of carbamazepine, valproate, and topiramate. The same tests were repeated after 1 month therapy.
Results: Before the administration of the AEDs the patient group was compared with the control group. The test time of TMT parts B increased and error numbers increased. The mistake in reading words of the Stroop-test increased and the time taken reading colours increased. The mean executive time of Tower of Hanoi increased and the total scores declined. After therapy the difference of neuropsychological index between the 3 subgroups was significant. They were digits forward, the vocabulary total, the reading words time of the Stroop-test, the mistake of reading words, the correcting numbers of the Stroop reading colours and the mean planning time of the Tower of Hanoi.
Conclusion: 1) Newly diagnosed adult patients with epilepsy had neuropsychological dysfunction before administrating AEDs. There may be links with brain diseases, seizure frequency and subclinical

epilepsy discharge. 2) Different AEDs have different effects on neuropsychological function because of their different chemical structures and mechanisms. 3) We believe that the test of the digit span and verbal fluency mirroring the cognitive function of the frontal lobe can be used as an early sensitive neuropsychological index to examine injury cognition induced by topiramate.

p1231
Inhibition of the Multidrug Transporter P-Glycoprotein by XR9576 Improves Seizure Control in Phenytoin-treated Chronic Epileptic Rats
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Purpose: Over-expression of multidrug transporters such as P-glycoprotein (P-gp or ABCB1) might be one of the mechanisms that could play a role in the development of pharmacoresistance by preventing anti-epileptic drugs (AEDs) to reach their neuronal targets. Nevertheless, definitive proof of a significant role of P-gp in pharmacoresistance is still lacking. Here we tested whether P-gp contributes to pharmacoresistance to phenytoin (PHT) using a specific P-gp inhibitor in a model of spontaneous seizures in rats.
Methods: The effects of PHT on spontaneous seizure activity were investigated in the electrical post-status epilepticus rat model for temporal lobe epilepsy, before and after administration of XR9576, a selective inhibitor of P-gp.
Results: A 7 day treatment with PHT (50 mg/kg) only partially suppressed spontaneous seizure activity (first day: 16±44%). However, seizures were effectively controlled by PHT in all rats when XR9576 was co-administered (96±5%). A 7 day treatment with 12 mg/kg XR9576 was effective only during the first 3 days of treatment. Longer seizure control (during 4 days) was obtained using 24 mg/kg XR9576.
Conclusion: These findings establish the proof of principle that specific inhibition of the multidrug transporter P-gp can significantly improve the anticonvulsive action of PHT. The fact that co-administration of XR9576 with PHT leads to a significant improved seizure control, indicates that administration of AEDs in combination with this P-gp inhibitor might be a promising therapeutic strategy to control seizures in pharmacoresistant patients.

p1232
Anticonvulsant Activity of the Newest Acid Benzylamide Derivative: Comparison in Epilepsy Experimental Models
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Purpose: It was previously documented that some of benzylamide derivatives may show anticonvulsant properties. The aim of this study was to evaluate the anticonvulsant action of three acid benzylamides: nicotinic (Nic-BZA), isonicotinic (INic-BZA) and two fluorinate picolinic acid (2FPic-BZA) derivatives (all drugs are presumed antagonist of AMPA/KA receptors) in two seizure models: maximal electroshock- or pentylenetetrazol-induced convulsions in mice. 2FPic- and Nic-BZA have shown rapid and short activity, whilst INic-BZA is a long acting drug.
Methods: Pentylenetetrazol was administered subcutaneously at a dose equal to its CD97 for the clonic phase. The current intensity for the maximal electroshock-induced convulsions was 25 Ma, delivered through ear-clip electrodes. The endpoint for electroconvulsions was tonic extension of the hind limbs. Moreover, the effect of studied agents on motor performance in the chimney test was evaluated and presented as a TD50 value. Therapeutic index could thus be calculated as TD50/ED50 ratio.
Results: 2FPic-BZA inhibited convulsions at the respective ED50 values: maximal electroshock - 34 mg/kg, and pentylenetetrazol - 56 mg/kg. Also, Nic-BZA exhibited anticonvulsant activity - its ED50s for the inhibition of seizures follow in maximal electroshock - 36 mg/kg and in pentylenetetrazol - 37 mg/kg. Moreover, INic-BZA protected against maximal electroshock- or pentylenetetrazol-induced seizures at doses of 92 and 134 mg/kg, respectively. The therapeutic index calculated for 2FPic-BZA, evaluated in the two seizure models was 1.8 (for pentylenetetrazole) and 3.6 (for maximal electroshock). In comparison, the therapeutic indices of Nic-BZA and INic-BZA were 6.6 and 2.2 for maximal electroshock or 6.5 and 1.5 for pentylenetetrazol, respectively.
Conclusion: The data show promising anticonvulsant properties of benzylamide acid derivatives. Supported by a grant from Committee for Scientific Investigations No 3P05F 033 23

p1233
Hippocampus in TLE Patients: Multidimensional Framing with Neuronavigation, EcoG, MRI and Histology.
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Purpose: The development of pre-surgical MRI evaluation and the access to anatomically well-preserved surgical specimens of the hippocampus obtained from temporal lobe epilepsy (TLE) patients open new possibilities for understanding the basic mechanisms involved in epileptogenesis. The aim of the present investigation is to perform a refined morphological study of hippocampal anatomy and cytoarchitecture in TLE patients by using different digital 3D reconstruction systems.
Methods: Pre-surgical MRI study included volumetric reconstruction of atrophic hippocampi from five refractory TLE patients. Electrocorticography (ECoG) was performed during surgery in order to map hippocampal discharges. After surgery, the entire hippocampus was histologically processed and the contours of each histological section through the long axis of the hippocampus were outlined using a digital acquisition system. Finally, MRI, ECoG and histological 3D reconstructions were superimposed and analysed using specific graphic software.
Results: Since removed tissue was cut along the same plan used for MRI acquisition, histological analysis was performed within the same reference as the MRI scan for each patient. A little volumetric shrinkage was observed when comparing MRI and histological reconstructions, but the macroscopic landmarks were preserved. The 3D reconstruction of the internal hippocampal contours allowed the visualization of the actual position of the Ammon's horn and dentate gyrus into the patient's head. Moreover, cytoarchitectural abnormalities of these structures, such as pyramidal cell loss and granular cell dispersion, were spatially correlated with the distribution of electrographic discharges.
Conclusion: This original approach allowed precise spatial correlations between neuroanatomic alterations that are known to occur at different scales within the hippocampus of TLE patients. This work was supported by FAPESP, CNPq and CAPES from Brazil.

p1234
Remacemide Blocks Metaphit-induced Audiogenic Seizures in Rodents
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Purpose: We investigated the effect of remacemide (remacemide hydrochloride), a low-affinity, non-competitive NMDA antagonist, on metaphit (1-(1-(3-isothiocyanatophenyl)cyclohexyl)-piperidine)-induced audiogenic seizures in rats and mice.
Methods: Metaphit was administered intraperitoneally (i.p.) in doses of 10 and 80 mg/kg to Wistar rats (n=12) and Swiss albino mice (n=7), respectively. Rats were exposed to intense audio stimulation (100□3 dB, 60 s) at hourly intervals after metaphit injection, and mice only once, 24 h post-injection. Remacemide (50 mg/kg, i.p.) was injected to metaphit-treated rats (n=8) after the 8th AGS testing. Mice (n=8) were injected with remacemide (50 mg/kg, i.p.) 23.5 h after metaphit, and 30 min before sound stimulation. Audiogenic seizures were scored according to the scale: 1) wild running, 2) wild running followed by clonic convulsions, and 3) wild running, clonic and tonic convulsions. We analysed the incidence of seizures, latencies to convulsions, seizure severity, and lethality.
Results: Metaphit-induced audiogenic seizures in rats increased gradually, reached a peak 7-12 h after the injection (10/12, 2.2±0.3), then decreased and disappeared 31 h later. In the experimental group six out of eight rats, which had seizures in the 8th testing, were injected with remacemide. Remacemide blocked seizures in these animals for two hours, and then convulsions reappeared. All mice treated with metaphit only (80 mg/kg, i.p.) exhibited audiogenic seizures 24 h later (latency 5±4 s, severity 2.8±0.3). One animal died during convulsions.
Conclusion: Remacemide (50 mg/kg, i.p.) completely abolished the occurrence of metaphit-induced audiogenic seizures in mice and rats (Fisher's exact probability test, $p<0.01$).

p1235
Combined Treatment with Dapsone plus Primidone against Kainic Acid-induced Seizures in Rats
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Purpose: To evaluate the ability of dapsone (DDS) in combination with primidone (P), to attenuate the kainic acid-induced seizures (KA) in rats.
Methods: DDS and P were ip injected into male Wistar rats (200-250 g), 30 minutes before 10 mg/Kg kainic acid. Rats were randomly allocated into one of the following groups: 1) control, administered with vehicles + KA, 2) DDS 6.25 group, administered with 6.25 mg/Kg of DDS + KA, 3) DDS 12.5 group, administered with 12.5 mg/Kg of DDS + KA , 4) P group, administered with 30 mg/Kg of P + KA, 5) DDS 6.25 + P group, administered with 6.25 mg/Kg DDS + 30 mg/Kg of P+ KA, 6) DDS 12.5 + P group, administered with 12. 5 mg/Kg + 30 mg/Kg of P + KA. The occurrence of Limbic ('wet-dog shakes') and tonic-clonic seizures was recorded by digital video camera.
Results: DDS and P reduced the number of limbic seizures, by -72% (DDS 6.25 group) and -90% (DDS 12.5 groups) and by -88% (P group) as compared to control group. The combination of DDS 6.25 and P reduced by 94% the limbic seizure frequency, but only by 50%, when the high DDS dose was used (DDS 12.5 + P group). Only the combination of DDS at the high dose (DDS 12.5 + P group) was able to fully prevent tonic-clonic seizures.
Conclusion: The combination of DDS + P is effective to attenuate both limbic and tonic-clonic seizures in the KA model.

Wednesday 31st August and Thursday 1st September 2005
13:15 – 14:15
Poster Session
Clinical Neurophysiology

p1236
Recurrent Ictal Sinus Arrest and Syncope with Right Temporal Seizure Onset
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Purpose: To describe and discuss a case of cardiac sinus arrest and syncope with right temporal seizure onset.
Methods: Case report and literature review.
Results: A 40 years old right handed woman with recurring uninvestigated syncope was hospitalised after three episodes of déjà vu, nausea, vomiting and brief loss of consciousness, with spontaneous recovery, once with urinary incontinence. During EEG recording the same day, she had two right temporal onset seizures and ictal sinus arrest, one lasting 11 seconds, with brief alteration of awareness. MRI was unremarkable. She was treated with carbamazepine and a permanent pacemaker. There has been no recurrence in four years. Ictal bradyarrhythmias are increasingly reported, typically associated with temporal or frontal seizure onset. Electrophysiological data suggest a left amygdala or hippocampal area for arrhythmogenesis although some reports note that bilateral ictal spread was necessary for AV block to occur. Unilateral studies have shown AV block with left temporal electrical stimulation. In this case, only scalp EEG was available and two apparent right temporal seizures each led to sinus arrest. The reported vomiting with other events is consistent with right temporal onset in this patient.
Conclusion: Life-threatening cardiac arrhythmias can be triggered by seizures especially of frontal or temporal onset. These are a possible mechanism for some sudden unexpected deaths in epilepsy. Although a left-sided predominance for ictal cardiac arrhythmias has been reported, the present case suggests that unilateral right temporal seizure onset may also trigger these potentially lethal events. Several mechanisms may thus operate to cause ictal cardiac arrest.

p1237
Active Observation Paradigms Perform Better than Passive Measurements in Seizure Anticipation
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Purpose: Seizure anticipation may afford a means of preventing seizure occurrence altogether. Seizure clustering may be reliably anticipated by the relative phase clustering index (rPCI) by application of intermittent low-amplitude intracranial electrical stimulation (ICES) (Kalitzin et al, Clin Neurophysiol, 2005). Others have used passive measures in anticipating seizure clustering. We now compare the performance of two active observation paradigms, rPCI and signal amplitude demodulation (ADM) requiring low-amplitude ICES, against two passive descriptors, signal energy (SE) and signal speed (SS).
Methods: We studied 4 patients undergoing invasive seizure monitoring during presurgical evaluation for pharmacoresistant seizures. In 3 cases both active and passive paradigms were obtained. The fourth patient served as a control case, with measurements obtained only interictally. We calculated SE similar to Litt et al, Neuron, 2001 and SS using technique similar to Cerf and el-Ouasdad, Biol Cybern, 2000.
Results: We show that although all descriptors were able to identify at least some evidence of impending seizures, performance of ADM was less robust while performance of SE and SS was strongly influenced by the sleep/awake cycles. Only rPCI performed well in all three cases investigated, e.g. rPCI correctly identified both the site of seizure onset and estimated time to next seizure.

Conclusion: We agree with Meiwald et al, Physica D, 2004, that passive observation descriptors are not reliable enough for clinical application of seizure anticipation. We show that active observation paradigms are superior in identifying impending seizures and that those paradigms are useful in a clinical setting. We advocate the use of rPCI over ADM.

p1238
Improving the Interpretation of the Ictal Scalp Electroencephalogram: A New Muscle Artefact Removal Technique
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Purpose: The aim of this study was to investigate the potential clinical relevance of a recently developed method for muscle artefact removal in the ictal electroencephalogram (EEG).
Methods: One ictal EEG of 26 patients with refractory partial epilepsy and an ictal onset zone that was well-defined during a presurgical evaluation, were processed with a new subspace-based muscle artefact removal technique. The artefact-free recordings were compared with the band pass (0.3-35 Hz) filtered original EEGs by an unblinded neurologist.
Results: In 24 of 26 cases (92%) muscle artefact significantly contaminated the ictal EEGs. In all 24 cases the ictal EEG was easier to interpret after the muscle artefact was removed. The time of ictal onset on EEG was detected earlier in 9 out of 26 cases (35%), the onset of the seizure was better localised in 7 out of 26 (27%) and the ictal-pattern of the onset was located in a higher frequency range for 8 out of 26 cases (31%). Localised ictal-onset beta activity was observed only after removal of muscle artefact in 5 patients (19%). The muscle artefact removal technique did not degrade the EEG signal in any of the patients.
Conclusion: Our muscle artefact removal subspace-based technique was easy to implement, fast and user-friendly in a clinical environment, and improved the interpretation of ictal EEG in a clinically significant way in around 50% of patients. We are currently conducting the same study with two blinded EEG readers and a larger sample of ictal EEGs.

p1239
Secondary Hippocampal Epileptogenesis in Gelastic Epilepsy
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Purpose: So far, epileptogenesis in gelastic epilepsy due to hypothalamic hamartomas is incompletely understood. Whereas some evidence from intrahypothalamic recordings, ictal SPECT and from successful surgical therapy points to a central role of the hamartoma in seizure generation, other reports have pointed to an extrahypothalamic seizure origin. This study investigates interictal and ictal recordings obtained from 5 patients who underwent invasive depth electrode recordings from both hypothalamic hamartoma and extrahypothalamic sites with regard to evidence for secondary hippocampal epileptogenesis.
Methods: EEG data from 5 patients with pharmacoresistant focal epilepsy with gelastic, complex partial and secondarily generalised tonic-clonic seizures undergoing invasive intracranial recordings including hypothalamic hamartoma were investigated. Interictal discharges were classified as temporarily independent in the hypothalamus and extrahypothalamic areas. Ictal onset zones were classified as initially present in the hamartoma or initially only present at extrahypothalamic recording sites. EEG recordings were correlated with seizure outcome.
Results: In all 5 patients, both intrahypothalamic and extrahypothalamic interictal spiking was observed which was temporarily independent. In 2 patients, isolated hippocampal ictal onset was shown; they, however, achieved complete seizure freedom following interstitial radiosurgery of the hypothalamic hamartoma without touching the extrahypothalamic seizure onset zones.
Conclusion: Depth recordings from the hypothalamic hamartoma and from hippocampal sites gave evidence of temporarily independent generation of both interictal and ictal epileptic activity. The fact that 2 patients with hippocampal seizure onset and independent hippocampal interictal spiking became seizure free by radiosurgical destruction of the hypothalamic hamartoma alone may be interpreted as evidence for secondary epileptogenesis in the hippocampi; at the time of therapeutic intervention, secondary foci had not reached complete independence from the primary, intrahypothalamic focus.

p1240
Non-invasively Recorded Regional Polyspikes are Suggestive of Cortical Dysplasia as Aetiology of Focal Epilepsies
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Purpose: To evaluate the relative frequency of regional polyspikes in focal epilepsies secondary to cortical dysplasia.
Methods: We performed a data search for the term 'regional polyspikes' in the data base of our Epilepsy Monitoring Unit. Patients with generalised epilepsies and Lennox-Gastaut syndrome were excluded. Regional interictal epileptiform discharges were recorded in 514 patients with non-invasive EEG.
Results: We identified 29 patients with regional polyspikes and focal epilepsies. Another 485 patients showed regional epileptiform discharges other than polyspikes. The polyspikes were significantly more frequently localised to the extratemporal (76%; n=22) than temporal (24%; n=7) regions ($p<0.01$). In contrast, regional epileptiform discharges other than polyspikes were significantly more frequently localised to the temporal lobes (71%; n=324) than extratemporally (29%; n=161) ($p<0.01$). The aetiology of the epilepsy was significantly more frequently cortical dysplasia in the group of patients with regional polyspikes (31%, 9 of 29 patients) than in the other patients with regional epileptiform discharges (5.1%, 25 of 485 patients) ($p<0.01$).
Conclusion: Non-invasively recorded regional polyspikes point to cortical dysplasias as aetiology of predominantly extratemporal epilepsies.

p1241
Interictal EEG in Temporal Lobe Epilepsy in Childhood
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Purpose: To clarify the value of interictal discharges and verify which extratemporal regions may also show epileptiform activity in temporal lobe epilepsy (TLE) in childhood.
Methods: We studied 53 consecutive patients, from 2 to 18 years old (mean age = 11.32 years; 28 male) with TLE. Each patient had 1 to 15 interictal EEG recordings (mean: 5.6; total = 297 EEGs). Video-EEG monitoring was performed on 40 patients. All patients had MRI. The findings were compared with a control-group of 53 consecutive TLE adult outpatients with hippocampal atrophy. Each adult patient underwent 3 to 21 routine EEGs (mean: 10.67; total = 566).
Results: Our data showed that interictal EEGs of children with TLE present extratemporal epileptiform discharges more frequently than EEGs of adults with TLE. Although we found epileptiform discharges in all extratemporal cerebral regions, they occurred mostly in frontal and parietal areas. 25 children and 10 adults had frontal epileptiform

discharges (p=0.001). When only children with hippocampal atrophy (30) were compared with adults, we had similar findings (p=0.007). Our data showed variable findings concerning other extratemporal regions.
Conclusion: Our findings may suggest a close interaction between frontal and temporal lobes in children with epilepsy and provides further evidence of the existence of a medial temporal/limbic neural network.

p1242
Misleading Patterns of EEG Activity During Stereoelectroencephalography
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Purpose: Although intracranial recordings by stereotactic depth electroencephalography (SEEG) can overcome some of the limitations of surface EEG, it is not unusual during SEEG to observe certain interictal patterns which may lead to errors in localising or lateralising the epileptogenic zone.
Methods: Among patients referred to the Sainte-Anne Hospital for the surgical treatment of drug-resistant partial seizures, all EEG patterns considered as misleading on SEEG recordings, performed over 3-4 days and as described by Bancaud et al (1969), were documented.
Results: Misleading patterns of epileptiform aspect presented a high degree of variability in shape (alteration of background activity and slow waves or paroxysmal events such as spikes, spike-slow waves, etc), spatial distribution (focal or regional), time of occurrence during SEEG sessions (early or late after electrode implantation) and sensitivity to activation techniques (hyperventilation, sleep, photic stimulation, etc). For example, in a patient falling asleep spikes may be recorded from the normal hippocampus and rhythmic spike discharges (5Hz) recorded from the cingulate gyrus (area 23) do not necessarily indicate that this structure is implicated in epileptogenesis.
Conclusion: Long-term monitoring of epilepsy patients with depth electrodes has revealed certain distinctive EEG patterns which bear no relationship to seizure generation. As they have little or no practical value for diagnosis they must be distinguished from truly abnormal activities related to epileptogenesis. Special training and experience in the recognition of pathological and physiological intracerebral EEG patterns is needed for EEG technicians and neurologists dealing with refractory epilepsy.

p1243
Dipole Analysis of Epileptiform Discharges in EEG Among Patients with Epilepsy
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Purpose: To demonstrate the origin of epileptiform and physiological waves using dipole analysis.
Methods: A total of 32 long term EEGs obtained from 12 epilepsy patients with generalised epilepsy and 20 with partial epilepsy were used for dipole analysis. More than 360 epileptiform discharges of various forms has been submitted in this analysis. We analysed interictal small spikes, sharp waves, spike- and wave complexes (SWK), epileptic and nonepileptic K complexes as well as alpha waves, emg artefacts, vertex sharp waves. The individual components from complexes has been evaluated separately.
Results: In the group of generalised epilepsies there was a striking diffuse arrangement of spiking component of SWK during generalised epileptiform discharges in contrast to the slow component of SWK. According to dipole modelling it has been shown that slow components have their origin in deep mesencephalic and thalamic regions. The origin of focal spiking is clearly related to the side of origin of epileptic discharges and the type of epileptic syndromes.
Conclusion: Interictal dipole modelling contributes to a better localisation of the underlying brain source of epileptic discharges.

p1244
Cortical Synchronisation before Generalised Absence Seizure: A Magneto-encephalographic Study
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Purpose: Cortical activity modifications leading to generalised absences seizures (GAS), i.e. the origin of the associated bilateral spike-wave discharges (SWD), remain unknown. Using a new non-invasive technique characterising the phase synchronisation between sources located on the neocortex, we explore the cortical synchrony several seconds prior to the initiation of GAS, in order to understand these transition mechanisms.
Methods: Four spontaneous GAS were recorded from 2 patients in an eyes-closed resting condition using a whole-head MEG device. We then solved the inverse problem (Brainstorm Matlab toolbox, http://neuroimage.usc.edu/brainstorm/) to estimate the basis of magnetic resonance image (MRI) cortically located sources activity from which originates the MEG signal. To characterise the synchronisation between brain regions, we performed a time-frequency analysis of activity of these sources, and detected their common instantaneous frequencies. The cortical areas determined as synchronous across time-frequency windows of interest were finally projected onto the patient brain.
Results: A synchronisation phenomenon preceding the GAS onset by 1.5 s was detected in a theta frequency band (5-7Hz). While projecting the corresponding synchronous cortical patches onto the patient brain, a region restricted to frontal and pre-central location was revealed. Such patterns were very reproducible across the four seizures.
Conclusion: These observations suggest a cortical synchronisation prior to the occurrence of the absence SWD. This confirms the importance of the cortical activity in the initiation of GAS, as recently reported using high density EEG (Holmes, M. D. et al. Epilepsia 2004; 45(12): 1568-1579).

p1245
Principal and Independent Component Analysis of Automatically Detected Positive Temporal Sharp Waves for Source Localisation in Neonates
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Purpose: Positive temporal sharp waves (PTSW) are pathological transients in the EEG of premature and full term neonates. They might be associated with ischemia, periventricular leukomalacia or intraventricular haemorrhage. Dipole source localisation of PTSWs can be indicative of focal cerebral dysfunction. We designed an automated spatio-temporal method to extracts PTSWs and to detect the clusters of neuronal activities for source localisation in neonates.
Methods: The EEG data of three neonates with PTSW were included. To find sharp wave candidates, template matching (TM) method was used. Then, to reduce data space by discarding the small components, principal component analysis (PCA) was performed. Considering the hypothesis that PTSW is composed of contributions from statistically independent sources, independent component analysis (ICA) was applied to separate the sources. A separate dipole fitting procedure was performed for each step. The final output of the algorithm was the set of significant clusters with their average dipole location and time series.
Results: PTSWs were detected successfully by our adapted TM method. By refining these candidates by PCA, much of the noise was removed from the signal subspace. The PCA-processed signal subspace was decomposed into independent components by ICA. Applying the dipole fit method, our results showed that PCA processing of PTSWs can restrict the area of the dipole clusters. ICA

indicated a good estimation of the sources by separating independent sources resulting in different spatial clusters of dipoles.
Conclusion: The presented procedure can be useful to the physician as an automated method to refine PTSWs for source localisation.

p1246
Anticipated Detection of Epilepsy Seizure Onset with a Novel On-line Disharmony Index
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Purpose: An approach to the problem of seizure prediction aimed to provide a computationally effective method for real-time application with standard scalp EEG recordings is presented.
Methods: One control record performed during steady interictal interval and 10 preseizure records lasting 15-20 minutes with standard scalp EEG 32 channels from 3 subjects suffering from pharmacoresistant medial temporal lobe epilepsy have been used. A disharmony index based on multiple abrupt changes of EEG spectral features is introduced to characterise the pre-ictal phase. The amount of changes into the time unit is considered as a predictor. A new computationally effective on-line algorithm to solve the basic problem of single change detection is proposed. Control records were used to estimate the parameters of the algorithm for each patient and preseizure records were used to evaluate the method.
Results: We observed a reliable prediction of 30 seizures for 3 patients with an average anticipation time of 10.5, 12.6, 16.3 minutes (with respective variances equal to 3.1, 4.1, 2.6). The anticipation times ranged between 7.5 and 21 minutes. Only 1 false positive occurred in the control records.
Conclusion: The proposed algorithm offers a computationally effective method to be applied in real time applications. Additional efforts are oriented towards decreasing the probability of false positive and further evaluation is under way. This study was partially supported by a grant of the Swiss National Science Foundation SCOPES 7IP 62620.

p1247
Detailed Separation in Time Space and Frequency of Ictal EEG in order to Visualize Complex Initiation and Propagation Patterns of Epileptic Seizures
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Purpose: Extracranial recording of ictal EEG is a mandatory part of presurgical epilepsy evaluations. In the clinic the interpretation of these recordings is currently mainly based on visual inspection of the traces. We present a method to quantify the results, which may considerably facilitate the interpretations, and also provide additional information that cannot be obtained from mere visual analysis.
Methods: In 1-10 seizures of around 60 patients the Fast Fourier Transform (FFT) was used to decompose the ictal activity into its frequency components. For several consecutive 2 second periods during seizure development, a distributed source model was used to determine the power of each frequency (3-10 Hz) within different regions of interest (ROI:s) in the brain. The temporal and spatial development of the ictal activity during a seizure could thus be determined, and both frequency changes within a region and propagation of the activity between regions could be visualized.
Results: Different propagation patterns were obtained for patients with different focus locations. For instance, seizures of mesial temporal origin had a different frequency development over time than neocortical temporal seizures, and the ictal activity in patients with right temporal foci tended to propagate more to extratemporal areas than in patients with left temporal foci.
Conclusion: The ictal propagation patterns, when put in relation to the results of other neuroimaging techniques, may provide additional important information about the epileptic source. The relative simplicity of the technique also makes it suitable as a routine clinical tool in presurgical epilepsy evaluations.

p1248
Evaluation of Health-related Quality of Life in Patients with Intractable Epilepsy
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Purpose: To evaluate health-related quality of life (QOL) in patients with intractable epilepsy.
Methods: To investigate the following domains of QOL as proposed by the World Health Organization by the commonly use scale in China and social questionnaire.
Results: Results showed that 23% of intractable epilepsy patients had not received free education for 9 years. Out of 323 marriage age patients, 38.6% were single and 22.9% were divorced. 317 patients experienced serious adverse reactions and these included ataxia, skin eruption, consciousness, hepatic function damage and foetal death. There were 132 cases with depression and another 124 cases who showed postictal psychosis or delirium. 67 patients developed alternating psychosis and 48 cases showed interictal schizophreniform psychosis. Of 400 patients, 242 depended on familial or social care.
Conclusion: For intractable epilepsy patients, the health-related quality of life needs significant changes.

p1249
Contributing Factors to Atypical Language Dominance in Patients with Left Epileptic Foci
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Purpose: Several studies have shown an increased incidence of atypical language dominance (right language dominance or bilateral language dominance) in patients with left hemisphere epileptic foci. We retrospectively investigated the incidence and contributing factors of atypical language dominance (AL), determined by intracarotid amobarbital procedure (IAP, Wada test), in patients with left or right hemispheric focal epilepsies.
Methods: We included 162 epilepsy patients (89 males,73 females) whose language dominance was determined by IAP at our centre from 2000 to 2004. The items of language test in IAP included spontaneous speech (6 points), understanding (2 points), repetition (2 points). The language lateralisation index (L) was computed according to the formula L=(score IAP right -score IAP left)/(score IAP right + score IAP left). L has a value between 1 and -1; 1 expressing complete left language dominance (LD) and -1 indicating complete right hemispheric language dominance. Patients were classified into LD if L is more than 0.8, and AL (right, incomplete left or right, and bilateral dominant) if L is below 0.8. Clinical information was obtained from medical records including age, gender, age at onset of epilepsy, duration of epilepsy, frequency of seizures, risk factors, risk factors onset age, and lateralisation of MRI or EEG.
Results: 72 patients (38 male, 52.8%) had left hemispheric foci. Of them, 25 patients (34.7%) had AL. Univariate analyses revealed that in left epileptic foci, AL was significantly associated with early epilepsy onset age (AL:12.10±0.07 years old, LD:17.66±11.56 years old, p=.047), and early risk factors onset age (AL:1.92±0.74 years old, LD:5.28±0.79 years old, p=.020). Of 74 patients with right hemisphere foci (male 37 patients, 52.9%), only 4 patients (5.4%) had AL. Univariate analyses showed that less frequent seizure frequency (AL:1-11/years, DL:>=1/month) was associated with AL in patients with right epileptic foci (p=.007). There is no significant association with gender, age, duration of epilepsy, risk factors, and localisation of

lesion. Logistic regression analysis revealed that age at onset of epilepsy was independently associated with atypical language dominance in the left epileptic foci.
Conclusion: AL in left epileptic foci had an incidence of 34.7% and was associated with age at onset of epilepsy and that in the right epileptic foci associated with less frequent incidence.

p1250
Frequent Mobile Phone Usage and EEG Characteristics
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Purpose: Magnetobiological research in the last few years pointed to different effects of mobile phone usage on the human organism, especially to different grades of brain activation. It is known that omnidirectional antennas radiate so that sometimes more than 50% of the magnetic power of the phone acts on the user's head. It is known that mobile phones operate at 900-1800 MHz and the spectrum of a realistic device may be several hundreds of GHz wide, particularly in the digital mobile phone system.
Methods: During our everyday EEG registration in our neurophysiological laboratory we noticed a number of persons who complained about headaches and whose anamnesis registered frequent mobile phone usage for professional purposes (frequent and long duration calls). So we selected persons whose headaches could not be related to any other aetiology. We registered EEG by using the standard procedure with hyperventilation (HV) and intermittent photostimulation (IFS) lasting 20 minutes. 87 persons, 17-55 years old, 35 female and 52 male were examined.
Results: During the registration of electroencephalographic (EEG) activity the characteristic bioelectrical change was a generalised desynchronisation with no notable changes during HV and IFS. We registered no specific epileptic phenomena. However, in these persons we found sleeping disorders and increased irritability in behaviour.
Conclusion: The registered EEG changes enable us to give the examined persons advice to reduce the duration and frequency of using the mobile phone. A possible explanation may be experimentally registered pericellular, perivascular and perifascicular oedema of brain structures, provoked by this type of electromagnetic radiation in experimental animals. All findings point to the importance of continuing investigations into the effects and possible consequences of mobile phones on different organic systems.

p1251
Head Deviation (HD) in Brain Mapping and Epilepsy
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Purpose: Head deviation (HD) is considered as the condition which strongly suggests lateralisation, and is considered to be an important clinical sign. These HD may be observed not only with epilepsy but also brain mapping. We studied the three points (time lapse until HD happens, the anatomical position where HD happens, laterality of HD) in cases who had HD with bipolar stimulation by depth electrodes.
Methods: 20 (epilepsy and brain tumour cases) patients who performed the bipolar stimulus with depth electrodes were analysed. 4 cases (2 male, 2 female, average age 39.5 yrs) showed the HD. Stimulus conditions were 50Hz, 0.5msec, and 5 to 6 mA.
Results: For time lapse until HD happens, one case presented the HD at the same time with stimulus, 1 case in less than 5 seconds and two cases needed more than 10 seconds. For the anatomical point of view, the HD was induced for all cases by the white matter stimulus of the position of Brodmann 6 and 8. For laterality of HD, all 4 head rotation was in the stimulus and opposite side.
Conclusion: As one of the functional mappings of HD induction, the influence of the white matter around the Brodmann 6 and 8 could be considered, and all directions of HD of this part were opposite.

p1252
Interhemispheric Functional Integration of the Frontal and Parietal Areas with the Model of Epilepsy
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Purpose: The aim of the study was to analyse the functional associations of frontal areas with parietal, temporal and occipital areas of contralateral hemispheres in patients with symptomatic epilepsy.
Methods: The changes of higher integrative (mental) functions were evaluated in separated groups with different lateralisation and localisation of epileptic focus (51 patients, 31 women, 20 men, mean age of 34 years, S.D. 5.5). The mapping with the help of 'MBN'-neurocartograph (by EEG spectral power and coherence) was used for analysis of the brain bioelectrical activity.
Results: The controversial literature data and our examinations deserve special attention. There is numerous evidence for separate right- and left-hemisphere epilepsies: clinical examinations and literature data mainly confirmed this viewpoint. Our results (electrophysiological, psychological, clinical) displayed that in a number of cases in epilepsy, functional communications between the frontal area and the somatosensory region of contralateral hemispheres may cause the 'additional' clinical and behavioural symptomatic of epilepsy, which is affected by contralateral hemisphere dysfunction. The statistical analysis of brain bioelectrical activity showed an increase of spectral power and coherence in EEG delta band in the frontal area of one hemisphere and in the parietal brain regions of the contralateral hemisphere.
Conclusion: According to our results and literature data, the features of cortical interhemispheric associations (of frontal and parieto-temporal areas of contralateral hemisphere) is known to be not pathognomonic for epilepsy and reflects one from the forms of functional flexibility that causes a new level of reorganisation of integrative activity.

p1253
MEG Detects a Higher Proportion of Focal Interictal Epileptic Discharges in Spontaneous Sleep Compared to EEG
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Purpose: This study explores the effect of background activity on visual MEG and EEG spike detection in simultaneous interictal sleep recordings. Since MEG is indifferent to radial activity, e.g. sleep changes, a higher ratio of spikes unique to MEG compared to EEG was presumed in overlapping sleep activity.
Methods: We examined 14 patients with focal epilepsy aged 3.5-17 years. 122-channel whole-head MEGs and 33 channel EEGs were recorded simultaneously for 20-40 min. Segments of artefacts or bilateral polyspikes (>2 ED/200 ms) were excluded. EEG and MEG data was split into 28 data segments, which were blinded and independently reviewed as to ED by 4 experienced neurophysiologists. Segments were matched and ED detected by ≥3 investigators identified as unequivocal spikes: MEG>EEG (difference ≥3 raters), EEG>MEG (ditto) and EEG=MEG (≥3 raters each). Simultaneous sleep changes (spindles, vertex waves, K-complexes, slow wave sleep) were visually determined in ED-segments (+/- 500 ms).
Results: Of 4704 detected ED, 1387 unequivocal spikes were identified; 689 spikes unique to MEG (54% within EEG sleep changes) and 136 spikes unique to EEG (21% sleep). 562 spikes were identified in both modalities (42% sleep). A significantly higher rate of MEG spikes was associated with vertex waves or other sleep changes compared to EEG and EEG/MEG spikes.
Conclusion: Altogether more spikes were detected by MEG compared to EEG. Beside focus localisation and source orientation, overlapping

sleep changes contribute to this discrepancy. In sleep, the MEG enhancement of tangential over radial sources leads to higher spike detection rates in simultaneous recordings.

p1254
Does Magnetoencephalography Improve the Presurgical Evaluation of Epilepsy?
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Purpose: To asses the usefulness of magnetoencephalography (MEG) in presurgical evaluation of epilepsy in relation to EEG.
Methods: 15 patients with focal intractable epilepsies have been evaluated (6 temporal, 9 extra-temporal). All patients underwent long term video EEG-scalp and MEG. Interictal and ictal epileptiform activity (EA) recorded in EEG and/or MEG were classified as 'lobar', 'hemispheric' or 'nonlocalisable' depending on the epileptogenic zone outlined. Diagnosis was supported by postoperative seizures improving (11p) or accurate localisation obtained with invasive recording in non operated patients (4p).
Results: Interictal EA in EEG were 'lobar' in 66.6% (10 p), 'hemispheric' in 20% (3 p) and 'nonlocalisable' in 13.3% (2 p). Considering data from ictal EEG, localisation became to 'lobar' in 86.7% (13 p) and hemispheric in 13.3% (2 p). Abnormalities recorded in MEG were 'lobar' in 46.7% (7 p), 'hemispheric' in 46.7% (7 p) and 'nonlocalizable' in 6.7% (1 p). 3 of the 'hemispheric' patients suffered seizures during the MEG. The ictal origin was 'lobar' in all of them, improving the localisation to 'lobar' in 66.7% (10 p).
Conclusion: A) Interictal video EEG-scalp studies show higher accuracy than MEG in localisation of EA. B) The EEG localisation rate increases if ictal EEG data are used. C) Although unusual, MEG recorded seizures have shown very high localisation power. D) MEG is not an election method in presurgical evaluation of epilepsy and it would only provide additional information.

p1255
Loss of Deep Cortical Fissures in Polymicrogyria Requires Simultaneous EEG with MEG Source Analysis
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Purpose: Multiple source analysis of interictal EEG and MEG spikes was used to define irritative zones in polymicrogyria (PMG). MEG/EEG discrepancy was assumed since MEG predominantly depicts signals from tangential, fissural neurons, drastically reduced in PMG.
Methods: We examined 7 patients with focal epilepsy and unilateral PMG in MRI, aged 7.5-19 years. 122-channel whole-head MEGs and 32-channel EEGs were recorded simultaneously for 25-40 min. Interictal spikes were identified visually and used as templates for similar spatio-temporal spike patterns (BESA□). Similar spikes (r>0.85) were averaged, high-pass filtered (5 Hz), enhancing spike onset, and subjected to multiple spatio-temporal source analysis. Source localisation was visualised and compared to the lesion by superposition on T1-weighted MRI.
Results: 9 spike types were identified in 7 patients (2 types in 2 patients). In 8/9 EEG and 7/9 MEG spike types, sources modelling spike onset activity were localised within the lesion. In 2 spike types, EEG onset preceded MEG significantly (19/25 ms) and reflected radial activity within the lesion. MEG spike onset activity was once mislocalised to the normal hemisphere, depicting propagation. In addition, distances of simultaneous EEG/MEG onset sources were conspicuously high (9-47mm). In 2 simultaneous spike types MEG localised in more peripheral PMG parts, where fissures re-emerged.
Conclusion: MEG/EEG incongruity relates to deep fissure absence in PMG. Twice EEG alone detected the radial onset while MEG localised the propagation of interictal spike activity. In two further cases, MEG localised to the periphery of the irritative zone. Simultaneous MEG/EEG and multiple source analysis prevent MEG misinterpretation.

p1256
Clinical and Ictal Video-EEG Characteristics of 28 Cases with Infantile Spasms
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Purpose: The aim of the study is to investigate the clinical, interictal and ictal video-EEG characteristics of 28 cases with IS and evaluate the clinical significance of early diagnoses and treatment.
Methods: Clinical observations and video-EEG monitoring were analysed and followed up for 28 babies with IS.
Results: 28 babies (19 male, 9 female; aged 2~16 months with an average of 6.5 months) were diagnosed with IS after presenting with clinical spasms and hypsarrhythmia at the onset of the initial seizures. All cases were involved in the axial musculature with three generally divided types including in flexion, extension or mixed by 12, 9 and 7 cases respectively. After analysing 64 occurrences of clinical spasms and video-EEG recordings across all babies, the spasm patterns of the group were clinically classified as follows: symmetric spasms in 14 cases, asymmetric/asynchronous spasms in 8 cases, focal or hemispasms in 6 cases, spasms combined with
partial seizures in 8 cases, spasms preceded by brief atonia in 2 cases, subclinical spasms in 5 cases; in addition, subtle spasms were found alone or coexisting in most of the cases. Interictal EEG showed typical and atypical hypsarrhythmia in 8 and 20 cases respectively, focal poly-spike/sharp and slow waves or hemihypsarrhythmia in 5 cases; at least three different patterns of ictal-EEG were associated with clinical spasms: fast wave bursts, diffuse polyphasic high slow voltage wave complex and desynchronisation or decremental activity, in which the prominent positivity of the polyphasic high voltage slow wave complex of negative-positive- negative deflection was usually parallel with clinical tonic or tonic spasms. Video-EEG monitoring was more valuable than the routine EEG for the early diagnosis and treatment of IS, particularly for those babies with a history of hypoxic-ischemic encephalopathy and subclinical spasms. Although most of the clinical spasms were usually symmetric, focal lesions could not be excluded. EEGs were not always synchronous and symmetric.
Conclusion: IS are a special type of epileptic seizure as well as an epileptic syndrome with different patterns, and could be associated with partial and other types of seizures; video-EEG was valuable in its early diagnosis and treatment.

p1257
Is Sleep Activated Epileptic Activity in Children a Common Feature that is Seldom Diagnosed?
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Purpose: Sleep activated epileptic activity (SAEA) is a well know EEG phenomenon. Landau-Kleffner syndrome (LKS) and the continuous spike wave during slow sleep (CSWS) syndrome are partly characterised by this. The SAEA is not limited to these disorders, but is also reported in other diseases such as autistic spectrum disorder (ASD and in attention deficit and hyperactivity disorder (ADHD). However, the reports are relative few and diverse. This study was undertaken to help characterise the SAEA in patients referred to our epilepsy centre.
Methods: All long-term recordings since June 2004 with increased epileptic activity during sleep were included. Indexes of epileptic activity for slow-wave- (SWI3) and REM-sleep (RI3), and for the

wake period (AI3) were calculated. Patient information was mainly collected from referrals. This abstract reflects the analysis of 50 of the recordings.
Results: A total of 180 recordings were included which is 20% of all recordings in the period and 40% of recordings in children. There were 11 without epilepsy. The mean age was 10.6 years (SD 3.8 years). There was information on ADHD in 30%, ASD in 9% and LKS in 15% of the referrals for these recordings. Total number of spikes during sleep varied from 871 to 49677 with a mean of 16508. The mean SWI3 was 46.7% (range 6.3%-92%). The SWI3/AI3 had a median of 10.4. There was a good correlation between inter spike interval and the SWI3.
Conclusion: SAEA is common in our population and is recorded almost exclusively in children. Besides epilepsy, ADHD was the most common diagnosis in these patients. It is our opinion that appreciation of this EEG phenomenon and its clinical implications is insufficient.

p1258
Clinical and Therapeutic Approach of Children with Abnormal Electroencephalogram without Seizures
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Purpose: To analyse the clinical features, therapeutic approach and outcome of a paediatric population with EEG alterations and without seizures.
Methods: 32 abnormal EEGs of 30 subjects without a history of epilepsy were selected from the EEGs requested between 1999 and 2002. The patients had complained of headaches, syncope, altered behaviour, learning difficulties and other non epileptic paroxysmal disorders. The EEG changes considered were: lentification (focal or diffuse) and paroxystic activity (focal or generalised). Clinical registrations of these patients were analysed.
Results: The 32 EEGs were performed on children aged between 2 and 14 years. 32% girls and 68% boys. A familiar history of epilepsy was referred in 32% of these children. Around 10% had a history of febrile convulsions and for 35% the neurological examination was not normal. 21 subjects (70%) were treated, 7 with carbamazepine and 14 with valproic acid. 85% of this group normalised the EEG and in 43% the clinical outcome was favourable. The mean follow-up time was 2.6 years and the final diagnosis changed in 28%.
Conclusion: A significant part of this group had a familiar history of epilepsy. Although there was no evidence of seizures, pharmacological treatment was started in the majority, after a positive evolution of the EEG pattern. The clinical benefit was not evident for all children studied. The subclinical EEG alterations and the neurologic complaints of these patients may be manifestations of a subjacent pathological process in the central nervous system.

p1259
Absence-tonic Seizures: An Unusual Seizure Phenotype
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Purpose: To describe a hitherto unreported idiopathic generalised seizure semiology.
Methods: Clinical and observational report with video telemetry.
Results: A 15-year-old boy with moderate learning difficulties and communication problems was admitted for evaluation of his epilepsy. He presented with episodes of behavioural arrest since 9 years of age, which were diagnosed as 'absences'. They have remained refractory to treatment. Clinical and neurological examination was within normal limits. There was no family history of epilepsy. MRI brain was reportedly normal. Present attacks consist of staring, cessation of activity followed by sudden stiffening, abduction of arms and vocalisation. This may be followed by confusion or automatisms .The entire event lasted 30s to 1 minute and could occur 3-4 times /day despite treatment with valproate, lamotrigine, topiramate and clobazam. EEG showed generalised 2½ -5 Hz spike-wave discharges during the 'absence' period followed by a run of 12-15Hz polyspikes during the tonic phase. Only generalised spike-wave bursts were seen in sleep, without clinical correlates.
Conclusion: Although tonic-absence seizures have rarely been reported (1), the sequence appears to be reversed in this patient with the occurrence of 'absence-tonic' attacks. This semiology has not been described previously. The occurrence of fast bursts following the spike-wave discharges as a fixed sequence suggests an unusual switch from thalamic to cortical dominance in the genesis of these seizures. Further studies may provide instructive insights into the mechanisms of generalised absence-type epilepsies. References (1) Shih TT, Hirsch LJ. : Epilepsia. 2003 Mar; 44(3): 461-5

p1260
Is Hyperventilation an Effective 'Activating' Procedure in Routine Clinical EEG Studies in Children?
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Purpose: This study was designed to determine the actual value of voluntary hyperventilation (HV) in routine clinical EEG in provoking epileptiform EEG abnormalities in a series of children with generalised epilepsy .
Methods: Consecutive EEG records of 275 children (ages 3–18 years; average 11 years; 34.5% females) with generalised epilepsy (generalised tonic-clonic seizures in 245 and absence seizures in 30), consistent with epileptiform discharges in baseline EEG (typical spike and wave, TSW in 40%; atypical spike and wave, ASW in 56.4%; and periodic lateralised epileptiform discharges, PLEDs in 3.6%) were reviewed. The patients underwent 5 minutes of voluntary HV during standard EEG recordings. All EEGs were recorded and interpreted by the author.
Results: Of the 275 EEG records, only 11.6% HV revealed increased interictal epileptiform discharges (IEDs) as evidenced by increase in frequency during HV when compared with the baseline EEG and in 0.7% ictal epileptiform discharges without clinical seizure. None of the 275 children elicited clinical seizure during HV .
Conclusion: The value of voluntary HV as an 'activating' procedure in routine clinical EEG studies, even in children with generalised epilepsy, was questioned in this study .

p1261
Cefepime Induced Encephalopathy and Triphasic Waves in Two Asian Patients
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Purpose: We report 2 Asian patients, 1 had pre-existing renal failure while the other had prior liver cirrhosis. Both developed encephalopathy and triphasic waves while being treated with cefepime.
Methods: Case reports
Results: Patient 1: 77 year old Chinese man with renal failure on haemodialysis presented with acute pancreatitis. After 6 days of ceftriaxone, antibiotic cover was changed to cefepime, 2 grams twice a day. Four days later, he became confused and developed myoclonus. EEG showed triphasic waves. There was mild, transient liver enzyme elevation. Ammonia level was normal. There was no change in serum urea, creatinine and electrolyte levels. Three days after cefepime cessation, he was less confused. Repeat EEG showed absence of triphasic waves. Patient 2: 71-year-old Indian man with a history of alcohol-related cirrhosis presented with malignant otitis media. After treatment with ciprofloxacin and ceftriaxone for 2 weeks, he was given cefepime, 2 grams twice a day. Three days later he became disorientated with asterixis. Triphasic waves were recorded. Liver function remained unchanged. Renal function and ammonia level were normal. Two days after discontinuation of cefepime, encephalopathy subsided. A week later, no triphasic waves were seen.

Conclusion: Cefepime-induced encephalopathy and triphasic waves, with and without status epilepticus, have been reported only in non-Asian patients with renal failure. Our report shows that cefepime toxicity should be considered for Asian patients who develop encephalopathy and triphasic waves, especially with (1) pre-existing kidney/liver impairment, (2) prior use of another cephalosporin, and/or (3) no significant deterioration of renal and hepatic function.

p1262
Effects of Topiramate on the Excitability of the Human Motor Cortex; A Transcranial Magnetic Stimulation Study
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Purpose: To clarify the mechanisms underlying the anticonvulsant activity of topiramate (TPM).
Methods: The effects of TPM on motor cortex excitability were examined with a range of transcranial magnetic stimulation (TMS) protocols, before and after double-blind administration of TPM or placebo in 20 healthy volunteers over a period of four weeks. TMS measures included: 1) the resting and active motor threshold (RMT-AMT) to TMS, which reflect changes in the membrane excitability at cortical and spinal level; 2) the short latency intracortical inhibition (SICI) and the cortical silent period (SP), which are both believed to reflect the excitability of inhibitory GABAergic cortical circuits; 3) the intracortical facilitation (ICF) that is thought to depend upon the activity of intracortical glutamatergic excitatory circuits.
Results: TPM produced a statistically significant decrease in ICF, as compared with placebo and baseline measures. We also found an increase in SICI, and a decrease in RMT, AMT, and SP duration; however, the changes in motor cortex excitability as measured by these parameters did not differ significantly from those observed after placebo administration.
Conclusion: These results indicate that TPM modulates glutamatergic neurotransmission by blocking AMPA/kainate non-NMDA receptor activity and by enhancing NMDA-modulated transmission, similar to that described in experimental studies. The net effect is a decrease in the high frequency glutamatergic neurotransmission that determines a decrease in motor cortex excitability to TMS. Our study thus provides in vivo neurophysiological evidence that the anticonvulsant properties in humans of TPM result mainly from an interaction with the glutamatergic AMPA/kainate receptors.

p1263
Levetiracetam Add-on Therapy has no Effect on EEG Background Frequency in Epilepsy Patients
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Purpose: Computerised analysis of EEG background frequency has become an important tool in the investigation of cognitive functions. Therapy with the traditional antiepileptic drugs (AEDs) has been associated with a slowing of EEG background rhythms. So far, it has not been tested whether the relatively new AED, Levetiracetam (LEV) has a detrimental effect on the EEG background frequency.
Methods: 28 patients with drug-resistant epilepsy were included. The patients received LEV as add-on therapy according to the study-design. All subjects underwent structured EEG recording at baseline after two months and again after four months of LEV therapy. Data of the occipital electrodes were analysed using Fast Fourier Transform (FFT). The following parameters from FFT were included: peak frequency within the alpha band, percentages of total power within alpha, theta, delta and beta bands.
Results: A six month-treatment with LEV add-therapy showed no negative effect on any of the measures analysed, it did not lead to a lower peak frequency or a lower percentage of total power within the alpha band. In addition, no power increase within the theta and delta activities could be observed. In the course of LEV therapy we could notice an increase of the percentage of total power within the beta band ($p = 0.027$).
Conclusion: Our findings demonstrate that LEV add-on therapy is not associated with a slowing of the EEG background rhythm. This is in accordance with recent reports of our own lab and others showing that LEV add-on therapy has no negative effects on cognitive functions, either.

p1264
Effect of Valproate on Silent Period and Corticomotor Excitability
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Purpose: To investigate by transcranial magnetic stimulation (TMS) the effects of valproate on silent period (SP) and corticomotor threshold (Thr).
Methods: 30 patients with generalised epilepsy (median age 25 years) were studied at baseline and re-examined 4 (S1) and 16 (S2) weeks after the administration of valproate (mean dose 1080 mg). TMS was performed with a Magstim 200 stimulator and a figure of eight coil (recording, FDI). Thr was measured at 1% steps. SPs were measured using a recently described protocol. Briefly, SPs were elicited at 5% increments from 0 to 100% maximum stimulus intensity (SI). At each SI, 4 SPs were obtained and the average value of SP duration was used to construct a stimulus/response (S/R) curve of SI vs. SP. The resulting S/R curves were then fitted to a Boltzman function and were statistically compared.
Results: Valproate increased Thr from 36.5 ± 5.99% at baseline to 41.02 ± 7.84 at S1 ($p<0.0001$, paired t-test). In a subgroup of 13 patients, Thr increased from 36.42 ± 6.6% at baseline to 40.03 ± 8.07% at S1 ($p<0.05$) with no further increases occurring at S2 (41.4 ± 8.24%, $p>0.05$, ANOVA and Tukey-Kramer post-test). Regarding SP, the Max value of the S/R curve decreased from 253.4 ms at baseline to 225.5 ms at S1 ($p<0.01$, Mann-Whitney U test). The other best-fit values of the S/R curves (V50, Slope) were not significantly affected.
Conclusion: Valproate, in common with other Na channel blockers, increases Thr. In addition, it reduces Max SP duration, an effect probably mediated by GABA A receptor activation.

p1265
Effects of Sleep Deprivation on Cortical Excitability in Patients Affected by Juvenile Myoclonic Epilepsy: A Combined Transcranial Magnetic Stimulation and EEG Study
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Purpose: To investigate the effect of sleep deprivation on corticospinal excitability in patients affected by juvenile myoclonic epilepsy (JME) using different parameters of transcranial magnetic stimulation (TMS).
Methods: 10 patients with JME and 10 normal subjects underwent partial sleep deprivation. Motor threshold (MT), motor evoked potential amplitude (MEP) and silent period (SP) were recorded from the thenar eminence (TE) muscles. Short latency intracortical inhibition (SICI) and short latency facilitation (SICF) were studied using paired magnetic stimulation. The TMS recording was performed before and after sleep deprivation. Coregistration EEG and TMS was performed.
Results: Sleep deprivation induced in patients a significant decrease in SICI and an increase in SICF after sleep deprivation, which was associated with increased paroxysmal activity. A significant decrease in the MT was observed. No significant changes in any TMS parameters were noted in normal subjects after sleep deprivation. The F wave was unchanged by sleep deprivation in both control subjects and in patients with JME.

Conclusion: In patients with JME, sleep deprivation produces increases in corticospinal excitability in motor areas as measured by different TMS parameters.

p1266
Predictive Value of Specific Video Tape Sequences in Photosensitive Epilepsy Patients
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Purpose: To assess the value of specific video tape sequences in predicting the risk for TV-induced seizures using television sets (TV 50 Hz) and video tape made of 4 sequences.
Methods: We studied 65 epilepsy patients with generalised photoparoxysmal responses (PPR) during intermittent light stimulation (ILS). 29 (group A) had television induced-seizures. 36 (group B) didn't experience seizures while watching television (20/36 had seizures induced by other visual stimuli than television and 16/36 had no visually-induced seizures). The video tape sequences were presented on a 50Hz TV set. The video tape was made of 4 sequences previously demonstrated as epileptogenic. The 1st is characterised by a moving pattern, the 2nd by a high rate of contrast with moving objects, the 3rd by a moving coloured picture and the 4th by a 12Hz red/blue flicker. EEG-video recordings were performed to obtain correlations between each video tape sequence and PPR.
Results: Electroencephalographic activation by at least 1 of the 4 sequences was obtained in 48/65 patients without any difference between the two groups: PPR were obtained in 20/29 in group A and 28/36 in group B. No difference was found regarding the photosensitivity range between the 2 groups. However, sequence 2 induced PPR in 10/29 patients in group A. By contrast, no patient in group B had EEG activation with this sequence (0/36) (p=0,0001). Activation by sequence 2 in group A patients was more frequent in subjects who had PPR at frequency ³ 40 Hz during ILS (p=0.045). In group B, 25/36 had PPR with sequence 4 while 9/29 in group A (p=0.002).
Conclusion: Presentation of video tape using TV 50 Hz sets during EEG recording might be useful to predict the risk of television-induced seizures in photosensitive epilepsy patients. However, video sequences consisting of high luminosity and moving objects (sequence 2) seem to be the most relevant to predict television-induced seizures. By contrast, video sequences consisting of 12 Hz red and blue flicker have no predictive value of TV- induced seizure in daily life.

p1267
EEG Seizure Prediction Using Entropy Measure
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Purpose: The interactions between neurons for seizure generation are known to be nonlinear in nature. The strength of coupling between functionally different cortical regions can be analysed by the nonlinear interdependence of the degree of synchronisation. Entropy measure can quantify statistical nonlinear interdependencies between two random variables. We applied this measure to detect seizures and to investigate whether if it can be used for seizure prediction.
Methods: EEG signals were recorded from 3 epileptic patients. Then the regularity of the single EEG channels and the mutual regularity and predictability between channel pairs were measured through the evaluation of the joint entropy of the segmented EEG. Mutual regularity index (MRI) was derived to analyse short data segments and to quantify the interdependence of coupled EEG channels even when there is no a priori hypothesis on the model of the signal generating mechanism.
Results: In all seizures, a preictal state was reflected by a decrease in values of MRI starting before seizure onset. Its duration was different for different seizures. This decrease in synchronisation occurred well in advance. It can be described as successive changes in brain dynamics starting before the seizure. The neurons within these regions might be initiated by abnormally discharging neurons that recruit neighbouring neurons into a critical mass leading to a focal or generalised synchronisation.
Conclusion: The degree of synchronisation between EEG signals from different recording sites has been analysed. The distinct drop in synchronisation before seizures that was usually not found during the interictal period has been demonstrated.

p1268
Newly Diagnosed Epilepsy in the Elderly: Age-Related Influence of Sleep Depth on Interictal Epileptiform Abnormalities
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Purpose: Few data are available on the diagnostic yield of sleep EEG recordings in elderly epilepsy (E) patients.
Methods: We analysed clinical and EEG data concerning 20 consecutive patients with E (cryptogenic focal in 8 subjects; remote symptomatic focal in 7; undetermined in 5 with exclusively sleep-related convulsive seizures) which had performed standard EEG (SEEG) and 24 hour ambulatory EEG (AEEG) at the first referral for seizure onset at age 60 years. We considered the presence of IEAs during SEEGs and sleep periods in AEEGs. IEAs throughout sleep periods were quantified by a spike index (SI) and coupled with sleep stages. Elderly patients (group A) were compared to 20 patients with seizure onset at 25-40 years of age (group B), matched up for epileptic syndrome and gender.
Results: Focal IEAs were detected in SEEG of 3/20 subjects of group A and 10/20 of group B. All patients in group A showed IEAs during NREM sleep (7/20 exclusively during stages 3-4). IEAs during NREM sleep were found in 14/20 subjects in the group B. SIs calculated in group A showed an increase linked to NREM sleep depth (mean SI ± s.d.: stages 1-2 = 0.6 ± 1.2, range 0.0-3.0; stages 3-4 = 1.7 ± 2.2, range.1.0 -7.6). Mean SIs in groups B did not show differences between NREM sleep 1-2 and 3-4. Repeated measure ANOVA revealed significant differences between groups A and B in the increase of the SI values from 1-2 to 3-4 stages (p = 0.012). IEAs during stages 3-4 in elderly with non-symptomatic E were clearly lateralised, isolated, high amplitude spikes or sharp-waves on anterior temporal regions.
Conclusion: Our findings confirm low IEA rates on SEEG in elderly subjects. AEEG documented a higher propensity to IEAs during NREM stages 3-4 in the elderly compared to a younger group. Focal sleep-related IEAs in elderly showed a peculiar morphologic and topographical pattern.

p1269
Diazepam Effect on EEG During Status Epilepticus
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Purpose: To determine the effect of intravenous diazepam treatment on EEG during status epilepticus (SE).
Methods: We retrospectively studied the duration of disappearance of epileptiform activity after diazepam intravenously (response time) and its relation to duration and aetiology of SE, using data from the Marmara University School of Medicine, Neurology Department SE registry.
Results: 53 patients with SE who had EEG, 16 male and 37 female, aged 17-88 years (mean 39.5 years) were recruited from the SE registry. According to the response time to administration of diazepam, patients were divided into four subgroups: group I (response time range 20-60 seconds), Group II (response time range 61-120 seconds), group III (response time range 121-180 seconds) and group IV (response time range 181-360 seconds). The duration of SE before administration of diazepam was 12.5 (±7.28) in the first group and 19.78 (±19.59) in the last group. According to the aetiology, metabolic and central nervous system (CNS) tumours were the earliest responders with 98 and 90 seconds respectively. CNS infections and

cerebrovascular diseases (CVD) were the latest responders with 124.4 and 140 seconds, respectively. While the mean response time of patients who died was 160 seconds, the mean response time of the others was 100 seconds.
Conclusion: These findings demonstrate the inverse relation between the effect of diazepam administration and seizure duration during status epilepticus. According to aetiological factors, it takes a longer time to observe the effect of diazepam in CVD and CNS infections. The response time may have a role in predicting outcome of status epilepticus treatment and in order to see the effect of diazepam, we should take the EEG longer.

p1270
Motor Cortex Excitability and Cognitive Functions in Epilepsy Patients with Mesial Temporal Sclerosis
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Purpose: In this study we aimed to investigate cortical motor excitability (CME) and cognitive functions in epilepsy patients with mesial temporal sclerosis (MTS).
Methods: The study group consisted of 11 patients (6 male, 5 female; age between 20-43) and age-sex-educational level matched to 10 control subjects. CME and cognitive functions were evaluated using transcranial magnetic stimulation (TMS), neuropsychological tests [Rey Auditory Verbal Learning Test (RAVLT), Wechsler Memory Scale-III (WMS-III) visual memory test, The Wisconsin Card Sorting Test (WCST), digit span forwards and backwards, trial making tests (A-B)] and P300 recordings.
Results: In the patient group, while the ipsilateral cortical silent period was longer; motor evoked potential amplitude and motor threshold values were reduced compared to the control group ($p<0.05$). Mean N200 and P300 latencies were longer in patients than in the control group ($p<0.05$). In addition the mean P300 amplitude was statistically reduced in patients compared to the control group ($p<0.05$). There were statistically significant differences in RAVLT and WMS-III visual memory test between patients and the control group ($p<0.05$). There was a negative correlation between P300 latency and WMS-III visual memory test ($r = - 0.60$, $p<0.05$).
Conclusion: Our results indicated that CME was increased and cognitive functions, especially memory and attention, were impaired in epilepsy patients with MTS.

Wednesday 31st August and Thursday 1st September 2005
13:15 – 14:15
Poster Session
Paediatric Epileptology

p1271
Epilepsy in Denmark: Incidence, Prevalence and Validation of Diagnosis
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Purpose: Large study populations are needed to study the association between epilepsy and factors with low frequency e.g. mortality.
Methods: We report the findings from The Danish National Hospital Register (LPR), which contains information on all epilepsy discharges from Danish hospitals from 1977-2002; outpatients have been included in the register since 1995.
Results: Validation: epilepsy diagnosis was validated in 188 registered cases of epilepsy and among these cases the diagnoses were confirmed in 153 patients (positive predictive value 81%, 95% CI: 75% – 87%). Incidence: the incidence of epilepsy was higher in men than in women, with an exception of ages 10–20 years in which the incidence rate was higher in women. The incidence rate was highly age dependant with a high incidence in the youngest children, declining to a low level of 5–10 new cases per 100,000 person years between 20 and 40 years, followed by a gradual increase thereafter. Prevalence: overall prevalence ranged between 0.4 and 0.8% of the population. The prevalence of epilepsy was age dependant with the lowest prevalence between 40-60 years for women and between 25-60 for men. For most age groups, the prevalence of epilepsy was higher for men than for women, with an exception of the age groups between 16 and 25.
Conclusion: We confirmed the epilepsy diagnosis in 81% of registered cases. The incidence and prevalence rates of epilepsy were similar to incidence rates from other, but smaller populations.

p1272
Childhood Epilepsy in Latin-American: A Systematic Review of its Prevalence
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Purpose: We conducted a systematic review and analysis of prevalence studies of epilepsy amongst children in Latin-America, in order to establish its magnitude, which may be a starting point in discussing an approach to the existing treatment gap.
Methods: We searched MEDLINE, IMBIOMED, and LILACS (Latin-American and Caribbean biomedical database). We included studies exploring the prevalence of epilepsy in childhood (0-14 years old) through standardised data collection questionnaires, with reports of raw population numbers, and a clear definition of epilepsy. Studies with acute symptomatic seizures, certain seizure patterns, and specific epileptic syndromes were excluded. Reviews, editorials, abstracts, and letters were not included. Type of population (urban or rural), gender, year of study, and method of ascertainment, were obtained from each study.
Results: The search yielded 1518 publications in MEDLINE, 96 in LILACS, and 99 in IMBIOMED. Application of exclusion criteria resulted in 30 studies; of these, only 17 presented prevalence information in children. The median prevalence was 13.5 per 1000 children (range: 7.5-44.3), with no differences between rural and urban populations (13.8 vs. 17.2, $p=0.35$). The method of ascertainment was similar in all studies: questionnaire and neurological evaluation, with the exception of one, which reviewed health records. Information was available only for Bolivia, Brazil, Ecuador, Chile, Colombia, Cuba, Guatemala, Mexico, Panama and Peru.
Conclusion: The prevalence of epilepsy in Latin-American children is no different from other portions of the southern hemisphere, but indeed higher rates are seen when compared with developed countries. Sources of variability in prevalence rates will be explored.

p1273
Epidemiological Characteristics of Children's Epilepsy in Yakutia
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Purpose: To study epileptic morbidity, frequency, aetiologic factors and clinical forms of epilepsy among children in the Republic of Sakha (Yakutia).
Methods: We examined 1309 children with epilepsy at the age of 1 month and up to 18 years, during 2000-2003. We used epidemiological, clinical methods and statistical analysis.
Results: The frequency of epilepsy has become 5.2 per 1000 of the child population in Yakutia. Frequency of symptomatic forms of epilepsy is 3.0, idiopathic epilepsy is 1.3, cryptogenic epilepsy is 0.9 per 1000. Morbidity of epilepsy among children in the Republic of

Sakha (Yakutia) is 114 per 100,000 of the child population. 400 patients with full known anamnesis are analysed and examined. Prenatal disorders of the brain are the most frequent reasons and a risk factor of epilepsy is 79.75%. Hereditary predisposition is 12.75%, febrile seizures as the next factor are met in 12.5% of cases, 7% of brain traumas and 7% of affective respiratory attacks in anamnesis, neuroinfections as aetiological factors account for 6%, 0.75% is for postvaccinal complications. Symptomatic focal forms of epilepsy dominate (55.8%) over idiopathic generalised (21.6%) and other forms. 20.4% are marked as symptomatic temporal lobe epilepsy, 15.2% as frontal lobe and 12.6% as a multifocal form.
Conclusion: 1) Frequency of epilepsy is 5.2 per 1000, primary morbidity is 114 per 100,000 of the child population in Yakutia. 2) Epilepsy is thus determined as a multifactorial disease. 3) The analysis of clinical forms correlation reveals a dominance of symptomatic over idiopathic and cryptogenic.

p1274
Incidence and Distribution of Epileptic Syndromes in Children
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Purpose: We carried out an epidemiological survey of childhood epilepsy within a large population in Okayama Prefecture, Japan. The patients were categorised according to the International Classification (ILAE, 1989) to clarify the incidence and distribution of epilepsies and epileptic syndromes in the general population.
Methods: Background population under 13 years of age was 250,997. The list of children with active epilepsy under 13 years of age was collected from the medical records of 83 hospitals or clinics. The patients diagnosed with epilepsy according to clinical and EEG findings were put on the list even if patients had had a single seizure or seizures induced by fever. EEGs were conducted in 99.8% of the total cases in this series. 2,220 cases were identified.
Results: The incidences of various types of epileptic syndromes were presented. 2,030 (91.4%) of the 2,220 could be classified into three major categories of the ILAE Classification. They consisted of 1,556 cases (76.7%) with localisation-related epilepsy (LRE), 453 cases (22.3%) with generalised epilepsy (GE) and 21 cases (1.0%) with undetermined epilepsy (UE). Detailed classification into subdivision categories of the ILAE Classification could be conducted in 142 (9.1%) of the 1,556 cases with LRE, 187 (41.3%) of the 453 cases with GE and 17 (81.0%) of the 21 cases with UE, respectively. On the other hand, a total of 1,721 (84.8%) of the 2,030 cases could not be classified into subdivision categories.
Conclusion: The majority of the cases with epilepsy should not be classified into the category as other epilepsies not defined above (ILAE, 1989) but should be given some appropriate classification items.

p1275
Assessment of Clinical Utility of Recent Proposals of the ILAE Task Force on Classification and Terminology for the Diagnosis and Classification of Patients Attending an Epilepsy Centre in Nepal
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Purpose: Application of the new recommendations from the ILAE task force on classification and terminology for categorising epilepsy patients and to assess its utility for diagnosis and proper management in an Epilepsy Centre in Nepal.
Methods: A retrospective analysis of all patients (n=604) referred to the centre from all over Nepal from November 1997 to March 2005 was carried out. Data included description of events from an eye witness, EEG, CT and MRI of the brain and other specific investigations. The diagnosis was reviewed and a classification attempted keeping in mind the recent ILAE Task Force proposals. (Jerome Engel, Jr. Epilepsia 2001;42:796).
Results: 604 patients with paroxysmal events were referred. 34 were not included in the study for lack of adequate data. Of the 570 cases, 21 (3.6%) could not be diagnosed satisfactorily. 57 (10%) had non-epileptic paroxysmal events. Of the 492 cases with seizures 97 (19.7%) were cases of idiopathic epilepsies, 22 (4.4%) of epileptic encephalopathies of which West syndrome was the commonest and of the 184 (37.4%) of symptomatic epilepsies, neurocysticercosis constituted 118 cases (24% of all the seizure cases). 77 (15.6%) were cases of probably symptomatic epilepsy. Only 25 (5%) patients with recurrent seizures could not be classified appropriately according to the ILAE classification.
Conclusion: The ILAE 1989 Classification of epilepsies and epileptic syndromes when applied flexibly according to the recent proposals made by the ILAE Task Force is found clinically very useful in diagnosis, prognostication and treatment of epilepsy, particularly in a developing country like Nepal.

p1276
Profile of Recurrent Seizures: A Rural Hospital Based Study
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Purpose: To find the incidence, aetiological factors, epilepsy syndromes and evaluation of therapy for recurrent seizures in children.
Methods: Patients attending the Seizure Disorder Clinic, ICH and RC, GRG, Madurai observation and questionnaire about seizure semiology and follow up and evaluation of imaging and EEG.
Results: Of the 240 patients attending the Epilepsy Clinic, 154 patients are on regular follow up. 30 patients have a high recurrence rate of more than 2 per month. (18% of total cases are on regular follow up n = 154). The patients having high recurrence symptomatic seizures (generalised seizures and localisation related seizures) account for 16 cases. Among the aetiological factors related to recurrent symptomatic seizures, infections account for 10 cases, birth asphyxia accounts for 4 cases, genetic syndrome accounts for 1 case and developmental lesion accounts for 1 case. Regarding therapy, primary drugs available are phenobarbitone, phenytoin, valproate and carbamazepine. We added clonazepam in 2 cases of West syndrome and seizure recurrence reduced from 10/day to 2/ day. Lamotrigine was added in 1 case of Lennox Gastaut syndrome and the response was good. In one case of symptomatic related epilepsy topiramate was added, recurrence rate reduced from2/day to 6/month. Because of poor socioeconomic status, newer antiepileptic drugs are affordable by only limited patients. Diagnosing epileptic syndromes becomes difficult in recognition of seizure semiology. Infections like tuberculosis and neurocysticercosis are responsible for most of the recurrent symptomatic seizures. Prevention and early treatment of infections will reduce the burden of management of recurrent seizures.
Conclusion: Presented for its social problems.

p1277
Clinical Profile and Spectrum of Epilepsy in Rural Maharashtra
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Purpose: The study is from an outreach epilepsy clinic conducted at rural Maharashtra 550 kms away from Mumbai. The clinic was conducted once every 6 weeks for a period of 2 years. The aim was to study the clinical profile of epilepsy, to offer affordable treatment with minimum investigations and to educate the patients.
Methods: 183 patients registered over a period of two years; 17 were not included in the study group as they had nonepileptic events. A detailed clinical history including seizure type and frequency, age of onset, birth history, family history and developmental history was taken in all. Neurological examination was performed. EEG was done when indicated, except in those with financial constraints. Seizures

and syndromes were classified according to ILAE Classification (1981). Appropriate AEDs were prescribed and a regular follow up was advised.
Results: The median age of onset was 2.35 years. 99 (59.6%) were males. Seizure types were as follows: GTC (48%), partial (38%), myoclonic (3.61%), absence (1.2%), both generalised and focal (3%), unclassifiable (6%). 14.5% had remote symptomatic epilepsy, perinatal insult being the commonest aetiology. Mean follow up of 8.4 months was obtained in 80 (48.19%) patients; 30 (37.5%) showing complete freedom from seizures while 16 (20%) showed good control.
Conclusion: Seizure freedom can be obtained in a large number of epilepsy patients from rural areas by simple clinical classification and appropriate AEDs.

p1278
Clinical Profile of Paediatric Epilepsies: A Study from a Tertiary Referral Centre of Eastern India
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Purpose: Epilepsy in the paediatric age group differs from adults in respect of prevalence, aetiology, pharmacokinetics and pharmacodynamics of antiepileptics and response to treatment. The objective of this study was to evaluate the clinical presentation, aetiology, response to treatment and to find out prognostic factors of paediatric epilepsy patients.
Methods: A total 90 paediatric patients (below 12 years of age) were included who attended the epilepsy clinic and paediatric neurology clinic of the Institute between March 2003 to February 2004. They were evaluated by detailed history, clinical examination and investigations to find out the type of seizure and possible aetiology. Reduction of 50% or more seizures was considered a good response to treatment.
Results: Of the 90 children 57.7% were boys and 42.3% were girls. Most of them were between 1-4 years of age (44%). In 44.4% patients the onset of seizure was below 1 year of age. 48% had localisation-related epilepsies and 44% had generalised seizures. 55% patients were good-responders. Poor-responders had seizure onset below 1 year of age, localisation-related epilepsies, and associated mental retardation or motor disability.
Conclusion: Early onset seizure, associated mental retardation and motor disability, localisation-related epilepsies and myoclonic epilepsies had poor prognosis in the paediatric cases of epilepsy in our study.

p1279
Use of New Classification (Engel, 2001) for Epilepsies in India
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Purpose: To evaluate the benefits of use and difficulties of the new classification of seizure types and epilepsies.
Methods: 902 persons with epilepsy attending a specialty epilepsy clinic with a national and regional drain, were evaluated using the new classification proposed by Engel from January 2002 to February 2005 based on history, clinical features, EEG, brain imaging (CT/MRI scan) and V-EEG in selected cases. Key terms were used as described in the classification. Seizure types were classified as self-limiting vs continuous, generalised vs focal and the syndromic classification was used with inclusion of conditions with seizures that do not require a diagnosis of epilepsy, such as febrile seizures and alcohol withdrawal seizures, using as many of the five axis as applicable in each case.
Results: The results are discussed in detail with the various difficulties and ease of use of the classification at the specialty clinic level. Some epileptic encephalopathies were difficult to classify.
Conclusion: However, being a useful system of classification that could be used easily by the end user with variable application for use, it needs education of various evaluators for its successful use.

p1280
Childhood Symptomatic Epilepsy: Clinical Profile, Seizure Control and Intellectual Handicap in Rural Region of Western India
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Purpose: To determine the prevalence, clinical profile, seizure control and intellectual function in children with symptomatic epilepsy from a community clinic conducted in Sawantwadi, a small town in rural Western India.
Methods: We carried out a detailed review of records of every child with seizures who attended the clinic from October 2002 until the current date. Children with a history of perinatal insult, developmental delay, CNS infections or positive neuroimaging findings were considered as having symptomatic epilepsy. Seizures and syndromes were classified according to ILAE Classification (1981). Appropriate AEDs were prescribed and a regular follow up was advised.
Results: Out of a total of 166 children studied, in 39 (23.5%) there was historic, clinical or radiological evidence to suggest underlying brain damage/defect. In this group of children with symptomatic epilepsy, the mean age of onset was 2.16 (sd + 4.88); partial seizures (51.28%) were more common than generalised seizures; a history of perinatal insult was present in 25 (64.1%) and developmental delay or mental retardation was seen 28 (71.79%). Mean follow up was 10.15 months. At the end of follow up 31.57% of children were refractory to treatment.
Conclusion: Perinatal insult is the commonest cause of symptomatic epilepsy in children residing in the rural region of Western India. Therefore there is a need within the community for better perinatal care.

p1281
Prevalence of Febrile Convulsions in an Urban Population of a Metropolitan City of India through Random Sample Survey
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Purpose: To determine the prevalence of febrile convulsion through a door-to-door random sample survey in the city of Kolkata.
Methods: The metropolitan area of the city of Kolkata was stratified and areas from all strata were randomly selected using a table of random numbers. This was to ensure proper representation of all sections of the people of the city in the study group. We conducted a two-stage survey in the city between March 2003 through February 2004. Initially field workers screened all patients with seizure disorders. Subsequently neurologists undertook a comprehensive examination of all the screened positive cases and carefully studied their investigational and treatment records.
Results: Out of the total surveyed population of 52,377 (men 27,415, women 24,962) there were 597 persons with seizure disorders. Of them 288 had active epilepsy, 28 had epilepsy in remission, 40 had single seizure, and 9 had non-epileptic events. A total of 211 persons were detected to have febrile convulsions (men 115, women 96) with a period prevalence rate of 4.02 per 1000 populations. Of them 56 persons (men 38, women 18) had active febrile convulsions i.e. children aged 6 years or less, providing a period prevalence of 11.95 (men 15.36, women 8.14) per 1000 persons. The mean age of onset was 1 year and 8 months. Only 6 (10.7%) had atypical febrile convulsions. 14 (25%) had a positive family history and 25 (43%) had a single episode of seizure.

Conclusion: This random sample population-based study in the city of Kolkata showed a high prevalence of febrile convulsions.

p1282
Risks of Febrile Seizure Transformation to Epilepsy
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Purpose: To determine risk factors and their meaning for transformation of febrile seizures (FS) to epilepsy.
Methods: Clinical records and patient history were studied for three groups of patients. The 1st group included 32 children (20 boys, 12 girls) aged 8-14 years, who had different forms of epilepsy and FS. The 2nd included 34 children (16 boys, 18 girls) aged 8-14 years, who had a history of FS but no epilepsy. The 3rd group included 40 children (26 boys, 14 girls) aged 1-5 years, who had at least one FS. Special attention was paid to the presence of focality, a degree of febrility, duration of seizures, relapse of seizures during 24-48 hours after 1st FS, age of first and last FS, general number of FS, frequency of FS, presence of FS and epilepsy in relatives, AED prescription.
Results: The frequency of focal FS was 10.6 times greater in children from the 1st group, a relapse of FS in 1-4 months was 7.4 times more frequent, FS longer then 3 minutes occurred 2.4 times, FS provocation by subfebrile temperature was 2.1 in those aged less than 1 year or older than 4 was 1.8, mental retardation in 1.6. A prescription of AED decreased the frequency of epilepsy in the 3rd group where one or more of mentioned factors were present. to 2.5%; that is below the known 4-15% of transformation.
Conclusion: Therefore an AED prescription is highly recommended if one or more of the above listed factors have been revealed.

p1283
Risk of Seizure Recurrence Following a First Unprovoked Seizure in Korean Children: An Extended Follow-up
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Purpose: To evaluate the long-term recurrence risk and risk factors following a first unprovoked seizure in Korean children.
Methods: From June 1994, 409 children who visited our paediatric epilepsy clinic within 7 days after their first unprovoked seizure were enrolled and followed prospectively from the day of the first seizure to July 2004 for a mean of 41 months. Seizures were classified by ILAE guidelines as idiopathic, cryptogenic, or remote symptomatic. Potential risk factors for recurrence were analysed by Cox's proportional hazard model and survival analysis was performed using the Kaplan-Meier analysis.
Results: 177 (43.3%) children experienced a recurrence within the mean period, 7.6 months after their first seizure. The cumulative probability of seizure recurrence was 28.5%, 38.6%, 46.3%, 49.7%, and 53.6% at 6 months, 1, 2, 4, and 6 years, respectively. In the overall group, aetiology of seizure (remote symptomatic, cryptogenic) and abnormal EEG were risk factors. In idiopathic and cryptogenic cases, abnormal EEG was a common risk factor. Additionally, in cryptogenic cases, onset age (>3 years) and prior complex febrile convulsions were associated with an increased risk (relative risk, 15.90; 95% confidence interval 2.03~124.4, $p<0.001$).
Conclusion: The recurrence risk observed in Korean children was similar to that in western countries. While children with an idiopathic first seizure and normal EEG had a particularly favourable prognosis, children with a cryptogenic first seizure aged more than 3 years and a prior complex febrile convulsion showed a very high risk of recurrence, suggesting the need for immediate long-term AED treatment.

p1284
Clinical Outcome of Children after Generalised Convulsive Status Epilepticus in a Tertiary Government Hospital: A Prospective Study
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Purpose: To determine outcome after generalised convulsive status epilepticus (GCSE) and factors affecting outcome.
Methods: A prospective cohort study of all patients <19 years old after GCSE in Philippine General Hospital over 7 months was conducted. Demographic data, seizure characteristics, baseline neurodevelopmental status, therapeutics, complications of status epilepticus (SE) and hospitalisation were determined. Outcomes (good/no neurologic sequelae or poor/death or sequelae) were noted on discharge, 2 weeks and 1 month after SE. Effects of age, neurodevelopmental status, aetiology, time before treatment and duration of SE on outcome were analysed independently.
Results: 33 Filipinos (mean age: 5.25 +/- 5.23 years) were included. 45% were <3 years old. Baseline neurodevelopmental status was normal in 52%. SE was epilepsy related in 48% and acute symptomatic in 52%. Majority (76%) had seizures >1 hour. Treatment was initiated >1 hour from seizure onset in 46%. Complications of SE were noted in 45%. Outcome was poor in 60% of children <3 years old, 52% of those with normal neurodevelopmental status, 59% of acute symptomatic cases, 53% treated >1 hour after seizure onset and 52% of those with >1 hour seizures. However, association between these factors and outcome was not statistically significant ($p<0.05$). Outcome at 2 weeks and 1 month remained unchanged.
Conclusion: A trend to poor outcome occurred in patients <3 years old, with normal baseline neurodevelopmental status, time before treatment initiation >1 hour, seizure duration >1 hour and in acute symptomatic SE.

p1285
Partial Idiopathic Epilepsy in Children: Does Continuous Antiepileptic Therapy after the First Seizure Provide Safety?
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Purpose: To find the answer of a frequent dilemma: does the commencement of continuous antiepileptic therapy after the first seizure give a child significant protection from recidivity?
Methods: This study was conducted at the Children and Youth Health Care Institute in Novi Sad, for a year during 2003-2004. We present data from children with diagnosed partial idiopathic epilepsy followed for one year.
Results: At The Institute for Child and Youth Health Care in Novi Sad all children hospitalised after the first partial idiopathic seizure were observed for a year. The group consisting of 33 observed children did not show any significant difference in sex, the type of seizure (partial or partial with secondary generalisation), the time of appearance of seizure (vigilance, during sleep/or awakening), the result of neuroimaging of the central nervous system, psychological examination and lateralisation of epileptical activity in EEG. Most of the children belonging to this group (nine of them) were 10-12 years old. Electroencephalogram (EEG) was carried out for all hospitalised children during sleep and for 76% of children in vigilance. Statistically significant differences in the appearance of specific changes in EEG during sleep and vigilance were not noticed. Continuous therapy was applied in 42.4% children while 57.6% children were left without therapy. 18.2% of children observed during the year had recidivity of seizures without any difference in characteristics comparing to the first seizure. 21% of the children who were not treated with antiepileptic drugs and 14% of the children who had antiepileptic therapy, disregarding the type of drug, had recidivit seizures. The coefficient of correlation between these two groups of

children is very low (0.11) which clearly shows that the commencement of continuous antiepileptic therapy after the first idiopathic partial epileptic seizure did not provide children with significant protection from recidivity.
Conclusion: Our results clearly show that starting continuous antiepileptic therapy after the first idiopathic partial epileptic seizure did not provide children significant protection from recidivity during the first year after the first attack.

p1286
Risk Factors for Children with Epilepsy: A Population-based Study over Six Years
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Purpose: Epilepsy is the most common serious neurological disorder and numerous factors are believed to predispose children to seizures. The aim of this study is to analyse the magnitude of the risk factors for epilepsy.
Methods: We included in the study 366 children (201 males, 165 females; aged 0-18 years) diagnosed with different types of epilepsies in our clinic in the last 6 years. All children present two or more epileptic seizures. 132 (36.,07%) children were diagnosed with partial epilepsy, 234 (63.93%) with generalised epilepsy. Pearson correlations were used for all variables.
Results: Some children had multiple risk factors. Perinatal factors (gestational age, prematurity, neonatal asphyxia, neonatal seizures) and prenatal risk factors (abdominal trauma, maternal infection, vaginal bleeding, medications, mother age 35 years, radiologic examen) were major risk factors (100%) for symptomatic epilepsy. A family history of epilepsy was present in 23.77% of patients (60.92% were diagnosed with idiopathic epilepsy) and represents an important risk factor. Febrile seizures were a major risk factor for symptomatic epilepsy (62.96%) and also cerebral palsy and mental retardation (100%).
Conclusion: Our data suggest that a family history of seizures increased the risk for idiopathic epilepsy. There was a modest genetic predisposition to seizures in children with symptomatic epilepsy. However our results suggest a much stronger association between prenatal/perinatal risk factors and symptomatic epilepsy.

p1287
Factors Predicting Neurodevelopmental Outcome in Infantile Epilepsy
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Purpose: To identify factors predicting outcome in patients with cerebral palsy and epilepsy. To evaluate significance of continuity of epileptiform activity for cognition and functional independence.
Methods: 121 patients with cerebral palsy (CP) and epilepsy were studied and followed. Ages ranged from 1 to 4 years. Mean follow up 3 years. Neurodevelopment and cognition were evaluated by Baeley Infant Development Scale, functional independence by WiiFIM. Patients were divided into 2 groups. Group A: 69 patients with epileptic encephalopathy (EE), Group B: 52 with partial epilepsy. Group A was divided into 2 subgroups according to EEG patterns, continuous or subcontinuous epileptiform activity (EA). At age 3-3.5 years all patients were evaluated for functional independence, cognition , seizure control, evolution of epilepsy syndrome.
Results: Severity of CP was similar in both groups. Comparative analysis of groups showed that in total, patients of group B had significantly better seizure control ($p<0.01$); functional independence was higher by 1.5 points; cognitive outcome was better ($p<0.05$). Signs predicting negative outcome included onset of seizures before 12 months, existence of neonatal seizures, existence of several seizure types. In subgroup of group A with continuous EA seizure control was reached in 50.9%, while in subgroup with subcontinuous EA in 72%. Difference was statistically significant ($p=0.01$). Cognitive outcome differed significantly ($p<0.01$), functional independence was lower by 1 point. Signs predicting negative outcome were early onset seizures and continuous EA on EEG.
Conclusion: In patients with cerebral palsy early onset multiple seizure types with continuous EA on EEG are predictors of poor seizure control, cognitive deterioration and low functional independence.

p1288
Epilepsy in Children with Intellectual Disabilities
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Purpose: Epilepsy is one of the most serious and common neural disorders among children with intellectual disabilities. Comorbidity of epilepsy and intellectual disability shows itself as a major challenge. Study of epilepsy in children with an intellectual disability was the aim of this survey.
Methods: This study was carried out in 2002. Data which we needed was collected by reviewing the medical records of 4361 children with intellectual disabilities and by interviewing 116 parents who had children with comorbidity of epilepsy and an intellectual disability.
Results: The prevalence of epilepsy in the children studied was 10.55% and 60.5% of the children with epilepsy had had at least one seizure attack during the last two years. Phenobarbital was the most common drug consumed by children with epilepsy. Periodic care for children was carried out by parents for 45.7% of the children, and 87.1% of parents didn't know anything about the side effects of the drug which their child was consuming.
Conclusion: It is necessary to implement an educational programme on epilepsy for parents who have children with comorbidity of epilepsy and intellectual disability.

p1289
Prognosis of Epilepsy after Withdrawing Antiepileptic Drugs in 143 Chilean Children
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Purpose: To determine the outcome of children with epilepsy after the withdrawal of antiepileptic drugs (AED) and to show the significant predictor factors that could be responsible for seizure recurrence.
Methods: 143 children from the epilepsy program were included, 80 (55.9%) males and 63 (44.1%) females, who were at least two years seizure-free and began progressive AED withdrawal. We obtained follow-up medians: to epilepsy onset 48 months (range: 1-185); to the onset of AED 53 months (range: 1-185); duration of seizure-free treatment was 28 months (range: 24-65) and 4 months (range: 1-16) to progressive AED withdrawal. Observation time after AED withdrawal was 28 months (range: 1-116). The epilepsy study group included the following: cryptogenic 57 (37.1%), idiopathic 71 (29.7%) and symptomatic 19 (13.3%) patients. Among these children, 78 (54.5%) had generalised seizures, 53 (37.1%) partial, 11 (7.7%) mixed and 1 (0.7%) had unclassified seizures. Statistical significance and survival analysis were calculated (Mantel method/life-table method/Kaplan-Meier survival analysis).
Results: In the study, 43 (30.1%) patients had recurrence; among these, 12 had recurrence during the decrease of medication. Only two factors had statistical significance: children with symptomatic epilepsy ($p=0.0011$) and the fact of presenting a specific electroencephalogram at AED withdrawal. Median for time survival is 60 months.
Conclusion: This study confirmed that one third of the children who began either partial or complete AED withdrawal presented recurrence and nearly one third occurred at the time of medication tapering. Likewise other studies, symptomatic epilepsy and specific changes on the electroencephalogram could be predictor factors for recurrence.

p1290
Electroclinical Correlations and Early Outcome of Neonatal Siezures
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Purpose: Identification of electroclinical forms of seizures, and evaluation of early neurodevelopmental outcomes.
Methods: 79 neonates were included in the research group according to the following criteria: 38-40 weeks of gestation, II, III level of HIE by Sarnat without other neurological complications, clinically manifested seizures/related to uncertain conditions, registered ictal, background EEG. Observation duration was up to 4 months. Neurological assessment was studied: at age 2-3 days by means of Dubovits full scale; at 1-2 months by means of Dubovits infant neurological assessment screening test; at 4 months by means of Dubovits infant assessment full scale and Bailey infant development screening test (10-11 p-low, 8-9 p–medium, 0-7 p-high risk group, accordingly, mild, moderate, severe outcome). In all cases polygraphic EEG investigation and neurosonography were carried out, and most of patients underwent MRI and CT.
Results: Three forms of seizures were identified: electroclinical ictal EEG discharge with clinical manifestation; electrographic 2≤ sec. paroxysmal EEG discharge without clinical manifestation; clinical paroxysmal, abnormal movements without ictal EEG-discharge. Early neurodevelopmental outcome was: electrographic seizures 77.8% severe, 22.2% moderate, 0% mild; clinical seizures 63.6% severe, 22.7% moderate, 13.6% mild; electroclinical seizures 35.4% severe, 18.7% moderate, 45.,8% mild. Lethality: electrographic seizures 33.3%, clinical seizures 13.6%, electroclinical seizures 8%. Correlations with 4 groups of background EEG (mild, moderate, severe, very severe): I 95% electroclinical and 5% clinical seizures; II 77% electroclinical and 33.3% clinical seizures; III 12.5% electrographic, 35% electroclinical, 52.5% clinical seizures; IV-18.2% electrographic, 41% electroclinical, 41% clinical seizures.
Conclusion: Electroclinical seizure have a statistically reliable correlation with an early neurodevelopmental outcome. Electrographic seizures display the highest correlation with mortality, severe neurodevelopmental outcome and severe background EEG disorders.

p1291
Study of Relation between Clinical Features and Outcomes of Infantile Spasms
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Purpose: To evaluate the outcomes of infantile spasms and to elucidate the differences in the outcome related to aetiology.
Methods: Medical records of 127 patients admitted in Fudan University Children's Hospital between January 1998 and June 2002 who were followed regularly for more than one year, were reviewed. The following clinical features were assessed: demographic data, seizure details (age of onset, type, frequency, duration, aetiology and treatment), developmental status, neurological findings at presentation and electroencephalographic (EEG), neuroimaging, metabolic, haematologic and chemistry testing were reviewed. These variables were compared among three groups: cryptogenic, symptomatic and idiopathic groups.
Results: The mean age of seizure onset was 6.7±3.1 months (range=1.8~12); the mean duration of follow-up from onset of seizures was 28±16 months (range= 6-54). The underlying causes could be determined in 72% of patients. Congenital malformations and perinatal asphyxia were two commonest causes. 28% of patients had idiopathic or cryptogenic spasms. The EEG appearances were hypsarrhythmia, general or focal slow spike and waves or burst-suppression. ACTH, valproate, clonazepam, nitrazepam, phenobarbital, topiramate, lamotrigine were used in the therapy of this group. 76.8% of patients had symptomatic spasms that were refractory to routine therapy and subsequentially had severe retardation. 61% of children had idiopathic spasms controlled with antiepileptic drugs.
Conclusion: Infantile spasm prognosis depends on the aetiology, age of onset (<4 months), EEG appearance, initial seizure frequency and antiepileptic drug effects on seizures.

p1292
Clinical Characteristics and Therapy of West Syndrome
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Purpose: To study clinical features and outcome of treatment of West syndrome.
Methods: Retrospective study of 82 cases of West syndrome during the period 2002-2004.
Results: The mean age in this study was 5.04 months, boys occupied 63% and girls occupied 37%. Flexion spasm was found in 96%, extension spasms 4%. Among 82 cases, 34 (41%) cases belonged to symptomatic (callosal agenesis 2/34, microdysgenesis 13/43, hydranencephaly 1/34, hypoxia ischemic 11/34, post cerebral haemorrhage 4/34, tuberous sclerosis 1/34, post meningitis 2/34); 48 (59%) cryptogenic. A delay in psychomotor development or a regression accompanies the onset of spasm in 91% cases. High voltage 1-3 Hz waves with multifocal asynchronous spikes and sharp waves of varying morphology and amplitude were 89%, fragment unilateral hypsarrhythmia, or alternating with bursts of polyspikes mildly asymmetric burst; suppression pattern with more prominent theta activity were 11%. In Vietnam the most commonly acceptable protocol of therapy is vitamin B6 100mg/day and this, along with valproic acid ranged from 25.07 to 40 mg/kg/day was used in 74 cases. Valproic acid with benzodiazepines was used in 2 cases. Vigabatrin was used in 20 cases, dose 50-100 mg/kg/day. Valproic acid with prednisolone was used in 50 cases; prednisolone dose 1-2 mg/kg for two weeks. Seizure free in 43.9%, reduction of seizures in 53.6%, intrastable seizure in 2.5% was achieved.
Conclusion: WS mostly began under 5 months, mostly hypsarrhythmia in EEG. The treatment for cryptogenic preference is valproic acid, for symptomatic the preference is vigabatrin. Steroid is the second choice or as an add on therapy, benzodiazepine is used as an add on therapy.

p1293
West Syndrome in Novi Sad: A Twelve Year Study
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Purpose: To estimate the epidemiological and clinical features of West syndrome in the area of Novi Sad, the capital of the autonomic province of Vojvodina, for the 12 year period between 1993-2004.
Methods: Population study based on retrospective analysis of hospital records of the Department of Developmental Neurology and Epileptology of the Institute of Health Care for Children and Adolescence Novi Sad, as the reference tertiary level institution for the children from the area. In calculations of disease frequency, appropriate parameters were used.
Results: In the period studied, there were 9 patients diagnosed as West syndrome (4 males and 5 females). The average annual incidence of the disease was 0.24/1000 (95% CI 0.11-0.46). 6 patients (66.6%) were registered in generations 1999-2003. Cumulative probability of the disease was 1/4167. Prevalence of the disease on the day of 31 December 2004 was 0.24/1000 (95% CI 0.11-0.46). Regarding aetiology, all patients had a symptomatic form of the disease (1 tuberous sclerosis, 1 developmental brain malformation, 7 severe perinatal asphyxia). Until the end of the study, except for a patient with tuberous sclerosis who is without seizures and drug therapy, the other patients remained with mental and neurological deficits of

varied degrees, being on antiepileptic polytherapy with satisfactory seizure control.
Conclusion: The investigated period in the area pointed to West syndrome as rather a rare syndrome of sporadic appearance, with the majority of cases clustered since 1999. All registered patients in the investigated period had symptomatic aetiology of the disease and a mostly unfavourable long term prognosis.

p1294
Outcome of West Syndrome: Indian Experience
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Purpose: Infantile spasms are associated with increased risk of autism. No single treatment is more efficacious. We evaluated the 3 year outcome of West syndrome irrespective of aetiology and treatment.
Methods: Review of 37 cases of infantile spasms of more than 3 years of age was done for cognition, seizures and abnormal EEG. The treatment modalities were not standardised and ACTH/prednisolone/vigabatrine were used depending on availability. The outcome was measured in terms of persistence of seizures, abnormal EEG and psychomotor development with respect to aetiology and treatment lag. Parent interviews were conducted for Autism behaviour checklist.
Results: Aetiology of symptomatic West was perinatal insult in 22/37 cases, 2 had early West following severe HIE, sequel of encephalitis (2) and error of metabolism (2). Two pairs of siblings with no proven neurometabolic disorder did poorly despite a short treatment lag in the younger sibling. 25 of the 30 symptomatic West had microcephaly, gross motor dysfunction and refractory seizures. Autistic spectrum was observed in 3 and LG syndrome in 2. Evaluation of 7 cases of cryptogenic West, 1 with a short treatment gap was attending regular school while 6 with longer (3 months) showed autistic spectrum (3) and specific language disorder (3). EEG abnormalities and seizures persisted in 3.
Conclusion: Poor outcome in symptomatic West is contributed to by underlying pre-existing pathology which is largely preventable with good perinatal care. Autistic spectrum and specific language dysfunction could be avoided in the cryptogenic cases with a short treatment lag.

p1295
Cerebrospinal fluid Interleukin-6 Levels in Patients with West Syndrome
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Purpose: Elevated cytokine response has been reported in patients with epileptic seizures. The objective of this study is to investigate the possible role of interleukin-6 (IL-6) in the pathogenesis of infantile spasms in West syndrome (WS). We measured IL-6 levels in cerebrospinal fluid (CSF) obtained from the newly diagnosed patients with WS.
Methods: 12 patients with WS (Group I) were classified as symptomatic WS (Group IA) in 8 and as cryptogenic WS (Group IB) in 4. The results were compared with control groups including patients with tonic-clonic seizures associated with two different kinds of inflammation of the central nervous system; Group IIA (infection): bacterial meningitis/encephalitis and Group IIB (trauma): post-traumatic seizures.
Results: There was no statistically significant difference between the mean values of CSF IL-6 levels in patients with WS (2.95±2.31 pg/ml) and those of subgroups of WS (Group IA: 2.26±2.01 pg/ml and Group IB: 4.33±2.52 pg/ml). Both control groups had more highly increased IL-6 levels in CSF (Group IIA: 193.05±185.52 pg/ml and Group IIB: 112.74±167.44 pg /ml) than those of patients with WS. Elevated IL-6 response in patients with tonic-clonic seizures associated with inflammation of the central nervous system might be due to the seizures themselves or related to the underling aetiology (infection or trauma).
Conclusion: No elevated IL-6 response was found in patients with infantile spasms.

p1296
Lacunae in the Diagnosis and Appropriate Treatment of West Syndrome
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Purpose: To highlight the lacunae in the diagnosis and appropriate treatment of West Syndrome (WS). To see if early recognition and appropriate treatment change the long term prognosis.
Methods: A study of 1000 cases of unequivocal childhood epilepsy from a tertiary paediatric epilepsy clinic. Details of history regarding birth, family, seizure onset, associated seizures, EEG, MRI, neurodevelopmental status and classification into symptomatic or cryptogenic were recorded. Onset of appropriate treatment, i.e. based on internationally recognised protocols for the treatment of West syndrome. Patients were followed up and seizure control assessed at 6 months and again at 24 months.
Results: Incidence of WS was 13.3%. Male:female 2.57:1. Perinatal insult in 67%. Consanguinity in 7.5%, family history of epilepsy was 4.5%. Average age of onset of infantile spasms (IS) was 6.95 months. 63% had isolated IS while 37% had associated seizure types. 25% had normal mentation at time of onset with 75% having delayed development. Patients were grouped with respect to the time lag from seizure onset to time of appropriate treatment. Group1: treated at time of seizure onset 19.5%. Group 2: treated within 1 month of seizure onset 18%. Group 3: treated after 1 month of seizure onset 63%. 4% of these never saw a doctor, while 96% were diagnosed as having epilepsy but treated with AEDs other than those in the protocol. 19% were cryptogenic. EEG showed hypsarrythmia in 79%. Initial seizure control at 6 months (>50% reduction) was 69%, 95%, 77% for the 3 groups. Long term seizure control for 24 months: 92%, 91.6%, 75% for the 3 groups.
Conclusion: West syndrome is one of the commonest early epileptic encephalopathies of infancy. The long term prognosis for epilepsy and neurodevelopment is better if diagnosed early, treated immediately and correctly.

p1297
Dravet Syndrome: Effect of New Antiepileptic Drugs
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Purpose: Dravet syndrome is a severe neurologic epileptic condition that affects an initially normal infant. The first seizure occurs before one year of age. It is usually a unilateral and febrile fit lasting for more than 20 minutes. Epileptic seizures then repeat in spite of multiple anti epileptic drugs. The development slows down in the second year of life and the child eventually has a severe developmental delay.
Methods: Our retrospective work concerns 30 children with Dravet syndrome (16 female and 14 male) from the west of France.
Results: There was a familial history of epileptic seizures in 58%. The mean age of onset was 6 ± 3 months. During the follow-up, children had frequent changes in treatment usually without effect on seizure frequency. New drugs like stiripentol and topiramate seemed to be useful with good effects on epilepsy. There were about 6.4 ± 3.6 treatment regimen changes before stiripentol and 1.9 ± 3.2 after and 7.4 ± 5.5 before topiramate and 0.4 ± 1.5 after. More seizures occurred in the first year; more severe was the developmental delay.
Conclusion: Early diagnosis is important to allow early use of these new anti epileptic treatments to reduce the number of seizures and improve the prognosis.

p1298
Polymorphisms of GABRG2 Gene in Korean Febrile Seizure Patients
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Purpose: Febrile seizures are characterised by a heterogenous phenotype segregating as an autosomal dominant trait with incomplete penetrance. Mutations in GABRG2 gene were identified in two families with generalised epilepsy with febrile seizures plus (GEFS+) and two families with absence epilepsy and febrile seizures (FSs). The present study assessed the role of the GABRG2 gene in GEFS+ and FS in the Korean population.
Methods: 20 GEFS+, 60 FSs and 97 control subjects were selected throughout a collaborative study of the Catholic Child Neurology Research Group. The SNP11135 and SNP211037 of GABRG2 were screened by DHPLC. DNA fragments showing variant chromatograms were subsequently sequenced.
Results: A total of 177 individuals (20 GEFS+, 60 FSs and 97 control) were screened. There were no significant differences in allelic frequencies (CC, C/T and T/T) of SNP11135176 in GABRG2 among the patients with GEFS+, FSs and control subjects (65% vs. 60.6% vs. 70.1%, 30% vs. 31.8% vs. 24.7% and 5% vs. 7.6% vs. 5.2%). There were small differences in allelic frequencies of SNP211037 in GABRG2 among the patients with GEFS+, FSs and control subjects (10% vs. 35.5% vs. 12.8%, 60% vs. 54.5% vs. 59.6% and 30% vs. 12.1% vs. 27.7%).
Conclusion: These data suggest that genomic variations of GABRG2 might be one of the susceptibility factors for FSs in the Korean population. This work was supported by the Korean Ministry of Health and Welfare Grant HMP-00-GN-01-0002.

p1299
Myoclonic Astatic Epilepsy (MAE) Longitudinal Electroclinical Study of 25 cases
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Purpose: In spite of its inclusion in the International Classification of Epilepsies, MAE, probably because of the lack of adequate electroclinical studies, is insufficiently defined and is considered by AA more a conceptual category of myoclonic epilepsy than a well defined syndrome. In order to outline how MAE is a form of epilepsy with well defined electroclinical features, we report the results of an electroclinical study of 25 subjects aged between 4 and 32 years (mean age 11 yrs) suffering from MAE, followed since onset for a mean period of 7 yrs 3 mths.
Methods: Only subjects without neuropsychological impairment at onset and with EEG-polygraphic recording of the seizures characterising the onset period and the evolution, have been considered.
Results: 84% are males; 44% have familial antecedents for epilepsy or FS. The age at onset is between 2 and 4.5 yrs. The interictal picture at onset is characterised by rhythmic theta activity in 60% and generalised S-W isolated or in brief bursts in 64%. Within 3 months from onset 4 types of seizures appear: generalised convulsive seizures isolated (12%) or in clusters (64%), massive myoclonias with generalised PS-W (92%), myoclonic-atonic or atonic attacks with drop or head drop (88%) and brief tonic-vibratory seizures mainly nocturnal (60%). Moreover 48% of subjects also have atypical absences. The subjects also have a peculiar type of long lasting (50%) or brief (40%) epileptic status. In 80% of cases the seizures stop after a brief period of correct treatment (PB or VPA with ETS and clonazepam and in same cases hydrocortisone). At follow-up 45% are normal, 40% have learning problems, 15% cognitive impairment.
Conclusion: MAE is a well defined idiopathic myoclonic epilepsy often starting with a stormy onset realising an epileptic encephalopathy but having a relatively good prognosis if correctly recognised and treated.

p1300
Myoclonic-astatic Epilepsy: Clinical and Electroencephalographic Features
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Purpose: To assess the clinical aspects of myoclonic-astatic epilepsy (MAE) in 9 of our patients, in particular seizure types, response to treatment and EEG features, trying to define any peculiar EEG pattern.
Methods: We retrospectively reviewed the clinical features, namely the response to treatment and the EEG findings and evolution of patients with the diagnosis of MAE.
Results: Included were nine boys, with seizure onset between 19 months and 3 years, 10 months old. The first seizures were tonic-clonic in all patients, being febrile in six, followed by other seizure types (days to two months later). All had myoclonic and atonic seizures (myoclonic-astatic seizures), as well as atypical absences. Seizure control was achieved in all but 1 patient. 7 patients had delayed psychomotor development, severe in 1. Sequential EEGs showed, in all patients and in at least one EEG, irregular spikes or polyspikes and slow waves, at a frequency of 3-6 Hz, generalised, or in the paracentral regions; theta waves were also frequently found in these areas. In those patients who achieved remission, both psychomotor development and EEG recordings improved or normalised.
Conclusion: Myoclonic astatic epilepsy is often mistaken for Lennox-Gastaut syndrome (LGS), but has significant differences concerning therapeutic options and the prognosis is usually much better, as shown in our small group of patients. EEG recordings are helpful in the diagnosis, with polyspike and wave discharges faster than in LGS, both generalised or located in the paracentral regions, as well as a characteristic slow-wave pattern also in the central areas.

p1301
Electro-clinical Features of Myoclonic Seizures in Infants and Children
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Purpose: This study was performed to demonstrate the clinical and electrophysiological characteristics of myoclonic seizures in infants and children.
Methods: 51 patients (27 males and 24 females) showed myoclonic seizures during long-term video-EEG monitoring (VEM). The mean age on VEM was four years and one month. The aetiology was cryptogenic in 17 patients (33%) and symptomatic in 34 patients (67%). Ictal semiology, and interictal and ictal EEG were analysed.
Results: 26 patients (51%) had myoclonic seizures only, while 25 patients (49%) also experienced other types of seizures. The types of accompanying seizures were partial seizures (7), tonic spasms (7), atonic seizures (6), absence seizures (6), and generalised tonic or clonic seizures (4). In patients with myoclonic seizures only, there were diffuse or bilateral polyspike/spike discharges or polyspike/spike and wave complexes (26), theta or delta bursts (14), and diffuse attenuation of the background activity (BGA) (7) with ictal rhythm. In patients with tonic spasms, bilateral high amplitude slow waves mixed with spike discharges were present. Diffuse or bilateral spike and wave discharges (3), diffuse attenuation of the BGA (2), and diffuse theta or delta bursts (1) were observed in patients who had accompanying atonic seizures. Abnormalities in the interictal BGA were found in 31 patients (61%), and epileptiform discharges were revealed in 43 patients (84%).

Conclusion: About 50% of myoclonic seizure patients experienced other types of seizures, with the ictal EEG pattern of accompanying seizures different to the ictal semiology. Therefore, VEM is necessary for accurate diagnosis and classification of seizure and epileptic syndrome especially for intractable myoclonic seizure patients.

p1302
Benign Myoclonic Epilepsy Associated with Afebrile Generalised Tonic-clonic Seizures (GTCS): A Spectrum of Benign Myoclonic Epilepsy in Infants (BMEI)
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Purpose: We have encountered patients manifesting primarily myoclonic seizures, and afebrile GTCS developing during infancy, who ultimately showed a benign prognosis. As their clinical manifestations resembled those of BMEI except for a presence of afebrile GTCS, we studied detailed electro-clinical manifestations and discussed the nosological place of these patients.
Methods: Subjects were 5 patients with BMEI and 8 patients who manifested with myoclonic seizures, preceding recurrent afebrile GTCS and benign prognosis (BME with GTCS). The myoclonic seizures were confirmed either by ictal EEG, polygraph or video-polygraph. We retrospectively reviewed medical records, EEGs and neuroimaging findings and compared the electro-clinical features between the two groups.
Results: BME with GTCS was preceded by afebrile GTCS ranging in frequency from 2 to more than 10 times, although these seizures were replaced by myoclonic seizures within 8 months. EEG showed normal to mild disturbance of background activity and generalised spike and wave complexes at 2-3Hz. There were no significant differences in the age at onset of myoclonic seizures (BMEI group; 1y10m-3y2m, mean 2y6m vs. BME with GTCS group; 0y6m-5y2mo, mean 2y11m), active period of epileptic seizures (3m-31m, mean 15m vs. 4m-19m, mean 10m), age at remission of seizures (2y8m-5y11m, mean 3y7mo vs. 0y11m-5y5m, mean 3y6m) or mental prognosis (IQ= 61-112, mean 85 vs. 61-121, mean 96) between the two groups ($P>0.05$).
Conclusion: BME with GTCS appears to have a higher prevalence and to form a syndromic spectrum with BMEI.

p1303
Outcome for Children with Juvenile Absence Epilepsy
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Purpose: While the incidence and natural history of childhood absence epilepsy is known, those of juvenile absence epilepsy (JAE) are less established. The objective of this work was to evaluate the incidence and outcome of patients with JAE.
Methods: Consecutive patients with JAE were retrieved from 3 paediatric neurology outpatient clinics in Israel. Inclusion criteria included onset of epilepsy after the age of 10 years, and follow-up until at least age 15 years. Patients with EEG suggestive of myoclonic epilepsy (polyspike and wave) were excluded from the study.
Results: 16 patients (9 females, 7 males) fulfilled the inclusion criteria for JAE. These patients constituted 15% of all patients with absence. The patients presented with epilepsy at a mean age of 12 years (range 10-16.5). Follow-up was performed at a mean age of 20 years (range 15-30). Family history of epilepsy was present in 31% of patients. Neurodevelopmental status was normal in all patients. Generalised tonic-clonic seizures occurred in 53% of patients, and 41% responded to the first antiepileptic drug. At follow-up, 64% were seizure-free.
Conclusion: The remission rate of JAE is less favourable than childhood absence, and more patients suffer from generalised tonic-clonic seizures.

p1304
Evaluation of Demographic and Clinical Characteristics of Juvenile Myoclonic Epilepsy
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Purpose: Epilepsy is a chronic disease of the nervous system with different cause. Juvenile myoclonic epilepsy (JME) is one of the most common idiopathic generalised seizures that include about 5-11% of epilepsies. According to clinical characteristics of JME, this disease cannot be diagnosed correctly in a clinic and attempting to do so results in inappropriate treatment. Patients need life-long treatment as long as the condition is uncontrolled. The aim of this study was to evaluate the characteristics of JME and then treat it appropriately.
Methods: This prospective observational study was done from March 2003 to September 2004 in epilepsy clinics at Isfahan University. Of 985 epilepsy patients, 50 had JME selected according to patient history, clinical observation and EEG findings. Clinical, demographic and treatment characteristics were recorded from special questionnaires. Patients were followed every 3 months for 1 year.
Results: 5% of epileptic cases were JME. Female to male ratio was 3.5. Mean age of onset was 13 years. Familial history was positive in 38% of cases and precipitating factors were positive in 60%. About 79% of those factors were due to stress, flashing lights, somnolence and fatigue. All patients were treated. Finally, 84% of patients responded to treatment completely and 14% responded partially and only 2% were refractory to the treatment.
Conclusion: In this research women to men ratio was 3.5. Our clinical findings were similar to those in the previous study. Most precipitating factors could be prevented with simple recommendations and response to treatment was very good. Patients should take antiepileptic drugs for long life.

p1305
Specific Learning Disabilities in Children with Rolandic Epilepsy
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Purpose: In this study we evaluated a group of children affected by Rolandic Epilepsy referred in succession at the UONPIA DH Dpt in Varese with an accurate protocol of neuropsychological tests in order to show the prevalence of specific learning disabilities.
Methods: 18 children, 9 males and 9 females (mean age 9.3 yrs), were evaluated with awake and sleep EEG records and a specific neuropsychological battery: WISC-R, Continuous Performance Test, TEMA subtests, Visual Motor Integration Test, language tests (ITPA and TCGB subtests), reading and writing tests (MT tests, Sartori-Tressoldi battery) and calculus tests (Biancardi-Nicoletti battery).
Results: The mean age of epilepsy onset is 7.5 yrs. 14 patients (77.7%) show an active rolandic focus, 9 of which (50%) show a marked sleep activation (> 50% of slow sleep). 10 subjects (55.5%) show specific reading or writing impairments and 4 of them are also discalculic. 7 out of 10 children with specific reading and writing disabilities show marked interictal epileptiform discharges during sleep (> 50% of sleep), and for 6 of them this condition is detected in different EEG records for more than a year. Children with specific learning impairments also show an age of epilepsy onset significantly lower than those who don't show learning difficulties (6.3 yrs vs 9 yrs; $p=0.01$).
Conclusion: This work shows a high prevalence of specific learning disabilities in subjects with Rolandic epilepsy and makes a mandatory indication for an accurate analysis and follow up of the neuropsychological competences, particularly reading and writing abilities.

p1306
Are Dyslexia and Dyscalculia Present in Rolandic Epilepsy?
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Purpose: To evaluate the prevalence of dyslexia and dyscalculia in a group of Italian children with Rolandic Epilepsy (RE). Moreover, an attempt was made to find correlations with age of onset of seizures, duration of active epilepsy, frequency and localisation of epileptic discharge.
Methods: We studied 15 children aged 8-11 years, affected by RE. They underwent a cognitive evaluation (WISC-R and Raven test), specific evaluations for dyslexia (MT tests by Cornoldi and reading tests by Sartori) and dyscalculia (BDE by Biancardi-Nicoletti), neuroimaging studies and EEG recordings, both when awake and asleep.
Results: Only preliminary results are available at the moment, as the study will end in June 2005.
Conclusion: RE is the most frequent epileptic form in childhood and is regarded as an example of benign focal epilepsy with a good long-term outcome. Nevertheless, there are studies indicating that children with RE have more scholastic and neuropsychological problems than controls. (Deonna T. et al. Epileptic Disorder 2000; 2: 59-66). The aetiology of cognitive dysfunction in RE is unknown. There are two hypotheses: firstly that EEG discharge may interfere with cognitive processing, secondly that EEG traits and cognitive impairments are independent symptoms of a common, underlying pathology. (Carlsson G. et al. Epileptic Disorder 2000; 2: S63-66). When reviewing the literature, little can be found on dyslexia and dyscalculia in RE. But, interestingly, numerical processing seems to be localised to parietal lobes (Landerl K. et al. Cognition 2004; 93: 99-125) while in dyslexia there could be a difference in functional organisation of parieto-occipital areas. (Leisman G. Brain Cogn 2002; 48: 425-431). From here came our interest in dyslexia and dyscalculia in RE.

p1307
Acoustic Variations According to the Epileptic Focus in Benign Rolandic Epilepsy
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Purpose: Although normal neuropsychological developments are expected in benign rolandic epilepsy (BRE), but subtle specific interference with language functions may be suspected. The aims of this study are to investigate the speech problems in BRE according to the seizure focus in EEG and semiology.
Methods: We prospectively performed standardised full speech assessments in 14 patients [right (7 patients), left (7 patients) centrotemporal spikes in EEG] who met the BRE criteria by ILAE. A computerized speech laboratory used to assess the speech characteristics. Laryngeal articulation pattern, voicing analysis, habitual pitch, voice onset time (VOT), word duration (TD) and vowel formants were compared by acoustic parameters before antiepileptic medication.
Results: The error pattern of laryngeal articulation in BRE was exclusively a substitution of stop consonants; these errors showed more frequently in the left group (16% vs 25%). VOT of stop consonants and TD of words in both groups were more prolonged than in the normal control group, especially in the left group (Table 2). The first formant of vowel /o/ and second formant of /e/ were significantly decreased in the left group ($p<0.05$). The right group showed a narrower pitch range (192.9+/- 54.0 Hz) and energy range in spontaneous speech (14.2 +/- 6.4 dB) than the left group (233.3 +/- 12.5 Hz and 19.4 +/- 9.4 dB). Duration of counting in the left group slower than in the right group (8.6 +/- 1.7 vs 7.9 +/- 1.8 sec).
Conclusion: BRE patients, especially those in the left origin group have speech problems. We recommend logopedic and phoniatric evaluations of speech in BRE patients.

p1308
Centro-temporal Spikes and Non-paroxysmal Epileptic Disorders
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Purpose: Centro-temporal spikes (CTS) are present in the EEG of 2% of normal children and in siblings of patients with rolandic epilepsy. In about 25% of patients with rolandic epilepsy disorders of speech, language, visual gnosis, education, affection and behaviour appear. The purpose of the study was to investigate a possibility of causation of neuropsychological, psychic and behavioural symptomatology in some patients without seizures by CTS.
Methods: Among 150 consecutive patients of 3-16 years attending the Psychiatric Department without a history of seizures, 16 (10.6%) had CTS in routine EEG. In 6 of them night sleep EEG was studied. All were studied by a psychiatrist, neurologist, psychologist, logopaedist. 7 were examined using MRI.
Results: CTS in 10 patients prevailed in left hemisphere, in 3, in the right, and in 3 were bilateral. In 3 patients there was continuous spike and wave activity in slow sleep. 75% of the patients had speech and language disorders, 37% visual and space agnosia, 44% behavioural disorders, 37% hyperactivity and deficit of attention, 19% autistic disorder, 81% educational, 31% pervasive developmental disorders. In 75% of the patients the disorders combined. The children with continuous spike and wave activity in slow sleep were the most handicapped. The type of disorder correlated with localisation of CTS in EEG. All the patients were treated by depakine chrono (15-30 mg/kg/day). In 14 followed-up patients CTS disappeared. 12 patients followed-up $\geq$6 months had significant improvement of speech, language, cognition and behaviour.
Conclusion: In a significant number of patients with speech, neuropsychological, emotional, educational and behavioural disorders the latter were caused by CTS. They can be successfully treated by sustained release valproate-depakine chrono, which suppresses epileptic discharges in EEG and prevents progression of the related epileptic encephalopathy.

p1309
Acute Symptomatic Seizures With or Without Status Epilepticus in Children
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Purpose: Acute symptomatic seizures differ from epilepsy in that they have a clearly identifiable proximate cause and they are not characterised by a tendency to recur spontaneously. But we hypothesised that acute symptomatic seizures with status epilepticus (SE) have an increased risk of subsequent seizures than those without status epilepticus.
Methods: We retrospectively studied 568 children with seizures who visited our hospital from January 1995 to December 2003. Among those children, 109 patients were determined as having provoked seizures, and the patients were followed up for 1 year.
Results: 109 children had acute symptomatic seizures. The ages of first seizures were 1.58 ± 2.53 years. Causes in order of frequency were acute gastroenteritis (33.0%), meningitis/abscess (31.2%), encephalitis/encephalopathy (19.3%), others (16.5). At one year follow-up, the incidence of unprovoked seizures was 28.4% for children with acute symptomatic seizures. The risk of unprovoked seizures was significantly greater for children with acute symptomatic seizures with SE (100%) than those without SE (22%).
Conclusion: The leading cause of acute symptomatic seizures was acute gastroenteritis. The incidence of subsequent unprovoked seizure

was highest in the group of encephalitis/encephalopathy. The risk of subsequent unprovoked seizures was greater for those with SE than those without SE. The risk of subsequent unprovoked seizures is determined by underlying precipitation factors and children with acute symptomatic seizures with SE should be followed up carefully.

p1310
Characteristics of Status Epilepticus in Children Caused by Central Nervous System Infections
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Purpose: To evaluate the characteristics of status epilepticus (SE) caused by central nervous system (CNS) infections.
Methods: The investigation included 277 patients aged from 2 months to 16 years with SE treated at the Institute for Mother and Child Health of Serbia in the period from 1994-2004. SE were caused by CNS infections in 38 patients (14% of all SE). We studied the aetiology of CNS infections, types and duration of SE, and response to antiepileptic drugs in control of SE.
Results: Bacterial meningitis was diagnosed in 16 patients, viral encephalitis in 18, mycoplasma pneumonia encephalitis in 1, tuberculous meningoencephalitis in 1, cerebral abscess in 1, subacute sclerosing panencephalitis in 1 patient. The most frequent type of SE was generalised tonic clonic SE in 22 patients (primary in 13 and secondary in 9), partial SE in 6, epilepsy partialis continua in 6 and multifocal myoclonic seizures in 4 patients. 50% of the patients had refractory SE. In the control of SE, midazolam in continuous intravenous infusion was effective in 26 (mean dose 0,38 mg/kg/h, mean duration 60 hours), thiopental in 3, phenobarbital in 4, diazepam I.V. in 2 and midazolam I.V. bolus in 2 patients. Artificial ventilation was necessary in 14 patients, and 3 patients died.
Conclusion: In our study CNS infections took part in 14% of the aetiology of all SE. The most frequent type was generalised tonic-clonic SE. Seizures were resistant to antiepileptic drugs and most effective control of SE was midazolam in continuous intravenous infusion in high doses.

p1311
Aetiology of Symptomatic Epilepsies in the First Three Years of Life: A Study Based on Neuroimaging
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Purpose: 1) To determine the aetiology of infantile symptomatic epilepsy with onset within the first three years of life using neuroimaging. 2) To identify risk factors for the most common aetiology found i.e. neonatal hypoglycaemic brain injury (NHBI).
Methods: The study was conducted at a tertiary care outpatient service. Consecutive patients were recruited prospectively. Seizure details, developmental milestones, perinatal histories and response to therapy were obtained from the caregiver and supplemented with birth records. Two radiologists, blinded to the clinical history reviewed the cranial imaging and suggested an aetiological diagnosis using standard criteria. The patients were ascribed an aetiological diagnosis. The categories were perinatal encephaloclastic (PE) e.g. perinatal hypoxic-ischaemic encephalopathy, NHBI etc, developmental (DV) e.g. tuberous sclerosis, cortical dysplasia etc and others. Risk factors were compared in the NHBI group and DV control group by univariate analysis. Neurological findings were compared in the different perinatal groups. Types of seizures and response to treatment were studied only in the HBI group.
Results: 63 boys and 37 girls were recruited. Mean age of seizure onset was 13.9 months. PE aetiologies were seen in 50 patients, DV in 28, 5 had postnatal aetiologies. 17 remained undefined. NHBI was seen in 23 patients. In 88/100 patients there was complete agreement between the two radiologists about the imaging findings. The kappa coefficient for diagnosis of NHBI was 0.83, for HIE it was 0.79, for PVL it was 0.63 and for developmental anomalies it was 1. Low birth weight (LBW), poor feeding and lower section caesarean section delivery were found to be significant risk factors for NHBI. The clinical features that separated the NHBI group from other perinatal aetiologies were lack of spasticity/dystonia. Infantile spasms were the commonest seizure type in children with NHBI.
Conclusion: 1) PE events were the commonest cause of symptomatic epilepsy with onset in the first three years of life. 2) NHBI emerged as the single most common aetiology. 3) LBW, poor feeding and LSCS delivery are significant risk factors for NHBI. 4) A characteristic clinical profile was seen in children with NHBI.

p1312
Epileptic Encephalopathy after Application of Triple Vaccine (DPT)
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Purpose: To present 4 cases in which just after the application of the vaccine (diphtheria, pertussis and tetanus) the patients have experienced frequent convulsions and signals of severe encephalopathy and to question the vaccine's casual value in the determination of the encephalopathy as a neurological sequelae.
Methods: Report of 4 cases presenting strong indications which suggest a casual relation between the application of the dose of DPT and neurological after-effects, mainly encephalopathy.
Results: In our reports, 3 cases showed reactions within 24 hours and 1 case within 36 hours. Among all of them there were no previous alterations related to psychomotor development; in 3 of them the convulsions occurred at the start of the clinic and they evolved with spasms, autist pautas, tetraparesis, hypotonia or hypertonia. Two cases have evolved with severe mental deficiency and aphasia. The EEG accused hypsarrhytmia in 2 cases and diffuse cerebral pain in another. The cerebral CT scan was normal in only one case and in the others it presented cerebral atrophy.
Conclusion: The encephalopathy has significative importance as a neurological sequelae of complications resulting from the application of the DPT vaccine and this vaccine should be questioned on its casual and non coincident value.

p1313
Control of Epilepsy in Children Suffering from Cerebral Palsy, with Respect to their Etiology and Tomographic Cerebral Injury Background: Clinical Experience at the Teletón Rehabilitation Centre for Children in Mexico
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Purpose: We described the relationship between cerebral palsy-aetiologies and the cerebral injuries in the epilepsy control.
Methods: A total of 398 subjects were included in this retrospective study. Both female and male subjects under 18 years old with evidence of epilepsy related to cerebral palsy (CP). For comparison analysis purposes the entire population was divided in two mayor groups: 1) CP based on its aetiology and 2) CP based on cerebral injury background by means of computer tomography (CT). The first group was subdivided into cerebral-vascular disease (CVD); cerebral malformation (CM); related causes (RC). The second group was subdivided into diffuse injury (DI); focal location injury (FLI); basal ganglia injury (BGI); cerebral dysgenesia (CD); hydrocephaly (H); and non-TC evidence (N). The impact of the epileptic seizures was determined according to the cerebral injury background and its aetiology through the M-L chi square test.
Results: The findings after clinical surveillance and statistical analysis, were able to affirm that seizures of the first group were controlled according to the following results: CVD 77.9% (n=276); CM 72% (n=86); RC 86% (n=36), non statistical significance was found in these subgroups ($p < 0.28$). The second group showed that DI

70.7% (n=150); FLI 82.4% (n=102); BGI 87.5% (n=16); CD 79.3% (n=82); H 77.8% (n=36); N 83.3% (n=12), statistical significance was found in these subgroups ($p < 0.04$).
Conclusion: Summarising, cerebral injury in children suffering from cerebral palsy has a prognostic reliance value in the control of epilepsy, regardless of its aetiology.

p1314
Spectrum of Epilepsy in Terminal 1p36 Deletion Syndrome
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Purpose: Seizures are often associated with terminal 1p36 deletions but poorly described. In order to better determine the spectrum of this epilepsy, we studied 19 patients with a confirmed 1p36 deletion syndrome.
Methods: Based on clinical charts, we retrospectively analysed the evolution of electroclinical features of this epilepsy.
Results: Median age of patients was 4 years. All subjects had mental retardation and presented characteristic dysmorphic features. Self abusive and autistic behaviour were observed in 10 cases. 13 patients had a history of seizures. The median age of first seizure was 3 months. Neonatal seizures were observed in 1 patient. Type of seizures included infantile spasms in 9 cases (45%), myoclonic seizures in 6, generalised tonic-clonic seizures in 5, complex partial seizures in 5 and simple partial seizures in 1 case. EEG was abnormal in all cases. Electroencephalogram findings showed hypsarrhythmia in 8 patients (40%), generalised paroxysmal spikes in 10 and focal paroxysmal anomalies in 4 cases. Among patients with abnormalities on EEG, 8 had a normal EEG before onset of epilepsy. Brain MRI was normal in 3 cases and showed mild cortical atrophy in 12 cases. Epilepsy was severe and resistant to antiepileptic drugs in 9 cases while benign forms of epilepsy were observed in 4. Severe epilepsy was specifically associated to infantile spasms.
Conclusion: Infantile spasms are common findings in 1p36 deletion syndrome and are usually associated with a poor clinical outcome. We suggest that infantile spasms, severe mental retardation and dysmorphic features in an infant might evoke a suspicion of 1p36 deletion syndrome.

p1315
Angelman Syndrome: Series Review from Kuwait
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Purpose: Angelman syndrome is a neurogenetic syndrome with unique clinical features including facial appearance, developmental delay, severe speech deficit, with ataxic gait and behavioural disorder. The confirmation of diagnosis is possible by genetic tests in nearly 80% of cases. The clinical features in AS manifests variably from infancy until years later. Our purpose is to review the clinical findings, electrophysiological and genetic studies in our series.
Methods: We present a case review of 6 children with a clinical phenotype consistent with AS among children attending our Neurology out- patient clinic. We reviewed the literature of AS, the clinical phenotype and the mechanisms speculated in children with AS with and without genetic defects. We also discussed the importance of clinical clues, the electroencephalographic features for early diagnosis, and their relevance to well defined syndromes mimicking AS.
Results: The phenotypic features for all patients were conclusive. However, the electrophysiological changes were characteristic for one patient. A diagnosis of AS was confirmed in 3 children by molecular genetic tests.
Conclusion: A high index of suspicion in developmentally delayed children with peculiar behavioural patterns, absent articulation and clumsy gait, helps in prompting a diagnosis of AS. Despite advances in molecular diagnosis, there is a need for awareness among paediatricians working in developmental, genetic and child neurology units and to consider the possibility of AS in any child without an obvious diagnosis for developmental delay. Extended research in genetic services might disclose novel results.

p1316
Onset of Seizures and the Course of Epilepsy and Developmental Disabilities in Patients with Cortical Dysplasia
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Purpose: There is little known about factors that play a role in the outbreak of first signs of epilepsy and developmental delay in patients with cortical dysplasia (CD). In this study we asses the onset and the course of clinical manifestations of epilepsy and deterioration of development in patients with CD. We thereby looked for possible (epileptogenic) triggers.
Methods: The study is a retrospective descriptive study. Until now we found 10 patients having CD diagnosed by 1.5 Tesla MRI. Features that indicate the onset of seizures and deterioration were traced in patient files. We looked for reported coincidental health problems. We described type and localisation of CD in relation with seizure type, seizure frequency, EEG findings, cognitive impairment (CI) and motor impairment.
Results: CD was diagnosed in 10 patients, 6 female, aged 24 -51. In 3 patients we saw mild CI, 1 had moderate CI, 2 had severe CI and 3 had profound CI. Seizures developed age <1 year in 4 patients, age 3 years in 1 patient and > 4 years in 5 patients. In 4 patients there was coincidence with fever or flu. Developmental delay before age 1 year was reported in 6 patients. Impairment of motor skills is present in 5 patients. First signs of motor developmental deterioration were seen respectively at the ages of 0;0, 0;3, 0;4, 3 and 20 years.
Conclusion: Onset of seizures can be after 10 years of age in patients with CD. Factors that might play a role in triggering first signs are worth investigating.

p1317
Epilepsy Associated with Idiopathic Megalencephaly
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Purpose: Idiopathic megalencephaly (IM) is often associated with some neurological problems, such as epilepsy, developmental motor, learning or autistic disorders. The aim of the study was to characterise the epilepsy in patients with IM and analyse its relation to neurological and developmental disorders.
Methods: 11 cases, aged 1-13 years, with IM were diagnosed among children with epilepsy over a 4 year period. All patients were studied clinically, psychologically and neurophysiologically and followed up for a period of 6 months - 5 years. Symptomatic megalencephaly and syndromatic cases were excluded clinically and by additional investigations.
Results: Megalencephaly was familial in 5 and sporadic in 6 cases. 3 patients had only a single secondary generalised tonic-clonic seizure, 1 child - two febrile seizures, 1 typical absences, 1 generalised myoclonic seizures and 5 partial and/or secondarily generalised seizures. Mild mental retardation was revealed in 2 cases, borderline intelligence in 2. The remaining children had normal intellect. ADHD occurred in 4 patients. None had autistic features. EEG showed focal and generalised paroxysmal activity in 3 children, only generalised

paroxysmal activity in one, only focal or bifocal in 6 and no pathology in the child with febrile seizures. All children, except the one with febrile seizures, received antiepileptic drugs and 8 of them were seizure free. 2 patients with mental retardation were difficult to control, 1 of them without any seizure reduction. MRI abnormalities were revealed in 1 of the 6 patients that underwent brain MRI.
Conclusion: In epilepsy patients with IM, partial epilepsy with secondarily generalised seizures prevailed. Epilepsy was mostly benign (10 of 11 patients were seizure free for at least 6 months). ADHD was the most common associated disorder in epilepsy IM cases. Mental retardation may correlate with resistant epilepsy. This study indicates the need for further studies on prevalence, aetiology and prognosis of epilepsy, associated with IM.

p1318
Epileptic Seizures Associated with Neuronal Heterotopia
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Purpose: The aim of the study is to correlate epileptic seizures with neuronal heterotopia, in different cortical malformations.
Methods: We retrospectively evaluated all case records of patients diagnosed in our department with symptomatic epilepsy due to neuronal heterotopia between 2003 and 2004. We classified as simple heterotopia where no other malformation was found and complex heterotopia where a more complex cortical malformation was associated. The differences and common features between simple or complex heterotopia were outlined.
Results: Neuronal heterotopia was diagnosed in 14 patients (9 females and 5 males), with ages 1-18 years. 7 patients had simple and 7 patients complex heterotopia (Aicardi syndrome, hemimegalencephaly etc). All patients had partial seizures, associated with generalised seizures in 11 patients (78.5%). The clinical exam showed neuro-psychological modification in 71.4% of patients with complex and only 28.5% of patients with simple heterotopia. The epileptic seizures were controlled by antiepileptic drugs in 8 patients (57.1%).
Conclusion: Results clearly show that neuronal heterotopia is commonly manifested as partial seizures with frequent generalisation. The response to antiepileptic treatment is good for a high percentage, regardless of whether there is simple or complex heterotopia. The degree of association with a modified clinical exam is much higher in complex heterotopia. Neuronal heterotopia is known to be frequently manifested as epilepsy, but to conclude whether this is the main aetiology of epileptic seizures in cortical malformations, further comparative studies with different cortical malformations with or without neuronal heterotopia are necessary.

p1319
Lissencephaly Type I: Clinical and Imaging Features in 19 Cases
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Purpose: We analyse the clinical and neuroimaging features of 19 patients diagnosed with lissencephaly type I. Lissencephaly (agyria-pachygyria) is a severe neuronal migration disorder, characterised by absence of gyri and sulci (agyria) or by their reduction to broad, flat gyri and shallow sulci (pachygyria).
Methods: Patients were evaluated from the clinical, electroencephalographic (EEG) and neuroradiological points of view. Their ages at the time of the first presentation ranged from 7 weeks to 14 years. All patients were investigated by cranial computed tomography (CT) and 5 by cranial magnetic resonance (MR) imaging. 17 patients were classified as isolated lissencephaly, 1 had Miller-Dieker syndrome and 1 had subcortical band heterotopia.
Results: 14 patients (74%) experienced epileptic seizures with onset during the first year of life. 8 patients (57%) had epileptic seizures resistant to conventional treatment. Clinically, 10 patients (53%) had microcephaly, 11 patients had spastic quadriplegia (58%) and 6 (32%) had facial dysmorphism. Mental retardation was observed in all cases, and was severe in 18 cases.
Conclusion: Lissencephaly type I should be investigated in the aetiology of early-onset childhood epilepsy and it should be considered in children with developmental delay with or without microcephaly and facial dysmorphism.

p1320
Early Onset Epilepsy in Focal Cortical Dysplasia
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Purpose: With focal cortical dysplasia (FCD), characteristics of epileptic seizures and syndromes have been reported in infancy and childhood, but neonatal onset seems to be rare. Therefore recognition of FCD may be delayed in this age group when an early diagnosis is especially important.
Methods: We report on 14 cases of children with epilepsy onset before the age of two months and a later discovery of FCD, followed at Saint Vincent de Paul Hospital, between 1986 and 1999. Medical records were reviewed, with a focus on seizure and syndrome presentation, response to treatment, EEG recordings, MRI data and clinical outcome.
Results: All children presented focal seizures, associated with epileptic spasms in 8 cases. Two EEG patterns were observed: hemi-suppression-burst, or slow wave and high voltage spike focus on serial EEG. FCD was frontal (n=4), occipital or occipito-temporal (n=5), and the remaining 5 patients had a central, parietal, fronto-parietal and fronto-temporal FCD. 10 patients received GVB with a dramatic improvement in 3 of them. Vigabatrin was stopped after 3 years of treatment for 2 of these 3 children, followed by recurrence of seizures, extremely difficult to control. In spite of focal cortical resection all children remained with seizures; hemispherotomy was performed on 2 patients with complete cessation of seizures. Longterm psycho-motor outcome was encouraging in our series.
Conclusion: In early onset epilepsy, with focal seizures associated or not to epileptic spasms, EEG may orientate the diagnosis of FCD, and the medical treatment with vigabatrin. Epilepsy surgery may be indicated in case of pharmaco resistance.

p1321
Epileptic Spectrum in Tuberous Sclerosis Complex
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Purpose: Tuberous sclerosis complex (TSC) is frequently associated with refractory seizures and developmental delay in children. Our purpose is to analyse epilepsy, AEDs (antiepileptic drugs) therapy and cognitive development in patients with TSC.
Methods: We revised data of 5 patients with TSC (diagnostic criteria revised by Gomez, 1999), with respect to the onset, type of epilepsy, neuroimaging, cognitive and mental alterations (using the Griffiths Mental Development Scales, 1996 Revision), response to antiepileptic therapy.
Results: The mean age is 3 years and 10 months (range: 16 months - 5.6 years). The onset of seizures was 2-13 months (mean age: 5.3 months). Age of diagnosis ranged between 6 and 14 months in 3 patients, 1 was diagnosed in first day of life with echocardiography and cerebral ultrasonography, and in 1 newborn at 32 weeks' gestation with cardiac rhabdomyomas. 2 patients had a diagnosis by neuroimaging (tubers, subependymal giant cell astrocytomas, subependymal nodules) and genetic testing (mutation in TSC2 gene). 3 patients had multiple lesions (retinal hamartomas, shagreen patch, facial angiofibroma and cerebral lesions). Epilepsy began as infantile spasms in 2 patients, as complex partial seizures, absences and

myoclonic jerks in 3 patients. 2 patients with monotherapy (topiramate; carbamazepine) are seizure free, while the other patients with polytherapy (2 with topiramate-vigabatrin-carbamazepine; 1 with topiramate-valproate) had a reduction of seizure frequency and intensity. All patients have global intellectual impairment.
Conclusion: In TSC mental retardation shows a stronger relationship with stormy onset and poor control of seizures.

p1322
Characterising Magnetoencephalographic Spike Sources in Tuberous Sclerosis Complex
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Purpose: Tuberous sclerosis complex (TSC) often causes medically intractable seizures. Magnetoencephalography (MEG) may provide an excellent tool for localising epileptiform discharges. This study classifies MEG spike sources (MEGSSs) from TSC patients and correlates them to EEG and MRI results.
Methods: 7 children with TSC and intractable epilepsy underwent prolonged video-EEG, MEG, and MRI.
Results: MEGSSs distributed as clusters (6 or more spike sources, 1 cm or less between sources) or additional scatters (fewer than 6 spike sources regardless of distance between sources; sources with more than 1 cm between sources regardless of number of sources). 2 patients had single, unilateral clusters with additional scatters; these predominantly lateralised MEGSSs correlated to prominent tuber regions and ictal/interictal EEG zones. 2 patients had bilateral clusters and scatters; the bilateral cluster locations did not correlate with multiple prominent tuber regions, bilateral or diffuse interictal discharges, or various seizure patterns and history. 3 patients had only bilateral scatters. Scatter regions partly overlapped EEG interictal/ictal-onset regions in all 3 patients, except generalised seizures in 1 patient. In 1 patient with equally bilateral scatters, a prominent tuber and interictal/ictal-onset zones in the right frontal region was overlapped by scattered MEGSSs.
Conclusion: MEG adds information to EEG and MRI studies for localisation of epileptogenic zones in TSC children. Single clusters and additional scatters in the unilateral hemisphere predicted the primary epileptogenic zone or hemisphere; bilateral or multiple clusters indicated bilateral primary and potential epileptogenic zones; bilateral scatters without clusters may bury epileptogenic zones within the extensive area of scattered MEGSSs.

p1323
Agenesis of Corpus Callosum with Epilepsy in Children: Clinical Correlation
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Purpose: The corpus callosum is a main connecting structure between the two cerebral hemispheres. Corpus callosum have a tract of fibres that connect the cerebral cortex of the contralateral motor, sensory and cognitive performances of the brain. Agenesis of the corpus callosum is a rare congenital anomaly which may be partial (hypoplasia) or complete. This anomaly may be isolated or associated with other cerebral malformations. The aim of the present study is to reveal the correlation between isolated agenesis of the corpus callosum and epilepsy in children.
Methods: In 90 children with malformation of the brain found on magnetic resonance imaging, isolated agenesis of the corpus callosum was evident in 14 (aged 8 months to 12 years).
Results: One child has complete agenesis of the corpus callosum and 13 children have hypoplasia. 6 were girls and 8 were boys (1:1.3). All cases had various neurological problems (difficulty of movement, cerebral palsy, dyslexia). 9 patients had some degree of intellectual impairment and developmental delay. Most cases (10: 71.4%) had some form of epilepsy: 4 children (40%) suffered from generalised tonic-clonic seizures, 4 (40%) had complex focal fits with secondary generalisation. 2 (20%) had polymorphic seizures. 60% of all cases had heavy and frequent attacks of seizures and were very difficult to treat by AED therapy. The attacks began from 1 month to 5 years of age.
Conclusion: Finally, we conclude that the determining factors in the development of epilepsy in the children, and especially in the prognosis of our patients, are agenesis of the corpus callosum.

p1324
Mitochondrial Diseases in Children with Epilepsy
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Purpose: Mitochondrial diseases (MD) represent a heterogeneous group of multisystem disorders which preferentially affect tissues with high energetic demands, and are often manifested in children. The brain is highly dependent on oxidative metabolism, and encephalopathy and epilepsy are common manifestations of many of these conditions.
Methods: We examined 24 children (36 months-16 years) suspected of having MD.
Results: Elevated serum lactate level, hypotonia, exercise intolerance, cardiac disrythmia, migraine headaches, vomiting and delayed speech affected most of these patients. Breath-holding spells and/or febrile convulsions were seen in 3 of the patients, 8 had complex partial, secondarily generalised seizures. The EEG showed the wave asymmetry, decreased functional level of brain activity, non-specific spikes or epileptiform discharges with temporal or medial frontal lobe localisation even in children without clinical seizures. MRI findings showed mild or moderate temporal lobe cortical atrophy, periventricular leukomalacia and stroke-like lesions. SPECT results in 10 children showed decreased and uneven perfusion of brain tissue. An increase of auto-antibodies and the level of glutamate receptor subunits GluR1and NR2A in blood serum, reflecting neuron membrane damage, was revealed in all children. Genetic examination showed that in A3243G, A11084G (MELAS), cytochrome C oxidase syndrome, epilepsy developed as the first sign. The first manifestation of ATP synthase 6 mutation was dilated cardiomyopathy in 4 out of 5 patients; recurrent stroke-like episodes and seizures developed later. In 16S rRNA, tRNA lysine, multiple mtDNA mutations, epilepsy developed later than the somatic signs.
Conclusion: It's very important to improve our knowledge of MD for searching new therapy options for these rare disorders.

p1325
Rasmussen's Encephalitis in India: Clinical Features and Treatment Outcome
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Purpose: To study the clinical features and treatment outcome of Rasmussen's encephalitis in India.
Methods: Retrospectively data were extracted from hospital records of patients diagnosed with RE. For inclusion, patients should be premorbidly normal, develop refractory seizures or epilepsia partialis

continua (EPC) and progressive hemiparesis and/or typical radiological features.
Results: 20 patients; 11 female and 9 male, had RE during last 10 years. Median age at onset was 5.5 years (2.5-19 years). Symptoms began as seizures in all patients. Seizures consisted of simple partial in 18 patients, complex partial in 17, with secondary generalisation in 9 and recurrent status in 6. 13 patients had EPC. Hemiparesis occurred at onset in 2 patients, after a mean of 20.5 months in 11 patients, while 7 had not noticed weakness but examination revealed weakness. Antecedent illness occurred in 5 patients. 10 patients had cognitive decline. Expressive speech dysfunction occurred in 14. At presentation all patients were on multiple anti-epileptic drugs (AEDs) with no benefit. EEG showed epileptiform discharges ipsilaterally (16), bilaterally (4), PLEDS (3) and electrographic seizures (4). Brain atrophy on MRI was hemispheric (10), perisylvian (6) or focal (1). 13 had inflammatory signal changes. 6 patients received immunotherapy: 2 had transient improvement but needed surgery later, 1 remained static, 1 had partial improvement, 2 had no benefit. 11 subjects were offered surgery: 4 declined; 7 underwent hemispherotomy: 5 were seizure free, 1 had marked seizure reduction, 1 had progression of RE contralaterally.
Conclusion: RE is a devastating epileptic syndrome predominantly affecting children. Response to AEDs is poor and immunotherapy unpredictable. Early hemispherotomy is advantageous.

p1326
Rasmussen Encephalitis Associated to Ipsilateral Mesial Sclerosis: Posthemispherectomy Evolution
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Purpose: To describe a boy with Rasmussen encephalitis associated to ipsilateral mesial sclerosis, whose early diagnosis and treatment originated a favourable evolution.
Methods: A 6 year old boy with a three year history of partial epilepsy, began having myoclonic jerks involving the right leg. These jerks quickly became a status epilepticus partialis continuous and progressive deterioration of their superior cerebral functions occurred. There was no history of previous infection. Three months later he was admitted into our hospital showing a flaccid hemiparesis of crural predominance. The WPPSI test showed as moderate mental retardation. The MRI demonstrated left cerebral hemiatrophy, small gliotic nodules in white matter and signs of ipsilateral hippocampal sclerosis. Video EEG revealed left continuous specific epileptic activity, ipsilateral continuous slowness and abnormal sleep structures. The SPECT demonstrated an avascular left posterior parietal area, without zones of hyperperfusion. The PET revealed an hypometabolic left parieto-occipital and ipsilateral mesial temporal areas. Oligoclonal bands were absent. The cerebral biopsy revealed neuronal and glial loss, gliosis of white matter, perineuronal edema and lymphoplasmocytic infiltrated. After five months of follow-up a modified functional hemispherectomy of the left hemisphere was performed.
Results: He showed absence of seizures after the immediate postoperative period. One month after surgery he had a noninvalidating right flaccid hemiparesis with crural predominance and a recovering motor aphasia.
Conclusion: The early diagnosis and modified functional hemispherectomy allowed to get the boy free of seizures and without important sequelae. The relation between mesial sclerosis and ipsilateral Rasmussen encephalitis will have to be investigated.

p1327
Rasmussen's Encephalitis: Medical or Surgical Treatment?
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Purpose: Rasmussen's encephalitis is a rare but severe epileptic syndrome in childhood. This is a auto-immune chronic encephalitis clinically characterised by epilepsia partialis continua and progressive hemiparesis and cognitive deficit. The aim of this study was to evaluate different medical treatments and comparing them with hemispherotomy.
Methods: This is a retrospective study including 6 patients recruiting, over a 15 year period, in two paediatric neurology departments. All were female; mean age at the time of diagnosis was 5.6 years (2.6 to 11.2 years). Efficacy was judged on seizure frequency reduction (≥ 50%) and a stop in the progression of motor and cognitive deficits.
Results: IV immunoglobulines and indomethacin, used respectively in 1 and 2 cases, were not effective. When thalidomide was used, in 2 children, a reduction of seizure frequency was observed during 9 months in only 1 case. Plasmapheresis, used alone in 1 case, associated with IV immunoglobulines in 3 cases, was partially effective in 3 children (the frequency of seizures was reduced and hemiparesis remained stable from 5 to 7 months). High dose IV methylprednisolone improved seizure frequency but was not able to stop or reduce the progression of motor and cognitive deficit. Surgical treatment, right hemispherotomy, has been done in 4 children. In all cases, seizures ceased. After the surgical procedure, hemiparesis worsened transitorily in 3 children, but 6 months later the motor deficit was similar to before the hemispherotomy. Cognitive deficit remained stable in 2 cases (aged 8 and 12 years), and was improved in the younger child for whom hemispherotomy was performed early (3.5 years). However, in the older child, hemiparesis and cognitive deficit remained more severe than before the surgical procedure.
Conclusion: Medical treatments may be, at best, transitory and partially effective but are not able to stop the progression of motor and cognitive deficits. Hemispherotomy is, at present, the only effective treatment. Clinical observations of functional prognosis improvement when hemispherotomy is performed early are also supported by the ability for cerebral functional reorganisation in children.

p1328
Comparison of Epilepsy Frequency, Seizure Type, and Electroencephalographic Abnormalities in Patients with Primary Autism and Patients with Secondary Autism
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Purpose: Epilepsy has been described as a part of the autistic child symptomatology. Epilepsy frequency ranges from 5% to 38%. Any type of seizure can be present. Both prevalence and seizure type may vary according to the population studied and according to the autistic disorder aetiology: primary or secondary. The aim of this series is to describe and compare the frequency of epilepsy in patients with primary and secondary autism, predominant seizure type, electroencephalographic abnormalities and underlying diseases most frequently associated with secondary autism.
Methods: 59 clinical files of patients with primary or secondary autistic disorders were reviewed, retrospectively and prospectively. These two groups were compared regarding epilepsy frequency, seizure type and electroencephalographic abnormalities using square chi.
Results: From the 59 patients with autism, 30 (50.8%) have epilepsy and 6 (20%) belonged to the primary autism and 24 (80%) to the secondary autism group. The secondary autism group had a higher incidence of epilepsy. Lennox Gastaut syndrome was the pathology most frequently associated to autism. In both groups, the most prominent seizure type was generalised tonic-clonic seizures in 4

cases (13.8%) for the primary autism group and 13 (43.3% for the secondary autism group.
Conclusion: Epilepsy occurred more frequently in the secondary autism group, although the prevalence of 20% of epilepsy in the primary autism group remains significant, maybe because of genetic factors. Autism could be a sequelae of the Lennox Gastaut syndrome.

p1329
Clinical Characteristics in Autistic Children with Epilepsy
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Purpose: Autism spectrum disorders are of a different seriousness of developmental disorders. One third of the population with autism develops seizures under eighteen years of age.
Methods: We examined the case reports of our 27 patients with autism and epilepsy retrospectively. The data of pre/peri/postnatal periods, level of intellectual and language functions, the onset of seizures, the epileptic syndromes, and the treatment of epilepsy were analysed.
Results: None of our patients had perinatal complications or postnatally acquired causes of neurological damage that increased the risk of developing seizures. Abnormal neurological signs were not found. CT and/or MRI were normal in all patients. They were divided into three groups on the basis of the peak of epilepsy onset. There were differences in the types of seizures, the results of treatment, IQ range, language abilities, and the possibilities of development and socialisation among the three groups
Conclusion: The seizures, starting in puberty, were well controlled, without substantial effect of previous life level. Epilepsy onset in early childhood, under two years of age, and associated with typical infantile autism, showed the poorest prognosis. The treatment of epilepsy was very difficult and possibilities of development were also poor.

p1330
Family Predictors of Psychopathology in Children with Epilepsy
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Purpose: Based on social interactional and ecological perspectives (e.g., Bronfenbrenner, 1986; 22 (6): 723-742) we examined epilepsy-related factors and distinct family factors as contributors to psychopathology in children with epilepsy. We hypothesised that proximal family factors (parent-child relationship quality) would exert the greatest influence on child psychopathology, above distal (parental characteristics) and contextual family factors (other family relationships), and epilepsy-related factors (duration and severity). We also hypothesised that proximal factors would mediate the effects of epilepsy-related factors, distal factors and contextual factors.
Methods: Parents of 91 children (M = 8.5 years, sd = 2.42) referred for epilepsy were asked to fill out questionnaires concerning child psychopathology, parent-child relationship quality, parental confidence in parenting, parental depression, problems with family adaptation, and marital satisfaction. Epilepsy-related factors were derived from medical files.
Results: Regression analyses indicated that epilepsy-related factors were nonsignificant contributors of child psychopathology, whereas proximal ($p < .001$), distal ($p < .01$), and contextual family factors ($p < .05$) were all significant contributors. However, when the effects of other family factors were controlled for, only proximal factors remained significant contributors of psychopathology ($p < .001$). Tests of mediation showed that distal and contextual factors influenced psychopathology through proximal factors ($p < .001$).
Conclusion: The treatment of psychopathology in children with epilepsy should particularly focus on the influence of parent-child relationship quality and one should be aware that effects of the broader family system might adversely influence parent-child relationship quality. Detailed information will be presented at the congress.

p1331
Behavioural and Psychiatric Profile in a Sample of Greek Children with Epilepsy
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Purpose: To examine behavioural issues and psychiatric profiles in children with epilepsy and potential differences between children with idiopathic and those with cryptogenic/symptomatic epilepsy.
Methods: The study sample included 52 patients consecutively seen in our epilepsy clinic (20 males), mean age 9.5 years, 29 with idiopathic epilepsy syndromes (subgroup A), partial and generalised and 23 with cryptogenic and symptomatic epilepsies (subgroup B). The Child Behaviour Checklist (standardised for Greek children) was followed by child and family interviews by psychiatrists. Comparisons with the Greek community sample were performed. Statistical analysis included comparisons between the subgroups, via t test and two-way ANOVA.
Results: Valid questionnaires: 44 out of 52. With the exception of anxious/depressed ($p=0.9$), delinquent ($p=0.11$), aggressive ($p=0.29$) and externalising ($p=0.29$), all percentages in the total sample of 44 children were significantly different (at $p<0.01$) from 10%. The t test showed significant differences between subgroups A and B in the social ($p=0.007$) and withdrawn categories ($p=0.047$). Two-way ANOVA performed in order to account for sex differences between the subgroups (24.14% males in A and 59.10% in B), demonstrated significant differences for the thought problems category ($p=0.007$).
Conclusion: The Child Behaviour Checklist demonstrated problems in the areas measured by the withdrawn, somatic, social problems, thought problems, attention, internalizing and total problems scales for the entire group. The two subgroups were not differentiated through the items examined in this study. Contrary to findings from other studies the anxious/depressed scores were low.

p1332
Non-epileptic Events in Paediatric Population
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Purpose: Although psychogenic seizures (pseudoseizures) make up the majority of non-epileptic events both in adults and the paediatric population, the spectrum is much wider and also includes physiologic and organic aetiologies in the latter. Limited data is available in the paediatric population on non-epileptic events.
Methods: We reviewed the data on the paediatric patients (age 1 month to 18 years) who underwent at least 24 hours long-term video EEG monitoring. Patients with possible simple partial seizures without any EEG correlation or with uninterpretable EEGs were excluded as were neonatal patients. All EEGs and video events were first reviewed by an EEG fellow then by an attending physician, Board certified in clinical neurophysiology. Predominantly motor-behavioural events without any EEG correlation were classified as stereotyped movements in children < 1 year old and as behavioural events in children older than 1 year with some degree of mental retardation or developmental delay.
Results: 416 children were included in the study. Of these, 94 (23%) patients were diagnosed with non-epileptic events. 54 patients were male (57.4%) and the mean age was 8.1 years. 15 patients (16%) also had concomitant epilepsy. Psychogenic seizures were the most common and occurred in 36 (38.3%) patients. The majority of patients (26 patients, 72.2%) with psychogenic seizures were adolescents (age ≥12) and female (23, 64%). Behavioural events were the second most common type of non-epileptic event seen in 25 patients (26.6%). All

patients with behavioural events had a mild-to-moderate degree of mental retardation. Other diagnostic categories included stereotyped movements (10 patients, 10.6%), parasomnias (6 patients, 6.4%), nonepileptic myoclonus (5 patients, 5.3%); daydreaming, breath holding spells and nocturnal enuresis (2 patients each, 2.1%), and extremity tremor, presyncope, paroxysmal non-kinesigenic choreoathetosis, gastroesophageal reflux disease, choreoathetosis and migraine were seen in 1 patient each (1.1%).
Conclusion: Paroxysmal non-epileptic events are common in the paediatric population. Non-epileptic events occurred in about one-quarter of our paediatric patients who underwent at least 24-hour LTM. Psychogenic seizures were the most common diagnosis in this population and occurred mostly in adolescents warranting psychological counselling in this age group.

p1333
Pattern of Cerebral Activity Maintained Two Years After Prolonged Febrile Convulsions in Children
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Purpose: The effect of prolonged febrile convulsions (PFC) on the electrical brain activity development is unclear. Temporal lobe epilepsy has been linked to the occurrence of febrile convulsions at a young age. One concern is to develop non-invasive predictive methods to identify at risk patients.
Methods: We retrospectively studied 4 infants aged 16 months tested one month post PFC and 6 infants aged 50 months tested 2 years post PFC. These infants were compared to control groups of equivalent ages. We used achromatic 1 Hz pattern visual evoked potentials (pVEPs) recordings. Stimulus related power spectral analysis (FFT) has been performed.
Results: We observed significant differences in quantitative power spectral amplitude values of frequency bands between infants who have presented PFC and their control groups. In fact, both PFC groups of infants show significantly more delta activity (1-3 Hz) ($p < 0.0005$) and less beta (14-29 Hz) ($p < 0.001$) and gamma (30-50 Hz) ($p < 0.001$) activity over occipital, parietal, temporal and frontal regions compared to their controls.
Conclusion: Enhanced slow frequency activity and suppression of higher frequency activity in the brain of PFC infants treating visual stimuli, are observed both 1 month and 2 years after the episode. Longitudinal studies are necessary to relate this pattern of activity to the appearance of epilepsy at later ages.

p1334
Study of the Significance of Photoparoxysmal Responses and Spontaneous Epileptiform Discharges in Childhood Epilepsy
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Purpose: This study examines photoparoxysmal responses (PPRs) and their relationship to epileptic seizures in the paediatric population.
Methods: A retrospective analysis of abnormal electroencephalogram (EEG) reports in children (from birth to 18 years) was performed. EEG requisitions and reports over a ten year interval (1989-1998)were reviewed for the presence of a PPR. Data was abstracted from the EEG requisitions, reports, and clinical records. Abnormalities of the background rhythm, morphology and location of spontaneous epileptiform discharges (SEDs) were documented.
Results: 78 children (208 records) met the study criteria. The mean age for PPRs was 10.18 years (95% CI: 9.49 – 10.87). The majority (81.58%) of children with a PPR fell between ages 6 and 16 years. Abnormal background rhythms were associated with a PPR in 37 (32.46%) records. There was no statistical association between the presence of abnormal background rhythms and the presence of a PPR. SEDs were associated with a PPR in 93 (81.58%) records, and the majority (70.97%) had epileptiform discharges that were generalised. The remaining epileptiform discharges were focal. The most common location of the focal SEDs was the bilateral frontal region (22.22%). 55 (70.51%) had generalised seizures, while 19 patients (24.36%) had partial seizures. There was no statistical association between PPR type (4 types classified) and seizure type. Idiopathic generalised epilepsy was the most frequently encountered syndromic diagnosis. Idiopathic partial and symptomatic focal and generalised epilepsy syndromes were also recognised.
Conclusion: Photoparoxysmal responses are associated with partial as well as generalised seizure disorders. Financial support for this research is from a grant from the Children's Hospital Foundation of Manitoba and the Health Sciences Centre Medical Staff Council Fellowship Committee.

p1335
Defining the Exact Time of a Severe Perinatal Asphyxial Insult: Can Amplitude Modulated EEG Assist?
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Purpose: The exact time an infant experiences a severe hypoxic ischaemic insult prior to delivery may have important clinical and medicolegal implications. Until now perinatologists have had to rely on antenatal foetal monitoring, often an imprecise process. In experimental animals EEG seizure activity occurs at a fairly well defined time after a hypoxic ischaemic insult, for example 6-8 hours in newborn lambs (Williams C, Gunn A et al). We wished to ascertain whether such a precise time of onset of seizure activity also occurs in humans.
Methods: Amplitude modulated EEG has been routinely used to monitor severely asphyxiated infants at Wellington Hospital since 1989, initially with the single channel CFM (Devices Ltd) and since 2003 with the dual channel BRM2 (Brainz Ltd NZ). We reviewed all case notes where records showed a EEG had been employed in the first week of life, and also extracted case notes in all asphyxiated infants to confirm whether aEEG had been used. From these records one of us (JT) extracted details of the perinatal history of those infants in whom the timing of the insults could be defined with a degree of certainty (acute prolapsed cord, acute abruption, acute shoulder dystocia etc) and the other (TVS) examined the aEEG to define the onset of electrical seizure activity, defined as a sustained burst pattern exceeding 20 mcV or a prolonged period (more than 2 minutes) of baseline exceeding 14 mcV. The time to onset of seizure activity from insult was calculated in these infants. Preterm infants, those with a history of intrauterine growth restriction and those with congenital cerebral malformations were excluded.
Results: 144 infants' case notes and aEEG traces were examined, as well as post mortem reports where available. 82 infants were initially excluded, mainly because they did not reach our criteria for severe asphyxia, but this group included also 5 infants with cerebral/subarachnoid haemorrhage as a cause for seizures rather than asphyxia. In 13 infants the aEEG was judged to have been applied too late after birth to yield useful results (>36 hours). In 29 infants the timing of the asphyxial event could not be made with certainty. In the remaining 10 infants the onset of seizure activity on the aEEG occurred at a mean time of 17.75 hrs (range 12-22 hrs). In no infant was electrical seizure activity seen in the first 12 hours, although aEEG was not applied until 2.5-11 hours (mean 7 hrs). Apparent clinical seizure activity was not accompanied by aEEG evidence of such in the first 18 hours in any infant where the aEEG was applied at the time infants with evidence of intracerebral or subarachnoid blood (not necessarily associated with evidence of asphyxia) tended to have early seizures. Our study confirmed the value of long aEEG examinations in asphyxiated infants as a depressed aEEG can be seen both prior to the onset of seizures and again after seizure activity has settled.
Conclusion: In this group of asphyxiated infants where the timing of asphyxia was known with some certainty, electrical evidence of

seizure activity was not seen in the first 12 hours after the asphyxial event, and usually occurred at about 18 hours. We confirmed clinicians often describe seizure activity in infants in the first 12 hours of life where there is no convincing aEEG evidence of such. Subarachnoid or intracerebral blood was possibly associated with earlier onset seizures but this group was very small. In spite of extracting case notes going back 17 years we were only able to find 10 suitable infants for this study. These findings may have important medicolegal implications and should be repeated in a prospective multicentre study.

p1336
Value of Long-term EEG Monitoring in the Diagnosis of Epilepsy in Children
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Purpose: Long-term EEG monitoring (LTEM) can be used for the diagnosis and monitoring of epilepsy treatment in children. The aim of the study was to evaluate the usefulness of LTEM in the detection of paroxysmal EEG activity in children subjected to observation due to seizure disorders.
Methods: The analysis was made on a group of 126 children admitted to the Department of Developmental Neurology, Poznan University of Medical Science in the year 2004, to diagnose and monitor the treatment of epilepsy, including the use of LTEM.
Results: 68 (54.0%) children from the group of 126 were admitted for diagnostic evaluation; 58 (46.0%) for monitoring treatment. EEG activity during wakefulness was recorded in all patients. Physiological sleep was recorded in 100 (79.4%) patients. Clinical events in the form of seizures were recorded in 33 (26.2%) patients, in 20 (15.9%) cases during wakefulness and in 13 (10.3%) during sleep. Correlation of the clinical event with the EEG paroxysmal activity was declared in 15 (11.09%) children. Seizure-like epileptiform EEG changes during wakefulness were found in 63 (50.0%) patients and during sleep in 82 (82.0%).
Conclusion: The results show that the LTEM monitoring is an effective epilepsy diagnostic tool as it detects paroxysmal activity better than the standard EEG. It also makes it possible to record EEG activity during a clinical seizure and to verify whether the seizure is of epileptic or psychogenic nature. By enabling the recording of EEG activity during physiological sleep it contributes to better detection of paroxysmal EEG activity.

p1337
Simultaneous Recording of Electroencephalography (EEG) and Near Infrared Spectroscopy (NIRS) in a 3 Months Old Infant Suffering from Refractory Epilepsy
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Purpose: This study aimed to analyse the interactions between electric and metabolic activities by EEG and near infrared spectroscopy, during ictal and interictal periods, in an infant suffering from refractory partial epilepsy.
Methods: S.B. was a 3 months old boy, presenting sub-continuous partial pharmaco-resistant seizures from birth. A multimodal monitoring approach was proposed. It consisted in the simultaneous monitoring of video-EEG (11 electrodes) and near infrared spectroscopy (3 emitters and 1 detector placed over the left hemisphere) at bedside. Several seizures were recorded with this bimodal apparatus.
Results: S.B.'s interictal EEG activity consisted of rapid activities associated with asynchronous suppression-burst. Seizures consisted of left hemispheric rapid activities (about 1 minute) followed by post-ictal theta activities (about 40 seconds). Seizures were associated with an increase of oxygenated haemoglobin starting a few seconds before the electroclinical seizure onset. The end of seizures was associated with a period of long-lasting metabolic undershoot, ending beyond the post-ictal theta activities.
Conclusion: The expected neurovascular coupling can still be maintained during the seizures, despite a constant interictal disorganised neuronal activity. These results highlight the interest of coupling elaborate electric and metabolic investigations in the course of seizures, particularly by the use of EEG and near infrared spectroscopy, in the monitoring and clinical follow-up of infants suffering from intractable epilepsy.

p1338
Variability of the Hemodynamic Response of Spike Related EEG-fMRI in Children with Focal Epilepsies
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Purpose: Heterogeneous BOLD responses to interictal spikes have been reported in adult patients with focal epilepsies. We used the spike related EEG-fMRI technique as recently described in children (Boor et al. Epilepsia 2003: 44: 688-92) to learn about brain areas that are active during interictal spikes in children with focal epilepsies and analyse the hemodynamic response to interictal spikes in children and juveniles with focal epilepsies.
Methods: We recorded EEG and fMRI simultaneously in 12 children with focal epilepsies aged 3.4 – 11.9 (median 7.4) years, using a 16 channel EEG and an 1.5 Tesla MRI scanner. We marked the onset of each gradient artefact on the EEG, before we removed these artefacts from the EEG, using a commercially available software. This enabled us to mark the spike peaks, which were the events in our EEG-fMRI paradigm. The event (=spike) related fMRI analysis was performed for positive and negative BOLD effects using Brain Voyager software.
Results: We found BOLD responses to interictal spikes in 7 patients (3 'positive' and 4 'negative') in the expected brain regions according to seizure semiology and surface EEG. However, the hemodynamic responses of the maximum BOLD effects in comparison to the 'standard hemodynamic response' showed several seconds of time shifts between individuals, both for positive and for negative BOLD responses.
Conclusion: The analysis of the interictal spike related EEG-fMRI in focal epilepsies should include the time course of the HRF. Positive as well as negative BOLD responses may indicate the brain regions involved with the occurrence of interictal spikes.

p1339
Contemporary Neurovisualization Methods (Magnetic Resonance Imaging and Spectroscopy) in the Diagnostics of Temporal Epilepsy
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Purpose: To define the correlation between the results of structural and metabolic disturbances in focally conditioned areas in the case of temporal epilepsy in children using contemporary neurovisualisation methods, magnetic resonance imaging and spectroscopy (MRI and 1HMRS).
Methods: 54 children with epilepsy aged 2 months to 9 years are examined by MRI and MRS using 1.5 T magnetom vision (SIEMENS). MRS are obtained with SVS STEAM method with the following parameters: TE=20, 135, 155, 175, 200, 270mc. TM=13.7mc, TR=1500mc, VOI=15*15*15mm3, NS=128. The examination was carried out under the condition of water signal suppression. Site localisation for SVS STEAM: both hemispheres of

the brain (temporoparietal lobes), hippocampal areas (positioning was performed by axial T2W images).
Results: 11 (20.4%) of the examined children, aged 5 to 9 years, had temporal epilepsy, 90.9% of them had perinatal diagnosis. Fits started at the age of 1.5 to 6 years, they were focal, secondary-generalised, generalised or mixed nature; frequency was 1 per month to 10 fits per day. In the neurological status no rough focal symptoms were identified. In 6 (54.4%) children medial temporal sclerosis (decrease in volume of the hippocampus) has been revealed using MRI. In the rest of the children no structural changes were found. All examined data of MRS spectra of the temporal and hippocampal areas showed alterations in the level of cerebral metabolite concentrations, represented as a decrease of N-acetylaspartate (NAA) peak, and decreasing N-acetylaspartate/creatinine ratio (NAA/Cr). 10-14% decrease in peak of NAA in the temporal area of one of the hemispheres, mostly left, evidenced a pathological process ($p<0,05$). NAA/Cr ratio in the examined area was 0.98+/-0.1 (n=1.21+/-0.1). The data indicated deceleration of energetic processes, processes of myelogenesis and neuronal deficiency (atrophic process) in the examined area.
Conclusion: In the absence of clear clinical symptoms, specific epileptic activity on EEG and structural changes (MRI) in the temporal area of the brain, objectively confirm the diagnosis 'temporal epilepsy' is possible using the data of quantitative characteristics of the level of cerebral metabolite concentration in the area.

p1340
Role of Brain Metabolites Ration in Detection of Epileptic Nides in Symptomatic Childhood Epilepsies
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Purpose: The aim of the work was to investigate the peculiarities of brain metabolites ratio disturbances in both ipsilateral and contralateral epileptic nides in symptomatic childhood epilepsies.
Methods: We examined 40 children suffering from epileptic seizures aged 1 to 16 years. Comparative clinical analysis, analysis of the level of brain metabolites ratio NAA/Cr (NAA - N-acetyl aspartate, Cr - creatine, phosphocreatine), Cho/Cr (Cho - choline-containing compounds), mIns/Cr (mIns – myoinositol) and results of MRI and EEG have been studied; brain metabolites ratios were received on the basis of brain 1H MRS.
Results: Comparison of brain metabolites ratios in patients with symptomatic epilepsies and controls have indicated bilateral reliable reduction of NAA/Cr ($p<0.01$) and reliable increasing of Cho/Cr; mIns/Cr ($p<0.01$). In the majority of cases, the greatest reduction in NAA/Cr was ipsilateral seizure focus, determined by clinical, MRI and EEG, including those with bilateral abnormalities.
Conclusion: Determined bilateral abnormalities of cerebral brain metabolites in symptomatic epilepsies point out an existence of several epileptic nides in the brain. Therapeutic actions should be directed both on epileptic seizure cessation and on correction of transmitters and energetic chains of the cerebral metabolism.

p1341
Circadian Rhythm of Melatonin Secretion in Children with Epilepsy
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Purpose: Numerous aspects of human physiology are greatly influenced by the time of day. Examples of circadian rhythms include the sleep-wake circle, daily rhythms of hormonal production or body temperature as well as rhythms in cognitive ability. Changes in the function of the circadian timing system may contribute to the development of a number of diseases. Certain forms of childhood epilepsy, with frequent night seizures, may be one such example when irregular sleep-wake cycle/changes in melatonin secretion and, consequently, worsened sleep quality may trigger seizures. The effect of melatonin on seizures has been reported in some individual cases, however mechanisms of its antiepileptic activity remain to be investigated. The aim of the present study was to search for the relationship between the melatonin secretion cycle and irregular sleep patterns in children with epilepsy, and to investigate their influence on seizure time and frequency.
Methods: 10 children with epilepsy and 19 age-matched controls were investigated. The subjects presented with different forms of epilepsy, 8 were using different antiepileptic drugs. Clinical investigation included routine EEG analysis, hepatic enzyme (ALT, AspTA), MRI and sexual maturity scores. The questionnaire and sleep diary was used to evaluate sleeping patterns and sleep disturbances. Daily body temperature, heart rate and blood pressure were sampled in parallel with the measurements of i) melatonin concentration in saliva, ii) melatonin metabolite 6-sulfatoxymelatonin levels in the urine. Analysis was performed using immunoassay (ELISA kits, Bühlmann Laboratories AG, Switzerland).
Results: Preliminary results showed higher nocturnal levels of melatonin in the saliva of children with epilepsy (ex. at 24 hr mean levels of 41 pg/ml vs 7.4 pg/ml of control group). There was high inter-subject variability in both children's groups. Individual temporal patterns of hormone levels will be presented in the selected cases.
Conclusion: Thus, preliminary results suggest that children having nocturnal seizures have irregular sleep-wake cycles and altered daily melatonin secretion.

p1342
Ictal Video-polysomnography and EEG Spectral Analysis in a Severe Case of Panayiotopoulos Syndrome
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Purpose: To report a child with a severe form of Panayiotopoulos syndrome (PS), video-EEG recording of an autonomic seizure and the results of all-night video-polysomnography.
Methods: An 8 year old boy was referred for sleep studies because of headache and paroxysmal sleep disorder. From age 3 years, he had frequent nocturnal autonomic seizures of 1-2 per month and of 5-20 minutes duration each. They all occurred during early morning sleep and consisted of pallor, tachycardia, vomiting, unilateral eye deviation and mildly impaired consciousness followed by severe headache. In addition, at age 7 years he experienced 3 visual seizures of multicoloured spheric hallucinations lasting 10-30 sec. each. Numerous previous EEG were reported as normal. The child had standard all-night video polysomnography. Video-EEG data were evaluated visually and by means of quantitative spectral analysis. Corresponding polysomnographic scoring was evaluated.
Results: The interictal sleep EEG showed functional spikes mainly in the right occipital electrodes. Clinically, the recorded seizure started with tachycardia long before eye deviation and vomiting. Spectral analysis of the electrographic seizure, which lasted for 20 minutes, showed focal onset in the right occipital areas followed by widespread recruitment of extra-occipital cortical regions. Sleep organisation was normal.
Conclusion: PS may manifest with frequent autonomic seizures without convulsions (Panayiotopoulos C.P. 2004; Epilepsy Behav.) and normal EEGs for many years. Paroxysmal sleep disorder may be another cause of misdiagnosis. Autonomic manifestations at seizure onset (tachycardia) may be inconspicuous occurring long before other more apparent symptoms (eye deviation and vomiting). Despite frequent seizures sleep EEG and structure patterns were normal. Gastaut-type occipital seizures may develop later favouring a continuum between the two disorders.

p1343
Anoxic-epileptic Seizures in Cornelia de Lange Syndrome: Case Report of Epileptic Seizures Induced by Obstructive Apnea
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Purpose: To report epileptic seizures following recurrent obstructive apnea in Cornelia de Lange syndrome (CdLS).
Methods: Case-sheet review
Results: The diagnosis of CdLS in a boy now age 3 years was made by typical phenotypic features. Since aged 10 months the boy had recurrent respiratory infections with obstructive apnea leading to cyanosis and loss of consciousness. Approximately 25% of apnoeas were followed by clonic jerks of his right limbs or all four limbs. The epileptic component usually lasted 10 minutes, but once it became status epilepticus. He never had unprovoked epileptic seizures. His MRI showed dysgenesis of the corpus callosum and reduced cerebral volume. After his first admission he was diagnosed with symptomatic epilepsy and was given carbamazepine and phenobarbital, without benefit. Significant improvement occurred after his mother was taught to extract mucus from his upper airways before obstruction occurred. Because of his peculiar saliva and mucus he needs suction of his upper airways almost every day. With this management, he no longer has obstructive apnea and has had no epileptic seizures since July 2004. Anti-epileptic drugs were withdrawn in October 2004.
Conclusion: The events in this child were anoxic-epileptic seizures (AES), that is epileptic seizures triggered by syncopes (Stephenson JBP et al. Epileptic Disord 2004;6:15-19). This is the first description of AES in CdLS. Even when recurrent epileptic seizures occur in patients with known cerebral pathology, the diagnosis of symptomatic epilepsy should not be uncritically accepted.

p1344
Epilepsy and Migraine in a Cortical Dysplasia: A Case Report
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Purpose: Migraine and epilepsy are two different syndromes which often show an overlapping of symptoms in childhood. A relationship between epilepsy and migraine has been postulated. Migraine and epilepsy are highly comorbid, but the nature of their association remains unclear. ICHD-II codes in point 7.6 for headache attributed to epileptic seizures occurring between the migrainous aura and the headache phase of migraine.
Methods: Case report
Results: MS aged 18 years came to our observation affected by West syndrome since the age of 10 months. A familiarity with mental and language retardation was present in the maternal relatives. Therapy with ACTH and VPA resulted in remission of the crises after 3 months. Brain magnetic resonance imaging (MRI) revealed polymicrogyric dysplasia of the left frontal parietal region. EEG revealed left-sided temporal and occipital OP discharges until the age of 6 years. VPA was stopped at the age of 6 years. Neuropsychological assessment showed mental retardation (IQ=70) with dyslexia and dyscalculia present until now. Neurological examination revealed motor clumsiness and lack of coordination of the right hand. At age 7 the boy suffered from headache diagnosed as migraine without aura (5 crises at year). A new MRI showed the same cortical dysplasia and SPECT showed modification on the frontal and occipital areas. At age 15, he experienced an abrupt onset of two generalised tonic-clonic crises. EEG revealed OP discharges during light stimulation and hyperpnoea. Therapy was started with oxcarbazepine stopping the seizures and migraine.
Conclusion: Exceptionally, reversible brain MRI abnormalities following migraine and seizures have been postulated. There are few descriptions, however, of patients suffering from cortical dysplasia and 2 diseases comorbid.

p1345
Hot Water Epilepsy and Cerebral Malformation
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Purpose: To present the case of a 1½ year old boy with an abnormal development and a history of seizures after immersion in warm water. These reflex seizures were followed after a period by unprovoked seizures.
Methods: The patient was born at term, after a pregnancy with a history of oligohydramnios, by C-section, with a birth weight of 2700g and an Apgar score of 9. The family history is unremarkable. On follow-up it was noted that he had an abnormal psychomotor development. Shortly before his first birthday he started to present seizures while bathing and he came to our clinic for evaluation.
Results: The clinical examination revealed a boy with microcephaly and slightly dysmorphic features, with retarded motor and cognitive development. He undertook a video-EEG recording while bathing, and shortly after immersion in the warm water he had a complex partial seizure with unresponsiveness, staring, generalised hypotonia, followed by slow recovery and oral automatisms and yawning. The EEG showed generalised slowing. His cardiac rhythm was normal during the seizure. The cerebral MRI showed pachygyria. After 3 months he began to also have unprovoked seizures, while on treatment with valproic acid.
Conclusion: Reflex seizures during bathing (hot water epilepsy) are usually a benign condition with a yet unexplained pathogenic mechanism. Our case is one of the few reports of this form of epilepsy in children with abnormal development and abnormal cerebral MRI, and in whom this is not as benign as previously reported.

p1346
Temporal Lobe Epilepsy Associated with Hippocampal Sclerosis and Contralateral Middle Fossa Arachnoid Cyst
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Purpose: We report a 11 year old boy with temporal lobe epilepsy associated with right hippocampal sclerosis and a contralateral arachnoid cyst in the middle cranial fossa. Arachnoid cysts are congenital lesions frequently detected incidentally. Their common location is in the middle cranial fossa. The relationship of arachnoid cyst and epilepsy is controversial and it is unlikely that a mass effect of the cyst is the cause of the epilepsy. In these patients the epileptic discharges on the EEG do not always coincide with the location of the cyst. Evidence of arachnoid cyst in the middle cranial fossa is not a typical structural abnormality on MRI in patients with temporal lobe epilepsy. Our patient ictal EEG recording showed the epileptogenic area located on the opposite side of arachnoid cyst, and we needed further diagnostic tests to provide relevant information about the lateralisation and localisation of the epileptogenic focus.
Methods: The boy, aged 11, was born after uneventful pregnancy and delivery. There was no history of epilepsy or other neurological disease in his family. His psychomotor development was normal until the age of 8 years when he experienced complex partial seizures typical of focus in the temporal lobe, sometimes occurring during concomitant febrile illness. The seizures were preceded by emotional auras with fear and anxiety followed by alteration of consciousness with reduction of reactivity, oro-alimentary automatisms, clonic version of the head and eyes, clonic/tonic facial motor symptoms and slurred speech. We reviewed EEG, MRI, MRI spectroscopy, and SPECT data.
Results: Interictal EEG showed normal background activity with spike and slow wave discharges exhibiting maximal amplitudes and phase reversal at the electrodes T4 and T6, permitting localisation of this

abnormal activity to the right temporal lobe. Ictal EEG showed pattern consisted of high-frequency spike discharges at the same electrodes. MRI disclosed arachnoid cyst in the left middle cranial fossa contralaterally to the EEG abnormality, and atrophic right hippocampus with hyperintensity on T2-weighted images. MRI spectroscopy showed low NAA in the right hippocampal region, and interictal single photon emission computed tomography (SPECT) brain perfusion imaging examination revealed hypoperfusion in the right temporal lobe, especially in the hippocampal region.
Conclusion: In our patient the arachnoid cyst in the left middle cranial fossa was not considered to be the direct cause of epilepsy, instead the seizures were attributed to contralateral hippocampal sclerosis. As EEG findings showed the epileptogenic area far from MRI abnormality, we used MRI spectroscopy and SPECT to clarify the discrepancy between MRI and EEG. This underlines the necessity of a multimodal and individualised approach to localising the epileptogenic focus

p1347
Practice Parameters of Diagnostic and Therapeutic Procedures in Asperger Syndrome and Childhood Epilepsy: A Case Report
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Purpose: There is an increasing scientific interest in the association between Asperger Syndrome and epilepsy in childhood. The clinical diagnosis of epilepsy in Autistic Spectrum Disorders is complicated and comprehensive. Practice parameters of these matters have been presented in a paper.
Methods: We present the analysis of a 3 year follow-up of a 10 year old boy without an evident pathology of prenatal and perinatal periods. From early childhood, he demonstrated symptomatology of Asperger Syndrome. At the age of 7, the boy had paroxysmal events characterised by a change of facial expression, impaired consciousness, and automatisms, followed by postictal confusion. The difficulty was to classify the seizures. During the next year the frequency of epileptic seizures and symptoms of ADHD increased. The neuroimaging findings of CT and MR of brain were normal. Standard EEG recordings and Holter -EEG showed bitemporal paroxysmal discharges on normal background activity. The boy's cognitive abilities were affected with a low level of cognitive abilities and disharmonic profiles. He was given antiepileptic treatment of valproic acid with tailored add-on CBZ and specific management for AS.
Results: On the basis of clinical pictures, analysis of EEG recordings and data he was diagnosed with complex partial seizures. The next psychological examination revealed improvement in IQ, better concentration and social abilities. The use of tailored AEDs positively influenced the decreased frequency of seizures
Conclusion: The primary problem is an early correct diagnosis of seizures and use of tailored antiepileptic treatment. It gives a chance for better quality of life. The topographic distribution of discharges in the EEG is also important in the classification of epilepsy.

p1348
Idiopathic Partial Epilepsy in a Child with Balanced Translocation T(13;22) (Q22.3-Q11.23)
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Purpose: We report on a child with idiopathic partial epilepsy and balanced translocation t(13;22) (q22.3-q11.23); this is a clinical contribution to genetic definition of the idiopathic partial epilepsies.
Methods: Evaluation of clinical, electroencephalographic, neuroradiological features and molecular genetic analysis.
Results: The child, born of non-consanguineous parents without a family history of epilepsy, presented , at age 7 years 4 months, nocturnal deep breathing and tonic-clonic seizures secondarily generalised lasting about 20'. After six months the child presented a similar nocturnal seizure lasting a few minutes. The interictal EEG shows focal sharp-waves in the left frontocentral region spreading in the temporal lobe and a sporadic tendency to generalisation in sleeping record. There is no evidence of brain structural damage to MRI, and no neurological dysfunction on clinical examination. The genetic analysis, normal in the parents, shows de novo balanced translocation t(13;22) (q22.3-q11.23). No features typical of De George syndrome, nor mental delay are present.
Conclusion: The ictal semeiology and EEG features of our child are evocative of the familial partial epilepsy with variable foci (FPEVF). This epileptic syndrome, autosomal dominant with incomplete penetrance, was mapped on chromosome 22q11-q12 between markers D22S1144-D22S685 in two large French-Canadian families (Xiong I et al. Am J Hum Genet 1999;65:1698-1710). This linkage was confirmed recently in a Dutch family (Callenbach PM et al. Epilepsia 2003;44:1298-1305) but not in a precedent study in an Australian family (locus in chromosome 2q) indicating genetic heterogeneity (Scheffer IE et al. Ann Neurol 1998;44:890:899). We have started a molecular genetic analysis to verify if, in our child, the translocation breakage is included between the known markers on Chr. 22q11-q12. In this case our report should give an important contribution to the definition of the role of this chromosomic region in idiopathic partial epilepsies and may be useful for identification of the gene involved in the FPEVF.

p1349
Paroxysmal Movement Disorder - Seizures and Spindle-like EEG Rhythms: Further Evidence of Peculiar Basal Ganglia Implication in Maple Syrup Urine Disease (MSUD).
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Purpose: MSUD is a rare autosomal recessive disorder affecting branched-chain-amino-acid metabolism, responsible for rapid neurological degradation. In the classic neonatal form, dystonic movements of arms and pedalling are pathognomonic signs. Convulsions may be difficult to distinguish from abnormal movements. We report a first video-EEG analysis of seizures and non epileptic movements in MSUD.
Methods: We report the case of a full term healthy newborn with uncomplicated pregnancy and delivery, breastfed for 8 days. Three days after artificial alimentation weight loss, hypoglycaemia, lethargy, respiratory distress, alternating hypertonia and hypotonia appeared. Biochemical screening was positive for leucinosis. Video-EEG was performed in intensive care at admission.
Results: Video-EEG allowed us to differentiate fronto-central tonic and versive epileptic seizures from similar paroxystic tonic non-epileptic movements. Typical non epileptic movements found in MSUD such as boxing and pedalling were also recorded. The interictal EEG showed spindle-like bursts in rolandic regions, called 'comb-like-rhythm', considered as a characteristic rhythm in MSUD.
Conclusion: Pathophysiological mechanisms in leucine-metabolism disorders are not completely understood. Recent neuro-imaging and experimental findings indicate a selective vulnerability of basal ganglia neurons to neurotoxic metabolites. We postulate that the unusual 'comb-like-rhythm' reflect a liberation of thalamocortical oscillators possibly due to altered basal ganglia inhibition. The peculiar tonic seizure semiology might be a further evidence that in MSUD seizures and dystonic non-epileptic attacks share the same neuronal circuits.

p1350
Peri-oral Myoclonia with Absence in a Child with Cerebral Frontal MRI Changes
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Purpose: We report a new and atypical case of peri-oral myoclonia with absence, a rare epileptic syndrome recently described by Panayiotopoulos et al (1994), with no effective treatment.
Methods: A 15-year old teenager with no particular personal and family history was referred to our centre for absence seizures that were refractory to treatment with lamotrigine. Clinical and neurological examinations were normal. His mother highlighted that during the absence fits, she noticed labial shivering and twitching. It is also noteworthy that a month after the onset of absence seizures, he presented a tonic-clonic fit. Cerebral T2-weighted MRI showed bilateral frontal hypersignal. A video electroencephalogram revealed that peri-oral myoclonia was concomitantly associated with generalised 3-4 Hz spike-waves. We added sodium valproate to his base-line treatment with lamotrigine. Lamotrigine was subsequently withdrawn.
Results: One month after starting sodium valproate, the patient had no more absences, and the EEG became normal.
Conclusion: We report an atypical case of peri-oral myoclonia with absence in which abnormal cerebral MRI changes were detected. It could be argued that our present case is a variant of the condition described by Panayiotopoulos as peri-oral myoclonia with absence, with the additional finding of cerebral MRI frontal disorders. Conversely, this patient may be viewed as a case with frontal cerebral abnormalities presenting with peri-oral myoclonia and absence. At the present state of knowledge, it is not known if such a distinction makes any valid difference. However, this observation probably widens the spectrum of findings in this newly described entity. Furthermore, while this condition is known to be refractory to treatment, our patient did respond favourably to sodium valproate. Our follow-up should, however, be continued beyond the 2-month window of opportunity over which period this observation was made. This would validate more appropriately our therapeutic results.

p1351
Withdrawal of Lamotrigine Caused by Sudden Weaning of a Newborn: A Case Report
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Purpose: Worldwide studies concerning the benefit of the new antiepileptic drugs (AED) in pregnancy seem to focus on the quality of women's life, the absence of the AED teratogenicity and less on the therapy of the newborn's withdrawal symptoms.
Methods: We present the case of a 6 weeks old infant, admitted in the newborn-ward for loss of appetite, neuromotor hyperexcitability, irritability that occurred after 2 weeks from sudden weaning caused by a new maternal epileptic seizure. The infant was born after a pregnancy with chronic treatment with 7 weeks 200mg/day phenobarbital switched progressively with 200 mg/day lamotrigine. There are reports that lamotrigine crosses the placenta with the same plasma level, declining progressively at 72 hours postpartum at 72% those of the mother, at 40-70% in milk and induced withdrawal in 1-2 weeks after breastfeeding stopped (Tran TA et al. Neurology, 2002;59:251-255).
Results: The absence of other clinical symptoms, normal investigation results and permanent indirect AED therapy of the newborn, suggest that the symptoms were induced by lamotrigine withdrawal. We have started a test therapy with a 1mg/kg/day dose with total recovery in 48 hours. After 1 month of discontinuing therapy the neuromotor development became normal.
Conclusion: 1) Withdrawal for newborns represents a new delicate situation and a diagnosis by exclusion. 2) Even though modern neurological therapy protocols for pregnancy exist, they are absent in newborn cases with withdrawal of AED when breastfeeding is not available. 3) Epilepsy management with all its out coming aspects of life still has lacunas.

p1352
Challenge of Pyridoxine Dependency: Case Report and Review of Literature
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Purpose: Apnea, bradycardia, and alteration of consciousness upon initial IV pyridoxine administration are diagnostic of pyridoxine dependency.
Methods: MM is a 3 year old girl with an infantile epileptic encephalopathy characterised by hyperalertness, irritability, weight loss, and intractable multifocal seizures. She became apnoeic, hypotensive, and unresponsive with IV infusion of 100-mg pyridoxine at age 5 months. She is now only on pyridoxine.
Results: Pyridoxine dependency is a rare clinical syndrome characterised by infantile seizures and an encephalopathy. Seizures types include myoclonic jerks, clonic, and tonic seizures. There is an associated encephalopathy characterised by hyperalertness, irritability, tremulousness, abnormal cry and startle. Systemic signs may also be present with temperature instability, abdominal distension, vomiting, hepatomegaly, and respiratory distress. Electroencephalography may be normal, show immature sleep patterns, or show epileptiform, generalised rhythmic slow, or suppression-burst patterns. Administration of IV pyridoxine during electroencephalography produces rapid normalisation of the background.
Conclusion: Infants with untreated pyridoxine dependency also have apnea, bradycardia, hypotension, hypotonia, alternation of consciousness and coma upon first IV pyridoxine administration. Indeed, in one report, this occurred in all 4 infants with pyridoxine dependency treated with IV pyridoxine, while the fifth, was treated with oral pyridoxine without any autonomic changes (Nabbout R et al. Arch Dis Child Fetal Neonatal Ed. 1999 Sep;81(2):F125-9). It has also been reported when pyridoxine was given via enteral tube. Pyridoxine, however, has been used extensively to treat infantile spasms and there are no reports of this phenomenon in non-pyridoxine dependent infants. Therefore, this response to pyridoxine is diagnostic of pyridoxine dependency and is therapeutic.

p1353
Portuguese Version of the Quality of Life in Epilepsy Inventory for Adolescents: AD-48 Translation
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Purpose: Portuguese adaptation of the Quality of Life In epilepsy Inventory for Adolescents (QOLIE-AD-48)
Methods: The adaptation process of the QOLIE-AD-48 into Portuguese included the following phases: authorization of the author for the adaptation, translation into Portuguese, assessment of item comprehension, back-translation into English, development of a consensual version, and formal assessment of its validity and reliability. The QOLIE-AD-48 contains 48 items in 80 subscales: epilepsy impact (12 items), memory/concentration (10), attitudes toward epilepsy (4), physical functioning (5), stigma (6), social support (4), school behaviour (4) and health perceptions (3).
Results: A bilingual translator conducted translation into Portuguese. The first Portuguese version was back translated and discussed by a panel of experts until agreement was reached on item wording according to content correspondence. The final version was tested in a pilot study including 10 adolescents with epilepsy, which confirmed a high level of item acceptance and comprehension.

Conclusion: The QOLIE-AD-48 is a robust measure, with good psychometric characteristics, for evaluating the quality of life in adolescents with epilepsy, which includes a six-item stigma subscale. We decided to adapt a specific measure with the same level of validity and reliability as the original version, while ensuring the cultural accuracy of the newly adapted version. Acknowledgment: Joyce Cramer for assistance in the conceptualisation of an inventory for adolescents.

p1354
Development and Validation of a Measure of the Impact of Epilepsy on an Adolescent's Quality of Life: Glasgow Epilepsy Outcome Scale-Adolescents (GEOS-AD)
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Purpose: To develop and validate a measure of the impact of epilepsy on an adolescent's quality of life (QoL) that is based on direct exploration of the adolescent's views.
Methods: Initial scale development was based on data generated through qualitative methods (focus groups) in a previous study (McEwan et al Seizure 2004;13:15-31). The draft measure was piloted (n=30) and refined using correlational methods. Psychometric properties were established by means of a field trial (n=78).
Results: An initial item pool of 76 was refined to 50. The structure of the measure mirrored the conceptual model derived from the focus group study; Part 1 covered issues relating to adolescent development (identity formation) with five subscales, and Part 2 covered epilepsy related issues with four sub-scales. The GEOS-AD had good internal consistency (a 0.91). Correlations with measures of concurrent and construct validity were acceptable and it discriminated on dimensions of clinical importance. Participant feedback suggested the measure has excellent face validity and potential clinical utility.
Conclusion: The GEOS-AD is a direct measure of how adolescents perceive epilepsy to impact on their QoL. It has sound psychometric properties. It provides a potentially useful clinical outcome tool and should contribute to our understanding of the impact of epilepsy on an adolescent's QoL.

p1355
Parental View of Epilepsy and Quality of Life in Rett Syndrome
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Purpose: Few instruments exist to measure the impact of epilepsy on the quality of life in Rett Syndrome (RS). In order to better define and provide detailed information on seizure characteristics and their impact on quality of life in RS, we performed an extensive socio-medical survey among members of the French association for Rett Syndrome (AFSR).
Methods: We attempted to describe seizure characteristics, parental opinion and quality of life related to RS by using a newly developed self administered questionnaire, sent by post to parents of AFSR.
Results: 200 completed questionnaires were returned. Mean age of patients was 14.8 ± 8.1 years (3-42), 70% had epileptic seizures and mean age at first seizure was 7.3 years ± 5.1 (1-24). No statistical difference was found between the age of first seizure, diagnosis of epilepsy and introduction of treatment. Epilepsy had a negative impact on child and family life (68% of cases), strongly correlated to the existence of generalised, prolonged, cyanotic and drug-resistant seizures, on the child's level of alertness and progress in communication skills and psycho-social consequences such as fear of seizures, and difficulty in finding home care aids.
Conclusion: We identified major concerns of parents with RS that determine the impact of epilepsy on children and their family's quality of life. Hence, we suggest using a brief 12 item questionnaire during a clinical visit, to assess the impact of epilepsy on quality of life.

p1356
Open-label Extension Study of the Efficacy and Safety of Rufinamide Adjunctive Therapy in Patients with Lennox-Gastaut Syndrome
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Purpose: To evaluate the long-term safety and efficacy of open label adjunctive rufinamide in patients with Lennox-Gastaut Syndrome (LGS).
Methods: Patients who completed a multicentre, double-blind, placebo-controlled, randomised, parallel-group study of rufinamide adjunctive therapy were eligible. After a 14 day double-blind conversion phase, the open-label period began and rufinamide doses could be modified between 10-45 mg/kg/day, given bid or tid. Efficacy was assessed as follows: i) percent seizure frequency per 28 days, ii) percent patients with 50% to 75% reduction in seizure frequency (response rate), and iii) tolerance to efficacy. Safety was evaluated by adverse events (AEs) and discontinuations.
Results: Of the 139 eligible patients, 124 continued into the open label extension phase and were treated for a median of 432 days (range 10-1149 days). Mean age was 14.2 years (range 4-37 years) and median rufinamide daily dose was 1800 mg (range 103-4865 mg/day). A reduction in median total seizure frequency was observed at 6 (-42.6%), 12 (-55%), 18 (-52.8%), 24 (-64.1%), 30 (-69.6%), and 36 (-79.3%) months. 45 (36.9%) and 26 (21.3%) patients had a 50% and 75% overall response rate for total seizures, respectively. No evidence of tolerance to rufinamide was noted. 12 patients discontinued due to AEs. The most common AEs were vomiting (30.6%), pyrexia (25.8%), upper respiratory tract infection (21.8%), and somnolence (21.0%). 2 deaths occurred and were judged not to be related to rufinamide.
Conclusion: Long-term adjunctive rufinamide treatment was effective and well tolerated for the treatment of seizures in patients with LGS.

p1357
Racial and Ethnic Bias in the Selection of Therapy for Epilepsy
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Purpose: Racial bias has been described in the selection of therapy for arthritis, renal disease, ischemic heart disease and epilepsy. Children with intractable epilepsy may be candidates for the vagus nerve stimulator (VNS), ketogenic diet, or resective epilepsy surgery. There are no published reports of a racial disparity for the treatment of intractable epilepsy at a paediatric health centre. Texas Children's Hospital's referral base consists of Hispanic (43.6%), white (40.2%), black (10.3%) and Asian (4.7%) patients. The presence of a racial bias will be determined by comparison of this demography with patients who have received nonpharmacological therapy.
Methods: Electronic medical records were reviewed. Data from patients who received VNS (n=153), resective epilepsy surgery (n=86), and the ketogenic diet (n=53) were compared to the U.S. census bureau demographic data.
Results: VNS patients were 25% Hispanic (n=38), 60% white (n=92), 10% black (n=16), and 3% Asian (n=5). Resective epilepsy surgery

patients were 34% Hispanic (n=29), 55% white (n=47), 5% black (n=4), and 2% Asian (n=2). Ketogenic diet patients were 26% Hispanic (n=14), 60% white (n=32), 8% black (n=4) and 4% Asian (n=2).
Conclusion: Our findings are consistent with previous reports that black patients undergo fewer resective epilepsy surgeries. The Hispanic population is underrepresented in patients treated with the ketogenic diet and vagus nerve stimulation. There was no discrepancy noted amongst white and Asian patients. This information should provide awareness to medical professionals in order to better serve their population, attempt to eliminate racial and ethnic bias, and address disparities in health care.

p1358
Safety and Efficacy of Clobazam in the Treatment of Epileptic Encephalopathies in Childhood
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Purpose: The use of clobazam in adults and in children with partial epilepsy enables a better knowledge about this drug, and its use in other types of epilepsy. The purpose of this study was to evaluate the safety and efficacy of clobazam as add-on therapy in children with epileptic encephalopathy.
Methods: This study was conducted at the paediatric epilepsy clinic of our university hospital. Children with epileptic encephalopathy under 18 years old were included. Clobazam was introduced as add-on therapy, starting with 5 mg/Kg/day. The dose was increased according to the minimally effective dose, up to the maximum tolerated dose. Data was obtained from clinical files and follow-up visits.
Results: 97 patients were included (39 girls), ages between 1 and 17 years (mean = 9.9). 26 patients had Lennox Gastaut syndrome, 7 myoclonic astatic epilepsy, 9 West syndrome and in 57 the type of epileptic encephalopathy could not be established. Clobazam dose ranged from 5 to 60 mg/day (mean = 37.5 mg/day). 40 patients presented adverse events, however, most of them were mild and transitory, and in only 11 patients clobazam needed to be withdrawn. 9 patients were seizure free after clobazam adjunctive therapy. In 11, seizure improvement was >75%, in 16 >50%, in 17 <50% and in 44 there was no modification in the seizure frequency. 3 patients were lost to follow-up. Among patients with seizure improvement, the results lasted for more than 1 year in 85%.
Conclusion: Clobazam is safe and effective in the treatment of generalised encephalopathies of childhood.

p1359
Effectiveness of Midazolam in the Treatment of Paediatric Status Epilepticus in an Intensive Care Unit
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Purpose: Status epilepticus (SE) is a common neurological medical emergency that is associated with significant morbidity and mortality in paediatric intensive care units (PICU). In this study the effectiveness of midazolam in the treatment of SE was investigated in a standard drug treatment regimen.
Methods: 27 children (aged 2 months to 18 years) with SE were included in the study. A departmental protocol for the treatment of SE was applied to all children. In the protocol, initial treatment of SE included rectal administration of two doses diazepam solution in the first step (0-10 min) and diphenylhydantoin or phenobarbital administration up to 20 mg/kg loading dose in the second step (11-30 min). Then midazolam infusion was initiated as a third antiepileptic drug with an initial bolus dose of 0.15 mg/kg. Maintenance of midazolam infusion was continued with a dose of 0.05 mg/kg increased as needed every 5 minutes up to 0.5 mg/kg.
Results: Between January 2000 and December 2003, twenty eight SE on 27 children were treated in the PICU. Only one of them (4%) was diagnosed as nonconvulsive status epilepticus. For operational definition, patients with SE were categorised as follows based on the observation of clinical seizures; initial SE: 8 (29%) children with seizures lasting longer than 10 to 30 minutes; established SE: 10 (36%) children with SE lasting between 30 and 60 minutes; refractory SE: 10 (36%) children with SE lasting longer than 60 minutes. Midazolam infusion was needed for 20 (72%) of 28 children treated with the departmental protocol. The midazolam infusion was found to be successful in terminating SE in 20 (95%) of 20 children. One child with refractory SE was treated with propofol infusion. Midazolam was well tolerated by all patients with no clinically significant cardiovascular changes. Overall mortality and morbidity were defined as 0% and 12.5% respectively.
Conclusion: Midazolam successfully terminated paediatric SE in the presented departmental protocol. Its potent antiepileptic effect, relatively safety record, makes midazolam a potentially important drug in the treatment of SE in PICU. Its optimal dosing and clinical usefulness in various settings needs further evaluation

p1360
Oral Administration of High Dose Diazepam in Children with Continuous Spike Waves during Slow Sleep
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Purpose: Epilepsy with continuous spike waves during slow sleep is a rare pathology, usually diagnosed in children around 4 years of age. Patients present with absences with or without generalised seizures, often with accompanying mental development delay. Treatment is difficult and even polytherapy is frequently ineffective. The aim of the study was to assess the effectiveness of oral administration of high dose diazepam in children with continuous spike waves during slow sleep.
Methods: 6 of our patients were treated with high doses of diazepam according to The Protocol from Massachusetts General Hospital (Dr E. Thiele). In late afternoon the patients were given 1mg/kg of diazepam orally; the total dose divided into 2 equal doses given 1 hour apart. EEG examination was performed each night. The patients underwent cardiac, respiratory and O2 saturation monitoring each night during the three weeks treatment.
Results: After 3 weeks EEG examination significant improvement was revealed in 5 cases. In those patients the therapy was subsequently continued for several weeks with lower doses (0.5mg/kg). Clinical effect (seizure control, development acceleration) was seen by the second month of the therapy. None of our patients showed severe adverse reactions to diazepam management. The only negative effects were agitation or sleepiness. The therapeutic effect of high dose diazepam remained up to 6 months and 4 of the patients required another course of diazepam.
Conclusion: In our study the use of high dose diazepam proved to be effective in gaining seizure control and mental development. However further observation is needed to determine its long time effectiveness and safety.

p1361
Reduction of Clinical Convulsive Crises and Epileptic Syndromes in Children Treated with Levetiracetam Added to Polytherapy
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Purpose: To determine the efficacy of levetiracetam in the control of clinical convulsive crises in epileptic syndromes in children. Although levetiracetam has been only approved for adults (1-19, 24), it has showed to be effective in children (3, 20-35).
Methods: Between September 2002 and January 2005, 24 children from our unit were treated with levetiracetam (40-50 Mg/Kg/day). Our retrospective-analytic study was carried out on 15 patients (aged 12

months - 13 years). All patients had their crisis diary checked before and after the addition of levetiracetam. The follow up was from 8 to 26 months (average 15 months). The patients were classified into three groups, according to the 1989 ILAE classification (36). The reduction of crises was rated as a percentage (%).
Results: We had 7 idiopathic syndromes, 3 symptomatic syndromes and 5 cryptogenic syndromes. We had 8 patients with partial epilepsies and 7 patients with generalised epilepsies. All groups showed significant reduction of epileptic crises (70% in more than 65% of patients). We observed no severe significant adverse reactions. In all patients the levetiracetam was added to polytherapy.
Conclusion: The fact of making a correct diagnosis of the epileptic syndromes goes in favour of taking a better therapy choice. The reduction of frequency of crises was significant. It was shown that levetiracetam has a wide range of action.

p1362
Retrospective Analysis of Keppra Efficacy and Tolerability in Childhood Epilepsy Syndromes
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Purpose: To evaluate Keppra efficacy and tolerability in children with partial and generalised epilepsies.
Methods: 45 children (25 boys, 20 girls) aged from 2 to 16 years were treated with Keppra for 6-12 months. 28 children had partial epilepsy, 5 had myoclonic-astatic epilepsy, 3 Dravet syndrome, 3 Lennox-Gastaut syndrome, 3 eyelid myoclonia with absences, 3 encephalopathy with CSWS. In all but 2 children Keppra was used as add-on medication (25 patients had 2 AEDs, 18 had 3 AEDs, 2 had LEV monotherapy), the dose varied from 25 to 45 mg/kg/day. Clinical efficacy and tolerability was assessed at the end of 6 months after therapy initiation.
Results: After 6 months of Keppra therapy 8 patients (17.8%) were seizure-free, in 17 (37.8%) reduction of seizure frequency > 50% was observed. Complete seizure control was achieved in 3 patients with partial epilepsy, 3 with myoclonic-astatic epilepsy, 2 with encephalopathy with CSWS (with disappearance of CSWS on the EEG). Side effects were recorded in 11 patients (24.4%), they were transitory and could be tolerable after reducing the dose either of Keppra or concomitant AEDs.
Conclusion: Keppra is a rather effective drug and can be recommended as a treatment option in children with partial epilepsy, myoclonic-astatic epilepsy and resistant CSWS.

p1363
Lamotrigine Monotherapy in Childhood Idiopathic Generalised Epilepsy
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Purpose: To confirm the efficacy of lamotrigine (LTG) monotherapy in childhood idiopathic generalised epilepsy (IGE).
Methods: We retrospectively reviewed the medical records of 30 children with idiopathic generalised epilepsy, who were diagnosed at the Division of Paediatric Neurology, Asan Medical Centre, between 1 March 1996 and 31 December 2003 and had taken LTG for more than 12 months.
Results: The entire study cohort included 30 patients with IGE. The included patients had generalised tonic-clonic seizures (with or without myoclonic jerks, without absence seizures), normal brain imaging finding, and generalised spike or polyspike-slow wave discharges on EEG. There was a male predominance (17/13). Mean age at seizure onset was 8.1±4.9 years, and LTG starting age was 10.6±4.5 years. Effectiveness of LTG was classified into G3 (seizure-free), G2 (50-100%), G1 (0-50%), and G0 (0%) according to the reduction rate of seizures or myoclonic jerks. Outcomes were as follows: G3 (20.66, 7%), G2 (7.23, 3%), G1 (3, 10%). Mean effective dose was 6.6±3.5mg/kg/day. Major side-effects were not detected.
Conclusion: LTG is an effective and safe antiepileptic drug as monotherapy for childhood IGE.

p1364
Pharmacokinetics of Zonisamide in Children with Epilepsy
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Purpose: Document pharmacokinetic (PK) characteristics of zonisamide in paediatrics.
Methods: Paediatric patients (n=33) with epilepsy (age 5-15 years) on stable doses of up to 2 AEDs were divided into 2 groups (Group 1: 5-11 years; Group 2: 12-15 years) and classified as receiving enzyme-inducing or noninducing AEDs. Open-label zonisamide was initiated (1 mg/kg/day) and titrated (7 weeks) to 12 mg/kg/day. Steady-state zonisamide PK was assessed on Days 13, 40, and 60 at 1, 7, 12 mg/kg/day, respectively. PK measurements included: maximum concentration (Cmax), time to Cmax (Tmax), area under the concentration-time curve to 12 hours (AUC0-12h), apparent oral clearance (CL/F), and total body weight-normalised CL/F (CL/F/TBW).
Results: A total of 33 patients enrolled (21 patients in Group 1, 12 patients in Group 2); and 31 were included in PK analysis. The maximum mean dose of zonisamide was 9.6 mg/kg/day. 16 patients (11 in Group 1; 5 in Group 2) were on stable doses of enzyme inducers. In noninduced patients, Cmax, AUC0-12h, and CL/F values were higher in older patients (Group 2), while CL/F/TBW values were lower in older patients; however, differences were not statistically significant. In all PK measurements for induced patients, no statistically significant differences were observed for both groups. Tmax was similar between groups on all days. In both groups, Cmax and AUC0-12h increased in a greater than dose-proportional manner from the 1- to the 7-mg/kg dose; however, these parameters were dose proportional from the 7- to the 12-mg/kg dose.
Conclusion: Zonisamide PK parameters were dose-dependent in children 5 to 15 years.

p1365
Follow-up Study of Infantile Spasms Treated by Vigabatrin
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Purpose: The aim of this study was to evaluate the efficacy of control of infantile spasms (IS) using vigabatrin (VGB) in newly diagnosed cases and to correlate with aetiology and outcome.
Methods: A prospective study was performed on 18 patients with IS treated with VGB as a first AED. The patients were regularly examined by paediatric neurologists at Sfax hospital, Tunisia. The following clinical features were assessed: onset, seizure type and evolution after treatment, electroencephalography data and motor and cognitive evolution.
Results: Among 18 patients, 9 (6 boys and 3 girls) have a good evolution after vigabatrin therapy protocol. In this group, the mean age of spasm onset was 5 months (3-9 months). EEG showed typical hypsarythmia and the cerebral MRI was normal in 7/9 patients and showed tubers in 2 patients. The interval between spasm onset and drug administration ranged from 7 days to 4 months. The interval of spasm control ranged from 7 days to 2 months and hypsarythmia disappeared from 17 days to 9 months. 4 children had normal psychomotor development and 1 was at school. The second half had a poor evolution after treatment with vigabatrin and corticotherapy (hydrocortisone) in second line. In this group, patients had early psychomotor retardation associated with neonatal seizures in 4 patients. The mean age of spasm onset was 6 months (3-15 months).

EEG showed an asymmetric pattern of hypsarythmia. MRI showed encephalomalacia (4/9 cases), cerebral malformation (3/9 cases), arterial infarct in 1 case, and was normal in the last case. All patients presented deep mental retardation, hypotonia and microcephaly at the last follow-up.
Conclusion: Vigabatrin therapy in IS was effective in idiopathic spasms and in tuberous sclerosis with good mental and motor evolution. In symptomatic IS, vigabatrin therapy was ineffective.

p1366
Use of Maturinol in Treatment of Polymorphous Convulsions in Children
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Purpose: It is generally known that management of polymorphous seizures is a challenging exercise as they often cause child disability or even death. The efficiency of maturinol in management of infant epilepsy manifested by polymorphous seizures was evaluated.
Methods: We followed up 42 children under 1 year old with polymorphous seizures resistant to traditional anticonvulsive therapy. These children underwent treatment with Maturinol (a suspension composed of pantogam, glucocorticoids, vitamins, ferments; agents accelerating maturation of the central nervous system and decreasing the excitability of neurons).
Results: There was a marked treatment effect ($p<0.05$) in the study group, as compared to the control group (25 infants receiving phenobarbital or valproate (Depakene, Convulsofin)).
Conclusion: Thus, we found that maturinol improves the metabolism of neurons, reduces excitability of the central nervous system, accelerates brain maturation and conduces the reduction of polymorphous seizures in infants. Moreover, it is practically nontoxic as compared to traditional antiepileptic drugs.

p1367
Delayed and Long-lasting Side Effects of Add-on Treatment with Topiramate in Drug-resistant Childhood Epilepsy
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Purpose: To assess the incidence and characteristics of side effects of adjunctive topiramate (TPM) in refractory childhood epilepsy.
Methods: An open, prospective, observational, uncontrolled study of TPM efficacy was carried out in 130 children aged 2 to 18 years. After a three-year follow-up, a retrospective analysis of the incidence and characteristics of all adverse reactions was made.
Results: In 30 children TPM was stopped after 1 to 3 months due to lack of efficacy or seizure increase, and 5 children were lost for follow-up. Hence, the medical documentation of 95 children was reviewed and analysed. In total, 51 children (53.7%) showed delayed and long-lasting adverse reactions. They were represented as follows: bradypsychia (n=16; 16.8%), weight loss (n=16; 16.8%), cognitive decline with or without language disturbances (n=15; 15.8%), paresthesias (n=2; 2.1%), anhydrosis (n=1; 1%), renal calculosis (n=1; 1%). Severe adverse reactions led to TPM discontinuation in 14 children (14.7%) despite evidence for good efficacy. Marked cognitive decline combined with at least one of the above side effects was the reason for stopping treatment in 7/43 (16.3%) children with previous normal intelligence, in 5/38 (13.2%) children with light to moderate intellectual deficit, and in 2/14 (14.3%) children with severe neuropsychological deficit. No specific drug combination was found to be predominantly associated with this type of adverse reaction to TPM.
Conclusion: Cognitive side effects are the most common long-lasting adverse reactions to add-on TPM in refractory paediatric epilepsy regardless of the previous cognitive level. When severe, they can lead to drug withdrawal despite good seizure control.

p1368
Effect of Carbamazepine Monotherapy on Thyroid Function in Children with Epilepsy
K. Voudris[1], A. Attilakos[1], E. Katsarou[1], S. Mastroyianni[1], A. Fotinou[1], A. Skardoutsou[1], A. Garoufi[1]

1) P and A Kyriakou' Children's Hospital, Athens, Greece

Purpose: The results of studies evaluating the effect of antiepileptic drugs on thyroid function in children are controversial. The aim of this study was to investigate by a prospective, self-controlled method, whether treatment with carbamazepine (CBZ) monotherapy has some effect on serum thyroid hormone concentrations in children with epilepsy.
Methods: Serum concentrations of triiodothyronine (T3), thyroxine (T4), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) were determined in 20 children with epilepsy (aged 2 to 13 years, mean age±sd=9.07±3.27 years), before and at 6, 12 and 24 months of CBZ monotherapy. Serum CBZ concentrations remained within the therapeutic range during the period of study.
Results: Serum levels of T3, T4 and FT4 were significantly decreased at 6 ($p=0.008$, $p=0.000$ and $p=0.000$, respectively), 12 ($p=0.005$, $p=0.000$ and $p=0.000$, respectively) and 24 ($p=0.003$, $p=0.000$ and $p=0.000$, respectively) months of treatment with CBZ monotherapy. Serum concentrations of TSH were significantly increased at 6 ($p=0.002$), 12 ($p=0.005$) and 24 ($p=0.013$) months of treatment with CBZ monotherapy.
Conclusion: Our results show that CBZ monotherapy may have a significant effect on serum thyroid hormone concentrations in children with epilepsy, early in the course of treatment. This suggests a need for early and careful monitoring of serum thyroid hormone concentrations in children receiving CBZ monotherapy.

p1369
Folic Acid Supplementation can Prevent some Blood Cell Abnormalities in Children Receiving Carbamazepine
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1) Department of Paediatrics, Shiraz Medical School, Shiraz, Iran

Purpose: Carbamazepine (CBZ) is a commonly used anticonvulsant agent, but it has been linked with different blood cell abnormalities. This study evaluated the effect of folic acid (FA) supplementation to prevent CBZ induced haematological derangements in children.
Methods: This prospective randomised clinical trial was conducted on children with epilepsy who received CBZ monotherapy. Group one received CBZ alone and group two, CBZ plus FA (1 mg/day). The two groups were matched appropriately. Each group included 41 children with epilepsy children. From all of the patients, baseline blood tests were obtained before starting medication and then serially. The patients were followed for at least one year.
Results: In group one, leukopenia was observed in 31.4% and neutropenia in 17.1% of the patients, but in group two these figures were 14.6% and 9.8% ($p=0.067$ and $p=0.331$ respectively) . At the end of the first year of follow up WBC and PMN counts were significantly higher in group two ($p=0.007$ and $p=0.001$ respectively). Haemoglobin concentration dropped in group one and had a slight rise in group two; the changes were significant. Platelet count, lymphocyte count, monocyte count and their changes in serial blood tests, did not differ significantly between the two groups.
Conclusion: Folic acid is a safe drug that can prevent some blood cell abnormalities linked to CBZ. It has a favourable effect on preventing leukopenia and haemoglobin drop in patients receiving CBZ, but its exact effect and the dose requirement in order to enhance its benefits, needs further research.

p1370
Long-term Efficacy of Depakine in Children with Partial Epilepsy
I. Grigore[1], G. Diaconu[1], M. Burlea[1], S. Badica[1]

1) University of Medicine and Pharmacy 'Gr. T. Popa', Iasi, Romania

Purpose: To evaluate the long-term efficacy of conventional depakine (VPA) and depakine chrono (VPA-SRF) in the treatment of epilepsy for children.
Methods: We included in the study 111 children diagnosed with different types of partial epilepsies (68 with symptomatic partial epilepsy, 43 with idiopathic partial epilepsy). 17 (15.31%) of patients receive other antiepileptic drugs (CBZ, CZP, PB) in mono or polytherapy. Patients whose weight was over 20 kg were administrated the VPA-SRF form and for children under 20 kg VPA was used. The doses of VPA/VPA-SRF were increased to 20-30 mg/kg/day. VPA or VPA-SRF was used either in monotherapy (86 patients) or polytherapy (25 patients). The results of treatment with VPA were evaluated depending on the following parameters: the frequency of epileptic seizures, side-effects and personal satisfaction of the patients.
Results: 61.26% of the children WERE seizure-free. A significant seizure reduction (> 50%) was observed in 10.81% of patients. A better total control of the seizures was observed in patients with idiopathic partial epilepsy who received VPA or VPA-SRF in monotherapy (100%). As add-on VPA or VPA-SRF was used only in symptomatic partial epilepsy, 56% of patients have a significant reduction (> 50%) of seizures.
Conclusion: This study confirms the long-term validity and tolerability of conventional depakine/depakine chrono in treatment of partial epilepsy for children. Treatment with depakine or depakine chrono in mono or polytherapy significantly decreased the seizure frequency and improved the quality of life of the children.

p1371
Oxcarbazepine in Paediatric Patients: EEG and Seizure Outcome
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1) Hacettepe University, Ankara, Turkey

Purpose: Oxcarbazepine (OXC) is a new antiepileptic drug (AED) used as both monotherapy and adjunctive therapy for the treatment of partial seizures with or without secondary generalisation. We studied the efficacy of OXC in paediatric patients with focal epileptiform discharges and/or partial seizures.
Methods: Medical records of 29 patients with focal epileptiform discharges and/or partial epilepsy maintained on OXC either as monotherapy or in combination with other AEDs were reviewed.
Results: Age at the time of evaluation was 4.5-20.5 years (mean: 10.7 years). Age at onset of seizures ranged between 6 months-11 years (mean: 4.8 years). 15 patients had symptomatic partial, 10 patients had idiopathic partial, and 1 patient had cryptogenic partial epilepsy. 3 patients had epileptiform discharges without manifest seizures, 1 of them was diagnosed with Landau-Kleffner syndrome. 62% of patients showed decreased seizure frequency by 50% or more. Follow-up EEG after treatment with OXC was available for 16 patients in a minimum of one month. Initial EEG studies showed epileptiform discharges activated during sleep in 16/29 of the patients. After treatment EEG showed persistence of sleep activated discharges in 4 patients with initial sleep activated discharges, in 4 repeat EEG was normal without epileptiform abnormality. 1 patient initially had ESES pattern and follow-up EEG showed consolidation of the discharges over the left. None of the patients suffered from side effects.
Conclusion: OXC can be safely be used in paediatric patients with partial epilepsies. Unlike other AEDs used for partial epilepsies, OXC does not seem to deteriorate EEG in patients with sleep activated discharges.

p1372
Demographics and Cost-effectiveness of the Vagus Nerve Stimulator (VNS) in Paediatric Epilepsy Patients
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1) Ohio State University, Children's Hospital, Columbus, Ohio, USA

Purpose: To examine the demographics of our paediatric epilepsy patients currently implanted with a vagus nerve stimulator (VNS) and as a secondary measure, review whether VNS reduced their epilepsy-related hospitalisations.
Methods: Clinical data for 75 VNS patients, (<18 years) who were followed at the Comprehensive Epilepsy Clinic over 2 years (2003-2004) was reviewed. All hospitalisations/emergency room visits for epilepsy or epilepsy-related conditions (i.e. falls, lacerations) in patients with >1 year of VNS therapy were calculated on an annual basis, pre and post-implantation (n=60).
Results: Average age at implantation was 9.28 years (range: 1.5-17 years; 50% girls). Duration of epilepsy prior to implantation was 6.69 years (range: 1-16.5 years). VNS therapy averaged 2.83 years (range: 0.1-7 years). Epilepsy syndromes included: localisation-related symptomatic 24 (32%), localisation-related idiopathic 5 (6%), generalised idiopathic 4 (5%), generalised symptomatic 12 (16%), Lennox-Gastaut syndrome 21 (28%), mixed 8 (11%) and infantile spasms 1 (1%). 4 patients discontinued VNS: infection, parental decision, emesis, seizure exacerbation. Average annual rate of hospitalisations pre-implantation was 0.91 (range: 0-8), vs 0.43 (range: 0-2.8) post-implantation. Pre-implantation, 18 patients (30%) had no hospital utilisation vs 45 (75%) post-implantation.
Conclusion: Although VNS is approved in the U.S. for intractable partial epilepsy in patients >14 years, much younger patients are implanted and the majority (61%) did not have localisation-related epilepsy. Side effects requiring discontinuation were low (5%). Post-implantation hospital utilisation decreased (47%), and 2.5 times more patients did not require hospitalisation. Lowered hospital utilisation can have a significant impact on the long-term cost-effectiveness of VNS therapy and decrease overall patient morbidity.

Sunday 28th August 2005
15:00 - 16:30
Grand Amphitheatre
Satellite Symposium
Merritt Putnam Symposium:Tolerance to Beneficial and Adverse Effects of Antiepileptic Therapy

Session Outline

The pharmacological treatment of epilepsy has made considerable progress during the last two decades due to improved knowledge of the clinical pharmacology of individual drugs and the development of promising new agents. One phenomenon which has received less attention is the development of tolerance to both the antiseizure and adverse effects of antiepileptic drugs (AEDs). The development of tolerance to the anticonvulsant effect of AEDs has been demonstrated in animal experiments for most AEDs. This tolerance may be differentiated into either 'pharmacokinetic' or 'pharmacodynamic' tolerance. Clinical evidence of the development of tolerance to AED effects is insufficient or, in the case of newer AEDs, does not yet exist. Moreover, confounding factors such as diagnostic errors, compliance issues or disease worsening may obscure clinical evidence of tolerance. The impact of tolerance to both the antiepileptic activity and to adverse effects should be more fully evaluated for its clinical relevance in the long-term treatment of epilepsy. Strategies should be based on knowledge of pharmacokinetic and pharmacodynamic changes over time in specific samples of patients as well as studies of basic mechanisms underlying these effects. Since genetic predisposition, age, and gender may predict a drug's metabolism and central nervous system effects, these factors should be considered in future research to ultimately guide clinical care.

Do AEDs Lose their Activity during Prolonged Treatment? The Evidence from Laboratory Studies
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Tolerance is defined as reduction in response to a drug after repeated administrations. Development of tolerance to a drug is an adaptive response of the body to prolonged drug exposure, and has been described for many drugs acting on either peripheral organs or the central nervous system. A variety of laboratory studies in different animal species have shown that, with the exception of valproate and tiagabine, all antiepileptic drugs (AEDs) that have been evaluated in this regard lose their activity during prolonged treatment. Such development of tolerance may lead to attenuation of side effects, but also to loss of efficacy of AEDs. AEDs for which loss of anticonvulsant activity during prolonged treatment has been demonstrated in laboratory studies are benzodiazepines, phenobarbital, primidone, phenytoin, carbamazepine, vigabatrin, levetiracetam, and lamotrigine. Two types of tolerance occur: (1) Pharmacokinetic (metabolic) tolerance due to induction of AED metabolizing enzymes, which has been shown for most first generation AEDs and is easily overcome by increasing dosage; and (2) pharmacodynamic (functional) tolerance due to "adaptation" of AED targets, e.g., by loss of receptor sensitivity, which has been experimentally shown for all AEDs that lose activity during prolonged treatment. Functional tolerance may lead to complete loss of AED activity and cross-tolerance to other AEDs. Thus, development of tolerance to the antiepileptic activity of an AED may be an important reason for failure of drug treatment. Whereas laboratory studies have convincingly demonstrated tolerance to first generation and some second generation AEDs, there is a lack of respective data for most novel AEDs. In view of the evidence from laboratory studies, it is highly likely that there is development of tolerance to newer AEDs (similar to that seen with benzodiazepines) in patients. Because of genome variability, this tolerance may affect only a portion of patients. Thus, there is a need for clinical studies to evaluate the impact of tolerance on drug treatment of epilepsy.

Do AEDs Lose their Efficacy during Prolonged Treatment? The Evidence from the Clinic
D. Schmidt[1]

1) Epilepsy Research Group, Berlin, Germany

There is convincing experimental evidence that various antiepileptic drugs (AEDs) such as benzodiazepines, carbamazepine, lamotrigine, levetiracetam, phenobarbital, primidone, and vigabatrin (but not valproate) lose their antiepileptic activity during prolonged treatment. In view of the laboratory evidence, it is likely that tolerance to antiepileptic activity will also occur in patients with epilepsy. A loss of the response to AEDs during prolonged treatment can and has been shown, as evidenced by a shift from responder to nonresponder status of individual patients during long-term clinical observations. Tolerance affects a subgroup of patients receiving benzodiazepines, carbamazepine, methsuximide, phenobarbital, phenytoin, and among the newer AEDs, gabapentin, lamotrigine, levetiracetam, topiramate and vigabatrin. Currently, a response shift during valproate treatment has not been demonstrated, but for many of the novel AEDs no data are available. Tolerance has been documented during treatment of newly diagnosed patients and during add-on treatment of chronic epilepsy. Although differences may exist among AEDs, tolerance appears to affect only a subgroup of responders of no more than 10% for most AEDs, perhaps due to genomic variation. Tolerance may thus be missed when only total group response is measured over duration of treatment. Individual patients switching from nonresponder to responder status may compensate or overcompensate for the loss of response in others resulting in a net gain of efficacy during prolonged treatment. Confounding factors, such as diagnostic errors or disease worsening with an increased seizure frequency, may also exist. A loss of response mimicking functional tolerance may be caused by lower plasma concentrations due to poor drug compliance or drug interactions. In addition, failure to maintain efficacy is routinely compensated by dose increments in clinical practice. If dose increments do not work, the epilepsy is considered drug resistant. Tolerance may contribute, at least in part, to the development of drug resistance following initial response. Thus there is a pressing need for well-controlled clinical studies assessing tolerance and its impact, if any, on long-term seizure outcome in epilepsy.

Exploring Potential Clinical Benefits of Tolerance to Adverse Effects of AEDs
F. Gilliam[1]

1) Comprehensive Epilepsy Center and the Neurological Institute, Columbia University, USA

Tolerance has been described for many antiepileptic drugs (AEDs), and is equivalent to efficacy in clinical relevance. It is unclear whether potency for antiseizure effects correlates with potency for adverse side effects in a given AED. The mechanism of action underlying an adverse effect of an AED may be similar to or different from that of its antiseizure effect. In certain circumstances, therefore, tolerance may develop to an adverse effect without reduction in antiseizure effect. Two observations have consistently been reported for most AEDs: 1) slower titration of the medication is associated with fewer and less severe adverse effects, and 2) some adverse effects attenuate over time on a specific AED. Although subjective adjustment to an adverse effect without an actual reduction must always be considered, accurate strategies to optimize the rate of initial exposure and rational estimation of the time to allow maximal attenuation of an adverse effect before discontinuation of the AED seems necessary for best utilization of available medications. These strategies should be based on knowledge of pharmacokinetic and pharmacodynamic changes over time in specific samples of patients. Since genetic predisposition, age, and gender may predict a drug's metabolism and central nervous system effects, these factors should be considered in future research to ultimately guide clinical care. This presentation will also review clinical and observational evidence supporting the potential for tolerance to certain adverse effects to provide a means for optimal use of available AEDs.

Monday 29th August 2005
12:00 - 13:30
Grand Amphitheatre
Satellite Symposium - Pfizer
Progress in the Treatment of Drug-Resistant Partial Epilepsy: Established and Evolving Therapies

Session Outline

One of the challenges facing clinicians in the treatment of partial epilepsy is inadequate seizure control due to drug resistance. Many patients (at least 50%) achieve seizure free status with their first prescribed antiepileptic drug (AED). Management approaches for the remaining patients who do not achieve seizure control include additional attempts at monotherapy or adjunctive therapy with a second AED. Currently, there are no universally accepted treatment algorithms that dictate which approach should be taken, and when, to treat these refractory patients. A substantial number of drugs are available for the purpose of adjunctive therapy with many introduced in just the last decade. These newer drugs differ from their predecessors by virtue of their mechanisms of action and efficacy and safety profiles, thus providing clinicians with criteria for making choices in combination therapy. The newest addition to this group of treatments used as adjunctive therapy in partial epilepsy is pregabalin which binds to the alpha-2-delta auxiliary protein associated with voltage-gated calcium channels. This binding has been linked to the anticonvulsant, analgesic, and anxiolytic effects observed in preclinical studies. Pregabalin, a new, effective, and well-tolerated treatment option, has recently been approved for adjunctive therapy in adults with partial seizures with or without secondary generalization. In addition, in the European Union and in several other countries,

pregabalin has also been approved for the treatment of either peripheral neuropathic pain or neuropathic pain in adults (dependent upon the individual country's approval). This symposium will present the latest information and views on the treatment of patients with drug resistant partial epilepsy. First, there will be a review of the evolution of pharmacologic therapies for epilepsy with a focus on how increased understanding of the functioning of the nervous system and the pathophysiology of epilepsy has driven this process. This will be followed by separate presentations that outline the rationale and clinical data supporting treatment approaches (ie, sequential monotherapy and adjunctive therapy) and drug choices in refractory partial epilepsy. These discussions will include information on efficacy, tolerability, safety, and mechanisms of action of drugs, and comorbid aspects of uncontrolled seizures in choosing a treatment approach.

The Evolution of Pharmacologic Therapies: Past, Present, and Future

B. Bourgeois[1]

1) Harvard Medical School, USA

The first use of bromide for the prevention of seizures by Locock in 1857 is usually considered to represent the beginning of effective pharmacologic therapy of epilepsy. Bromide was known to have a significant sedative effect and this prompted Hauptmann in 1912 to try another sedative compound to treat epilepsy, phenobarbital. The prevailing concept that sedation is necessary for seizure protection may have delayed the discovery of the antiseizure effect of phenytoin until 1938. Phenytoin had been synthesized in 1908, but was initially not evaluated as an antiepileptic compound, supposedly because it was found to have little or no sedative effect. This led to a new era during which several antiepileptic drugs were developed and marketed, of which 2 emerged as major established drugs, carbamazepine and valproate. By 1993, barbiturates, phenytoin, carbamazepine, and valproate accounted for the overwhelming majority of prescriptions for epilepsy. These drugs each have their specific spectrum of mild to severe side effects, and they are all involved in clinically significant pharmacokinetic interactions. Since 1993, after a hiatus of more than a decade, at least 8 newer drugs have become available in a large number of countries, with additional drugs marketed in a limited number of countries. Some of these drugs were developed on the basis of our improved understanding of the mechanisms of epilepsy. As a group, these newer drugs can be said to have a better side effect profile and less pharmacokinetic interactions, although this does not apply to each one of them. In addition to the availability of more drug options, the pharmacologic treatment of epilepsy during the past 25 years has been characterized by 2 major currents: the debate over the concept of monotherapy versus combination therapy, and more recently the better understanding of the concept and recognition of medical intractability.

Approaches to Drug Resistant Epilepsy: Sequential Monotherapy

E. Perucca[1]

1) Clinical Pharmacology Unit, University of Pavia, Italy

The majority of patients who become seizure free on antiepileptic drug (AED) therapy respond to the first drug that is given to them. Although there is universal agreement that treatment should be started with a single drug, the best strategy to be adopted in patients failing initial monotherapy is unclear. In the past, the most common policy was to add a second drug. However, with increased recognition of the advantages of single-drug therapy, many physicians now prefer to switch these patients to an alternative monotherapy, which has been found to result in seizure-free rates ranging between 15% and 44%. Alternative monotherapy is also a viable strategy in patients who do not respond to 2 or more sequential monotherapies, but seizure-free rates in these patients are much lower. There is a paucity of randomized controlled trials addressing the relative merits of sequential monotherapy versus adjunctive therapy in refractory partial epilepsy. The largest of such trials did not identify any major difference in outcome between the 2 treatment strategies (*Epilepsy Res*. 2003;57:1-13), but the confidence limits of the estimates were wide due to a relatively small sample size. Moreover, outcome is likely to depend on which specific AEDs are being substituted or combined. At the current state of knowledge, treatment decisions should probably be made on a case-by-case basis. Sequential monotherapy is definitely preferred in patients who failed the first treatment because of idiosyncratic adverse reactions, whereas early combination therapy can be justified in patients with prognostic indicators of a difficult-to-control epilepsy.

Approaches to Drug Resistant Epilepsy: Add-On Therapy

T. Tomson[1]

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While only few systematic attempts have been made to compare sequential monotherapy with add-on treatment, regulatory add-on trials have provided overwhelming evidence of the effectiveness of this strategy with most antiepileptic drugs (AEDs) for patients refractory to monotherapy. Systematic reviews of randomized controlled add-on trials have confirmed that all licensed new generation AEDs can be appropriate for adjunctive treatment of refractory partial seizures in adults, whereas documentation for other seizure disorders is scarce. The issue is thus not just to choose a strategy, sequential monotherapy or adjunctive treatment, but also to select the most suitable AED. With so many different old and new generation AEDs to choose from, the number of different combinations is practically endless. Unfortunately, we lack both direct comparisons of different new generation AEDs as add-on therapy as well as randomized studies assessing different specific AED combinations. The selection of a particular AED for adjunctive therapy will therefore be based on indirect evidence and individual factors. Although comparative studies are missing, various AEDs clearly differ in their efficacy, tolerability, and safety profiles as well as in pharmacokinetic properties. Such differences will help the physician to select the most appropriate adjunctive treatment for the patient, taking into account individual factors such as type of seizures and epilepsy, age, gender, comorbidity, and concomitant medication. There are observations to suggest that mechanisms of action may be another important criterion for selection of AEDs, in particular for adjunctive treatment, where it appears rational to combine drugs with different modes of action. The development of the newer generation AEDs has also brought new options in terms of mechanisms. The latest example is pregabalin, which binds to the alpha-2-delta auxiliary protein associated with voltage-gated calcium channels.

Tuesday 30th August 2005
12:00 - 13:30
Grand Amphitheatre
Satellite Symposium - UCB
The Evolution of the Epilepsies with Age

Session Outline

Most, if not all epileptic syndromes evolve with age i.e. some appear at a certain age and may vary over time, with some symptoms and/or abnormalities disappearing with age.
Idiopathic Generalised Epilepsies (IGE) comprise a range of entities based on seizure types and age of onset. However, with the exception of benign neonatal myoclonic epilepsy and juvenile absence epilepsy (JAE), most persist into adulthood, suggesting different genetic bases. JAE and juvenile myoclonic epilepsy (JME) begin near or after puberty and have a variable long-term evolution. Other less well defined syndromes and 'adult-onset' IGE can begin from young adulthood onwards and may have mixed features. Recognising these as IGEs rather than as partial epilepsies can have crucial prognostic implications.
Partial Epilepsies in neonates and young infants may resemble simple or complex partial events. The distinction of simple from complex partial seizures may not be possible if the alertness and awareness of the patient cannot be tested. Partial seizures may be present in both

benign idiopathic and symptomatic/ encephalopathic syndromes e.g. partial seizures in children with West syndrome, severe myoclonic epilepsy and Lennox Gastaut. Most commonly partial seizures, with or without secondary generalisation, are characteristic of benign epilepsy with centrotemporal spikes (Rolandic, BECTS). The latter's benign nature is recently challenged by reports of cognitive and behavioural difficulties in some children. Most partial seizures in young children are extra-temporal, while those of teens and adults are often of temporal lobe origin. During later childhood and adolescence partial seizure semiology becomes more like that in adults; mesial temporal sclerosis, neoplasms and vascular abnormalities are common aetiologies.

Epileptic Encephalopathies are particularly illustrative of the epilepsies' evolution with age. Certain seizures or EEG patterns are predominantly witnessed in young children, with Infantile Spasms (IS) being a typical example of such a seizure type. In West Syndrome, IS coincide with typical interictal abnormalities (hypsarrhythmia). Positive or negative cortical myoclonic jerks are observed in many epileptic encephalopaties such as Progressive Myoclonic Epilepsy, Lennox-Gastaut Syndrome and Continuous Spike and Wave Syndrome. A major challenge in managing epileptic encephalopathies is to preserve the patient's cognitive capabilities as far as possible.

Conclusions: all epilepsies evolve with age. Age and cerebral maturity either affect the clinical expression of interictal abnormalities and seizures or lead to recovery. AEDs can effectively reduce epileptic episodes and, although there are few studies of age-specific effects of AEDs on seizures, EEG abnormalities and cognitive development, the latest findings on new AEDs in adults are highly relevant to children and the elderly.

Tuesday 30th August 2005
17:30 – 19:00
Grand Amphitheatre
Satellite Symposium - Novartis
Safeguarding Developmental and Psyschosocial Outcomes of Childhood Epilepsy through Evidence-Based Management

Session Outline

One third of patients with epilepsy experience their first seizure during childhood, and approximately 1% of children are affected by this condition. The management of epilepsy in children has different issues from that in adults, primarily related to the growth and development processes that may affect or be affected by epilepsy treatment and due to an increased behavioural sensitivity to antiepileptic drugs (AEDs). The neonatal stage is characterized by rapid growth being affected by some AEDs. In turn, the accelerated growth affects factors such as hepatic metabolism, renal elimination and volume of distribution, which alters the pharmacokinetics of AED individually and making dose adjustments necessary. In addition, some AEDs may cause severe behavioural problems which may be of more negative impact than the seizures.

Although the older AEDs had proven efficacy and were widely used, their utility was hampered by undesirable adverse events and drug-drug interactions. The selection of AEDs for children with epilepsy, as in adults should be based on evidence from clinical studies systemically evaluating the efficacy, safety and tolerability, and pharmacokinetics of appropriate formulations in paediatric patients. However, AED treatment, particularly as monotherapy, has not been systemically investigated through well-designed clinical studies in the paediatric population, and extrapolation of data from studies conducted in older children and adults may be complicated by development, physiological and metabolic influences on drug pharmacokinetics. Consequently, several of the newer AEDs are not approved for paediatric use; oxcarbazepine is the only newer AED licensed for monotherapy in children (US ≥ 4 years old, EU > 6 years old) with partial seizures.

Patients with epilepsy are at an increased risk of cognitive impairment, as a result of the seizures themselves, psychosocial issues and the adverse effects of some AEDs. The major cognitive effects associated with AED therapy are impaired attention, vigilance, and mental and psychomotor speed. Although these cognitive effects are usually offset by the therapeutic benefit of AEDs in seizure reduction, they are of special concern in children, where they can impact negatively on school performance and psychosocial interactions. Furthermore, children with epilepsy often suffer from psychiatric comorbidities like attention-deficit hyperactivity disorder, anxiety and others leading to learning difficulties and other problems of psychosocial development. As a result, they frequently experience poor psychosocial outcomes due to numerous factors such as perceived stigma, behaviour problems and academic difficulties. Therefore, childhood epilepsy is a condition that affects and is affected by the whole family situation, and its management requires attention to more than seizure control.

This educational symposium will discuss the special problems related to choosing AEDs for children with epilepsy. In addition, new data from controlled clinical studies of newer AEDs with improved efficacy and safety profiles in children will be presented. Finally, the importance of comprehensive patient care that addresses the issues of cognitive impairment and the psychosocial aspects of childhood epilepsy will be outlined.