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8th European Congress on Epileptology, Berlin, Germany, 21 – 25 September 2008

Sunday 21 September 2008
14:30 – 16:00
Hall 1

VALEANT PHARMACEUTICALS SATELLITE SYMPOSIUM – NEURON-SPECIFIC M-CURRENT K+ CHANNELS: A NEW TARGET IN MANAGING EPILEPSY

E. Perucca
University of Pavia, Italy

Innovations in protein biology, coupled with genetic manipulations, have defined the structure and function of many of the voltage- and ligand-gated ion channels, channel subunits, and receptors that are the underpinnings of neuronal hyperexcitability and epilepsy. Of the currently available antiepileptic drugs (AEDs), no two act in the same way, but all target components of Na^+ channels, Ca^{2+} channels, the GABA system, glutamate receptors, or modulatory sites involved in transmitter release, alone or in combination. None targets primarily the endogenous braking action of M-type potassium current on repetitive firing and neuronal excitability. Although M-current was first identified in 1980 as a slowly activating, noninactivating voltage-gated subthreshold potassium current, its molecular correlates – a family of KCNQ (Kv7) channels – were only identified in 1996 and are now recognized as novel molecular targets for new AEDs. This symposium will address the need for AEDs with novel mechanisms, review recent discoveries related to the structure and function of neuron-specific potassium/M-current channels, and summarize the evidence that these channels are therapeutic targets in epilepsy based on preclinical and clinical studies with the potassium channel opener retigabine.

THE NEED FOR NOVEL ANTIEPILEPTIC DRUGS

J. French
New York University Comprehensive Epilepsy Center, New York, NY, USA

No Abstract Received.

ANATOMY AND PHYSIOLOGY OF M-CURRENT K+ CHANNELS

H. Lerche
University of Ulm, Ulm, Germany

Voltage-gated K+ channels of the KV7 (KCNQ) family underlie the so-called M current, a K+ current that is suppressed by activation of muscarinic acetylcholine receptors. This current is found in many neurons of the central nervous system and regulates their firing behavior. A major subcellular localization of these channels is the axon initial segment, the site of action potential generation at which also voltage-gated Na+ channels are concentrated. The functional role of M channels there is to serve as a brake for action potential firing. Therefore, pharmacological activation of these channels represents a potent anticonvulsant mechanism that is not in clinical use up to now.

KV7 channels (KV7.1-5) are encoded by five genes (KCNQ1-5). They have been identified in the last 10–15 years by discovering the causative genes for three autosomal dominant diseases: cardiac arrhythmia (long QT syndrome, KCNQ1), congenital deafness (KCNQ1 and KCNQ4), benign familial neonatal seizures (BFNS, KCNQ2 and KCNQ3), and peripheral nerve hyperexcitability (PNH, KCNQ2). The fifth member of this gene family (KCNQ5) is not affected in a disease so far. The phenotypic spectrum associated with KCNQ2 mutations is probably broader than initially thought (i.e. not only BFNS), as patients with severe epilepsies and developmental delay, or with Rolando epilepsy have been described. With regard to the underlying molecular pathophysiology, it has been shown that mutations in KCNQ2 and KCNQ3 decrease the resulting K+ current thereby explaining the occurrence of epileptic seizures by membrane depolarization and increased neuronal firing. Very subtle changes restricted to subthreshold voltages are sufficient to cause BFNS which proves in a human disease model that this is the relevant voltage range for these channels to modulate the firing rate. The two mutations associated with PNH induce much more severe channel dysfunction with a dominant negative effect on wild type (WT) channels.

KV7 channels represent interesting targets for new therapeutic approaches to diseases caused by neuronal hyperexcitability, such as epilepsy, neuropathic pain, and migraine. The molecular mechanism of KV7 activation by retigabine has been recently elucidated as a stabilization of the open conformation by binding to the pore region.

PHARMACOLOGY OF M-CURRENT K+ CHANNEL ACTIVATION

H. S. White
University of Utah, Salt Lake City, UT, USA

Much of what is known about the therapeutic potential of M-current activators is based on observations with retigabine (N-[2-amino-4-(-4-fluorobenzylamino)-phenyl]carbamic acid ethyl ester) since it is the only agent among the established and investigational antiepileptic drugs (AEDs) that enhances the M-current at therapeutic doses. By enhancing M-currents, retigabine decreases neuronal excitability by inhibiting spike-frequency adaptation. At concentrations (>10 μmol) higher than mean peak concentrations (2–6 μmol) achieved with therapeutic dosages of retigabine, retigabine may enhanceGABAA receptor-mediated chloride currents through a nonbenzodiazepine action. Seizure models in which retigabine has shown activity include electrical (MES), chemical (PTZ, picrotoxin, penicillin, kainate, i.c.v. administered NMDA), and genetic (genetically epilepsy prone rats and audiogenic seizure susceptible mice) seizures. Retigabine has been found to be effective in blocking the fully expressed behavioral seizure and decreasing the electrographic afterdischarge duration in the fully kindled rat model of partial epilepsy. It is also highly effective in two models of pharmacoresistant epilepsy, i.e., the mouse 6 Hz psychomotor seizure test and the amygdala-kindled rat rendered resistant to lamotrigine and other sodium channel blockers. Retigabine also prevents the acquisition of kindling in the amygdala kindled rat and enhances learning performance in a model of cerebral ischemia. The broad-spectrum activity of retigabine in animal seizure models demonstrates that the M-current plays an important role in the control of membrane excitability and control of seizure activity. Moreover, the preclinical profile of retigabine establishes the M-current as a legitimate molecular target for epilepsy management and for further development of M-current activators.

CLINICAL EVIDENCE FOR POTASSIUM/M-CURRENT CHANNELS AS A THERAPEUTIC TARGET IN EPILEPSY

J. French

New York University Comprehensive Epilepsy Center, New York, NY, USA

As the only antiepileptic drug (AED) to directly activate (open) KCNQ (Kv7) channels, which are the molecular correlates of M-current, retigabine provides the first opportunity to evaluate the potential of this new therapeutic class in epilepsy management. Its pharmacokinetic profile is characterized by a half-life of 8–10 hours, metabolism by hydrolysis/N-acetylation and glucuronidation (nonoxidative pathways), primarily renal elimination, and low potential for pharmacokinetic drug interactions. The efficacy and tolerability/safety of retigabine as adjunctive therapy in adults with partial-onset seizures has been established in double-blind, placebo-controlled trials, showing a clear-cut dose-response relationship. During 16 to 18 weeks of double-blind treatment, seizures were reduced >50% in 29%–40% of patients receiving retigabine 600–1200 mg/day vs. 17% of those assigned to placebo. Seizures were reduced >50% in 35%–50% of patients receiving retigabine 600–1200 mg/day vs. 22% of those assigned to placebo during the maintenance phase. Discontinuations due to adverse events were 9% in patients receiving placebo and 15%–28% in retigabine-treated patients, depending on retigabine dose, occurring most frequently during a titration period that allowed very little or no flexibility to improve tolerability or retention as the starting dosage of 300 mg/day (100 mg t.i.d.) retigabine was increased weekly in 150 mg/day increments to the assigned target dosage. The most commonly reported adverse events of retigabine as adjunctive therapy were nonspecific CNS effects observed with other AEDs, including dizziness, somnolence, and fatigue. In long-term, open-label therapy following dose-ranging study, patients were followed for a median period of 18 months and retigabine dosages were adjusted according to clinical response. The optimized dosage was <900 mg/day in ~80% of patients and 6% of patients were seizure-free for the last 12 months of retigabine therapy. Results of clinical studies with retigabine validate the therapeutic benefits of targeting KCNQ (Kv7) channels in the management of epilepsy.

Sunday 21 September 2008
16:30 – 18:00
Hall 1
Merritt-Putnam symposium – the role of inflammation in the development of epilepsy

IS INFLAMMATION A COMMON FACTOR IN VARIOUS FORMS OF EPILEPSY? EXPERIMENTAL OBSERVATIONS

A. Vezzani

Mario Negri Institute for Pharmocological Research, Milan, Italy

Inflammatory processes may contribute or predispose to the occurrence of seizures and cell death in various forms of epilepsy of different aetiologies. From a clinical standpoint, a role of inflammation in the pathophysiology of epilepsy was originally suggested by the demonstrated antiepileptic activity of selected powerful antiinflammatory drugs, including steroids. Moreover, markers of inflammation have been measured in the serum and cerebral spinal fluid of epilepsy patients. More recently, an increased expression of proinflammatory molecules has been demonstrated in glia and neurons from patients surgically treated for drug-resistant epilepsies, as well as in epilepsy disorders that do not feature an inflammatory pathophysiology, such as temporal lobe epilepsy [1]. Studies in experimental models show that the activation of specific inflammatory pathways can contribute the genesis and recurrence of seizures. This observation highlights the possibility that inflammation in the brain, induced for example by an initial precipitating injury occurring at birth or during the lifetime, initiates a cascade of events in the CNS that contributes to setting the basis for the late onset of epilepsy. Chronic inflammatory reactions in the brain can enhance neuronal excitability, endanger neuronal survival, and alter blood–brain barrier permeability [1–3]; each of these effects may contribute to epileptogenesis [4]. Experimental observations also show that seizures per se can trigger inflammation in the brain involving both the innate and the adaptive immune systems and sharing molecules and pathways also activated by systemic infection [5,6]. If a relation between inflammation and epilepsy were to be proven, it might open new opportunities for the treatment of seizures and possibly the retardation of epileptogenesis or progression of the disease.

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FEBRILE SEIZURES, BRAIN INFLAMMATION AND EPILEPSY

T. Baram

University of California at Irvine, Irvine, CA, USA

Multiple roles of inflammation in the development of epilepsy are emerging, and are a focus of intense study and debate. Inflammation may contribute to the initial events instigating epileptogenesis, to the epileptogenic process itself, as well as to the clinical (progressive) course of the established epilepsy. In addition, inflammatory mediators may have different roles in adult and neonatal / developing brains. Among seizures that occur during development, febrile seizures are intrinsically associated with the inflammatory processes that accompany fever. Therefore, the role of inflammatory mediators in the development of epilepsy is particularly intriguing in the context of the epileptogenic process that may be initiated by prolonged febrile seizures. Experimental models of prolonged febrile seizures enable study of the short-term mechanisms by which inflammation may contribute to febrile seizure generation. They also allow investigation of the mechanisms taking place over longer time scales, where inflammatory mediators contribute to the epileptogenic process that may follow prolonged and complex febrile seizures. This talk will commence with the important clinical questions and available background in human studies, will then present established and novel insights arising from the study of experimental models, and finally will discuss the relevance and impact of these studies on our understanding and management of febrile seizures and epileptogenesis.

SEIZURES, EPILEPSY AND INFLAMMATORY DISEASES OF THE CNS: A CLINICAL PERSPECTIVE

T. Keraenen

TAYS/Neurological Cl., Tampere, Finland

Seizures and epilepsy may accompany several inflammatory diseases affecting the CNS. These disorders may be primary CNS diseases or the CNS may be affected as a part of a systemic inflammatory process.

Multiple sclerosis (MS) is chronic inflammatory neurological disorder in which the risk of epilepsy is about three to seven times higher than in the general population [1]. Epilepsy seems to be associated with relapsing-remitting MS; it is unusual in primary progressing MS. Seizures are more likely to occur during acute relapses and may be the first manifestation of the disease. Seizures in MS are usually partial with or without secondary generalisation. The potential causes of seizures in MS include inflammation, oedema and/or demyelination in the cerebral cortex and the juxtacortical white matter.

Seizures may be a part of the CNS manifestation of several connective tissue diseases and vasculitides. Seizures occur in 10 to 40% of patients with neurological involvement of systemic lupus erythematosus (SLE). In 20 to 30% of patients, seizures are the first CNS symptom of SLE. In most cases seizures are acute and symptomatic, and often related to stroke [2]. The antiphospholipid syndrome (APS) is an autoimmune disorder characterized by arterial and/or venous thrombosis, recurrent foetal loss, thrombocytopoenia, and elevated levels of antiphospholipid antibodies (aPL). APS may be seen in patients with SLE, but APS may also appear as a primary disorder. Patients with primary APS reportedly have an increased prevalence of epilepsy [3]. Seizures may also occur in patients with polyarteritis nodosa, Wegener's granulomatosis and Sjögren's syndrome [4].

In many cases, seizures associated with inflammatory diseases occur during an acute CNS insult or metabolic derangement. However, also spontaneous recurring seizures occur after the acute flare of the inflammatory disorder. In summary, epileptic seizures are a common, and a clinically significant manifestation of inflammatory diseases affecting the brain.

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Monday 22 September 2008
07:30 – 09:00
Hall 2b
EUREPA Teaching Session
Childhood absence seizures, epilepsies, syndromes

PATHOPHYSIOLOGY OF HUMAN ABSENCE EPILEPSY

S. L. (Nico) Moshe
Albert Einstein College of Medicine of Yeshiva University, Bronx – New York, NY, USA

The pathophysiology of absence seizures remain a challenging topic. The available experimental data support the notion of a trigger zone within the thalamocortical system with a particular genetically determined epileptogenic susceptibility. During absence seizures, the trigger area becomes a part of the oscillating network, which constitutes an emerging property of the whole system. Whether there may be a discrete cortical focus initiating this process remains controversial. The data that have been accrued over the years have originated either from acute studies using the penicillin model or from two rodent models of absences – the Genetic Absence Epilepsy Rat from Strasbourg (GAERS) and the Wistar Albino Glaxo Rats from Rijswik (WAG/Rij). Studies in the two latter models suggest that the other regions of the brain that have a significant input to the thalamus or cortex and can influence or cause the system to generate a seizure. Whether this is the case in human absence epilepsy is unclear. There is a high degree of probability that even childhood absence epilepsy may be a heterogeneous condition. This is best seen when the ictal EEG discharges are analyzed. Indeed, Sogawa et al. have recently analyzed unprovoked ictal spike-wave discharges during wakefulness in 103 children between 3–12 years of age with documented childhood absence epilepsy. The results indicate that the 3Hz spike-wave discharges are not stereotyped. As an analogy to be the music form of sonata, 3Hz spike-wave discharges can be subdivided into multiple components. The existence and distribution of a particular component may reflect genetic variability and may predict response to specific treatments and outcome.

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CLINICAL VARIABILITY OF ABSENCE SEIZURES/ SYNDROMES IN CHILDHOOD AND ADOLESCENCE

A. Covanis
The Children Hospital Agia Sophia, Athens, Greece

GENETICS OF ABSENCE SEIZURES

D. Pinto
The Hospital For Sick Children, Toronto, ON, Canada

Monday 22 September 2008
07:30 – 09:00
Hall 5
EUREPA Teaching Session
Adult patients with epileptic encephalopathies of childhood

DRAVET SYNDROME BEYOND CHILDHOOD

C. Dravet
Marseille, France

THE LENNOX-GASTAUT SYNDROME PATIENT AS AN ADULT

M. Nikanorova
Danish Epilepsy Centre, Dianalund, Denmark

Lennox-Gastaut syndrome (LGS) is the severe epileptic encephalopathy of childhood, characterized by multiple seizure types,slow spike-waves on the EEG during wakefulness and bursts of fast rhythms during sleep, mental retardation and seizure intractability. LGS might be difficult to differentiate from myoclonic-astatic epilepsy and frontal lobe epilepsy with secondary bilateral synchrony. LGS is often overdiagnosed due to the concept that mental retardation and slow spike-waves are synonymous with it. The overall prognosis is considered to be unfavourable. Remission occurs only in cryptogenic cases, in not more than 7% of patients. Mortality rate in LGS is around 3–7%, and many deaths are related to accidents. In most of the cases epilepsy has a chronical course. Only 33–47% of patients maintain a complete LGS profile in adulthood, while in rest the evolution of seizure semiology and EEG-findings occurs. Tonic axial seizures and falls persist in the majority of cases, while atypical absences and myoclonic seizures may subside. Slow spike-waves are often transient and focal discharges are frequently seen over time. Thus, up to 33% of cryptogenic and 55% of symptomatic cases loose the characteristics of LGS and evolve into nonspecific generalized symptomatic epilepsies, severe epilepsy with multiple independent spike foci or localization-related epilepsies.

THE RASMUSSEN SYNDROME: A LONG-TERM PERSPECTIVE

C. Bien
University of Bonn, Bonn, Germany

Rasmussen syndrome (RS) is a chronic-progressive disorder mainly starting in childhood. The natural history of the condition has been delineated as follows: A ''prodromal period'' may last for up to several years, but is not an obligatory feature. If it occurs it is characterized by relatively minor signs and symptoms like mild hemiparesis or infrequent seizures. Thereafter, or, as the initial disease manifestation, the patient enters the ''acute stage'': He or she starts experiencing frequent intractable unilateral simple partial focal motor seizures, complex partial seizures or secondarily generalized seizures. During the disease course, particularly if inflammation spreads across the affected hemisphere, other seizure semiologies indicating newly recruited epileptogenic areas are frequently observed. Epilepsia partialis continua is observed in approximately 50% of the patients. Within a few months of the manifestation of epilepsy, progressive loss of neurological function associated with one hemisphere starts comes about, typically in the form of hemiparesis, hemianopia, cognitive deterioration and (if the dominant side is affected) aphasia. After on avarage 8–12 months, the main decline is over, and the patient passes into the ''residual stage'' with a stable neurological deficit. At this point seizure frequency is still high but lower compared with the ''acute stage''. In recent years, immunotherapy of patients diagnosed during the acute disease stage has been frequently used. Whereas positive effects on the neurological outcome have been documented, the seizures remain notoriously difficult to control. Hemispherectomy is highly effective for seizure control but only at the price of severe neurological impairments. It remains to be determined which patients on the long run profit most from immunotherapy (with better preservation of neurological functions) and which from hemispherectomy (with its high proportion of seizure-free patients). First experiences on long-term outcomes are presented.

Monday 22 September 2008
07:30 – 09:00
Hall 7
EUREPA Teaching Session
Pharmacogenomics: Its place in the clinical management of epilepsy

PHARMACOGENOMICS: HAS IT CHANGED CLINICAL PRACTICE IN OTHER FIELDS?

M. Pirmohamed
The University of Liverpool, Liverpool, UK

PHARMACOGENOMICS: WHY CONSIDER IT IN EPILEPSY?

N. Delanty
Royal College of Surgeons of Ireland And Beaumont Hospital, Dublin, Ireland

PHARMACOGENOMICS: HOW MIGHT IT INTEGRATE INTO PATIENT MANAGEMENT IN EPILEPSY?

M. Baulac
Hôpital Pitié-Salpêtrière, Paris, France

Monday 22 September 2008
07:30 – 09:00
Hall 9
EUREPA Teaching Session
How to get the most of your imaging – a workshop

HOW TO MAKE THE MOST OF YOUR MRI

H. Huppertz
Schweizerisches Epilepsiezentrum, Zurich, Switzerland

Cortical malformations are increasingly recognized as underlying cause of formerly cryptogenic focal epilepsy. In subtle cases, however, their diagnosis in MRI remains difficult. Three methods for postprocessing of MRI are presented which may improve lesion detection by enhancing image properties not readily accessible by visual analysis of conventional MRI. In morphometric MRI analysis a T_1-weighted volume data set is normalized and segmented. The distribution of gray and white matter is analyzed on a voxelwise basis and compared with a normal database. Based on this analysis, new feature maps are created which characterize three different signs of focal cortical dysplasia, i.e. abnormal thickness of the cortical ribbon, abnormal extension of gray matter into the white matter, and blurring of the gray-white matter junction. Curvilinear reformatting of 3D MRI data is a well-established tool to create and display serial convex planes parallel to the cortical surface. In contrast to the classical method requiring manual input, a novel operator-independent method for automatic curvilinear reformatting makes use of a set of predefined masks in order to remove the skull and outer regions of the brain step by step in layers of 2 mm thickness parallel to the brain surface. The serial convex planes enclosing the residual inner part of the brain are presented 3-dimensionally by volume rendering. The technique helps to visualize the gyral structure and the precise localization and extent of lesions and to identify subtle abnormalities difficult to detect in planar MRI slices. Skullstripping and volume rendering of the extracted brain (e.g., by use of MRIcro) is a simple and quick method for allowing a 3-dimensional view on the surface of the brain. This can help to detect abnormalities of the sulcal structure associated with cortical malformations.

PITFALLS IN PET IMAGING

A. Hammers
Imperial College London, London, UK

PET can be a very useful tool in the evaluation of patients with refractory focal epilepsy to determine whether they may be surgical candidates. This is particularly true when the mainstay of imaging in epilepsy, namely MRI, fails to demonstrate an abnormality. Several established PET tracers (e.g. flumazenil for visualizing GABAA receptor binding) and more recent tracers (e.g. MPPF or WAY100635 for visualising 5-HT1A receptor binding) can be useful, but clinical PET in most centres equates to FDG-PET. Thanks to the success of oncological imaging, it is expected that most centres will have or develop the capacity to obtain brain FDG PET in the future. In this part of the workshop, I will discuss prerequisites for clinical FDG PET imaging and present practical examples of successful and misleading visual and statistical data analysis. We will review the importance of the amount of activity injected and the timing of image acquisition. In terms of image artifacts, we will discuss practical examples of artifacts as they appear on images for visual analysis, and examples of artifacts when images are analyzed on a voxel-by-voxel basis, e.g. with Statistical Parametric Mapping (SPM). We will also discuss strategies to detect these artifacts, and finally possibilities of correcting them.

HOW TO DO SPECT

P. Dupont
Medical Imaging Center and Department of Nuclear Medicine, Leuven, Belgium

Many techniques are used to study different aspects of the brain of epileptic patients. In the presurgical work-up of a patient, it is essential to combine the structural and functional information derived from different modalities. One such modality is SPECT which is used to measure ictal and interictal cerebral perfusion. The SPECT perfusion tracers are trapped in the brain after the first pass. As a result, the tracer uptake and distribution, which are proportional to regional cerebral perfusion at the time of injection, remain unchanged for a few hours, independent of perfusion variations occurring after the fixation time. This gives a unique possibility for ictal imaging. To obtain the best sensitivity in detecting the epileptic zone, an interictal image is needed as well. This interictal image is acquired on a different day and in standardized conditions. To exclude differences between the ictal and interictal images which might be due to differences in generating both images, it is important to use the same camera, settings, reconstruction method and parameters. State-of-the-art acquisition has to be performed and the principles and recommendations will be discussed. The state-of-the-art analysis for perfusion SPECT in epilepsy is SISCOM (subtraction ictal SPECT coregistered on MRI) but also alternatives will be explained. For each analysis technique, we will highlight the pro and cons and we will show that it is essential to interpret the SPECT results in the context of the presurgical evaluation of a patient. Finally, a number of pitfalls of ictal/interictal perfusion SPECT will be shown. These include pitfalls related to technical issues and those having a more biological origin. Using optimal imaging strategies, it is possible to avoid these pitfalls.

PITFALLS IN fMRI IMAGING

M. Koepp
University College London, London, UK

There is sparse evidence-based data on clinical fMRI applications and accordant decision making. By assessing the functional impact and by clarifying the topographic relation of the pathology to eloquent brain areas, fMRI may be used to establish if surgery is appropriate for a given patient, and which specific risks will be associated with the surgery. Specific strategies and pitfalls of analyzing and interpreting diagnostic fMRI studies in individual patients will be highlighted in this session in relation to: 1. Data acquisition: fMRI primarily employs echo-planar imaging (EPI) techniques sensitive to the BOLD contrast. EPI is not particularly suited to recognize intracranial pathologies. T_2*-weighted EPI exhibits susceptibility artifacts and distortions, which increase the higher the field strengths of the MR scanner. Stimulus- or task-correlated motion can induce spurious activations. Unwarping geometric EPI distortions potentially improves registration and spatial accuracy of BOLD-fMRI. 2. Paradigm Design Sensory, cognitive or motor impairments or limited compliance often require individual adjustments to the fMRI paradigms. Rendering paradigm design optimal for an individual impedes standardization of clinical fMRI. In diagnostic fMRI, block designs prevail over event-related paradigms due to their efficiency. Instead of using uncontrolled ''resting'' states as the baseline for fMRI paradigms, a well-characterized active control condition that engages the patient in a task other than the task of- interest is usually a better choice 3. Data analysis For clinical decisions it is the predictive value of fMRI results that ultimately matters. This depends on the prevalence of true-positives vs. true-negatives within the sample tested. Positive predictive values are prevalence-conditioned, i.e., every test increasing the likelihood of positives within the sample will enhance the predictive value of affirmative fMRI exams. In clinical practice, however, it is often patients in whom other tests fail, yield inconclusive results, or cannot be conducted where diagnostic fMRI applications are pursued.

Monday 22 September 2008
09:00 – 11:00
Hall 1
Chairs' Symposium
Epilepsy as a disease and as a model

INTRODUCTORY REMARKS: EPILEPSY FROM BENCH TO BEDSIDE

C. Elger
Klinik Fuer Epileptologie, Bonn, Germany

Epilepsy is not a real disease but rather a state of the brain resulting in repeated seizures on a chronic basis. Therefore, it is not surprising that the models of epilepsy are numerous. However, the high number of epilepsy models must lead to the concept that epileptic seizures are rather unspecific and therefore, not suitable for investigating the basics of epilepsy in humans. When examining epilepsy as a disease, one must identify a certain syndrome, look for parallelities in adequate experimental models and then perhaps use it as a model to explain human problems. However, if the way back to the human disease is not undertaken, the results will stay on the level of an experimental epilepsy in a certain animal model. Modern epilepsy surgery has generated the unique chance to investigate human slices of the hippocampus down to the very basic processes and to compare these to animal models mimicking temporal lobe epilepsy of humans, at least based on the histology. From there, new and exciting data can be generated to explain the development of epileptogenicity in this type of epilepsy. However, the consequences for humans can not be determined at this moment. Besides investigations concerning epileptic data, one of the major comorbidities of temporal lobe epilepsy are memory deficits which can be investigated in humans to the fact that intercerebral recordings are undertaken in a portion of the patients. Our knowledge of the basic processes and the general aspects of human declarative memory has grown considerably on the basis of data derived from intercerebral recordings and epilepsy surgical procedures.

LOW-THRESHOLD CURRENTS AND INTRINSIC NEURONAL EXCITABILITY IN A MODEL OF TEMPORAL LOBE EPILEPSY

Y. Yaari
Hebrew University School of Medicine, Jerusalem, Israel

No Abstract Received.

THE YING AND YANG OF THE THALAMUS: SENSORY SIGNAL TRANSFER AND ABSENCE SEIZURES

H. Pape
Institute of Physiology I, Westfalische Wilhelms University Munster, Munster, Germany

Childhood absence epilepsy is characterized by sudden onset and offset episodes of bilaterally generalized spike-and-wave discharges (SWDs) in the thalamocortical system associated with a loss of consciousness. The SWDs most likely develop from naturally occurring rhythmic forms of network activities, and neurons in the thalamus make a most important contribution to these rhythms. This contribution is based on a dual mode of activity of thalamic neurons during different functional state of the brain. During periods of wakefulness and increased arousal, thalamic neurons generate tonic series of action potentials, thereby enabling the faithful transfer of incoming sensory signals from the periphery (eye, ear, skin…) to the cerebral cortex for final information processing. During periods of sleep, the same thalamic neurons generate burst discharges in a rhythmic-oscillatory fashion, which are synchronized in the thalamocortical network, are represented on the electroencephalogram as rhythmic slow sleep waves, and explain the dramatic reduction in sensory responsiveness of the brain during these states. Alterations of these mechanisms, in turn, can lead to SWDs characterizing absence seizures. Research over the last two decades progressed along two lines. Along

one line, candidate genes of absence epilepsy have been identified. Along a second, complementary line in genetic experimental models of human absence epilepsy, specific molecular, neuronal and synaptic mechanisms have been characterized which contribute to seizure generation and epileptogenesis in the thalamus. In a most simplified representation, these mechanisms interfere with the dual mode of thalamic neuronal activity (the ''yin and yang'') in that they prevent tonic activity and foster states of hyper-synchronized, rhythmic excitations and inhibitions in the synaptic network of the thalamus.

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MEMORIES AND EMOTIONS: MAPPING THE BRAIN WITH EEG

P. Chauvel
Hopital De La Timone, Marseille, France

No Abstract Received.

PROBING DEEP INTO THE CORTEX: BRAIN SRUCTURES GENERATING SEIZURES

P. Kahane
Grenoble University Hospital, Grenoble, France

No Abstract Received.

DESIGNING NEW AEDs: FROM BENCH AND ANIMAL MODELS TO BENEFITS IN REFRACTORY EPILEPSY

M. Bialer
The Hebrew University, Jerusalem, Israel

The new antiepileptic drugs (AEDs) currently in development can be divided into two categories: (1) drugs with completely new chemical structures such as ganaxolone, perampanel and retigabine, or the recently approved AEDs rufinamide (Inovelon) and lacosamide (Vimpat); (2) drugs that are derivatives of existing AEDs that can be regarded as second-generation or follow-up compounds of established AEDs. The following are second generation AEDs: eslicarbazepine acetate (Zebinex) (carbamazepine derivative or prodrug to oxcarbazepine active entity S-licarbazepine); valrocemide, valnoctamide and propylisopropylacetamide or PID (valproic acid derivatives); XP13512 (gabapentin prodrug) and brivaracetam (levetiracetam derivative). For any of these follow-up compounds to become successful, it must be superior to the first generation AED (most likely to become a generic product when the new AED is approved) and circumvent some of the side effects associated with its therapy. The development of new AEDs has been based on the utilization of animal models that were introduced with the discovery of phenytoin in 1938. Models with a similarly high predictive value do not exist in other CNS areas, such as migraine or bipolar disorder. Although there are a large number of models that could be utilized to screen for anticonvulsant activity, the maximal electroshock (MES) and subcutaneous metrazole (scMet) models remain the 'gold standard' in early stages of testing. Compounds active in either the MES or scMet models have generally been efficacious in clinical trials. The new AEDs discovered through the empirical approach of animal models have been more successful than the new AEDs discovered by a mechanism-based design (e.g. vigabatrin and tiagabine). The approach used so far for the discovery of new AEDs has advantages and disadvantages. The advantages are: (1) the use of easy models in intact rodents which detect anticonvulsant effects, regardless of the mechanisms of action involved; (2) the applicability of MES and scMet models to high-throughput screening, as demonstrated by the NIH Anticonvulsant Screening Program; (3) the possibility of using these models to assess pharmacokinetic/pharmacodynamic relationships which are valuable to guide human studies. Disadvantages are: (1) the notion that conventional models are likely to identify more of the 'same' new AEDs, e.g. drugs which share characteristics comparable to existing agents are unlikely to have a major impact on refractory epilepsies; (2) due to the heterogeneity of seizure disorders in humans, it is unlikely that a few animal models will predict the full therapeutic potential of a drug candidate; (3) anticonvulsant animal models are unlikely to predict human tolerability, an important consideration because in the clinical setting a high degree of efficacy may be prevented by dose-limiting adverse effects. One innovative approach to overcome the first disadvantage is to utilize animal models that display a phenotype consistent with pharmacoresistance, such as the phenytoin-resistant kindled rat, the lamotrigine-resistant kindled rat, and the 6-Hz psychomotor seizure model. A new AED can be successful if at least one of the following criteria are met: (1) greater effectiveness in refractory epilepsies; (2) ability to prevent or delay the onset of epilepsy (epileptogenesis); (3) usefulness in other nonepileptic CNS disorders and preferably superiority over existing drugs; (4) fewer adverse effects; e) improved ease of use (rapid titration, linear pharmacokinetics, lack of drug interactions and longer half-life). If a new drug candidate meets item '3' in the above criteria, there is a greater economic incentive for its development, as shown by the commercial success of those AEDs which are approved for other indications such as migraine prophylaxis (valproic acid, topiramate), neuropathic pain (gabapentin and pregabalin), and bipolar disorder (valproic acid, lamotrigine).

Monday 22 September 2008
14:30 – 16:00
Hall 1
Discussion Group
Analysis of brain function with antiepileptic drugs and therapeutic monitoring

BRAIN FUNCTION AND AED IN ANIMALS

H. Kubova
Academy of Sciences of the Czech Republic, Praha 4 – Krc, Czech Republic

Brain functions and AED in animals. Hana Kubova, Department of Developmental Epileptology, Institute of Physiology, Academy of Sciences of the Czech Republic, Prague, Czech Republic Routine testing of effects of AEDs involves the assessment of anticonvulsive activity in various models of chemically or electrically provoked epileptic seizures and search for important side effects like sedation, cognitive or motor impairment. Tests are usually performed using naïve adult animals exposed only to a single dose of tested drug. Thus possible changes of efficacy or severity of side effects with time of treatment are not studied and they can be overlooked in experimental studies. In spite of the fact that AEDs are frequently used in children, studies in immature experimental animals are rare. Some of these studies however suggest both quantitative and qualitative differences in sensitivity to the AEDs effects in various seizure models or behavioral tests between mature and immature brain. In addition, recent studies demonstrate that administration of some AEDs (phenobarbital, phenytoin, valproate, vigabatrine and benzodiazepines) can increase apoptosis in various brain structures, whereas administration of others (lamotrigine, levetiracetam or topiramate) does not affect programmed cell death. These studies suggest that even short exposure to certain AEDs during early development may lead to transient or permanent changes of brain functions. There is limited number of studies searching for long-term consequences of early exposure to AEDs on various behavioral parameters, but some changes of social and emotional behavior or cognitive functions were demonstrated in animals exposed to benzodiazepines or barbiturates early during postnatal development. The main principle of AEDs effects is alteration of brain excitability, thus exposure to AEDs may lead to transient or permanent changes of this parameter. Possible changes of brain excitability due to AEDs administration on seizure thresholds remains to be studied in details, but results of preliminary experiments indicate possible very selective long-term effects. Taken together, brain functions can be affected not only acutely when AEDs are still present in the organism. At least some AEDs can interfere with normal development and lead to alteration of various brain functions long-term after discontinuation of treatment.

MECHANISMS OF ACTION DETECTED BY TRANSCRANIAL MAGNETIC STIMULATION

W. Paulus
University Clinic Goettingen, Gottingen, Germany

No Abstract Received.

QUANTIFICATION OF EPILEPTOGENICITY IN HUMANS

H. Stefan
Epilepsy Centre, University Hospital Erlangen, Erlangen, Germany

Purpose: Quantification of epileptic activity often poses problems because the events are transcient and in addition to ictal clinical manifestations like seizures or status epilepticus. Interictal or ictaform epileptic activity can occur. Epileptic seizures recognized by subjective report of the patients often are missed. In different studies comparing the subjective report and objective EEG documentation 40 – 50% of the seizures occurring were missed by the patients' reports.

Method: In addition to the improvement of localizations of epileptic activity, also the quantification or the amount of epileptic activity is cutted out. Long-term EEG or video EEEG recordings are performed. Not only to improve the diagnostic yield, but also for therapeutic monitoring of epileptic activity during the course of treatment.

Results: Findings of objective documentation of epileptic seizure activity before and during treatment are demonstrated.

Conclusion: Objective documentation of seizure activity enables to prove the temporal onset of efficacy as well as of the superiority of new treatment approaches. This not only holds true for acute trials in clinical phase II or III studies, but is also of interest for monitoring in critically ill patients during status epilepticus.

Statement: The corresponding author and all coauthors confirm that the procedures were approved by the ethical standards of our institutional ethics committee and that patients' consent has been received to perform these investigations.

NEUROPSYCHOLOGICAL CHANGES DURING ANTIEPILEPTIC DRUG TREATMENT

A. Aldenkamp
Epilepsy Centre Kempenhaegh & Department Of Neurology, Heeze, The Netherlands

No Abstract Received.

Monday 22 September 2008
14:30 – 16:00
Hall 2b
Discussion Group
Structure modifications to improve antiepileptic drugs (AEDs) risk/benefit ratio

STRUCTURE-ACTIVITY RELATIONSHIPS (SAR) FOR AEDs

H. S. White
University of Utah, Salt Lake City, Utah, USA

No Abstract Received.

STRATEGIES FOR STRUCTURE MODIFICATIONS: CANDIDATE COMPOUNDS, RATIONALE, PREPARATION AND SCREENING

H. Klitgaard
UCB Pharma Scetor, Braine-L'Alleud, Belgium

Random screening of new chemical entities and structural variation of existing AEDs has been highly productive by identifying most of the classical AEDs and several derivatives of these – notably valproate and carbamazepine – with improved pharmacokinetic or safety profiles. These approaches have also contributed a Rational drug discovery was initially introduced to target mechanisms enhancing GABAergic or reducing glutamatergic neurotransmission. This resulted in the discovery of the GABA-elevating AEDs vigabatrin and tiagabine as well as a number of candidate AEDs antagonising the ionotropic glutamate receptors, NMDA and AMPA. More recently rational drug discovery has been applied successfully to optimise selectivity and affinity of new chemical entities towards novel targets identified by the antiepileptic mechanism of existing AEDs. Significant drug discovery efforts have been devoted to the ?2? protein, KCNQ2/3 potassium channels and the synaptic vesicle protein 2A (SV2A). These novel targets were identified from the antiepileptic mechanisms of gabapentin, retigabine and levetiracetam, respectively. Regarding the latter, more than 12,000 compounds were screened for their affinity for SV2A. This led to the identification of seletracetam and brivaracetam, both with 10-fold greater affinity than levetiracetam for the synaptic vesicle protein 2A.

Brivaracetam is in late clinical development based upon results showing that it confers a more potent and complete seizure suppression than levetiracetam in various animal models of seizures and epilepsy. Recent phase II clinical trials demonstrated that brivaracetam produced a significant, dose-dependent reduction in the frequency of seizures in adults with refractory, partial seizures. Remarkably, brivaracetam had an adverse effect profile undistinguishable from placebo. These results highlight that structure variation of existing AEDs has proven a productive approach for the generation of new AED candidates with improved risk/benefit ratios.

IMPROVING PHARMACOKINETICS AND SAFETY THROUGH STRUCTURAL MODIFICATIONS: LESSONS FROM VALPROIC ACID DERIVATIVES

M. Bialer
The Hebrew University, Jerusalem, Israel

Valproic acid (VPA) is one of the four first line antiepileptic drugs (AEDs). Although in animal models VPA is the least potent of the major AEDs, it has been established as an effective drug over the complete range of seizure types and is therefore a broad-spectrum anticonvulsant. VPA is also an effective (and FDA-approved) drug in migraine prophylaxis and in treatment of bipolar disorders. Two VPA amide derivatives, valrocemide and valnoctamide (racemate), are currently in phase II clinical trials for epilepsy and bipolar disorder, respectively. A VPA homologue (arundic acid or ONO-2506) is currently under clinical development for potential treatment of Alzheimer's and Parkinson's diseases. The use of VPA is limited by its two rare but potentially life-threatening side effects: teratogenicity and hepatotoxicity. While VPA's teratogenicity is associated with the parent compound, primarily due to its carboxylic acid moiety, its hepatotoxicity results from biotransformation into hepatotoxic metabolites with a terminal double bond, specifically 4-ene-VPA and 2,4-diene-VPA. Consequently, there is an incentive to develop a second generation VPA that possesses the following characteristics: (1) broad-spectrum anticonvulsant; (2) better potency than VPA in epilepsy and other CNS disorders; (3) lack of teratogenicity and hepatotoxicity; e) lack of weight gain. These characteristics will endow such a VPA derivative a promising potential to become a second generation to VPA drug. Following a series of structure-pharmacokinetic-pharmacodynamic relationship studies of VPA, we developed aliphatic and cyclopropyl VPA amide analogues and derivatives, designed to retain or enhance

anticonvulsant and CNS-activity in the treatment of neuropathic pain and bipolar disorder, while avoiding its teratogenicity and hepatotoxicity. From a pharmacokinetic standpoint amides are superior to esters due to their better metabolic stability and the higher likelihood that they will work as drugs on their own rather than prodrug to their corresponding acids. A metabolically stable amide derivative of VPA cannot form an acyl-CoA that is the first step in the formation of a recitative metabolite 2,4-diene-VPA that has been associated with VPA-induced hepatotoxicity. The leading aliphatic VPA amide derivatives that emerged from our studies were valproyl glycinamide or valrocemide and the enantiomers of propylisopropylacetamide (PID) (R)-PID and (S)-PID. These compounds were more potent than VPA in a wide range of anticonvulsant animal models as well as animal models for neuropathic pain and were nonteratogenic in a mouse model for VPA-associated teratogenicity. Unlike VPA, the cyclopropyl amide analogues of VPA: 2,2,3,3-tetramethylcyclopropanecarboxamide (TMCD), N-methyl-TMCD (MTMCD) and 2,2,3,3-tetramethylcyclopropanecarbonyl urea (TMC-Urea), possess two quaternary carbons in the ?-positions to the carbonyl and hence cannot be biotransformed into hepatotoxic metabolites with a terminal double bond. MTMCD and TMC-Urea were found to be broad-spectrum anticonvulsants. Furthermore they are nonteratogenic and most probably nonhepatotoxic. TMC-Urea was the most promising anticonvulsant compound with a protective index (PI=TD50/ED50) of 18.5 in the maximal electroshock (MES) test, compared to 1.6 for VPA. TMCD, MTMCD and TMC-Urea also possess an antiallodynic activity in a rat model of neuropathic pain and are 2 and 7 times more potent than VPA. Furthermore MTMCD is equipotent to VPA and lithium in various models for bipolar disorder. In conclusion, valrocemide, PID enantiomers, MTMCD and TMC-Urea are CNS-active amide derivatives of VPA that re more potent than VPA, due to their lipophilicity, better brain permeability and metabolic stability. The broad spectrum and potent anticonvulsant and CNS activity, along with their lack of teratogenicity (animal models) high safety margin and favourable pharmacokinetic profile, make these compounds attractive candidates to become new, potent and safe antiepileptics and CNS drugs.

STRUCTURAL AED ANALOGUES IN CLINICAL DEVELOPMENT: AN OVERVIEW

E. Perucca
University of Pavia, Pavia, Italy

Historically, structural modification of existing drugs has led to important therapeutic advances by allowing identification of novel compounds with improved pharmacokinetic and/or pharmacodynamic profile. In epilepsy, this drug discovery strategy has been applied repeatedly with considerable success since the introduction of phenytoin in 1938, and is being further pursued in modern times by taking advantage of advanced high throughput techniques and large-scale screening. Structural analogues of existing antiepileptic drugs which are currently in clinical development include: (1) brivaracetam, a pyrrolidone derivative which binds to synaptic vesicle protein type 2A (SV2A) with greater potency compared with levetiracetam, and is also endowed of weak sodium channel blocking activity; (2) seletracetam, another levetiracetam analogue which shows even greater affinity than brivaracetam as a SV2A ligand; (3) eslicarbazepine acetate, a third generation derivative of carbamazepine which behaves as a prodrug of eslicarbazepine (the S-enantiomer of the monohydroxyderivative of oxcarbazepine); (4) fluorofelbamate, a felbamate derivative whose metabolic pathway has been found, in vitro, to avoid the production of the reactive metabolite thought to be responsible for the idiosyncratic toxicity of felbamate; (5) JZP-4, a lamotrigine analogue which shows greater potency and efficacy than lamotrigine in experimental models of refractory epilepsy, antidepressant activity and antimania activity; (6) valrocemide, a valproic acid derivative with a potentially improved safety profile and (7) T2000, a nonsedating barbiturate endowed with anticonvulsant activity but being developed primarily in essential tremor. The rationale for the development of these compounds, and the pharmacological and clinical data obtained to date will be critically reviewed.

Monday 22 September 2008
14:30 – 16:00
Hall 5
Discussion Group
Lesion versus epilepsy driven hemisphere dominance in epilepsy?

LANGUAGE DOMINANCE RELATED TO EPILEPTIFORM ACTIVITY

F. Wormann
Bethel Epilepsy Centre, Bielefeld, Germany

Left temporal lobe seizures cause ictal and postictal speech disturbances in 75% of patients, suggesting that seizures are capable to disturb speech production at least transiently. It has been shown that series of seizures affected language lateralization by fMRI. In acquired epileptic aphasia Landau-Kleffner, even interictal epileptiform activity propagating to the language areas may contribute to permanent speech disturbances. Epilepsy associated factors influencing language reorganization can be investigated in patients with mesial temporal lobe epilepsy and hippocampal sclerosis (HS). These patients have the same pathology in the same location – clearly outside eloquent cortical language areas in the lateral frontal and temporal lobes. We examined patients with mesial temporal lobe epilepsy and HS using Wada test or language fMRI (Janszky et al, 2003 + 2006). We found that atypical language lateralization occured in 25% of patients and was associated with higher frequency of left-sided interictal epileptiform activity and with seizures spreading to the left temporo-lateral region. In patients with focal epilepsy, not only the known factors, i.e. the age at which some brain injury occurred and the localization of the lesion within the vicinity of eloquent cortex, but also the epileptic activity itself – interictal discharges and seizure spread – may influence language reorganization. Our findings suggest that not only structural elements but also functional factors do affect language organization. We hypothesise that under constant functional disturbances such as chronic epileptic activity, language representation can shift gradually from the left to right hemisphere – often without serious permanent aphasic symptoms.

References

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Janszky J, Mertens M, Janszky I, Ebner A, Woermann FG. Left sided inter-ictal epileptic activity induces shift of language lateralization in temporal lobe epilepsy – an fMRI study. Epilepsia 2006;47:921–927.

LANGUAGE fMRI AND TRACTOGRAPHY PRE- AND POSTSURGERY: EVIDENCE FOR STRUCTURAL AND FUNCTIONAL PLASTICITY

S. Bonelli
UCL Institute of Neurology, London, UK

Purpose: Patients with temporal lobe epilepsy (TLE) often present with impaired cognitive functions in particular language and memory function. Anterior temporal lobe resections (ATLR) benefit up to 70% of patients with intractable TLE but may be complicated by neuropsychological deficits such as naming difficulties following epilepsy surgery in the dominant hemisphere. Functional reorganisation can occur within unaffected ipsilateral brain regions or to the contralateral hemisphere. We investigated language function in patients with TLE using fMRI and tractography before and after surgery to detect evidence for structural and functional plasticity.

Methods: To date we scanned 25 patients with left TLE due to HS on a 3T GE-MRI scanner. All subjects performed fMRI language

paradigms including verbal fluency, verb generation and a reading task and MR tractography preoperatively and 4 months following surgery. All patients underwent standard neuropsychological testing pre- and postoperatively.

Results: FMRI analysis revealed significant left hippocampal fMRI activation for verbal fluency being correlated with better preoperative naming scores. Greater lateralization of fMRI activation to the dominant hemisphere was associated with greater decline in naming function, whilst greater preoperative fMRI activation in the nondominant hemisphere correlated with better postoperative naming outcome. Postoperatively, greater fMRI activation for verbal fluency in the nondominant hemisphere was significantly correlated with greater postoperative naming scores. Using MR tractography we demonstrated that greater lateralization of tracts to the dominant hemisphere was significantly correlated with greater naming deficits following surgery.

Conclusion: Both, language fMRI and tractography predict language deficits in patients undergoing ATLR in the dominant hemisphere. Furthermore, our findings provide evidence for effective reorganisation of language function to the contralateral hemisphere.

STABILITY OF LANGUAGE DOMINANCE PATTERNS FROM BEFORE TO AFTER SURGERY

W. Alpherts
Sein, Heemstede, The Netherlands

No Abstract Received.

POSTOPERATIVE RESHIFT OF RIGHT INTO LEFT HEMISPHERE LANGUAGE DOMINANCE

N. Fritz
University of Bonn, Bonn, Germany

The known influence of epileptic activity on functional organization of the brain raises the important question of change in language dominance after successful epilepsy surgery. Apart from general insights in plasticity of the brain, research in this field may affect prognosis of postoperative memory outcome in that a preoperative atypical language and memory dominance indicated by a ''crowding effect'' (marked nonverbal memory deficits, relatively preserved verbal and language performance) may not protect from postoperative verbal memory loss. This hypothesis was supported by the findings in three women with left temporal lobe epilepsy and a preoperative neuropsychological pattern characteristic for interhemispheric language transfer (''crowding effect''). After left-sided surgery they showed a recovery on nonverbval memory functions that exceeded a normal release of contralateral functions due to seizure control or retest effects (Gleissner et al., 2002). When investigating a larger group with left-sided temporal lobe epilepsy which also included men, Helmstaedter and colleagues (2004) found that right-sided dominant patients had better postoperative verbal memory outcome than patients with bilateral or left language dominance who showed significant memory loss. In patients with atypical language dominance, figural memory improved postoperatively only in women, while deteriorating in men. No relation to seizure outcome was found. A comparison of pre- and postoperative language dominance assessed by means of language fMRI was conducted in three patients with left temporal lobe epilepsy (Helmstaedter et al., 2006). In one patient, postoperative follow-up language fMRI indicated reversal of right into left dominance going along with unexpected losses in verbal memory performance. Overall, these findings suggest that postoperative plasticity of memory and language functions can be found in epilepsy patients and may depend on degree of preoperative language atypicality as well as gender and seizure outcome.

Monday 22 September 2008
14:30 – 16:00
Hall 6
Discussion Group
Pathophysiological role of GABAergic transmission in epilepsy

TONIC GABAERGIC INHIBITION IN EPILEPSY

M. Walter
Institute of Neurology UCL, London, UK

No Abstract Received.

GABAERGIC SYNCHRONIZATION AS A PROMOTER OF EPILEPTIFORM ACTIVITY

M. Avoli
La Sapienza University And The Montreal Institute, Montreal, Canada

GABA is the main inhibitory transmitter in the forebrain where it acts at both the ionotropic GABA type A and the metabotropic GABA type B receptors; GABA type A receptor activation is known to open channels that are permeable to Cl- and to a lesser extent bicarbonate. A homeostatic balance between excitatory and inhibitory mechanisms is essential for allowing meaningful information processing under physiological conditions. In addition, it is expected that interfering with GABA receptor-mediated inhibition causes the appearance of seizures. However, growing evidence indicates that GABA type A receptor-mediated conductances may also assist, support or shape epileptic hypersynchrony; these data have been obtained in vitro from rodent limbic structures such the entorhinal and perirhinal cortices or the amygadala, from the subiculum of patients presenting with temporal lobe epilepsy, and from the neocortex of epileptic patients with Taylor's type focal cortical dysplasia. These effects are presumably caused by (1) alterations in the KCC2 cotransporter leading to GABA type A receptor depolarizations due to the elevated internal Cl-; (2) glial and neuronal GABA type A receptor-dependent increases in extracellular K+ that directly depolarizes neighboring neurons; and (3) the ability of GABAergic cells to promote network oscillations at gamma frequencies. It should also be emphasized that in some of these experiments prolonged period of epileptiform synchrony that resemble electrographic seizures, are blocked either by preventing GABA release by activating ì-opioid receptors or by antagonists of the GABAA receptor. In conclusion, while blocking GABA receptor function consistently leads to neuronal hyperexcitability and short-lasting epileptiform events, data obtained from several in vitro models of epileptiform discharge indicate that GABA type A receptor-mediated mechanisms can also initiate and sustain ictal depolarizations.

PATHOPHYSIOLOGICAL ROLE OF CHLORIDE TRANSPORTERS IN EPILEPSY

K. Kaila
University of Helsinki, Department Of Biosciences, Helsinki, Finland

No Abstract Received.

GABA AND THE INITIATION OF ICTAL ACTIVITIES IN TISSUE FROM PATIENTS WITH TEMPORAL LOBE EPILEPSIES

R. Miles
INSERM EMI 224, CHU Pitié Salpêtrière, Paris, France

No Abstract Received.

Monday 22 September 2008
14:30 – 16:00
Hall 7
Discussion Group
How many immunomediated epileptic encephalopathies exist in children?

OVERVIEW OF CLINICAL ENTITIES

L. Fusco
Bambino Gesu Childrens Hospital, Rome, Italy

No Abstract Received.

IMMUNOLOGICAL MARKERS

D. Vincent
John Radcliffe Hospital, Oxford, UK

Immune mediated encephalopathies are beginning to be more widely recognized in adults, and to a certain extent in children. In adults, the best identified syndromes are the paraneoplastic conditions, associated with small cell lung cancers, ovarian, breast or other tumors. Most of these syndromes occur in middle-age and older individuals, as would be expected. They can involve the limbic system, brainstem, cerebellum or multiple levels of the CNS. Among younger patients, Ma2 antibodies are found in a form of limbic and hypothalamic encephalopathy with testicular tumors. And very recently, antibodies to NMDA receptors have been identified in young women with psychiatric or limbic presentations, dyskinesias, stupor often leading to coma. These patients usually have an ovarian teratoma. Both these conditions improve after removal of the tumor and immunotherapies to reduce the antibodies.

A nonparaneoplastic form of limbic encephalitis is associated with antibodies to voltage-gated potassium channels. These antibodies are also present in some patients with idiopathic epilepsy, with or without cognitive or other limbic defects. They tend to do very well with immunotherapies. They are almost always adults, and children with similar presentations have only rarely been found positive unfortunately.

Therefore, there are few antibodies identified so far in the majority of children with acute or subacute onset of encephalopathy. A few cases of NMDA receptor-antibody associated encephalopathies occur in young adults or children, and GluR3 antibodies may be present in some children with Rasmussen's encephalitis, although this is disputed. But the techniques available for measuring antibodies to different targets and identifying new antibodies are improving rapidly. There is an urgent need for the systematic study of childhood forms of encephalopathies.

DEVASTATING EPILEPTIC ENCEPHALOPATHIES

O. Dulac
Hopital Necker – Enfants Malades, Paris, France

No Abstract Received.

THERAPEUTIC PROSPECTIVES

C. Bien
University of Bonn, Bonn, Germany

The following inflammatory brain disorders without (apparent) infectious origin and typically associated with focal epileptic seizures have been delineated: Rasmussen encephalitis (RE), limbic encephalitis (LE), anti-*N*-methyl-D-aspartate-(NMDA-)receptor encephalitis, and steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT, formerly called ''Hashimoto encephalopathy''). All of these conditions occur in children and adults, however at very different ratios. In recent times, the process of diagnostic clarification has been the main focus of clinical research into these conditions. Treatment research has just begun. There is still no reliable evidence regarding the best possible therapies for these conditions. In this situation, recommendations can only be derived from case studies and from pathogenetic considerations. In RE, the paradigmatic epileptic immunopathy, there are data supporting a beneficial effect of early immunosuppressive and immunomodulatory interventions. For intractable seizures in RE patients with advanced disease, epilepsy surgery in the form of hemispherectomy in one of its modern variants is highly effective. Whereas for LE very little is known on effective means of treatment in childhood and adolescence, anti-NMDAR encephalitis and SREAT respond well to immunosuppression or immunomodulation. In anti-NMDAR encephalitis, ovarian teratomata need to be searched for because their removal seems to improve the outcome of affected patients (paraeneoplastic form of the condition).

Monday 22 September 2008
16:30 – 18:00
Hall 3

UCB SATELLITE SYMPOSIUM – RAISING EXPECTATIONS IN THE MANAGEMENT OF PARTIAL ONSET SEIZURES

G. Krauss, P. Patsalos†, and P. Ryvlin‡*
**Johns Hopkins University, Baltimore, USA; †Institute of Neurology, London, UK and ‡Hospices Civils de Lyon, Lyon, France*

Development of 'newer' AEDs is raising expectations in the management of partial-onset seizures. Monotherapy remains the treatment of choice for newly diagnosed epilepsy but the addition of a second AED may be considered after failure of one or two monotherapy drugs. Many of the 'newer' AEDs have unique mechanisms of action, suggesting that combinations of drugs with different mechanisms could have synergistic efficacy in controlling seizures. Reports of synergistic action of AEDs in animal models could have clinical relevance. However, there are no prospective, controlled studies reporting evidence of synergy in patients with epilepsy. The 'newer' AEDs are efficacious in patients who have failed 'older' AEDs and are generally better tolerated. 'Newer' AEDs have better pharmacokinetics with some closely approximating the ideal, characterized by good bioavailability, rapid achievement of steady-state plasma concentrations, linear and time-invariant kinetics and minimal protein binding. Adjunctive therapy with 'newer' AEDs may be facilitated by their low potential for drug-drug interactions and good CNS tolerability. Previous studies, mainly conducted with 'older' AEDs, have indicated that patients who do not respond to sequential monotherapy are unlikely to become seizure-free with polytherapy. However, recent clinical evidence has prompted a reevaluation of the role of combination therapy, suggesting that some patients may only become seizure free on a combination of two or three AEDs. The availability of expanded treatment options has made it possible to tailor the choice of therapy to specific patient populations. Further evidence-based guidance is required to inform clinicians on how and when to combine AEDs.

Monday 22 September 2008
18:30 – 20:00
Hall 3

EISAI SATELLITE SYMPOSIUM – WHAT TYPE OF DATA MAKES YOU PICK YOUR DRUG? AN EXPERT PANEL DISCUSSION

L. Sander, M. Baulac,† J. Cramer,‡ E. Trinka,§ and S. Wroe¶*
**Institute of Neurology, University College London, London, UK; †Pitié-Salpêtrière Hospital, APHP, Paris, France; ‡Yale University School of Medicine, New Haven, CT, USA; §University Hospital Innsbruck, Innsbruck, Austria, and ¶National Hospital for Neurology and Neurosurgery, London, UK*

What do you consider are the key factors that influence your prescribing decisions in epilepsy? There are often many different types of trials,

studies and data available to inform your decision; do you value one type above another when faced with such a wealth of evidence in the clinic? Are there different medical circumstances under which you perceive a particular type of evidence to have greater value? Do you make your decisions because you place more importance on one particular type of data or because the evidence available is more directly related to your individual patient? Randomized controlled trials are considered to be the gold standard for evidence in drug development, providing reliable information about efficacy and safety that allows the drug to be registered. Do the results of these trials reflect your everyday experience in clinical practice? Do they provide you with the information you need to advise your patient how they might respond over the long term? Alternatively, do you prefer to consider more naturalistic data gathered under less stringently controlled conditions over longer periods of time that could potentially provide a more representative view of drug utility? Or should greater emphasis be placed on the individual patient and the outcomes that affect quality of life? Alternative study designs may be less rigorous than randomized controlled trials but can deliver conclusions that might be more relevant and useful to everyday clinical practice postlaunch. Could a balanced interpretation based on the advantages and disadvantages of contrasting study designs help you in the decision-making process?

Tuesday 23 September 2008
07:30 – 09:00
Hall 2b
EUREPA Teaching Session
Pitfalls in Waking and Sleep EEG Diagnosis

UNUSUAL EEG ACTIVITIES IN WAKEFULNESS AND SLEEP

P. Gelisse
CHU Gui De Chouliac, Montepellier, France

This lecture covers the scope of the main features of unusual EEG wake and sleep activities in children and adults. The EEG must be a tool used to confirm clinical hypotheses. A patient should never be diagnosed as ''epileptic'' based merely on observation of spikes or similar abnormalities but in the absence of any semiological evidence. When in doubt, it is recommended to be cautious before attributing pathological significance to findings. During waking state, we will decribe alpha variants, posterior slow waves of youth, lambda waves, subclinical rhythmic electrographic discharges in adults, breach rhythm, hypersynchrony hyperventilation and photomyogenic response. During an EEG, patients can become drowsy or even fall asleep spontaneously and due to the close link between sleep and epilepsy, prolonged EEGs are often performed. It is therefore necessary to be knowledgeable about sleep patterns including hypnagogic hypersynchrony, frontal slow delta waves of drowsiness in elderly individuals, vertex waves, positive occipital sharp transients of sleep, post arousal hypersynchrony and frontal arousal rhythms in children. Unusual nonpathological activities observed in sleep are rhythmic temporal theta burst of drowsiness, benign sporadic sleep spikes, fourteen-and six Hz positive bursts, wicket spikes, six-hertz spike-and-wave bursts (phantom spike-and-wave bursts). Indeed, a more thorough knowledge of these elements is necessary so as not to misinterpreted them as pathological traits. But also, the presence of typical spikes or spike-waves does not necessarily indicate that a patient is epileptic. The clinical context is very important when interpreting an EEG.

PITFALLS IN ACTIVATION PROCEDURES

D. Kasteleijn Nolst Trenité
University La Sapienza, Rome, Italy

No Abstract Received.

PARTICULARITIES OF DEEP EEG RECORDINGS VERSUS SCALP EEG

A. Biraben
CHU De Rennes Hopital, Rennes, France

No Abstract Received.

Tuesday 23 September 2008
07:30 – 09:00
Hall 5
EUREPA Teaching Session
Limbic Circuitry, Emotions and Epilepsy. Structures Involved, Clinical Picture and Therapeutic Possibilities

LIMBIC STRUCTURES, EMOTIONS, AND EPILEPSY

F. Lopes da Silva
University Of Amsterdam, Amsterdam, The Netherlands

No Abstract Received.

SEMIOLOGY AND COGNITIVE ASSESSMENT OF SEIZURES WITH INTENSE EMOTIONAL COMPONENT

S. Meletti
University Of Modena And Reggio Emilia, Italy

In recent years the functional anatomy of brain networks involved in emotional processing has been the focus of many researches leading to considerable advances in our understanding of the mechanisms involved in both the expression and the perception of emotional signals. However, the majority of such studies concerned the way we judge and decode the emotions that are expressed from others. In other words, we have gathered considerable information on the brain networks engaged in the processing of facial and vocal signals that encode an emotion, such as fear or disgust. On the contrary, few studies have investigated the way we express our emotions, and the cerebral structures that are involved in the generation of facial, vocal, bodily, autonomic signals as well as the conscious feeling of experiencing an emotional state. Current knowledge on this is largely based upon the studies that used intra-cerebral electrical stimulation in man.

Here we analyze findings obtained from personal patients' populations that underwent long-term video-EEG monitoring and intra-cerebral electrical stimulation of the temporal lobe. We also take into analysis data from the published literature.

The aim of this presentation is to analyze emotional phenomena obtained in spontaneous seizures and by intracerebral electrical stimulation and to compare different anatomical, pathological, methodological variables that could potentially affect the probability to observe ictal emotions.

FUNCTIONAL AND STRUCTURAL APPROACH TO EMOTIONAL AND AUTONOMIC COMPONENTS IN EPILEPTIC SEIZURES

F. Bartolomei
Universite Aix Marseille II, Marseille, France

No Abstract Received.

INFLUENCE OF EPILEPSY SURGERY ON EMOTIONS AND AUTONOMIC COMPONENTS OF LIMBIC SEIZURES IN NONOPERATED PATIENTS

J. Wellmer
University Of Bonn Medical Center, Bonn, Germany

The presentation consists of two parts: (1) Influence of epilepsy surgery on emotions. There are many theories about what emotions are and how individual emotionality/susceptibility to emotions can be explained. The Component Process Model (CPM) by Klaus Scherer opens the possibility to measure changes in emotionality/susceptibility to emotions in individuals through their ability to react with an appropriate emotion to significant events, to regulate their emotional expression and feeling state in a situationally appropriate manner, and to show appropriate sensitivity to the emotional expression of social interaction partners. We discuss the utility of this concept for indentifying the impact of focal epilepsies and epilepsy surgery on emotions and present existing literature on this issue. (2) Autonomic components of limbic seizures in nonoperated patients. Seizures of different origin within the brain show autonomic components to a variable extent. We discuss the most frequent autonomic changes observed during seizures with regard to their localizing and lateralizing value as well as their clinical significance beyond presurgical evaluation (i.e. SUDEP).

Tuesday 23 September 2008
07:30 – 09:00
Hall 7
Workshop
EPICURE: EU funded research into functional genomics and neurobiology of epilepsy, a basis for new therapeutic strategies

THE GENETICS OF HUMAN EPILEPSIES

T. Sander
Cologne Centre for Genomics, Koln, Germany

Genetic factors play a predominant role in the aetiology of about 50% of all epilepsies. The underlying genetic architecture likely represents a biological continuum, in which a small fraction of familial epilepsies follows monogenic inheritance, whereas the majority of sporadic epilepsy patients presumably display a polygenic predisposition. Mutations in over 70 genes now define biological pathways leading to rare monogenic forms of epilepsy in hunans and animals. Many of the epilepsy genes identified in rare monogenic forms of idiopathic epilepsies encode voltage-gated or ligand-gated ion channels. However, the genetic basis of the common epilepsy syndromes with genetically complex predisposition remains elusive. The EPICURE consortium will accelerate progress in our research field by joining the resources and expertise of 29 research groups from 12 European countries (www.epicureproject.eu). Advances in high-throughput genotyping and large-scale sequencing technologies together with a better understanding of the structural organization of the human genome have improved the prospects to dissect configurations of functionally convergent susceptibility alleles tracing key molecular pathways of epileptogenesis. Only the comprehensive assembly of the most important susceptibility, genes will allow to assess individual risk profiles and to develop preventive therapy strategies.

FUNCTIONAL ANALYSIS OF ION CHANNEL MUTATIONS IN GENETIC EPILEPSIES AND PHARMACORESISTANCE

H. Lerche
University of Ulm, Ulm, Germany

Mutations associated with idiopathic epilepsies have been identified in genes encoding ion channels, in both rare monogenic epileptic syndromes and in some families with common idiopathic generalized epilepsies (IGE). Furthermore, genetic variants are likely to modulate the susceptibility to seizures and the effects of antiepileptic drugs. Among the targets of such epileptogenic mutations are channels crucial for the generation of action potentials and the regulation of neuronal firing such as voltage-gated sodium and potassium channels, as well as those involved in inhibitory synaptic transmission such as GABA(A) receptor subunits. Concerning genetic variability to pharmacotherapy, a sodium channel polymorphism has been shown to be associated with the dosage of sodium channel blocking drugs used as anticonvulsants in patients. We use in vitro techniques expressing such genetic variants in heterologous mammalian cells and cultured neurons, immunohistochemistry and gene-targeted mouse models in order to (1) characterize the biophysical consequences of genetic alterations associated with epilepsy and pharmacoresistance, (2) understand the functional role of the affected channels in different cell types and circuits of the mammalian brain, and (3) analyze the pathogenic role of mutations on the molecular, cellular, network and whole animal level. Our studies will not only enhance the understanding of epileptogenesis and pharmacoresistance, but hopefully also improve anticonvulsive therapies.

ACQUIRED CHANNELOPATHIES AND LOSS OF CONTROL EXCITATION

M. Walter
Institute of Neurology UCL, London, UK

Partial epilepsy frequently follows specific brain insults (e.g. stroke, head injury, status epilepticus). There is often a latent period between the insult and the development of epilepsy. During this period, there are alterations in neuronal excitability, receptor expression, synaptic transmission and network connectivity. Amongst these changes are alterations in voltage dependent- and ligand gated-channels that regulate neuronal and network excitability. Although many of these 'acquired channelopathies' lead to a loss of control of excitation, some are compensatory but may contribute to other aspects of the condition such as cognitive and memory dysfunction. Here I will discuss the acquired channelopathies in epilepsy. In particular I will concentrate on changes in ion channels in dendrities (potassium channels, HCN channels) and soma (calcium channels, sodium channels) that lead to the so-called 'epileptic neuron' and the complex changes in GABA(A) receptor mediated transmission that not only lead to hyperexcitability, but also may contribute to network dysfunction and impairments of cognition. Importantly, the elucidation of these acquired channelopathies have increased our understanding of the cellular mechanisms underlying epilepsy and may help us understand the role of mutations and polymorphisms in genes encoding for ion channels in epilepsy. Conversely, the discovery of gene mutations in epilepsy can inform our understanding of the role of such acquired channelopathies.

PHARMACOGENETICS OF REFRACTORY EPILEPSY

E. Perucca
University of Pavia, Pavia, Italy

About one third of patients with epilepsy are refractory to available pharmacological treatments. While the mechanisms responsible for drug resistance are probably multifactorial, increasing attention has focused in recent years on the potential role of genetically-related factors. Different genetically controlled mechanisms can potentially lead to failure to respond to an antiepileptic drug (AED). These include (1) occurrence of idiosyncratic adverse reactions in patients with specific genotypes, preventing stabilization of these patients on therapeutically effective regimens of one or more drugs; (2) genetically-related variability in the metabolism of AEDs, or in the transport of AEDs across the blood brain barrier, or at the site of the epileptogenic focus; and (3) genetically-mediated alterations in AED targets in the brain. The best example of genetically mediated idiosyncratic reactions to AEDs is represented by the association between the HLA-B*1502 allele (which is present with a higher frequency in Han Chinese and some other Asian ethnic groups) and serious skin reactions to carbamazepine and, possibly, phenytoin, lamotrigine and other AEDs (Man et al, Epilepsia 2007; 48: 1015–8). As far as pharmacokinetic mechanisms are concerned, genetic

polymorphisms affecting the expression of cytochrome P450 enzymes have been shown to influence clearance and dosage requirements of some AEDs, one example being the variation in phenytoin clearance in relation to CYP2C9 and CYP2C19 polymorphisms: this could lead to inadequate drug response by making dose adjustments difficult. Other lines of evidence suggest that multidrug resistance may be caused, at least in some cases, by an increased expression of drug transporter systems at the site of epileptic activity, a mechanism which may be also be under genetic control. The transporter studied most extensively in this respect is P-glycoprotein, encoded by the ABCB1 gene, and conflicting data have been produced on the possible role of the CC genotype of the ABCB1 3435C>T polymorphism in influencing responsiveness to AEDs (Tate and Sisodiya, Expert Opin Pharmacother 2007;8:1441–9). Studies addressing possible genetically mediated alterations in drug targets have focused especially on ion channels, and data have been provided that a functional polymorphism in the *SCN1A* gene may play a role in influencing the response to sodium channel blockers such as carbamazepine and phenytoin (Tate et al. Proc Natl Acad Sci USA 2005;102:5507–5512). The role of genes coding for a wide range of other AED targets is being specifically investigated as a subproject of the EPICURE study. Further breakthroughs in this area may also derive from ongoing genome-wide association studies.

Tuesday 23 September 2008
07:30 – 09:00
Hall 9
Workshop
Gap – junctions and epilepsy

GAP – JUNCTIONS AND CONNEXINS EXPRESSION IN THE CNS

D. Condorelli
University of Catania, Catania, Italy

No Abstract Received.

GAP JUNCTIONAL COMMUNICATION IN ASTROCYTES AND NEUROGLIAL INTERACTION

C. Giaume
Inserm U840, Paris, France

Gap junctional communication in astrocytes and neuroglial interaction In the central nervous system, glial cells and in particular astrocytes are characterized by a high level of connexin (Cx) expression. These membrane proteins are the constituents of gap junction channels allowing direct intercellular exchanges. In defined conditions, they can form also ''hemichannels'' that provide an alternative pathway for inside-outside exchanges. A common feature of these Cx channels is their permeability for ions as well as small signaling molecules (< 1–1.2 KDa) constituting a basis for dynamic neuroglial interaction that can lead, or be associated, to neuronal dysfunction in pathological situations. This is the case for several models of epilepsy in which changes in the expression level of astrocytic Cxs have been observed. In this context, this presentation will be focused on the following points. First, an up-date review on the properties of glial networks sustained by the expression of Cxs and hemichannels in astrocytes. Second, the listing of data indicating how glial networks and neuronal circuits interact. Third, the discussion of results arguing for a contribution of hemichannels and gap junction channels to the uptake and the trafficking of metabolic substrates. And finally, the presentation of data suggesting the participation of astrocyte metabolic networks to the maintainance of epileptic-like discharges in neurons. As a whole, such information will contribute to propose that now Cxs in glial cells should also be considered as potential targets for the development of alternative strategies to intervene in neurological pathologies including epilepsy.

PHYSIOLOGY OF GAP-JUNCTIONS

U. Heinemann
Johnannes-Muller-Institute of Physiology, Berlin, Germany

Gap junctions exist in many tissues and provide for exchange of small molecules and electrical charges. The underlying proteins form hemichannels in the plasma membrane which can fuse and provide for electrical and metabolic coupling between cells. Gap junctions permit in the liver that adrenergic input has only to reach some cells and the rest receive the receptive chemical signal through gap junction. In smooth muscles gap junction provide for directed propagation of signals in the vascular and intestine system. Gap junctions can be regulated. Thus, connexins and gap junctions are upregulated during pregnancy providing for more and more effective synchronized contraction of smooth muscle cells. In the central nervous system classical astrocytes are coupled through gap junctions providing for a network of coupled cells. The loss of one connexion has mild consequences. Animals which loose both connexins may present with spontaneous epileptiform discharges and show relative mild abnormalities in spatial K buffering. GAP junctions between neurons do also exist. They are important in the inferior olive where they provide for the synchronisation of the principal rhythmogenic cells, GABAergic input determines which GAP junctions are functionally active. In the hippocampus many basket cells are also coupled by gap junctions providing for enhanced contribution to generation of gamma oscillations. Gap junctions between principal cells have also been suggested but experimental proof is still rare. However, they have been suggested to be important for generation of network oscillations in the high frequency range of 200 – 600 Hz oscillatory activity. Evidence from my lab suggests that at least in some cases these high frequency oscillations can also be achieved by synaptic interactions in networks with recurrent excitatory interactions.

ANTIEPILEPTIC EFFECT OF GAP-JUNCTIONS BLOCKERS

H. Cock
St Georges Hospital, London, UK

The role of gap junctions are in the propagation and maintenance of seizures is increasingly recognized, and ex vivo (using ''epileptic'' brain slices from animal models and human surgical specimens) support that gap junction blockers may be antiepileptic. However systemic toxicity of gap-junction blockers has to some extent limited in vivo or clinical studies. However focal drug delivery techniques, increasingly used in other disease areas (e.g., neurooncology), which avoid systemic complications and thus broaden the range of potential agents, is also being investigated in epilepsy, to both enhance understanding about the role of gap junctions in, and provide proof in principle of possible therapeutic benefits. Gap junction blockers applied focally in vivo have proved effective in acute provocation models and more recently in the cortical tetanus toxin model in rats, which has frequent partial motor seizures, refractory to high doses of systemic agents including phenytoin and diazepam, and thus appears to be a clinically relevant model of refractory epilepsy. In this model, the effect of gap junction blockers delivered directly to the epileptic focus was assessed in freely moving unsedated animals. Injections of Carbenoxolone or mefenamic acid through a preimplanted cannula resulted in a clear reduction of seizure frequency (assessed both behaviorally and using EEG monitoring) compared to the predrug baseline, whereas injections of 0.9% saline had no effect. No additional sedation was required, and there were no observable side effects. As would be expected from a single pulse delivery, the duration of effect was short (20–30mins), but nonetheless of a clinically relevant magnitude (% time seizing reduced from 50–60% to 10–15%). Similar studies using longer term delivery methods and in a broader range of clinically relevant animal models now need to be conducted, in order to assess whether gap junctions as novel therapeutic targets can live up to the promise they offer.

Tuesday 23 September 2008
09:00 – 11:00
Hall 1
Main Session
Immune processes in epilepsy: basic and clinical issues

IMMUNE/INFLAMMATORY PROCESSES IN EPILEPSY: NEUROBIOLOGICAL ASPECTS

A. Vezzani
Mario Negri Institute For Pharmocological Research, Milan, Italy

Inflammation in CNS has been described in various neurological disorders; recent findings have shown markers of inflammation in glia and neurons in surgically resected human epileptogenic tissue from drug-resistant epilepsies of various etiologies. Markers of adaptive immunity can be also present depending on the type of epilepsy. Studies in rodent models of epilepsy show that proinflammatory cytokines are rapidly synthesized by glia during seizures, or after a brain injury that can prime epileptogenesis (e.g., neurotrauma). The release of cytokines from glia, or from cells of the adaptive immunity, may profoundly alter neuronal excitability; in particular, elevated levels of IL-1beta or complement activation in the rodent hippocampus induce proconvulsive effects, and anti-IL-1beta treatments reduce acute and chronic seizures. Recent insights into the mechanisms underlying these effects indicate that IL-1beta modifies the neuronal responses to glutamate and GABA. In particular, IL-1beta activates a novel intracellular pathway in hippocampal neurons that results in enhanced NMDA receptor-mediated calcium influx; TNF-alpha induces the recruitment at cell membrane of AMPA receptors more permeable to calcium, and induces internalization of GABA-A receptors. These cytokines can increase also the extracellular glutamate concentration by reducing astrocytic glutamate reuptake and priming its release by astrocytes. Systemic inflammation, mimicked by lipopolysaccaride injection, has also been reported to decrease seizure threshold in rodents. Elevated cytokine levels and downstream inflammatory mediators in brain, and/or activation of inflammatory pathways in the periphery, may also promote changes in brain microvasculature, including blood–brain barrier breakdown and angiogenesis which in turn may affect seizure threshold. Targeting inflammation may represent a new approach to control seizures and the associated neuropathological events.

INNATE IMMUNITY IN EPILEPSY: THE FOCUS ON TLE AND MALFORMATIONS OF CORTICAL DEVELOPMENT

E. Aronica
Academic Medical Centre, Amsterdam, The Netherlands

The immune system uses two types of defense mechanisms: innate and adaptive immunity. The innate immunity is constitutively present in CNS and relies on resident cells. Microglial cells represent the primary immune effectors cells, activated in response to different types of brain injury. However evidence is emerging that also the astrocytes are active players in the cerebral innate immune response. Recently both experimental and clinical evidence indicate the existence of a chronic inflammatory state in the epileptic brain. A rapid activation of both microglia and astroglial cells occurs in response to seizure activity and persists in the chronic phase in regions involved in the generation and spread of seizures. In addition activation of the innate immunity is associated with areas of blood brain barrier damage. Gene expression analysis in the post–status epilepticus model demonstrates that the immune response is the most prominent process changed during epileptogenesis and still up-regulated in the permanent epileptic state. Within the immune response, the complement cascade is prominently activated. Experimental evidence also demonstrates a prominent up-regulation of cytokines, chemokines and other key mediators of the inflammatory process (e.g. cox-2, plasminogen activators, vascular endothelial growth factor) which can alter the dynamics of the neuronal networks. These experimental findings have been recently corroborated by evidence of activation of inflammatory processes in human specimens from cases of drug-resistant focal epilepsies. Prominent activation of microglia and astroglial cells and activation of the complement cascade and proinflammatory cytokine-associated pathways occurs in patients with temporal lobe epilepsy (TLE) and hippocampal sclerosis as well as in specimens of patients with focal malformations of cortical development. The identification of cellular components and mediators of the inflammatory response during epileptogenesis and in chronic epileptic tissue is important for understanding the pathogenesis of epilepsy and may contribute to the development of new therapeutic strategies.

AUTOIMMUNE EPILEPSY: THE PUTATIVE PATHOGENIC ROLE OF GLUTAMATE RECEPTOR AUTOANTIBODIES

M. Levite
Weizmann Institute of Science & Mineuet Therapeutics, Rehovot, Israel

Neuro-autoimmunity to glutamate recptors: autoantibodies to glutamate receptors can damage the human brain in epilepsy, neuropsychiatric systemic lupus erythematosus and encephalitis Glutamate is the major excitatory central-nervous-system neurotransmitter. Now, glutamate-receptor (GluR) autoantibodies call for our serious attention, as they are found in many patients with epilepsy and systemic lupus erythematosus (SLE), and can unquestionably damage the brain. Glutamate/AMPA-receptor-subtype-3 (GluR3) autoantibodies were found thus far in 35% (78 of 222) of patients with different epilepsies studied worldwide. Glutamate/NMDA-receptor-subunits-R2A/B (NR2A or NR2B) autoantibodies, some of which cross-react with double-stranded (ds) DNA, were detected thus far in 35% of SLE patients, and suspected to contribute to their neuropsychiatric impairments, among them epileptic seizures. NR2-autoantibodies were also found in patients with epilepsy (18%), stroke and encephalitis (primarily paraneoplastic). Individual epilepsy patients have either GluR3-autoantibodies or NR2-autoantibodies or none, indicating no cross-reactivity. Some epilepsy patients have anti-dsDNA-which do not cross react with any of the glutamate-receptor autoantibodies. Human and animal studies show that GluR3-autoantibodies bind neurons, posses a unique ability to activate their glutamate-receptor antigen, can kill neurons by either excitotoxicity or complement activation, cause multiple brain pathology, induce and neurobehavioral/cognitive impairments, and augment seizure severity in GluR3B-immunized mice. NR2/dsDNA-autoantibodies, once present in the CNS, can also bind and subsequently kill hippocampal and cortical neurons, by an excitotoxic complement-independent mechanism. Based on all the above, we recommend that neurologists, especially epileptologists, should consider glutamate-receptor autoantibodies as autoimmune molecules which are frequently found among patients with epilepsy and neuropsychiartic lupus, and which may be pathogenic the brain, and therefore and screen for them, especially in intractable epilepsy and before brain surgery. If either GluR3 or NR2 autoantibodies are present in a given patient, primarily in the CSF, they may induce/contribute to the brain damage, neurobehavioral/cognitive/emotional impairments and seizures, and as such should be silenced or removed.

IMMUNE PROCESSES IN EPILEPSY AND THERAPEUTICAL OPTIONS

C. Bien
University of Bonn, Bonn, Germany

Immunological epileptology is an appealing field of research in disease mechanisms. At the same time, it generates concepts for therapeutic interventions in immune-mediated epilepsies. The most prominent example for such a pathophysiology-based extension of treatment options is the introduction of immuno-interventions in Rasmussen encephalitis: In earlier times, the progressive decline was followed without specific treatment up to a stage when hemispherectomy would no longer cause additional neurological deficits. Today's strategy is to inhibit the pathogenic immune reaction early on to improve the functional long-term outcome. Similar approaches are emerging in conditions like limbic encephalitis,

the most frequent cause of adult-onset temporal lobe epilepsy with hippocampal sclerosis. Again, early immuno-therapeutical intervention may prevent the transgression into a chronic, often intractable epilepsy with cognitive impairment. Further elucidation of immune-processes at the basis of epileptic brain diseases will to lead to an expanding immunotherapeutic armamentarium for patients with seizure-disorders.

Tuesday 23 September 2008
09:00 – 11:00
Hall 3
Main Session
Pharmacogenetics and pharmacogenomics in epilepsy

THE RECEPTOR SIDE: THE PHARMACOGENETIC PREDICTION OF PHARMACODYNAMIC RESPONSE

C. Elger
Klinik Fuer Epileptologie, Bonn, Germany

With an increasing number of antiepileptic drugs (AEDs) reaching the market without clearly reducing the amount of patients being pharmacoresistant, the question arises as to whether part of the pharmacoresistance is based on genetic abnormalities on the neuronal or other levels of the brain resulting in a reduced efficacy of AEDs. The second question which is still open is whether pharmacogenetic profiling of the patient would result in an exclusion of some AEDs on the long way of AED testing. A prerequesite for pharmacogenetic and pharmacogenomic views in AED therapy is the knowledge of the genetic basis of epilepsies as well as transporters, transmitter receptors, ion channels and intercellular pathways. On the other hand, genetic modifications of the metabolisms of the AED itself might be part of the problem. The theme of this symposium is to review the findings on these topics and relate them to practical consequences.

THE TRANSPORTER SIDE: MULTIPLE-DRUG TRANSPORTERS AND THEIR GENETIC VARIABILITY IN RELATION TO DRUG RESPONSE IN EPILEPSY

S. Sisodiya
Institute of Neurology, UCL, London, UK

In parallel with theoretical and practical developments in genetic association studies across human traits and diseases, research into genetic variability in multidrug transporters and its relationship with the clinical phenotype of drug response in epilepsy has evolved over the last few years. Sample sizes have grown and representation of variation in the genes in question has broadened. The current balance of opinion might suggest that common variation in the gene, ABCB1, encoding the best studied multidrug transporter, P-glycoprotein, may not have a large role to play. There is no good evidence to date that common variation in any other transporter-encoding genes influences drug response in epilepsy. Can we conclude either that multidrug transporters have no role in drug response in epilepsy or that genetic variability in their encoding genes have no role in drug response in epilepsy? To address these questions, the basic evidence and arguments will be reviewed within a framework for evaluation of multidrug transporter function. We can certainly conclude that, in the absence of additional information at this point, calls for trials of inhibitors of P-glycoprotein in drug-resistant epilepsy are premature. Without evidence that P-glycoprotein is contributing to drug resistance in individual patients, and without in vivo measures of the native function and therapeutic inhibition achieved of P-glycoprotein, any such trials would be difficult to interpret, and might lead to premature rejection of an approach that might be potentially valuable for at least a subset of patients. We also need to look beyond P-glycoprotein and ABCB1. A significant proportion of the genome encodes transporters of one form or another. It is now possible and appropriate to move to genome-wide analyses of well-characterized, large cohorts of patients in whom relevant definitions of drug response and resistance have been applied. Studies and approaches of this type will be discussed.

THE METABOLIZING PART: GENETIC VARIABILITY OF METABOLIZING ENZYMES IN EPILEPSY

M. Bialer
The Hebrew University, Jerusalem, Israel

Since the outcome of antiepileptic drug (AED) therapy is often unpredictable, the goal of personalized medicine is to use genetic testing to target therapy by identifying those patients unlikely to respond to an AED as well as those individuals that are likely to respond adversely to the same AED. Pharmacogenetics also assists in selecting the drug (AED) that is most likely to have the highest therapeutic cost-to-benefit ratio for an individual patient. Until the recent advances in genomics, pharmacogenetic research was conducted utilizing the phenotype-to-genotype approach. Patients who reacted exceptionally to drug response were compared to patients (individuals) with 'normal' response. With the explosion of genomics technology a reverse approach of genotype-to-phenotype is currently feasible whereby genetic polymorphism can serve as a starting point to assess whether genetic variability is indeed causative polymorphism and translates into phenotypic variability that might be of clinical relevance. Candidate genes for therapeutic and adverse response can be divided into three categories: pharmacokinetic, receptor/target and disease-modifying. Of all the pharmacokinetic genes involved in mediating drug response, those associated with drug metabolizing enzymes have been the focus of most pharmacogenetic research. Most drugs (AEDs) are eliminated by metabolism primarily mediated by cytochrome P450 (CYP) (e.g. phenytoin, carbamazepine, tiagabine, zonisamide). CYP2D6, CYP2C19 and CYP2C9 are known to be polymorphically expressed with sufficient variations to have an impact on drug therapy. None of the current AEDs are mainly eliminated by a CYP2D6-mediated metabolism. Phenytoin and phenobarbital are metabolized by CYP2C9 and CYP2C19 and are subject to the genetic polymorphism of these two CYPs. However the CYP2C9 or CYP2C19-mediated fraction metabolized (fm) of phenobarbital (<25%) is much smaller than the fm of phenytoin (90%). Thus, the clinically relevant effect of polymorphism is less likely in the case of phenobarbital than in the case of phenytoin. Severe phenytoin intoxication occurred in patients subsequently genotyped as homozygous for CYP2C9*3 and heterozygous for the CYP2C9*2 allele. The high CYP2C9-mediated fm of phenytoin prompted the idea to utilize phenytoin as a probe drug for CYP2C9 phenotyping. In some AEDs (e.g. lamotrigine, carisbamate) the primary metabolism is via glucuronidation mediated by the UDP-glucuronosyltransferases (UGTs). The UGTs catalyse the transfer of the glucuronic acid moiety from the cosubstrate UDP-glucuronic acid to functional groups on the drug (substrate), resulting in metabolite(s) with greater polarity and water solubility. Genetic polymorphisms have been identified in a wide array of UGTs (e.g. UGT1A1, UGT1A3, UGT1A4, UGT2B4, UGT2B7). However, as not all the known mutations in UGTs will translate to clinically relevant phenotypic changes, it is critical to conduct functional studies to correlated genotyping with phenotyping. The majority of the substrates are glucuronidated by multiple UGT enzymes, thereby making it difficult to know which UGT enzyme is predominately responsible for the metabolic glucuronidation. UGT1A1 is a major conjugating enzyme that is responsible for bilirubin homeostasis and the glucuronidation of various drugs. A common genetic polymorphism in the promoter region of the UGT1A1 gene, denoted as UGT1A1*28, leads to reduced enzyme expression and is associated with Gilbert's syndrome. Lamotrigine is mainly metabolized by N-glucuronidation (fm=85%) primarily mediated by UGT1A4. The major UGTs involved in the glucuronidation of valproic acid (fm=20–60%) and carisbamate (fm=44%) are not yet known. For AEDs extensively metabolized by polymorphic enzymes, knowledge of the enzyme polymorphism (e.g. CYP2C9 and CYP2C19 in the case of phenytoin), before the initiation of therapy could prevent concentration-related side effects. Based on this knowledge, the polymorphic drug would either not

be used in patients with mutant alleles regarded as 'poor metabolizers' or would be initiated at low dose.

INDUSTRY PERSPECTIVES OF PHARMACOGENETICS IN EPILEPSY

M. Franc
Johnson & Johnson Pharmaceutical Research and Development, Raritan, NJ, USA

Drug selection in the management of epilepsy remains largely empirical and often involves long periods of trial-and-error involving over 20 choices of antiepileptic drugs (AEDs). From a clinical perspective, knowing which patient to treat with which AED remains an important unmet medical need. From a business perspective, epilepsy therapeutics has become a highly competitive and fragmented market. Marginal clinical effect sizes in refractory patients (current target population) and the unknowns associated with AED mode of action pose a challenge to the pharmaceutical industry in delivering novel and efficacious AEDs. For these reasons, epilepsy is a priority therapeutic area for pharmacogenetic research and drug-linked diagnostics at Johnson & Johnson Pharmaceutical Research and Development. The major goals of pharmacogenetics in epilepsy are to replace the current practice of trial-and-error with a more rationalized, targeted approach and to help with the development of novel AEDs. The ability to predict treatment response would significantly benefit epilepsy patients and could provide a competitive advantage to innovator drugs. A multiattribute decision analysis (MADA) approach to determine the feasibility and added-value of pharmacogenetic research studies in the epilepsy portfolio will be presented. The MADA integrates objective information (e.g., data, calculated forecasts) and subjective information (e.g., judgments, estimations, opinions) for a set of predefined attributes, and requires the cooperation of experts from a range of divergent functional areas including genetics, medicine, pharmacology, statistics, commercial/marketing, and regulatory affairs. The assessment attributes relevant to pharmacogenetic studies conducted in industry include: added-value; scientific, technical, and statistical feasibility; regulatory impact; commercial impact; cost and resources; and timelines. Opportunities were made possible by the systematic collection of DNA in epilepsy clinical trials and a corporate commitment to research innovation.

Tuesday 23 September 2008
14:30 – 16:00
Hall 3
Discussion Group
Brain stimulation in epilepsy: exotic therapy or real perspective?

MAGNETIC BRAIN STIMULATION

W. Theodore
Epilepsy Research Branch, NINDS, Bethesda, MD, USA

No Abstract Received.

DC-STIMULATION

M. Nitsche
Georg-August University, Goettingen, Germany

Transcranial direct current stimulation for the treatment of epilepsy. Michael A. Nitsche, Georg-August-University, Dept. Clinical Neurophysiology, Goettingen, Germany Transcranial direct current stimulation (tDCS) has gained increasing interest as an efficient tool to modulate cortical excitability and activity of the human cerebral cortex noninvasively and painlessly in recent years. It was demonstrated that beyond its physiological impact tDCS is able to influence perceptual, cognitive and behavioral functions in healthy subjects as well as clinical symptoms in neuro-psychiatric diseases accompanied by enhanced or reduced cortical excitability, e.g. depression, stroke and pain syndromes. Since epilepsy correlates with an enhanced level of cortical excitability, its reduction by tDCS might evolve as a promising option. Slice and in vivo animal experiments have already demonstrated the efficacy of DC stimulation to reduce epileptic activity. A first pilot study in patients with pharmacoresistant focal epilepsy as well as some case reports show promising results. Future studies should encompass optimizing stimulation protocols to achieve clinically relevant effects.

DEEP BRAIN STIMULATION

K. Vonck
Ghent University Hospital, Ghent, Belgium

No Abstract Received.

DEEP BRAIN STIMULATION IN MYOCLONUS EPILEPSY

B. Steinhoff
Epilepsy Center Kork, Kehl-Kork, Germany

Up to now, vagal nerve stimulation (VNS) has been the main therapeutic stimulation approach in patients with therapy-refractory epilepsy who are not candidates for resective surgery. Based on the extensive experience available with the treatment of movement disorders, chronic high-frequency deep brain stimulation (DBS) may also be effective in patients with refractory epilepsy. A benefit is expected in epilepsy because of the connections that exist between the subthalamic nucleus (STN) and the superior colliculus (dorsal midbrain anticonvulsant zone). Individual case reports of successful DBS in different types of epilepsy have already been presented. Our group has meanwhile experience with five adult patients (four males, 28 – 33 years) with progressive myoclonic epilepsy syndromes PMES)who underwent chronic high-frequency DBS according to a study protocol that had been approved by the local ethical commission. Electrodes were implanted in the subthalamic nucleus (STN) in the first patient and additionally in the anterior thalamic nucleus (ATN) bilaterally in the following four cases. The DBS effects were compared with the baseline Video-EEG findings concerning myoclonic jerk and daily life performance eight weeks prior to the implantation and three-monthly afterwards. No complications occurred. The best effects were seen with STN but not with ATN stimulation in all patients. In the four patients with a sufficient follow-up reduction of myoclonic seizures by more than 50% was documented by video and by self-reports. All patients reported clinically relevant improvements of various capabilities such as free standing and walking or siginificantly improved fine motor abilities. The best effect was seen in the least impaired patient. DBS of the STN may be an effective treatment option for patients with PMES. Less impaired patients may benefit more markedly. In order to achieve more reliable data multicenter studies are urgently needed.

ACUTE STIMULATION OF THE BRAIN (NEUROPACE)

M. Morrell
Columbia Comprehensive Epilepsy Centre, New York, NY, USA

No Abstract Received.

Tuesday 23 September 2008
14:30 – 16:00
Hall 2b
Discussion Group
From gene profiling to identification of new antiepileptogenic targets

GENE EXPRESSION DURING EPILEPTOGENESIS IN THE RAT: ON THE SEARCH FOR ANTIEPILEPTOGENIC TARGETS

J. Gorter

CNS/Swammerdam Institute For Life Sciences, Amsterdam, The Netherlands

Microarray experiments with RNA from brain regions obtained at different time points after electrically or pharmacologically induced status epilepticus in the rat point to inflammation as a possible contributing epileptogenic factor. The overwhelming acute inflammatory response is reflected in a general and time dependent activation of multiple genes that code proteases, cytokines and other inflammatory substances. Expression of these genes can alter the dynamics of neuron-glia networks – for example, by potentiating glutamate release from neuronal and glial sources. Some over-activated genes may not only cause parenchymal inflammation but also inflammation of endothelial cells, leading to disruption of the blood–brain barrier – a feature that may further contribute to network instability. From this scenario it can be speculated that anti-inflammatory treatment could help to slow down the process of epileptogenesis or prevent further progression of the disease.

FROM PROFILING DATA TO FUNCTIONAL ANALYSIS OF GENES: FOCUS ON PLASMINOGEN SYSTEM.

A. Pitkänen

Epilepsy Research Laboratory, University of Kuopio, Kuopio, Finland

Assessment of molecular changes in the brain during epileptogenesis using large scale molecular profiling typically shows that about 300–700 genes have altered expression. Analysis of data with bioinformatics tools has provided views about the previously unexplored pathways that may contribute to cellular alterations during epileptogenesis, including neuronal/glial migration, angiogenesis, and axonal plasticity. One of these pathways is plasminogen activating system. During the past years we have investigated the changes and their functional consequences in urokinase-type plasminogen activator (uPA) and its receptor (uPAR). Both uPA and uPAR expression is increased during the first two weeks after SE-induced epileptogenesis. Interestingly the expression of both uPA and uPAR in glial cells in the molecular layer of the dentate gyrus is located at the region that limits the mossy fiber sprouting. Moreover, neuronal expression of uPAR in the epileptogenic hippocampus is located in surviving parvalbumin positive interneurons with lesser extent in the somatostatin positive interneurons. These observations in the context of data showing alterations in the seizure threshold both in uPA and uPAR knockout mice suggest that urokinase-type plasminogen activation system may contribute to plastic cellular alterations underlying the change in excitability during epileptogenesis.

HUMAN TEMPORAL LOBE EPILEPSY: FROM MICROARRAY TO BIOLOGICAL NETWORKS

A. Becker

University of Bonn, Bonn, Germany

In TLE, insults such as status epilepticus (SE) can induce chronic epilepsy. The complexity of histopathological alterations in the affected structure, the hippocampus, suggests expression alterations in various genes and pathways. Since many patients with pharmacoresistant TLE undergo surgical treatment with hippocampal removal for seizure control, we have the unique opportunity to analyze gene expression in human brain tissue. For obvious reasons, human hippocampi from early stages of epilepsy development are not available for gene expression analysis. In order to resolute regional and temporal patterns of gene expression in epilepsy development, we apply mRNA analyses in TLE animal models complementary to those in human tissue. Using microarrays, we have shown that ensembles of transcripts are increased at sequential stages of epileptogenesis. Early during epileptogenesis induced by a SE (day 3), many differentially expressed genes were associated with cellular stress and injury. Later during epileptogenesis (day 14 after status epilepticus), elements of the transcription machinery and molecules involved in synaptic reorganization showed upregulation. After the onset of chronic epileptic seizures, neurotransmitter receptors and ion channels as well as neuronal growth and signaling (e.g. synapsin-II) related transcripts were increased. These data suggest a critical role for transcription factors in orchestrating later phases of epileptogenesis. We have further addressed this issue with bioinformatics tools based on recently established approaches for promoter element prediction, and have examined the promoter regions of ion channel genes that are regulated in epilepsy models. We have identified shared transcription factor binding motifs, that are conserved e.g. in distance to transcription initiation sites and in orientation in co-regulated genes. Transcriptional control mechanisms for key steps in epileptogenesis will be presented. Our work is supported by Deutsche Forschungsgemeinschaft (SFB TR3), BMBF (NGFN and German Israeli Program), EPICURE, and the BONFOR program of the University of Bonn Medical Center.

GENOMIC APPROACHES TO DEVELOPMENTAL DISORDERS ASSOCIATED WITH EPILEPSY

E. Aronica

Academic Medical Centre, Amsterdam, The Netherlands

Genomic approaches to developmental disorders associated with epilepsy Malformations of cortical development (MCD) are recognized causes of developmental delay and pediatric epilepsy, which is often resistant to pharmacological treatment. The process of epileptogenesis in MCD is not fully understood and the detection of the mechanism(s) underlying epileptogenesis is complicated by the large variety of histopathological and molecular features of MCD. Recently, attention has been focused on a subgroup of focal MCD that share common cellular, molecular and histopathological features suggesting common pathogenic and epileptogenic mechanisms. These MCD are characterized by abnormal glioneuronal proliferation and include focal cortical dysplasia (FCD), Tuberous sclerosis complex (TSC) associated brain lesions (i.e. cortical tubers), hemimegalencephaly (HMEG) and low-grade glioneuronal tumors (i.e., gangliogliomas, GG). FCD and GG represent frequent neuropathological findings in surgical specimens from pediatric and young adult patients undergoing surgery for intractable epilepsy. The access to this clinically and histopathologically well-characterized neurosurgical material and the recent development of molecular biological technologies opens new perspectives for pediatric epilepsy research. Microarrays and Serial Analysis of Gene Expression (SAGE) are two major techniques used in gene expression profiling. In addition, a novel layer of gene regulation mediated by small noncoding RNAs (MicroRNAs, miRNA), acting as posttranscriptional regulators of gene expression, is emerging. An overview of recent data of gene expression profiles in focal MCD is presented along with a discussion of possible functional consequences of these changes and future directions. Furthermore a few suggestions regarding likely candidate genes involved in pathogenesis and/or epileptogenesis of focal MCD and target molecules for new therapeutical approaches are put forward.

SINGLE-CELL GENE EXPRESSION ANALYSIS: IMPLICATIONS FOR CORTICAL MALFORMATIONS

P. Crino

University of Pennsylvania Medical Centre, Philadelphia, PA, USA

No Abstract Received.

Tuesday 23 September 2008
14:30 – 16:00
Hall 5
Workshop
Hypermotor seizures: from definition to underlying networks

HYPERMOTOR SEIZURES: ARE THEY ALWAYS CLINICALLY THE SAME?

S. Noachtar
University of Munich, Munich, Germany

No Abstract Received.

DO HYPERMOTOR SEIZURES ALWAYS ORIGINATE FROM THE FRONTAL LOBE?

P. Kahane
Grenoble University Hospital, Grenoble, France

No Abstract Received.

HYPERMOTOR SEIZURES AND SLEEP: WHAT IS THE LINK?

F. Picard
University Hospital of Geneva, Geneva, Switzerland

Hypermotor seizures frequently occur during sleep, notably when they are part of the syndrome of Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE). Clinically ADNFLE does not differ from the more frequent sporadic cases of nocturnal frontal lobe epilepsy (NFLE). The seizures occur nearly exclusively during non-REM sleep stage 2. They often appear on transient physiological rhythmic oscillations specific of this sleep stage, the sleep spindles, which are generated by thalamocortical circuitry. A study of two MRI-negative NFLE patients with intracerebral EEG recordings showed that the last sleep spindle immediately preceding a seizure always had a longer duration than the others. This demonstrated a functional alteration of the sleep spindle-generating thalamocortical loop concomitant with the seizure onsets and suggested a thalamic participation in NFLE pathogenesis in these patients. As mutations of subunits of the neuronal nicotinic acetylcholine receptor (nAChR) have been identified in some families with ADNFLE, we decided to determine the regional distribution and density of nAChR in ADNFLE patients with mutations in comparison with healthy controls by PET using a nAChR agonist. We found a significant increase of nicotinic receptor density in mesencephalon and pons of the patients, but decreased density in the right dorsolateral prefrontal region. Brainstem cholinergic nuclei are known to project to the thalamus. Based on the known biochemical and cellular circuits in the brainstem, our results suggest that the nAChR density increase in the mesencephalon is involved in the pathophysiology of ADNFLE through the role of brainstem ascending cholinergic systems in arousal.

HYPERMOTOR SEIZURES: A RELEASE PHENOMENON OF INBORN BEHAVIORS?

C. Tassinari
University of Bologna, Bologna, Italy

No Abstract Received.

Tuesday 23 September 2008
14:30 – 16:00
Hall 6
Discussion Group
'Practical' epileptogenic zone: noninvasive definition in children

USEFULNESS AND LIMITS OF CLINICAL PHENOMENOLOGY?

L. Tassi
Centro Chirurgia Epilessia ''Claudio Munari,'' Milano, Italy

Anatomo-electro-clinical correlations permitted to define the site and the extension of the epileptogenic zone (EZ) in focal epilepsies and are mandatory in the presurgical workup. Clinical symptomatology represents an enormous ''reservoir'' of information, but the epileptologist must be able to make a correct use. It is particularly true in children, especially in very young patients. Every patient has a different, peculiar epilepsy, and a variety of signs and symptoms. The chronology of occurrence of every subjective manifestation and objectivable sign, defines the neuronal pathological network: ictal discharges, with different modality of duration and intensity, involve cortical and subcortical regions, determining a ''dysfunction'' of the EZ, but also of the bordering areas. This neuronal process accounts for minimal differences during distinct seizures in the same patient. The worst error, is to define the extension and localization of the EZ on the basis of a SINGLE sign or symptom. Seizures are the multimodal expression of the cortical involvement with a spatiotemporal dimension. Only the very initial clinical modifications rise to high localization value. On the other hand, only few signs or symptoms allow an accurate and unquestionable localization: auditory illusions and hallucinations, lateralized simple visual hallucinations, clonic/hypertonic modification of the limbs; oroalimentary automatism are generally associated with temporal lobe seizures. Other clinical modifications could be predominantly located in some regions. It is just the opposite for symptoms like oculo-cephalic deviations, gestural automatisms, the presence of a loss of contact, olfactory hallucinations (occurring in temporal but also during orbitary seizures). Finally every epileptologist owns precious information from the ictal semeiology of patients, but only the continuous correlation with neurophysiological and neuroradiological data could allow the definition of the pathway of propagation. Only very initial signs have a localization value and only few signs have a real localizing meaning.

SCALP EEG: TRUTHS AND PITFALLS?

E. Hirsch
Place de l'Hôpital, Strasbourg, France

Epilepsy surgery in children is a functional surgery: its goal is to perform the resection of the epileptic brain tissue while sparing the eloquent cortex. Prolonged scalp video-EEGs allow recording of all types of seizures and play a crucial role in localizing the ''practical e.g., what to remove'' epileptogenic zone. Detailed presurgical evaluation always requires the definition with scalp EEG of various zones that have a variable spatial relationship with the epileptogenic zone Truths: The fundamental objective of presurgical evaluation is to define, with precision, the location and exact extent of the epileptogenic zone. Ideally, the surgical resection should take out the entire epileptogenic zone sparing any adjacent cortex that is not part of the epileptogenic zone (morphologically normal or abnormal). Seizure onset zone: Noninvasive surface electrodes give an excellent overview of the brain, but usually can not detect the actual seizure-onset zone. Irritative zone: EEG and/or MEG are necessary to detect interictal spikes. EEG/fMRI can assist us in defining the exact volume of tissue that generates interictal spikes. Interictal spikes can be essentially considered as extremely focal ''EEG seizures'' that do not spread. Pitfalls: Generalized abnormalities on scalp electroencephalograms (EEG) are not uncommon in children with focal epilepsy. Children with exclusively generalized or multiregional EEG abnormalities and mental retardation are usually not considered surgical candidates, even when brain

lesions are seen on imaging. However generalized and multiregional EEG abnormalities, in the absence of dominant focus, may not preclude epilepsy surgery in children with a congenital or acquired lesion seen on MRI. Age related focal ''rolandic spikes''or generalized spikes might coexist with symptomatic focal spikes. Such EEG aspects are misleading and will be illustrated.

WHEN TO BELIEVE IN MORPHOLOGICAL BRAIN IMAGING?

W. Harkness
Great Ormond Street Hospital For Children, London, UK

No Abstract Received.

FUNCTIONAL BRAIN IMAGING: TO PERFORM OR NOT ?

C. Chiron
Hospital Necker, Paris, France

The success of cortical resection for intractable focal epilepsy is highly dependent on the accurate delineation of the epileptogenic zone (EZ). Gold standard for delineation lies on intracranial-EEG, an invasive exploration drawing based on the results of the noninvasive presurgery workup. This workup in children includes video-EEG, neuropsychological evaluation and high definition MRI, as well as FDG-PET and ictal/postictal SPECT when available. Although only class III-IV evidence are currently available showing that PET and SPECT tend to improve post-surgery outcome by making the EZ definition more accurate, both imaging methods provide an additional help in pediatric patients especially those with negative MRI, with difficult electroclinical semiology, or with discordant presurgery data. High quality is required for PET and SPECT be informative: lack of head movements during image acquisition, video-EEG simultaneously to ictal/postictal SPECT and comparison with interictal scans, close cooperation between nuclearists and neurologists. Using image comodalities (PET/SPECT/MRI) let to improve the sensibility of PET and SPECT to define the EZ as well as to image the epileptic network and to detect subtle epileptogenic lesions. Given the higher proportion of extratemporal lobe epilepsies in children than in adults, EZ is often more difficult to define. Noninvasive investigations therefore provide helpful additional data to localize the onset of seizures and to guide the intracranial recording in pediatric patients.

Tuesday 23 September 2008
14:30 – 16:00
Hall 7
Discussion Group
Any progress in the treatment of epilepsy in pregnancy?

MAJOR CONGENITAL MALFORMATIONS AND AEDS: WHAT HAVE WE LEARNED FROM THE PREGNANCY REGISTRIES?

D. Battino
FONDAZIONE I.R.C.C.S. Istituto Neurologico, C Besta, Milan, Italy

It is now 40 years since the first publications on fetal risks with antiepileptic drugs (AEDs). Since then the risk of major malformations in the offspring of women with treated epilepsy has been shown to be 2–3 times higher than in the general population, mainly due to the use of AEDs. The risk is higher with polytherapy and appears to be dose-related for valproate and possibly also lamotrigine. While it has been known that AEDs may differ with respect to the type of malformations they can induce, earlier studies have generally lacked the power to demonstrate differences between AEDs in their overall teratogenic potential. Epilepsy and pregnancy registries have been established to provide such information, which is essential for a rational management of women with epilepsy with child-bearing potential. Although most are prospective the existing registries vary in design, which needs to be considered when their results are compared. Some registries are driven by pharmaceutical companies and only provide data on pregnancy outcome related to the sponsor's own product. Others are generic national registries not primarily dedicated to the assessment of AEDs and often lack detail on the indications. Others are organized by independent research groups and are potentially more useful in that they publish comparative data. Data from the UK, North American, and Australian AED and pregnancy registries have so far indicated comparatively high malformation rates with valproate, 6.2.to 13.3%, lower with carbamazepine, 2.2 to 3.0%, and similarly low with lamotrigine, 1.4 to 3.2%. The number of exposures to other newer generation AEDs is still too low to allow meaningful conclusions. Additionally, malformation rates by different AEDs need to be compared with caution given the potential impact of confounding factors as will be discussed based on data from EURAP, the large International AED and pregnancy registry.

PRENATAL EXPOSURE TO AEDS AND LONG-TERM COGNITIVE DEVELOPMENT: ARE THERE DRUG SPECIFIC ADVERSE EFFECTS?

K. Eriksson
Tampere University Hospital, Ped. Neurology Unit, Tampere, Finland

Significant increase in the prevalence of mental retardation in children of mothers with epilepsy has not been identified even though larger studies are lacking. However, when the question whether children of mothers with epilepsy have specific cognitive defects compatible with normal intelligence have been addressed, an increased risk has been found – but not always attributable to AED exposure. The results of prospective clinic- or registry-based studies investigating the effect of phenytoin, phenobarbitone, primidone and carbamazepine have been contradictory with some studies showing and others not showing impaired cognition in AED-exposed children. A recent retrospective postal questionnaire from UK found that the need for additional educational support at school was significantly increased in valproate-exposed children compared to unexposed and carbamazepine-exposed children. Since then, other studies have suggested that exposure to valproate (alone or in combination therapy) may impair exclusively verbal IQ but these studies have been limited by either small number of valproate monotherapy exposed children or by the confounding effects of low maternal education and possibly also maternal epilepsy characteristics. In a population-based, evaluator-blinded, controlled study from Finland, the neurological and cognitive functioning of school-aged (6 years or older) children exposed to valproate monotherapy in utero was compared to matched non-exposed and carbamazepine exposed children. The prevalence of low intelligence was increased in valproate exposed children but spesific verbal IQ differences were not noted. However, also the mothers using valproate scored significantly lower in intelligence quotient tests and had also a significantly lower educational level, which may largely explain the results. No data to date have been published on the effects of newer-generation AEDs such as lamotrigine, levetiracetam, oxcarbazepine, topiramate or gabapentin on the prenatal exposure of these AEDs and long-term neurocognitive development of the offspring.

PREGNANCY INDUCED ALTERATIONS IN AED KINETICS: HOW CAN DOSAGE BE OPTIMIZED?

S. Johannessen
National Center For Epilepsy, Sandvika, Oslo, Norway

No Abstract Received.

MECHANISMS OF AED DEVELOPMENTAL TOXICITY: STATE OF THE ART AND COULD PREGNANCY REGISTRIES BE USED TO ADVANCE OUR UNDERSTANDING?

R. Finnell
Institute of Biosciences and Technology, Texas, USA

The management of pregnancies in women with seizure disorders has been a controversial area ever since the first reports of a possible teratogenic risk associated with antiepileptic drugs (AEDs) was first published in the mid-1960s. A robust literature has evolved including clinical case reports, epidemiological studies, and both In vitro and in vivo animal experiments. Recent contributions to this literature include data from Anticonvulsant Drug Pregnancy Registries, as industry has embraced postmarketing surveillance of their drugs as a means of identifying potential problems including potential teratogenic effects. This new data has enabled the American Academy of Neurology's working group on women with epilepsy to conclude that intrauterine first-trimester valproate (VPA) exposure contributes to the development of major congenital malformations (MCMs), especially when compared to other frontline AEDs. It is also probable that in utero exposure to AED polytherapy is associated with reduced cognitive outcomes compared to monotherapy, and in utero exposure to VPA probably reduces cognitive outcomes in children. The issue now is to better Identify who the high risk mother-infant pairs are, so that safer intervention strategies can be employed to reduce the risk of seizures and birth defects. This will require a more thorough understanding of the mechanisms underlying the teratogenicity of AEDs and the identification of genetic risk factors that put some mothers and their babies at increased risk for an adverse pregnancy outcome. In order to approach these two important issues, the following concepts will be covered in the presentation: Placing AED-induced birth defects in their proper context of all congenital malformations. Reviewing suspected teratogenic mechanisms of action of select AEDs. Discussing the potential of role of folic acid and folate pathway genes with regards to both the sensitivity to, and protection from, AED-induced birth defects. Consider novel screening methods to identify high risk AED complicated pregnancies.

Tuesday 23 September 2008
16:30 – 18:00
Hall 2b
Discussion Group
Can we replace the term ''generalized seizures''?

CORTICAL TRIGGER IN GENERALIZED SEIZURES IN RODENTS AND HUMANS

F. Lopes Da Silva
University of Amsterdam, Amsterdam, The Netherlands

No Abstract Received.

BRAINSTEM AND FOREBRAIN NETWORKS IN GENERALIZED SEIZURES IN RODENTS AND HUMANS

P. Mares
Institute Of Physiology, Prague 4, Czech Republic

Generalized seizures are either convulsive (generalized seizures with tonic and clonic phases, e.g. grand mal type) or nonconvulsive (absence seizures). There are substantial differences in pathophysiology of these two basic types of seizures and in the structures involved in their generation. Brainstem si responsible for initiation of generalized tonic–clonic seizures, the structure where the pattern is generated is with a high probability descending part of reticular formation, i.e., the structure regulationg muscle tone under physiological conditions. The brainstem generator can be triggered from various parts of the brain, including forebrain structures (basal ganglia, cerebral cortex). Final common path activated by the generator is represented by spinal motoneurons. Under normal conditions spinal cord is only an effector but if it is isolated from supraspinal regulation, it is able to generate the same pattern of generalized tonic–clonic seizures as an intect brain. Generalized absence seizures are forebrain seizures. They are started in cerebral cortex and involve thalamocortical mechanisms. Brainstem structures have mainly a permissive role in this type of generalized seizures – an optimal state for appearance of absence seizures is relaxed wakefulness, a decreased tonic influence of ascending reticular formation on cerebral cortex.

WHY SOME ANTIEPILEPTIC DRUGS ARE EFFECTIVE ON GENERALIZED SEIZURES?

D. Schmidt
Epilepsy Research Group, Berlin, Germany

Generalized seizures include absence seizures (ABS), myoclonic seizures (MYO) and primary generalized tonic–clonic seizures (PGTC) as seen in idiopathic generalized epilepsies. Several issues make it difficult to answer the question in the title. These issues include generally poor evidence for efficacy of antiepileptic drugs (AED), few experimental models and controversial pathophysiology of generalized seizures, and limited insight into the molecular targets (Table). Table. AEDs for treatment of individual generalized seizures and their molecular targets (adapted from Rogawski and Löscher, 2004).

Abbreviations: + generally accepted as useful, (+) less extensive evidence base, +/− may provoke seizures, Ca Calcium channels, HVA high voltage activated, NaF fast sodium current, NaP persistent sodium current, DMCM is a negative allosteric modulatory of GABA, GABA GABA A receptor AED Molecular target ABS MYO PGTC Valproate NaF?,NaP?,Ca T-type? + + + Lamotrigine NaF,Ca HVA + +/− ? Zonisamide NaF,Ca T-type (+) (+) ? Felbamate NaF,Ca HVA,GABA,NMDA (+) ? Topiramate NaF,NaP,CaHVA,GABA,NMDA (+) (+) + Ethosuximide NaP?, Ca T-type + Levetiracetam Ca HVA, reverses DMCM (+) (+) ? Benzodiazepines GABA + ?.

Summary: AEDs effective against generalized seizures share several molecular targets and have, in general, been less well evaluated for efficacy than partial seizures.

WHAT ARE GENERALIZED SEIZURES AND EPILEPSIES?

E. Hirsch
Place de l'Hôpital, Strasbourg, France

''Generalized seizures'' corresponds to an ictal manifestation whose initial semeiology indicates, or is consistent with, more than minimal involvement of both cerebral hemispheres. A system is a group of independent but interrelated elements (networks) comprising a unified whole. The more we learn about basic mechanisms of epilepsy, the more we realize that few, if any, clinically relevant epileptic phenomena are truly generalized or focal. All seizures begin somewhere, and although the brain can be diffusely involved in the seizure generation. Specific cortical and subcortical networks are involved in the genesis expression and control of generalized seizures. Animal and human data suggested that the so-called generalized seizures involve selective networks while sparing others. Does the term ''generalized'' have some clinical utility and justify his continue use despite the fact it is descriptively inaccurate. The most important near-term objective, therefore, may not be to find better terms to replace the concepts of generalized seizures and epilepsies, but to make sure that physicians understand all the subtleties of individual conditions, irrespective of how they might be classified.

Tuesday 23 September 2008
16:15 – 18:00
Hall 3
Bursary Award Symposium

RECOGNITION OF BASIC AND SOCIAL EMOTIONS THROUGH FACE AND VOICE IN PATIENTS WITH MEDIAL TEMPORAL LOBE EPILEPSY

G. Monti, F. Benuzzi, M. Pugnaghi, M. Molinari, P. Nichelli, and S. Meletti

University of Modena and Reggio Emila, NOCSAE Hospital, Modena, Italy

Purpose: Patients with chronic temporal lobe epilepsy can be impaired in tasks requiring to decode the emotions expressed by others. The present study evaluates the ability to recognise facial and prosodic expressions of both basic and social emotions.

Method: According to anatomo-electroclinical evaluation of presurgical drug-resistant TLE patients the following patients group were obtained: MTLE (n = 15), with patients showing MRI evidence of hippocampal sclerosis or other medial temporal lesion; lateral TLE (LTLE, N = 12), with patients having MRI evidence of lesions located in the neocortical temporal cortex. 30 normal subjects served as controls. Recognition of basic emotions was evaluated by tasks of facial expressions recognition and emotional prosody recognition. In addition subjects were presented with a 3 second video clip featuring the eye region of the face expressing of one of the following social emotions: flirtatious, suspicious, mocking and guilty.

Results: Relative to healthy controls MTLE patients were impaired in recognition of fear, sadness, angry, and disgust ($p < 0.01$ for all comparisons) both from facial and prosodic expressions. No difference was observed for the recognition of any basic emotions in LTLE versus healthy controls. MTLE patients also showed a generalized deficit in social emotions recognition respect to healthy controls. LTLE patients were impaired in recognition of only one specific social emotion (guilty) respect to healthy subjects.

Conclusion: Our results suggest that medial chronic temporal lobe epilepsy is associated to widespread impairment in processing basic and complex emotions both from facial and from prosodic cues.

EVALUATION OF ENANTIOSPECIFIC ANTIALLODYNIC ACTIVITY OF PROPYLISOPROPYLACETAMIDE, AN AMIDE DERIVATIVE OF A CHIRAL CONSTITUTIONAL ISOMER OF VALPROIC ACID

D. Kaufmann, B. Yagen, M. Tal, M. Devor, and M. Bialer

The Hebrew University of Jerusalem, Jerusalem, Israel

Propylisopropylacetamide (PID) is a chiral CNS-active constitutional isomer of valpromide, the amide derivative of the major antiepileptic drug valproic acid (VPA).

Purpose: a) To evaluate the enantiospecific activity of PID on tactile allodynia in the spinal nerve ligation (SNL) model of neuropathic pain in rats, b) To investigate enantioselectivity in the pharmacokinetics of (R)-PID and (S)-PID compared to (R,S)-PID, and c) To determine electrophysiologically PID's potential to affect tactile allodynia by suppressing ectopic afferent discharge in the peripheral nervous system (PNS).

Method: Racemic PID and its individual enantiomers were administered i.p to 10 rats in a crossover randomized double blind protocol and their antiallodynic ED50 values were evaluated. Plasma concentrations were determined by a gas chromatograph (G.C.) equipped with a chiral column following i.p. administration of 60 mg/kg of the racemic mixture and the two stereoisomers to rats. Electrophysiological recordings were made from the L5 dorsal root (DR) in 6 rats using the teased fiber method, followed by Passive observation of neural activity 60 min after i.p. administration of 80 mg/kg racemic PID.

Results: (R)-, (S)- and (R,S)-PID produced dose-related reversal of tactile allodynia with ED50 values of 46, 48, 42mg/kg, respectively. The individual PID enantiomers were not enantioselective in their antiallodynic activity. No sedative side effects were observed at these doses. (S)-PID had lower clearance (CL) and volume of distribution (V) than (R)-PID after administration of the individual enantiomers, compared to similarity in these parameters after administration of the racemic mixture. Systemic administration of (R,S)-PID did not suppress spontaneous ectopic afferent discharge generated in the injured peripheral nerve. Both of PID's enantiomers, and the racemate, are more potent antiallodynic agents than VPA (ED50=269mg/kg) and have similar potency to gabapentin. Consequently, they have the potential to become new drugs for treating neuropathic pain.

DO PERIICTAL CHANGES IN HEART RATE, QT TIME AND HEART RATE RECOVERY IDENTIFY PATIENTS AT HIGH RISK OF SUDEP?

R. Surges, J. Erhuero, C. Scott, J. Sander, and M. Walker

Institute of Neurology, London, UK

Purpose: Sudden unexplained death in epilepsy (SUDEP) may be due to cardiac excitability modulated by seizure activity. This study aims to identify ECG features which may help defining patients at risk.

Method: Periictal ECGs of patients with intractable focal epilepsies who underwent presurgical video-EEG telemetry and who later died suddenly were retrospectively assessed. Controls were matched for age, gender and date of video-EEG telemetry. ECG features were measured pre-, intra- and postictally. Heart rate (HR) was determined by measuring the shortest RR intervals. Postictal heart rate recovery (HRR) was assessed by comparing preictal HR to HR 5 minutes after seizure. Values expressed as mean±SEM.

Results: Each group comprised 19 patients (age 36±2 years; available seizures SUDEP: 51, control: 38). The relative change in maximal ictal HR was significantly higher in SUDEP patients (control 1.51±0.42 vs. SUDEP 1.74±0.47, p 0.02). HRR tended to be impaired in SUDEP, but did not reach statistical significance (Controls: 6.6±3.2 bpm, SUDEP: 12.3±2.7 bpm, p 0.17). No relevant differences in per-ictal QT intervals were detected. Cardiac arrhythmias occurred during the early postictal period in 4 SUDEP patients (in 26% of the seizures, all marked sinus arrhythmia) and in 4 controls (16% of the seizures; sinus arrhythmia in 3 seizures, supraventricular/ventricular extrasystoles in 3 seizures).

Conclusion: Periictal changes in heart activity may facilitate cardiac vulnerability leading to SUDEP. Patients suffering from refractory focal epilepsy with high relative increase in HR and impaired HRR may benefit from detailed cardiological assessment and preventive therapeutical measures.

PREDICTING EPILEPTIC SEIZURES: AN ASSESSMENT OF TWO DIFFERENT KINDS TO COMBINE PREDICTION METHODS

H. Feldwisch Genannt Drentrup,†, B. Schelter†, M. Jachan*,†, J. Nawrath†, R. Sandner†, A. Brandt†, J. Timmer*,†, and A. Schulze-Bonhage*,†*

**Bernstein Center For Computational Neuroscience Freiburg, Gemany and †University of Freiburg, Germany*

Purpose: Concerning the assessment of the predictability of epileptic seizures, a continuous and reliable analysis of neurophysiological

recordings of epilepsy patients is necessary. Recent work has indicated that methods from nonlinear dynamics can detect significant preseizure changes in the EEG at least for some patients. As a means to increase seizure prediction performance we tested whether or not two different kinds of combination of seizure prediction methods yield superior prediction results.

Method: A bivariate phase synchronization index (PSI) and the univariate ''Dynamical Similarity Index'' (SIM) were adapted for seizure prediction. The analysis of these prediction methods was based on long-term intracranial EEG data with continuous recordings of 8 patients for 7–11 days including 124 seizures. Approaches to combine methods were applied and compared to the individual methods. All results have been validated by a statistical test procedure (Schelter et al, Chaos 2006; 16: 013108).

Results: By evaluating the EEG data continuously and without knowledge of 'future' events, a prediction situation analogous to an online application was possible. For a fixed set of parameters, the mean sensitivity almost doubled from 28.4% for the individual methods to 52.8% for the ''AND'' combination, and to 43.1% for the ''OR'' combination. This reveals that correct predictions of both individual methods are stronger correlated than false predictions.

Conclusion: The presented combination of prediction methods is a promising new approach enhancing seizure prediction performance considerably. It enables to join the individual benefits of prediction methods in a complementary manner.

TRACTOGRAPHY OF MEYER'S LOOP AND TEMPORAL LOBE RESECTION

M. Yogarajah, N. Focke*, M. Cercignani*, J. Acheson*, S. Bonnelli*, G. Parker†, D. Alexander*, M. Symms*, A. McEvoy*, M. Koepp*, and J. Duncan**
**Institute Of Neurology And National Society For Epilepsy, UCL, UK and †Imaging Science and Biomedical Engineering, University of Manchester, UK*

Purpose: Visual field defects (VFD) can occur in up to 70% of patients following anterior temporal lobe resection (ATLR), and is most commonly a superior homonymous quadrantanopia, due to disruption of Meyer's loop. The anterior extent of Meyer's loop is not visualized on conventional imaging and there is much inter-individual variation, so the likelihood of a postoperative VFD cannot be accurately predicted. Using tractography to delineate the course and anterior extent of the optic radiation preoperatively, may help to reduce the risk of visual field defects following ATLR.

Method: We studied 19 patients who underwent ATLR, using diffusion tensor tractography to visualize the optic radiation preoperatively. Preoperative tracts were overlaid on postoperative high resolution MR images. Distances from the anterior edge of Meyer's loop to landmarks in the temporal lobe were calculated. All patients underwent postoperative Goldmann perimetry, and VFDs were quantified using a previously described method.

Results: In 8 patients VFDs ranging from 20 to 80% of a quadrant across both eyes were present, and in these patients disruption of Meyer's loop was apparent. The anterior extent of Meyer's loop ranged from 24 to 43 mm from the temporal pole. After adjusting for the anterior-posterior extent of resection a significant correlation between extent of the VFD and distance from the tip of Meyer's loop to the temporal pole was present.

Conclusion: Preoperative tractography is a promising method to visualize Meyer's loop, and assess an individual patient's risk of a VFD as a result of ATLR. Word Count = 242 words Please note that by the time of this conference more patients will have been enrolled in this study.

Tuesday 23 September 2008
16:30 – 18:00
Hall 5
Workshop
Sodium channel defects in genetics and pharmacogenetics of epilepsy

SCN1A AND *SCN2A* MUTATIONS IN EPILEPSY

P. De Jonghe
Neurogenetics Group, VIB, Antwerp, Belgium

No Abstract Received.

LESSONS FROM *SCN1A* KNOCKOUT MICE

M. Mantegazza
Besta Neurological Institute, Milano, Italy

No Abstract Received.

POTENTIAL ROLE OF A NEONATAL *SCN1A* SPLICE VARIANT IN DRUG RESPONSE

S. Schorge
Institute of Neurology, UCL, London, UK

No Abstract Received.

CORRELATION OF DRUG RESPONSE TO NA CHANNEL BLOCKERS IN VIVO AND IN VITRO

H. Beck
University of Bonn, Life And Brain Center, Bonn, Germany

No Abstract Received.

Tuesday 23 September 2008
16:30 – 18:00
Hall 6
Discussion Group
Crime and punishment: legal aspects of epilepsy and AED treatment

EPILEPSY AND MOTHERHOOD. WHAT ARE THE DANGERS OF MOTHERS WITH EPILEPSY INJURING THEIR CHILDREN?

P. Crawford
York District Hospital, York, UK

The risk of mothers with epilepsy accidentally injuring their children appears to be low and relates to seizure type, frequency and timing. The literature on this subject is sparse but an Indian study of child rearing in 20 mothers with epilepsy reported 3 incidents where a mother dropped a baby as a result of a seizure. An email survey of epileptologists with a special interest in women's issues revealed that few had encountered mothers accidentally harming a child as a result of a seizure. It was felt that counselling of the mother about safety issues may have reduced the risk of injury. However it was commented that the risk of injury to a child is frequently cited in custody proceedings. A survey of epilepsy specialist nurses revealed similar findings.

UNFORESEEN SIDE EFFECTS OF ANTIEPILEPTIC DRUGS

S. Schwabe
Sanofi Aventis Project Direction, Bridgewater, NJ, USA

Antiepileptic drugs are among the most complex pharmacological agents known. This is not surprising, since they are used to treat the epilepsies, some of the most complex diseases known. Epilepsy research (in the right hands!) nevertheless shows a higher success ratio than most CNS areas when measured as predictability from preclinical research to treatment in humans. In spite of this, the field has seen quite a few compounds that went on to show unforeseen and unforeseeable AE and efficacy profiles in clinical use. Examples of this could include felbamate and vigabatrine, among others. On the other hand, many AEDs have also gone on to prove efficacy in other indications, not seldom nonepileptic indications. Examples of this could include topamax and gabapentin, among others. This presentation will go over a selection of some of the more interesting cases, looking for commonalities between them.

ASSESSMENT OF MENTAL CAPACITY IN PEOPLE WITH EPILEPSY

M. Trimble
Institute of Neurology, London, UK

A brief over view of the laws relating to mental capacity in the UK including the newly introduced Mental Capacity Act (2005)will be presented. The difficulties of such assessments in patients with subtle neurocognitive abnormalities will form the centre of the lecture since it is such patients who are not well defined by the act and yet whom would appear to be vulnerable. There will be a brief discussion of the impact of seizures themselves on the mental state and also upon the development of psychoses ictal and interictal. Some practical guidelines for the assessment of mental capacity will be suggested.

EPILEPSY AND DRIVING – THE EUROPEAN PERSPECTIVE

E. Beghi
Mario Negri Institute For Pharmacological Research, Milan, Italy

As seizures represent a potential source of accidents and injuries, limitations on driving are justified for people with epilepsy. The European Council Directive 91/439/EEC on driving licenses reports 'a license may be issued or renewed subject to an examination by a competent medical authority and to regular medical check-ups. The authority shall decide on the state of the epilepsy or other disturbances of consciousness, its clinical form and progress (no seizures in the last two years, for example), the treatment received and the results thereof'. For commercial driving it states 'driving licenses shall not be issued for applicants or drivers suffering or liable to suffer from epileptic seizures or other sudden disturbances of the state of consciousness'. Unfortunately, differing regulations for a driving license are in act among the members of the European Union (and elsewhere in the world). This may be explained by the variability of published reports and by the differing interpretations of seizures and epilepsy. About one third of seizures may be provoked and, in that sense, they may disappear when the underlying epileptogenic condition is under control. Even unprovoked seizures may not recur in about one half of patients and in those with repeated unprovoked seizures, several epilepsy syndromes may be compatible with noncommercial driving. In addition, in patients with repeated unprovoked seizures in complete remission (with or without treatment), the risk of accidents and injuries is decreased and tends to be close to that of the general population. In the European Union, most member states require a two year period before granting or renewing a driving license. However, differing exceptions are in act for seizures and epilepsies not interfering with driving abilities. These include provoked seizures, isolated unprovoked seizures, seizures occurring during sleep, myoclonic seizures, simple partial seizures, seizures only on awakening, and seizure relapse after treatment discontinuation. All these issues have been discussed in a scientific report by the advisory board to the driving license committee of the European Union. However, a Europe wide legislation is still awaited.

Tuesday 23 September 2008
16:30 – 18:00
Hall 7
Discussion Group
Focal cortical dysplasia type I: are there electroclinical and seizure outcome differences between children and adults?

NEUROPATHOLOGICAL CHARACTERISTICS OF DIFFERENT TYPES OF FOCAL CORTICAL DYSPLASIA

I. Blumcke
Univ Medical School, FAU Erlangen, Erlangen, Germany

No Abstract Received.

FOCAL CORTICAL DYSPLASIA TYPE 1 IN ADULTS

L. Tassi
Centro Chirurgia Epilessia "Claudio Munari," Milano, Italy

Purpose: FCD is the most frequent neuropathological finding in epilepsy surgery populations. Type I FCD (architectural dysplasia, AD) in adults is often associated with other histopathological lesions, determining different clinical pictures. Methods. With a minimum follow-up of 1 year, 176 (22%) pts out of 784 operated on in the Claudio Munari Centre, showed a FCD type 1. Adults (>16 years) were 143 (18%). Anatomo-electro-clinical correlations were analyzed. Results. Five different subgroups were found: isolated FCD type I (34 pts, 24%), with a negative presurgical MRI in 44%, a predominant multilobar localization (12 pts, 35%) and a poor outcome (only 47% in Class I of Engel). In 65 pts (45%) with TLE, AD was associated with hippocampal sclerosis, the presence of Febrile Seizures (37 pts, 57%) and a good outcome (52 pts in Class I, 80%). Neoplastic benign lesions were found associated with AD in 24 pts (17%), with a predominant temporal location (79%) and an excellent outcome (87% in Class I). In 16 pts (11%) AD was associated with other cortical malformation, particularly with Periventricular Nodular Heterotopia (10/16 pts). In 50% the posterior part of the brain (TPO regions) were involved. The surgical outcome was good in 13 pts (Class I 81%). In the last group, 4 pts (3%) with a multilobar epilepsy and a poor outcome (only 1 pt in Class I), showed an association between AD and perinatal anoxo-ischemic pathology. Conclusions. In adults epilepsy surgery patients, FDC type I is probably a complex composite malformation. Only few cases showed an isolated AD, related with a poor outcome and a multilobar involvement. The surgical outcome can vary in the other subgroups in which AD was linked to other histopathologic lesions (hippocampal sclerosis, tumors, other cortical malformations, scars).

FOCAL CORTICAL DYSPLASIA TYPE 1 IN CHILDREN

P. Krsek
Epilepsy Center Motol, Prague, Czech Republic

Purpose: Focal Cortical Dysplasia (FCD) is the most frequent pathology in pediatric epilepsy surgery patients. Two major pathological variants are distinguished, FCD type I and type II. Adult patients with FCD type I have usually lobar involvement (most frequently temporal, coinciding with hippocampal sclerosis), only rarely mental retardation and predominatingly favorable postsurgical seizure outcome. Epilepsies caused by FCD type I in children have not been studied in detail.

Methods: We analyzed pediatric series at two recognized epilepsy surgery centers:

Behandlungszentrum Vogtareuth, Germany (24 cases) and Miami Children's Hospital, Florida (94 cases). Clinical, EEG, MRI, neuropsychological, surgical and seizure outcome data were retrospectively reviewed.

Results: Perinatal risk factors were commonly encountered in FCD type subjects. Majority of patients had very early seizure onset and frequent daily seizures. Children with FCD type I were more likely to manifest mental retardation than patients with FCD type II. We found no EEG abnormality distinctive for FCD type I. Typical MRI findings were lobar hypoplasia/atrophy together with less prominent gray/white matter junction blurring and white matter signal changes. Hippocampal sclerosis was frequently associated with FCD type I in adolescents, but not in young children and infants. Multilobar involvement was common in young children. Surgical outcomes were worse in FCD type I patients when compared to FCD type II group.

Conclusions: Children with FCD type I typically present within the first year of life, have multilobar involvement, no association with hippocampal sclerosis, very high seizure frequency and often mental retardation. The pathology is difficult to localize by both EEG and MRI; unfavorable surgical outcomes are therefore often in this group of young patients. Invasive EEG study should be considered when FCD type I is expected based on noninvasive tests.

Supported by Grants IGA NR/8843-4 and VZ 00000064203.

'MILD' CORTICAL DYSPLASIA – SEVERE EPILEPSY (SUMMARY AND OPENING THE DISCUSSION)

H. Holthausen
Epilepsy Center For Children And Adolescents, Vogtareuth, Germany

No Abstract Received.

Tuesday 23 September 2008
18:30 – 20:00
Hall 3
Janssen Cilag Satellite Symposium
Practical issues of drug therapy – how to avoid pitfalls

FIRST MONOTHERAPY – EVIDENCE AND EXPERIENCE

E. Ben-Menachem
Sahlgrenska University Hospital, Goteborg, Sweden

Adults with epilepsy need complete seizure control with tolerable drug side effects in order to work, drive, and lead a normal social life. Monotherapy is often the best way to achieve these goals. This stems from clinical experience showing that monotherapy offers fewer adverse effects (AEs), lower toxicity, and reduced risk for teratogenicity. Monotherapy also avoids the complex dosing regimens, poorer compliance, and increased treatment costs associated with polytherapy.

There is an abundance of data derived from clinical trials with defined efficacy outcomes and minimized potential for bias for treatment outcomes in newly or recently diagnosed patients. However, data are derived from clinical trials derived from a homogenous population and might not be easily applicable to the individual patient. The lecture discusses current treatment guidelines as well as their applicability to daily practice.

DRUG THERAPY IN THE ELDERLY – SOME EVIDENCE, BUT MORE EXPERIENCE

H. Stefan
Epilepsy Centre, University Hospital Erlangen, Erlangen, Germany

The elderly are the most rapidly growing segment of the population with an incidence of epilepsy in persons over 65 is higher than in any other age group. In nursing homes, its incidence is even higher than in community-dwelling persons of similar ages. About 10% of nursing home residents are being treated with antiepileptic drugs (AEDs), with an ''epilepsy/seizure'' indication reported for about 7.7% of this use. Many elderly patients are being treated with AEDs introduced before 1978–phenytoin, carbamazepine, valproate, and barbiturates. However, age-related changes in protein binding, decreases in hepatic and renal clearance, alterations in gastrointestinal absorption, and interactions with drugs used for other conditions make the choice of the best AED difficult. AEDs that do not interact with other drugs, are not metabolized by the liver, and are readily absorbed may offer benefits for the elderly. To complicate matters, the elderly are not a homogeneous population. Today there are many AEDs to choose from, and some of the newer AEDs have more favorable characteristics than the older ones. Choice of an AED should be made on an individual basis, considering the tolerability, efficacy, consequences of drug-drug interactions, and expenses associated with acute and chronic adverse effects. Randomized controlled data as well as data from daily practice are presented and discussed. Clinical skills rather than formulaic approaches are needed to match detailed knowledge of each patient's characteristics with the properties of the various AEDs.

FAILURE OF FIRST MONOTHERAPY – LITTLE EVIDENCE, BUT A LOT OF EXPERIENCE

B. Steinhoff
Epilepsy Center Kork, Kehl-Kork, Germany

For patients with documented epilepsy, anticonvulsant drugs are the mainstay of treatment. Modern outcome studies have demonstrated that around 60% to 70% of patients with newly diagnosed epilepsy enter long-term remission, mostly on a single antiepileptic drug. Patients unresponsive to initial monotherapy might benefit from an increased dose load, however, incremental doses are usually associated with increased adverse events. Subsequently, combinations of 2 or at most 3 drugs or sequential monotherapies are usually prescribed for those unresponsive to monotherapy. Choice of second or third drug is usually based on own experience. In addition, both polytherapy and some certain antiepileptic drugs can aggravate seizures. Few human data exists on synergistic effects of various combination therapies, for efficacy e.g., Valproic acid and lamotrigine or increase in adverse events, e.g., carbamazepine and lamotrigine. Patients are at risk for overtreatment, which does not bring efficacy but rather adverse effects.

The lecture will discuss strategies for optimal choices of second monotherapy, combination therapy and minimization of adverse events.

Wednesday 24 September 2008
07:30 – 09:00
Hall 2b
Workshop
Treating epileptic encephalopathies: state of the art

AGGRESSIVE TREATMENT FOR DEVASTATING DISEASE

U. Kramer
Sourasky Medical Center, Tel-Aviv, Israel

USEFUL, USELESS OR DANGEROUS AEDs

A. Arzimanoglou
Service Epilepsie, Sommeil Et EFNP – HFME – CHU Lyon, Bron Cedex, France

ARE IV IMMUNOGLOBULINES USEFUL: WHEN, HOW, FOR HOW LONG?

L. Lagae
University Hospitals KULeuven, Leuven, Belgium

The concept that the immune system plays a role in the epileptogenic process of some epileptic syndromes was first proposed more than 20 years ago. Since then, numerous studies have reported on the existence of a variety of immunological alterations in epileptic patients, on the observation of favourable responses of refractory epilepsy syndromes to immunomodulatory treatment, and on the association of certain well-known immune-mediated disease states with epilepsy (Billiau, Lagae Eur J Paed Neurol, 2005). More recently, genetic alterations in well known immunological pathways have been described in epilepsy syndromes and thereby justify well designed trials with immune-modulating therapies in epileptic encephalopathies. In an open-label study, we prospectively investigated the effect of IVIG on clinical, EEG and serum/CSF immunological parameters in patients with refractory childhood-onset epilepsy (Epilepsia, 2007). Thirteen patients (median age 6.9 years) with refractory epilepsy were given IVIG (add-on, 4 × 400 mg/kg/3 weeks). Seizure frequency, 24-h video-EEG, and CSF/serum immunological parameters and cytokine profiles (IL-6/IL-8/IL-12/IL-10) were documented before and after completion of the course. Seizure frequency was reduced by > or = 50% in four, and by 25%–50% in three patients. In contrast, variation in automatically recorded spike counts (1-h-wake and -sleep) did not correlate with clinical improvement. Serum immunological parameters showed variable deviations in eight patients and CSF immunoblotting showed oligoclonal bands in two patients. IL-6 and IL-8 were clearly detectable in CSF of all patients; the levels were significantly higher than those in plasma but remained unaffected by IVIG treatment. This study illustrates the potentials of IVIG in the epileptic encephalopathies, but the exact role and especially timing of IVIG treatment in these syndromes remains to be discussed.

SURGERY: CAN IT ONLY BE PALLIATIVE?

H. Cross
UCL Institute Of Child Health, St Albans, UK

Epileptic encephalopathy by definition implies that some developmental compromise is the result of ongoing epileptic activity. Within the current ILAE classification, certain epilepsy syndromes are listed as epileptic encephalopathies. They may be thought of as those syndromes most at risk of developing such. Children with early onset focal epilepsy are also at high risk of developmental compromise in the long term; it is presumed that the ongoing epileptic activity must be in part responsible and by this premise, some if not all is potentially reversible. Developmental outcome is improved with lesser duration of epilepsy prior to surgery suggesting a potential for improvement the earlier surgery is performed. What evidence have we that this is the case? Very few studies are able to demonstrate definitive improvement in cognitive ability. At the very least, a maintained IQ is demonstrated on group effect, namely maintained trajectory of learning postoperatively. It could be presumed that IQ, as a measure of ability relative to peers, would be likely to drop with time with ongoing seizures. All major surgical centres are able to quote individuals where significant gains have been demonstrated when there has been seizure control early in the natural course of the epilepsy. So is reversal of epileptic encephalopathy achievable? Ongoing seizure activity is not the whole story; underlying pathology and age of onset of seizures also influence outcome. Children with symptomatic focal epilepsy require assessment on an individual basis about the relative contribution of such, and an attempt made to achieve maximal seizure control, particularly in the very young, which in symptomatic focal epilepsy involves early consideration for surgery. Expectations for cognitive outcome must be discussed in each case, and outlined to the family. Surgery is still aimed at seizure control; developmental gains may be a secondary aim but cannot be guaranteed.

Wednesday 24 September 2008
07:30 – 09:00
Hall 5
EUREPA Teaching Session
Nonconvulsive status specific features and specific etiologies

NONCONVULSIVE STATUS IN THE RING CHROMOSOME 20 SYNDROME

S. Zuberi
Royal Hospital For Sick Children, Glasgow, UK

NONCONVULSIVE STATUS TRIGGERED BY ANTICONVULSANTS

P. Thomas
UF EEG Epileptologie Service De Neurologie, Nice, France

Treatment with antiepileptic drugs (AEDs) may provoke a paradoxical aggravation of epilepsy, both in adults and in children. Various mechanisms may be responsible, but the most puzzling is a truly inverse pharmacodynamic effect, with increased seizure activity sometimes associated with the appearance of new seizure types, that occurs without high drug level, drug tolerance, or encephalopathy. Idiopathic generalized epilepsies (IGE), a subgroup of epilepsies which are genetically determined and have no structural or anatomic cause, are often involved in this type of deterioration. In IGE, the use of ill-advised AEDs, especially carbamazepine (CBZ) and phenytoin (PHT), either in monotherapy or in combination, is a common problem, encountered in up to 69% of patients in recent series. Paradoxical aggravation in IGE usually results in subtle or overt increased seizures with or without new seizure types, associated with worsening of EEG abnormalities, and with a dramatic increase of confusional episodes, related to atypical nonconvulsive status epilepticus.

NONCONVULSIVE STATUS IN THE ELDERLY: DIAGNOSTIC PROBLEMS AND THERAPEUTIC ISSUES

J. Fernandez Torre
University Hospital Marques De Valdecilla, Santander, Spain

The diagnosis of nonconvulsive status epilepticus (NCSE) may be particularly challenging in older people. The high incidence of delirium, and the frequent coexistence of delirium and dementia between elderly subjects is responsible for this major difficulty. A high level of suspicion and the consideration of an urgent electroencephalogram (EEG) as the method of choice in the evaluation of these patients will be the clues to obtain an early and accurate diagnosis. In addition, the characterization and delineation of several typical pictures occurring in the elderly individuals can make easier its recognition, diagnosis and treatment. In general, ambulatory and comatose patients must be distinguished. In both groups, there are generalized and focal or partial forms of NCSE. From a practical point of view, we can differentiate the following situations: (1) NCSE in preexisting generalized or partial epilepsy; (2) NCSE as cause of abnormally prolonged postictal period following a generalized tonic–clonic seizure (GTCS); (3) subtle generalized NCSE (as the final phase of a GTCSE); (4) situation-related generalized NCSE (secondary to drugs, toxics, electroconvulsive therapy and metabolic disturbances); (5) NCSE occurring in elderly patients with acute brain injury and potentially epileptogenic lesions; and (6) NCSE in critically ill (comatose) elderly subjects. Although it is well-known that a definitive diagnosis of NCSE is obtained after a clinical and electroencephalographic resolution following the acute administration of intravenous benzodiazepines, this

approach has limitations because an immediate clinical improvement can be difficult to evaluate in an elderly patient under the hypnotic effects of these drugs. Moreover, the absence of a rapid clinical improvement is not always definite sign of encephalopathy because a delayed normalization of the mental state may occur in NCSE. Degenerative and metabolic encephalopathy may particularly mimic NCSE in these patients. In conclusion, NCSE in older people requires of an expert clinical and neurophysiological approach.

Wednesday 24 September 2008
07:30 – 09:00
Hall 7
EUREPA Teaching Session
Deficient energy metabolism presenting as epilteptic seizures or status epilepticus

THE ROLE OF MITOCHONDRIA IN EPILEPTOGENESIS

H. Pihko
Helsinki University Central Hospital, Hus, Finland

EPILEPTIC ENCEPHALOPATHY IN CHILDREN WITH TWINKLE – MUTATIONS

T. Lonnqvist
Helsinki University Central Hospital, Huch, Finland

Increasing number of neuromuscular diseases caused by defects in the nuclear-encoded proteins responsible for mitochondrial DNA (mtDNA) maintenance is detected. Especially, mutations in the genes whose products function directly at the replication fork, such as mitochondrial DNA polymerase ã (POLG), and replicative helicase Twinkle cause early and late onset neuromuscular disorders. Dominant mutations in PEO1 gene encoding Twinkle helicase cause pure external ophthalmoplegia (PEO) plus-syndromes, which are characterized by multiple mtDNA deletions in the muscle, brain and the heart of the patients. We have described recessive PEO1 mutations in homozygous form (Y508C) in 22 infantile onset spinocerebellar ataxia (IOSCA) patients and in compound heterozygous form (Y508C and A318T) in two brothers. Sarzi et al. have reported another homozygous recessive PEO1 mutation (T457I). The patients with either compound heterozygous Y508C and A318T or homozygous T457I mutations had mtDNA depletion in the liver. Recently we showed mtDNA depletion in the brain of IOSCA patients making IOSCA a representative of the tissue specific mtDNA depletion syndromes. We have followed-up 21 IOSCA patients and the two heterozygotes at HUCH. Severe epilepsy appeared in 13 IOSCA patients and in both heterozygotes. The epilepsy usually started as epilepsia partialis continua and progressed to a generalized status epilepticus lasting for several days. Six IOSCA patients and both heterozygotes have died because of this severe epileptic encephalopathy. Focal, stroke-like lesions were seen in MRI, and brain atrophy with focal laminar cortical necrosis and hippocampal damage on neuropathological examination. The treatment has been problematic because of lack of efficiency and potentially harmful side effects. VPA should be avoided, because it may precipitate fatal liver failure, and VPA and PHB may in addition impair respiratory chain activity. Oxcarbazepin causes hyponatremia and is ineffective. PHT is ineffective, and causes elevation of liver transaminases in IOSCA patients. Lamotrigine and levetiracetam are well tolerated, but not very effective. So far the best option for intravenous therapy has been midazolam as a continuous infusion at the onset of the status epilepticus. Recessive PEO1 mutations should be considered in patients with refractory epilepsy and ataxia or atypical progressive CP-like syndrome or liver involvement.

IMPAIRED GLUCOSE TRANSPORT INTO THE BRAIN

J. Klepper
Klinikum Aschaffenburg Childrens Hospital, Aschaffenburg, Germany

Wednesday 24 September 2008
07:30 – 09:00
Hall 9
EUREPA Teaching Session
Treating epilepsy

DIAGNOSIS AND MISDIAGNOSIS

P. Genton
Centre Saint Paul – HHG, Marseille, France

STARTING AND STOPING TREATMENT

A. Gil Nagel
Clinica Ruber International, Mirasierra, Spain

THE PLACE OF POLYTHERAPY

M. Brodie
Western Infirmary – Epilepsy Unit, Glasgow, UK

Around 60% of adolescent and adult patients with newly diagnosed epilepsy control on monotherapy, usually with their first (~50%) or second (~10%) antiepileptic drug (AED). A further 5–10% of this population will respond to polypharmacy. In our own series of 1099 newly diagnosed patients collated over 25 years, 61.7% became seizure-free on monotherapy, while only 6.5% were controlled for a year or more on AED combinations. All but 3 of these 71 patients received 2 drugs. Combining AEDs with different mechanisms of action may enhance their effectiveness, although the only partnership for which there is good clinical evidence of synergism is sodium valproate with lamotrigine. My current practice is to try one or two pharmacologically distinct monotherapy options prior to combining, with exception of patients with severe lesional epilepsy who respond well to their first AED. If at optimal dosing, he or she reports just a few sporadic seizures, I would add in a second AED at low dosage. There are a few useful pragmatic tips in combining AEDs. Firstly, drug burden is a function of dose as well as number of drugs and so avoiding a high dose of any of the pharmacological partners is more likely to provide good seizure control without unacceptable toxicity. Secondly, broad spectrum AEDs with multiple mechanisms of action probably provide the best chance of an optimal outcome. Avoiding combinations of AEDs with similar modes of action also seems a reasonable caveat. Seizure freedom must be the primary goal for every patient at the outset. However, polypharmacy brings with it substantial morbidity and so a palliative strategy will be necessary for many patients with truly refractory epilepsy. Nevertheless, there is increasing evidence that seizure-free rates are modestly increasing in parallel with the licensing of new AEDs with different mechanisms of action.

Wednesday 24 September 2008
09:00 – 11:00
Hall 1
Main Session
Predicting the response to AEDs

DO WE GET ANY HELP FROM ANIMAL MODELS?

G. Sills
University of Liverpool, Liverpool, UK

Preclinical models play an essential role in the discovery and development of new antiepileptic drugs (AEDs). The identification of candidate compounds in random screening, the demonstration of efficacy prior to first use in human volunteers, and the preliminary evaluation of effective doses, pharmacokinetics, and safety are all dependent on the use of experimental seizure models. Maximal electroshock (MES), pentylenetetrazol (PTZ) and the kindled rat are the most well-characterized models for the assessment of anticonvulsant efficacy and have been in widespread use for many decades. Attempts have been made to correlate activity in these models with potential clinical efficacy, based largely on pharmacological sensitivity to older AEDs. However, experience with newer antiepileptic agents has questioned this association. For example, several compounds, including lamotrigine, topiramate, zonisamide and levetiracetam, are reported to possess a broad spectrum of clinical effectiveness that is not reflected by their range of activity in animal models. Indeed, the lack of efficacy of levetiracetam against acute experimental seizures induced by MES and PTZ could, in theory, have curtailed the development of the drug and belies its effectiveness in chronic models. A revised approach to the use of preclinical models in the identification and development of AEDs is required, embracing a wider range of approaches with improved clinical predictability and sufficient sensitivity to select compounds with novel mechanisms of action. Employing more clinically relevant treatment protocols that consider the chronic and often adjunctive use of novel antiepileptic agents, dissecting out activity against individual components of the kindled seizure, and utilising recently described 'drug resistant' models all hold promise for improved characterisation of efficacy in preclinical studies and may ultimately ensure that new AEDs with the potential to address the therapeutic void of refractory epilepsy are not prematurely discarded.

WHICH ARE THE PROGNOSTIC FACTORS ACCORDING TO THE EPIDEMIOLOGICAL STUDIES?

F. Semah
Shfj – Cea, Orsay, France

The early prediction of intractability is a major challenge in epileptology. Some prognostic factors have been pointed out, most of which underlined that partial epilepsy is more difficult to control than idiopathic generalized epilepsy. The main predictors of intractability being the presence of a brain lesion demonstrated by neuroimaging or suggested by a neurological deficit or a developmental delay or defined by significant focal electroclinical abnormalities. Little is known about the relationships between the location of the epileptogenic area and the chance of being seizure-free in patients with partial epilepsy. Some data suggested that temporal lobe epilepsy is more difficult to control than other types of partial epilepsy, but this might only reflect the prognostic value of hippocampal sclerosis. We will review the data that have suggested that epileptic patients with MRI evidence of hippocampal sclerosis often suffered from medically refractory epilepsy. We will also discuss the pitfalls associated with hippocampal abnormalities detected by MRI. We will then focus on the prognostic factors in patients with malformations of cortical development. The response to the first AED is another early predictor of refractory epilepsy. At the time of diagnosis, several prognostic factors are now available to predict drug resistance, but further studies are needed to better delineate the specific role of each of these factors, and in particular, that of the various types of underlying brain abnormality.

WHY DO SOME PATIENTS LOSE THE INITIAL RESPONSE?

D. Schmidt
Epilepsy Research Group, Berlin, Germany

Development of tolerance, i.e., the reduction in response to a drug after repeated administrations, is an adaptive response of the body to prolonged exposure to the drug, and tolerance to antiepileptic drugs (AEDs) is no exception. Tolerance may lead to attenuation of side-effects but also to loss of efficacy of AEDs and is reversible after discontinuation of drug treatment. There are two major types of tolerance. Pharmacokinetic (metabolic) tolerance, which is due to induction of AED metabolizing enzymes and has been shown for most first generation AEDs, but is easy to overcome by increasing dosage. Pharmacodynamic (functional) tolerance, which is due to ''adaptation'' of AED targets, e.g., by loss of receptor sensitivity, and has been shown experimentally 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. Although there is convincing experimental evidence that almost all AEDs lose their antiepileptic activity during prolonged treatment, because of diverse confounding factors, detecting tolerance in patients with epilepsy is more difficult. But it can be done with careful assessment of decline during long-term individual patient response. After excluding confounding factors, tolerance to antiepileptic effect for most modern and old AEDs can be shown in small subgroups of responders by assessing same-patient reponse in individuals or groups. Why do some patients develop tolerance and others do not? Probably because the extent of tolerance in a given patient depends on the drug and individual, largely unidentified possibly genetic, factors. Whatever the reason(s), development of tolerance to the antiepileptic activity of an AED may be an important reason for failure of drug treatment in some patients.

CAN WE PREDICT THE RESPONSE FOR INDIVIDUAL PATIENTS?

R. Kälviäinen
Kuopio University Hospital, Kuopio, Finland

Can we predict the response for individual patients? Reetta Kälviäinen Epilepsies form a heterogenous group of disorders with unique clinical presentations, different underlying causes, different natural histories and different implications for management and treatment. Epidemiological studies give us some information about which patients are in greatest risk to become intractable and which patients have the best possibility to respond to AED treatment. It is, however, still difficult or even impossible to predict the response of an individual patient at the start of the treatment. We have identified from population of Kuopio University Hospital (pop. 250,000) in Finland all the patients with newly diagnosed focal epilepsy during 1988 to 2002 (N= 350). The patients had to be aged between 15 to 65 years at the time of diagnosis and with normal intelligence (intelligence quotient over 85). Patients with progressive neurological disorder, severe psychiatric or other medical condition or substance abuse were excluded. All patients underwent careful neurological, neurophysiological and neuropsychological evaluation at the time of diagnosis an before the drug treatment was started. From the year 1993 all the patients underwent also MRI evaluation. All patients have now had a prospective 5-year follow-up. Altogether 70% of the patients have achieved seizure-freedom, whereas 30% continue to have seizures or have been participated into our epilepsy surgery program. There was no statistically significant difference in the baseline number of seizures before start of the treatment, although there was slight tendency towards higher seizure numbers in the drug-resistant group. The drug-resistant group had also more remote symptomatic etiologies for the epilepsy than the seizure-free group. Six variables predicted 5-year seizure outcome: age at the time of diagnosis, presence of spike focus in EEG, partial complex or mixed seizure type, remote symptomatic etiology and moderately impaired memory performance. Explanations for poor response include also noncompliance and etiological factors, which were not detected at the time of diagnosis. We have created also a model for predicting individual response on the basis of the data gained from our dataset. Defining the type and especially the etiology of the epilepsy should be considered mandatory in the diagnostics of epilepsy because it offers the best guide to both management and predicting the individual response to the management and therapy. In future we may also have specific tools in certain types of epilepsies in further predicting the response for each patient.

Wednesday 24 September 2008
09:00 – 11:00
Hall 3
Main Session
Synaptopathies in epilepsy

REORGANIZATION OF THE INTERNEURONAL NETWORK IN THE EPILEPTIC HUMAN HIPPOCAMPUS

Z. Magloczky
Institute of Experimental Medicine, Hungarian Academy of Sciences, Szigony, Hungary

Changes of hippocampal GABAergic interneuronal circuits are known to play a central role in epileptogenesis. The selective loss of some interneuron types has been reported. Fate of functionally different hippocampal interneuron types have been investigated in two models of temporal lobe epilepsy (kainate and pilocarpine) and in surgically removed hippocampi of therapy resistant human TLE patients. A subset of perisomatic inhibitory cells contains parvalbumin (PV), they include axo-axonic and basket cells, and are responsible for controlling/synchronizing the output of principal cells. A decrease in their number was reported in epilepsy. Electron microscopic examination of pyramidal and granule cell bodies in PV-immunostained sections of the epileptic human hippocampus revealed that perisomatic innervation of the principal cells was preserved in both sclerotic and nonsclerotic samples. In addition, the ratio of the initial segment synapses increased among the postsynaptic targets, which might give rise to a more efficient regulation, and thereby an increased synchrony, of granule cell firing. Dendritic inhibitory interneurons display different sensitivities to excitotoxic damage in epilepsy. Those containing calbindin are well preserved, although their synaptic connections are changed. Namely, they terminate on other interneurons in larger proportion than in the control. In addition, the length of their synaptic active zones is increased. Calretinin (CR)-containing cells – responsible for synchronizing other inhibitory interneurons – are particularly sensitive to epilepsy in the human hippocampus. In animal models, their number was found to decrease soon after the first seizure. This suggests that synchronization of dendritic inhibitory cells might be impared in human epileptic hippocampi and consequently, an abnormal potentiation of excitatory inputs to pyramidal cells. Principal cell ensembles connected by potentiated synapses may be involved in seizure generation. Damage of even a small number of cells may cause serious disturbances of network activity, if those cells play a crucial role in the circuit.

SYNAPTIC, EXTRASYNAPTIC AND NONSYNAPTIC ION CHANNELS IN EPILEPSY

D. Kullmann
Institute of Neurology, London, UK

Numerous changes in the expression of voltage- and ligand-gated ion channels have been reported in experimental models of acquired limbic epilepsy. Establishing which of these changes contribute to the occurrence of seizures is notoriously difficult. Some of the more robust alterations affect GABAA receptors. Depending on their subunit composition these receptors mediate either fast inhibitory neurotransmission or tonic inhibition of neuronal excitability, but changes in either type of signalling can have unexpected effects on the input-output relationships of neurons. An alternative insight into the roles of synaptic and nonsynaptic ion channels in epilepsy comes from some rare single-gene disorders. These are increasingly amenable to investigation both in animal models and by genetic manipulation of neurons in vitro.

ALTERED FUNCTIONS OF INHIBITORY NETWORKS IN HUMAN AND RODENT TLE

U. Heinemann
Johnannes-Muller-Institute of Physiology, Berlin, Germany

Altered Functions of Inhibitory Networks in Human and Rodent TLE Uwe Heinemann, Else Tolner, Tamar Dugladze and Tengis Gloveli

Both in pilocarpine or kainate treated rats and in patients with temporal lobe epilepsy loss of principal cells far exceeds loss of interneurones. Yet, application of GABA receptor blockers does not induce epileptiform activity in such tissues. In fact stimulus induced responses show signs of disinhibitions. This is typical for the dentate gyrus of the hippocampus. We tested whether this is also true for the entorhinal cortex. In the entorhinal cortex deep layer stimulation or stimulation of the parasubiculum and presubiculum induces prolonged excitatory responses in superficial layers of the entorhinal cortex similar to those which are observed after application of bicuculline in the entorhinal cortex from normal animals. Histological analysis suggested loss of neurones in layer III of the EC in different models of TLE including human TLE. This loss was originally attributed to loss of inhibitory cells as the number of parvalbumin positive cells declined. However, counting of cells which express the enzyme GAD65/67 which produces GABA from glutamate revealed no cell loss suggesting that the number of GABAergic cells is preserved. Changes in glutamine and glutamate transport may have led to silencing of GABAergic neurones. We therefore tested for substitution of glutamine to the cerebrospinal fluid. This resulted in appearance of spontaneous epileptiform discharges in these preparations suggesting that glutamine supply to interneurones is not the cause of loss of inhibition. We suggest that this may be due to increased interaction between inhibitory interneurones. This would reflect in changes in rhythmic activities as well. Indeed we can show that there is change in the ability of generation of network oscillations in the neighbourhood of an epileptogenic lesion.

FUNCTIONAL CONSEQUENCES OF SYNAPTOPATHIES AT THE NETWORK LEVEL

C. Bernard
Inserm U751, Marseille, France

No Abstract Received.

Wednesday 24 September 2008
14:30 – 16:00
Hall 3
Neurobiology Symposium
Neuro-Glia signaling and epilepsy

ASTROCYTES IN THE EPILEPTIC BRAIN: ROLE IN SEIZURE GENERATION AND NEUROVASCULAR COUPLING IN EXPERIMENTAL MODELS

G. Carmignoto
University of Padova, Padova, Italy

No Abstract Received.

GLIA-NEURONAL SIGNALING DURING NEOCORTICAL EPILEPTOGENESIS

A. Friedman
Ben-Gurion University, Bersheva, Israel

Focal insults to the neocortex often involves vascular damage, and specifically breakdonw of the blood–brain barrier (BBB) and followed by the development of focal epilepsy. We have recently shown that in the rat neocortex long-lasting breakdown of the BBB or direct exposure to serum-derived albumin, or to transforming growth factor beta 1 (TGF-b1) leads within days to the generation of an epileptic focus. Significantly,

within hours following either treatment, and before the emergence of neuronal hyperexcitability, we observed a rapid up-regulation of the astrocytic marker, glial fibrillary acidic protein (GFAP). To study the role of astrocytes in epileptogenesis we investigated gene expression using gene array technology in all three models of epileptogenesis. Analyses of genomic expression patterns demonstrated a similar activation pattern for BBB opening, brain exposure to albumin or TGF-â1. Microarray analyses at different time points following treatment highlights the importance of early astrocytic activation. Importantly, the application of TGF-â pathway blockers suppressed the majority of the albumin-induced transcriptional changes associated with the epileptogenesis process and prevented the generation of epileptiform activity. Transcriptional changes predict reduced buffering capacity for both extracellular potassium and glutamate. A NEURON model was used to simulate the role of reduced astrocytic uptake of extracellular potassium and glutamate on excitatory synaptic potentials (EPSPs). The duration of a single excitatory postsynaptic potential was prolonged during the accumulation of glutamate and less sensitive to potassium accumulation. In contrast, during repetitive activation, glutamate accumulation was associated with frequency-dependent depression of EPSPs while potassium accumulation led to frequency and NMDA-dependent synaptic facilitation. Electrophysiological experiments in neocortical slices during albumin-induced epileptogemesis showed synaptic facilitation and seizure-like activity in response to stimulation at 10–20Hz. Our data indicate a TGF-â signaling pathway mediating a rapid astrocytic transformation, and consequent reduced potassium buffering as an underlying cause for neuronal hyper-excitability during epileptogenesis.

ASTROCYTE-NEURON COMMUNICATION IN HUMAN BRAIN TISSUE

G. Perea
Instituto Cajal, Spain

No Abstract Received.

A ROLE FOR ASTROCYTE DYSFUNCTION IN HUMAN EPILEPSY

C. Steinhauser
University of Bonn, Bonn, Germany

We have recently identified two distinct types of cells with astroglial properties, GluR cells and GluT cells, coexisting in mouse hippocampus. GluR cells express ionotropic glutamate receptors, receive synaptic input from neurons, and lack functional glutamate transporters and gap junction coupling. GluT cells, resembling bona fide astrocytes, display glutamate transporters, gap junction coupling, but lack ionotropic glutamate receptors. Both types of astroglial cells are also present in the hippocampus of patients presenting with intractable temporal lobe epilepsy (lesion-associated, nonsclerotic epilepsy). However, in patients suffering from hippocampal sclerosis, one of the most common forms of epilepsy, astrocytes almost completely disappears while the remaining GluR-cells undergo alterations of their glutamate receptors. These findings support the hypothesis that glial cells play a key role in the generation and/or spread of seizure activity in human epilepsy. This deleterious effect is brought about by (1) the abundant excitatory neurotransmitter glutamate and (2) impaired gap junction-mediated buffering of K+ and metabolites, leading to prolonged activation of cells in the hippocampus, a brain region crucially involved in learning, memory, and emotional processing. Analyses of more than a hundred brain specimens neurosurgically resected from epilepsy patients were used to substantiate this new insight. We have developed an animal model of epilepsy, unilateral intracortical kainate injection, resembling many of the morphological and functional changes observed in human epileptic hippocampus. Our findings challenge the common view of epileptogenesis according to which neurons are considered the prime targets affected in this disease.

Wednesday 24 September 2008
14:30 – 16:00
Hall 5
Discussion Group
Does prenatal exposure to carbamazepine or valproate impair cognitive development?

IMPACT OF PARENTAL EXPOSURE TO VALPROATE AND CARBAMAZEPINE ON COGNITION IN ANIMAL STUDIES

C. Frisch
University of Bonn, Bonn, Germany

There is evidence that valproate, and, to a lesser extent, carbamazepine, are cognitively teratogenic agents. In animal studies, cognitive teratogenicity of valproate was demonstrated several times, while the effects of carbamazepine are less clear. Accordingly, it was recently shown that rat juvenile cortical and hippocampal development was impaired by repeated intraperitoneal valproate application to dams, while for carbamezpine no clear-cut evidence was found. Furthermore, functional impairment on the cellular level was induced by valproate applied during different developmental episodes, and neuronal cell death in the developing brain was found to be induced by single anticonvulsive doses of valproate but not by such doses of carbamazepine. The effects of more distributed valproate application during pregnancy on these parameters and related behavioral processes are only partially known. Therefore, we established a self-application schedule by diluting valproate in the drinking water of pregnant Wistar rats. After application during whole pregnancy, high dosages with peak serum concentrations slightly above the therapeutic range induced early decrements in general activity and deficits in learning and memory. These impairments were paralleled by decreased cortical, cerebellar, and brainstem volumes, and cortical volume reduction was correlated with spatial acuity in the water maze. Unexpectedly, medium dosages led to improved water maze performance in 30 days old rats, and MRI analyses yielded increased hippocampal volumes in these animals. The results indicate that effects of valproate in utero on rat offspring cognitive capabilities depend on total drug load differentially affecting cerebral development. Furthermore, they point to the importance of the drug application schedule used in animal studies of teratogenicity.

CONFOUNDING FACTORS IN HUMANS: DOES MATERNAL EPILEPSY PER SE AFFECT COGNITIVE DEVELOPMENT IN THE OFFSPRING?

K. Eriksson
Tampere University Hospital, Ped. Neurology Unit, Tampere, Finland

The most important factors confounding the effect of in utero AED exposure on neurocognitive performance in offsprings of mothers with epilepsy include genetic traits associated with different seizure/epilepsy/epilepsy syndrome types and their etiologies, severity of mother's epilepsy (e.g. seizure control during and after pregnancy), AED treatment (number and doses), maternal (and paternal) intelligence, psychosocial and family environment (e.g. socioeconomic status, developmental support) and possible pre-, peri- or postnatal comorbidity of the child (e.g., chromosomal/genetic syndromes). When approaching this issue, many methodological problems arise; population-based, controlled studies with sufficient numbers for power would be needed but mainly hospital-based series with selected study groups exists, children should be at least 5–6 years of age for reliable long-term neurocognitive developmental test results etc. Almost all individual cognitive differences, when reliably measured, are moderately to substantially heritable and one of the most significant predictor of child's IQ and neurocognitive development is the IQ of the mother. Parent-offspring correlations are, however, confounded reflecting both the influence of genetic and environmental factors. The effects of various epilepsies/epilepsy syndromes, like e.g., idiopathic

generalized syndromes such as juvenile myoclonic epilepsy and focal epilepsies such as temporal lobe epilepsy, may in this respect be different. The mothers in the former 'valproate group' may be significantly different compared to the 'carbamazepine group' of focal epilepsies. They may have different genetic background as well as co-morbidities, which interfere with parenting interactions, and influence their socioeconomic status. All these factors can together impose a cumulative impact on the neurocognitive development of the offspring and serve as significant confounding factors when the causal relationship between drug exposure and children's complex neurocognitive outcomes are evaluated.

DOES PRENATAL VALPROATE EXPOSURE CAUSE COGNITIVE IMPAIRMENT?

N. Adab
University Hospital Coventry and Warwickshire, Lemington Spa, UK

One-third of people with epilepsy are women of childbearing age. Approximately 0.5% of pregnancies per year are exposed to antiepileptic drugs. Valproate remains the drug of choice for idiopathic generalized epilepsy, particularly juvenile myoclonic epilepsy. It is increasingly avoided in young women for fear of its teratogenic effects. Most research has focused on major malformations, but the data about longer term developmental effects remains poorly studied. This discussion will review the growing published evidence for prenatal valproate exposure on cognitive impairment and learning difficulties. A systematic Medline search was used to identify independent cohort studies. Both retrospective and prospective studies suggest that prenatal valproate exposure results in significantly lower development scores in preschool children and lower IQ, particularly verbal scores in school age children. There is growing interest in exploring specific cognitive deficits. In addition, behavioral problems including autistic spectrum disorders were found more commonly among children with valproate exoposure in utero. The limitations of the studies are examined and implications for the design of future research explored. Pharmacogenetic factors may have a role since not all pregnancies are affected. In the meantime for women with epilepsy and the practicing clinician, a decision has to be made balancing seizure freedom against the risks to the developing child.

IS PRENATAL CARBAMAZEPINE EXPOSURE SAFE FOR COGNITIVE DEVELOPMENT?

E. Gaily
Hospital For Children And Adolescents, Helsinki, Finland

Fetal exposure to carbamazepine (CBZ) as well as to other antiepileptic drugs during the first trimester of pregnancy increases the risk of major malformations. Less data are available on whether children exposed to CBZ in utero have a higher risk of cognitive dysfunction than nonexposed children. Three population-based prospective controlled evaluator-blinded studies have reported cognitive outcomes in children exposed to CBZ monotherapy. One study reported IQ scores obtained by Wechsler scales at age 5–11 years in Finnish children. The mean (SEM) full scale IQ was 99.7 (1.8) in 86 CBZ exposed and 97.6 (1.4) in 141 control children of mothers with no epilepsy. A Swedish study compared the results of the Griffiths test at 2–8 years between 35 carbamazepine-exposed children and 66 control children; no difference was observed. Pooled data on the prevalence of mental deficiency from two Finnish studies showed IQ under 70 in two of 105 children (1.9%). One of the two children with low IQ had West syndrome in infancy. The effects of CBZ monotherapy have also been investigated in three prospective studies which enrolled a total of 102 exposed mother-child pairs and controls through teratology counseling services. Two studies reported significantly lower developmental quotients in CBZ exposed children compared to nonexposed controls while one study found no difference. A retrospective study comprising 52 children exposed to CBZ monotherapy found no IQ difference compared to 80 unexposed controls. Another retrospective population-based study investigated the prevalence of autistic spectrum disorder; the risk was not statistically significantly increased in 80 children exposed to carbamazepine monotherapy compared to the general population. Population-based studies suggest that the risk of significant cognitive impairment after fetal exposure to carbamazepine monotherapy is low. However, the power of the existing studies is insufficient to exclude subtle IQ alterations.

Wednesday 24 September 2008
14:30 – 16:00
Hall 6
Discussion Group
Fast activity at seizure onset in human and animal temporal lobe

CHARACTERIZATION OF FAST DISCHARGE IN VARIOUS TYPE OF HUMAN PARTIAL EPILEPSIES

F. Bartolomei
Universite Aix Marseille II, Marseille, France

No Abstract Received.

ELECTROGRAPHIC PATTERNS OF SEIZURE ONSET: CAN THEY TELL US ABOUT THE TRIGGERING MECHANISMS?

A. Bragin
David Geffen School of Medicine At UCLA, Los Angeles, CA, USA

To correctly diagnose the mechanism(s) triggering seizures in a patient using a simple test, and prescribe the proper medications, is a dream of every practicing neurologist. There have been numerous attempts in clinical and basic science to elucidate mechanisms triggering seizures. In the clinical sciences, these efforts have contributed to approaches for classifying of seizures. There are several classifications of seizures and most of them assume that abnormal synchronization of neuronal discharges is the primary cause of seizure generation. Although standard analysis of EEG records is directed at determining the time of seizure onset and location of areas involved in the generation of epileptiform activity, existing technology has the capability of recording brain electrical activity from multiple sites, with high sampling rate. Electrical activity could be sampled in the frequency range of 0.1 Hz to 1 kHz allowing analysis of ultraslow activity and high frequency oscillations. This new technology reveals additional information which is largely not available from standard clinical practice. Such analysis of electrographic seizure onset patterns could reveal novel mechanisms seizure generation. Research leading to algorithms that analyze and classify seizure onset patterns automatically could extend the utility of EEG in clinical practice making it a more powerful diagnostic tool. Identification of the chemical correlates of different electrographic ictal onset patterns may help guide physicians in selecting a course of medical treatment that is tailored to each patient's personal needs.

FAST NETWORK OSCILLATIONS PRECEDING SEIZURES IN RAT HIPPOCAMPUS

P. Jefferys
The Medical School, Birmingham, UK

No Abstract Received.

NETWORK MECHANISMS OF FAST ACTIVITY AT SEIZURE ONSET IN THE ENTORHINAL CORTEX

M. De Curtis
Instituto Nazionale Neurologico, Milan, Italy

The network mechanisms responsible for the initiation of a focal seizure are largely unknown. A common seizure pattern onset observed in

patients with mesial temporal lobe epilepsy (TLE) is characterized by fast activity at 20–30 Hz. We reproduced this pattern in the temporal lobe of the in vitro isolated guinea pig brain, to study cellular and network mechanisms involved in its generation. Seizure-like events were induced by brief arterial perfusion of 50μM bicuculline in vitro. Intra, extracellular and K-selective recordings were performed in the entorhinal cortex (EC) during interictal-ictal transition. Principal EC neurons did not generate action potentials during ictal onset, whereas sustained firing was observed in putative interneurons. Within 5–10 seconds from seizure onset principal neurons generated a prominent firing, that correlated with the appearance of hypersynchronous bursting discharges. Fast activity correlated with rhythmic inhibitory potentials superimposed to a slow depolarization that developed concurrently with an increase in extracellular potassium, [K+]o. The amplitude decrease of rhythmic inhibitory potentials during the [K+]o rise suggests that progression of ictal discharge is promoted by a potassium-dependent change in reversal potential of inhibitory activity. These findings demonstrate a prominent role of inhibitory networks during the transition from the interictal state to seizure in the entorhinal cortex.

Wednesday 24 September 2008
14:30 – 16:00
Hall 7
Discussion Group
The nosology of the epilepsies: what is 'idiopathic generalized epilepsy'?

MOLECULAR GENETICS OF IGE

F. Zara
Institute Giannina Gaslini – Lab. Neurogenetics, Genova, Italy

No Abstract Received.

PET AND SPECT FINDINGS IN IGE

M. Koepp
University College London, London, UK

Juvenile myoclonic epilepsy (JME) is characterized by specific types of seizures, showing a lack of pathology using magnetic resonance imaging (MRI) and computed tomography scanning. However, JME is associated with a particular personality profile, and behavioral and neuropsychological studies have suggested the possible involvement of frontal lobe dysfunction. The development of highly sensitive neuroimaging techniques has provided a means of elucidating the underlying mechanisms of JME. Single photon and positron emission tomography have demonstrated cerebral blood flow (rCBF), neurotransmitter and metabolic changes. Compared to normal controls, the JME group showed a significant rCBF reduction in bilateral thalami, red nucleus, midbrain, pons, left hippocampus, and in the cerebelli, whereas rCBF increase in the left superior frontal gyrus suggesting an abnormal neural networks in the thalamus, hippocampus, brainstem and cerebellum associated with JME. A study using 11C-FMZ-PET demonstrated that GABAA-cBZR binding is globally increased in the cerebral cortex of patients with JME and other forms of IGE. Frontal lobe GABAA-cBZR binding was particularly elevated in patients with JME, but not in patients with other forms of IGE. Similarly, a study using PET to measure the uptake of 18F-fluoro-2-deoxyglucose (18FDG) demonstrated that JME is associated with frontal lobe abnormalities that may affect epileptogenic potential and cognitive functioning. Correlating with impaired performance during a visual working memory test, JME patients were shown to have reduced 18FDG uptake in the dorsolateral prefrontal cortex, premotor cortex and basal frontal cortex. Sensitive neuroimaging techniques provide evidence of the involvement of additional, possibly multifocal disease mechanisms – in particular involving the frontal lobes – in accordance with the findings of behavioral and neuropsychological studies. Current evidence therefore suggests that JME is a frontal lobe variant of a multiregional, thalamocortical 'network' epilepsy, rather than a generalized epilepsy syndrome.

MR IMAGING AND SPECTROSCOPY IN IGE

F. Wörmann
Bethel Epilepsy Centre, Bielefeld, Germany

Routine MRI in patients with idiopathic generalized epilepsy (IGE) is normal by visual inspection and definition. Quantitative MRI can, however, show subtle, but widespread cerebral structural changes in patients with IGE. When voxel-based morphometry (VBM) was used to analyze structural MRI data objectively, patients with juvenile myoclonic epilepsy were shown to have an increase in cortical gray matter in the mesial frontal lobes compared with normal subjects (Woermann et al., 1999). Other VBM studies in IGE showed diverging results, but implicated changes within the frontal lobes and thalami most often. Proton magnetic resonance spectroscopy (1H-MRS) provides information on certain brain metabolites. As N-acetyl aspartate (NAA) is thought to be a neuronal marker, a reduction in the level of NAA can be an indication of neuronal damage or dysfunction. Both prefrontal and thalamic NAA concentrations were found to be significantly lower in IGE patients than in controls. A negative correlation was found between NAA levels and duration of epilepsy, indicating that thalamic dysfunction in IGE may be progressive. In addition, 1H-MRS has revealed frontal lobe changes of other metabolite in IGE, by demonstrating increased levels of glutamate plus glutamine (GLX). This finding was thought to stand for an increased neuronal excitability in this region. 1H-MRS has also demonstrated elevated levels of GLX and GABA in the occipital lobes of patients with IGE. Results from quantitative MRI and 1H-MRS, suggest multi-focal changes in a system/network consisting of (frontal) cortex and thalami in IGE. Woermann FG, Free SL, Koepp MJ, Sisodiya SM.

Duncan JS. Abnormal cerebral structure in juvenile myoclonic epilepsy (JME) demonstrated with voxel-based analysis of MRI. Brain 1999;122:2101–2107.

REFLEX EPILEPTIC TRAITS IN IGE

P. Wolf
Danish Epilepsy Centre – Dianalund, Dianalund, Denmark

No Abstract Received.

Wednesday 24 September 2008
14:30 – 16:00
Hall 9
Discussion Group
Understanding dissociative (nonepileptic) seizures: mechanisms and presentations

PREDISPOSING, PRECIPITATING AND PERPETUATING FACTORS: AN OVERVIEW

M. Reuber
University of Sheffield, Sheffield, UK

No Abstract Received.

PHENOMENOLOGICAL ASPECTS OF DISSOCIATIVE SEIZURES: CLUES TO MECHANISMS

J. Mellers
Maudsley Hospital, London, UK

No Abstract Received.

STRESS PHYSIOLOGY AND EMOTIONAL PROCESSING IN DISSOCIATIVE (NONEPILEPTIC) SEIZURES

K. Roelofs
University of Leiden, Leiden, The Netherlands

Failure of cognitive and attentional functioning in patients with psychogenic nonepileptic seizures (PNES) is often assumed to be related to psychological stress factors, such as trauma history. Although interpersonal trauma is common in PNES, the proposed relation between trauma and the attentional functioning remains unstudied in these patients. We investigated the attentional processing of social threat cues in PNES in relation to interpersonal trauma reports and basal and stress-related activity of physiological stress systems (heart rate variability and salivary cortisol in particular). A masked emotional Stroop test, comparing color naming latencies for angry, neutral and happy faces, was administered to 19 unmedicated patients with PNES and 20 matched healthy controls, in neutral and stress conditions. Stress was induced by means of the Trier Social Stress Test. Compared to controls, patients displayed an increased attentional bias for masked angry faces in neutral conditions, which was correlated to self-reported sexual trauma. These results, together with the finding that patients showed decreased HRV, may reflect a state of hypervigilance to play part in patients with PNES. The relation with self-reported trauma, moreover, offers the first evidence suggesting early risk factors to play a role in the altered threat processing in PNES.

THE SUBJECTIVE SIDE OF DISSOCIATIVE (NONEPILEPTIC) SEIZURES AND THEIR PSYCHODYNAMICS: CONVERSATIONAL PATTERNS

M. Schondienst
Epilepsiezentrum Bethel, Bielefeld, Germany

No Abstract Received.

Wednesday 24 September 2008
16:30 – 18:00
Hall 3
New Drugs Symposium

PROGRESS REPORT ON NEW ANTIEPILEPTIC DRUGS IN DEVELOPMENT – AN UPDATE OF THE NINTH EILAT CONFERENCE (EILAT IX)

H. S. White
University of Utah, Salt Lake City, UT, USA

The Ninth Eilat Conference on New Antiepileptic Drugs (AEDs)-EILAT IX was held in Sitges, Spain from the 15th to 19th of June 2008. There were more than 300 basic scientists, clinical pharmacologists and neurologists from 25 countries in attendance. The main themes of the IX Eilat Conference included: (1) old and new AEDs in generalized epilepsies; (2) novel formulations and routes of administration of AEDs; (3) common targets and mechanisms of action of drugs for treating epilepsy and other central nervous system (CNS) disorders; and (4) opportunities and perspectives in new AED discovery. As with past Eilat conferences, a large part of the programme was devoted to a review of the investigational AEDs in development. In addition, updates on those AEDs introduced since 1989 were provided. At the present time, there are at least 15 investigational AEDs in various stages of development. Detailed presentations provided a review of the preclinical and clinical status for brivaracetam, carisbamate (RWJ-333369), 2-deoxy-glucose, eslicarbazepine acetate (BIA-2-093), ganaxolone, huperzine, JZP-4, lacosamide, NAX-5055, propylisopropylacetamide (PID), retigabine, T-2000, tonabersat, valrocemide and YKP-3089. A brief overview of the current status of these investigational AEDs will be provided.

AN UPDATE ON BRIVARACETAM DEVELOPMENT – SUPPORTED BY UCB SA

P. Von Rosenstiel
UCB SA, Braine L'Alleud, Belgium

EFFICACY AND SAFETY OF ESLICARBAZEPINE ACETATE (ESL) AS ADJUNCTIVE THERAPY FOR PARTIAL SEIZURES – SUPPORTED BY BIAL

E. Ben Menachem
Sahlgrenska University Hospital, Goteborg, Sweden

Wednesday 24 September 2008
14:30 – 16:00
Hall 2b
Discussion Group
Search of biomarkers for epileptogenesis

USE OF EEG IN SEARCH OF BIOMARKERS FOR EPILEPTOGENESIS – REVIEW OF ANIMAL DATA

P. Mares
Institute Of Physiology, Prague 4, Czech Republic

Status epilepticus represents the most common trigger of epileptogenesis in experimental animals. Status can be induced chemically (kainic acid, pilocarpine or lithium/pilocarpine) or electrically (stimulation of perforant path or hippocampus). Studies in adult laboratory animals can use long-term videoEEG monitoring to have longitudinal data from the same group of animals and to have exact data on the appearance of the first spontaneous seizure. Studies in developing animals (rats) have a disadvantage in the fast growth of the brain and skull; in addition, rat pups are fully dependent on mother care up to the age of 14 days, physiological weaning is at postnatal day 28. For these reasons is it impossible to perform real long-term monitoring and to have data similar to adult animals. All methods of induction of status epilepticus mentioned above are directed to limbic structures therefore it is always necessary to have recording electrodes not only in cerebral cortex but also in hippocampus. Spontaneous convulsive seizures may be preceded by nonconvulsive limbic seizures with epileptic activity only in limbic structures. Appearance of the first ictal EEG activity, i.e. the first spontaneous seizures is a sign of completed epileptogenesis or at least of its first step. It is important to have indicators for the phase preceding the first spontaneous seizure. Interictal activity can be registered in nearly all animals after status epilepticus but its predictive value is highly questionable. Different in vivo as well as in vitro stimulation methods (evoked potentials, epileptic afterdischarges) brought data on increased excitability mainly of limbic structures but our present abilities to predict appearance of seizures and thus recognize that the process of epileptogenesis is going on are very limited.

USE OF EEG IN SEARCH OF BIOMARKERS FOR EPILEPTOGENESIS – REVIEW OF HUMAN DATA

P. Halasz
Opni, Attila Ut, Hungary

Spike discharges are not acceptable as candidates for EEG surrogate marker (SM) in epilepsy. They do not occur in all people with epilepsy (FLE). Do occur in some people without epilepsy (as ''injury potentials'' or as genetic trait markers).

Their location does not accurately coincide with the seizure onset zone. No features of spikes correlate with severity of epilepsy. Can not predict when and whether a next seizure will occur. The relationship of seizures and spikes is not enough clear (chicken/egg question) Arguments in favor that high frequency oscillation(HFO) can be a good candidate for SM in epilepsy are growing. It is linked both to epilepsy related spikes (restricted experience with different kind of spikes) and seizure onset. It is present in the strictly localized seizure onset zone (exclusively?) and

not present in regional seizure onsets (not validated yet by postoperative outcome data and demonstrated only in few patients and selected etiologies). HFO seems to herald seizure onset in a restricted zone.

Manipulations that decreases HFO reduces the likelihood of seizures (experimental data). Had been found along the whole phylogenetic scale. Possible to detect with microwires (fast ripples) and also with ECoG and depth macroelectrodes (ripples). A drew back is that detectabilty is questionable without invasive electrodes (except MEG).

HYPES AND HOPES FOR MR/SPECT/PET IMAGING AS A SENSOR FOR EPILEPTOGENESIS

A. Nehlig
Inserm U 666, Strasbourg, France

Neuroimaging is currently used for assessment of epilepsy in humans and animal models. In animals, early imaging studies used autoradiography to assess regional changes in cerebral blood flow and metabolism but these approaches need the sacrifice of animals. Recently, SPECT and PET allowing the epileptogenic temporal follow-up have been miniaturized and represent attractive tools in epilepsy research. However, their definition is not as precise as autoradiography and does not allow accurate follow-up of metabolic and circulatory changes in small brain areas. Nevertheless, the development of new ligands allowing labeling of various receptors increases the possibilities of the temporal study of functional changes during epileptogenesis. In the last decade, MR techniques have been quite extensively used in animal models of epilepsy. Anatomical MRI showed the time-related involvement of brain structures in epileptogenesis in correlation with neuronal damage and astrogliosis. Diffusion-based imaging has given further information on the re-arrangement within tissue and localization of seizure foci. Diffusion-tensor imaging and manganese-enhanced MRI provide information on the establishment of new circuits. MR spectroscopy (MRS) using 1H, 31P is measuring the brain energy charge or metabolites (lactate, N-acetylaspartate, choline, creatine). Finally MRS using 13C-labelled substrates is giving promising information on the relations between astrocytes and neurons during epileptogenesis. BOLD functional MRI (fMRI) starts only to be developed in animal models. It is very promising since it allows measuring simultaneously cerebral blood volume and flow, and gives information on CMRO2, an index of neuronal activity. Finally, a combination between EEG, and fMRI, as in human epilepsy, would help unravel the electroclinical correlates of EEG activity and functional changes during epileptogenesis. Given that all these techniques have both advantages and limitations, they need to be combined to allow satisfactory temporal, functional and regional follow-up of the epileptogenic process.

CSF AS A CANDIDATE SOURCE FOR BIOMARKER IDENTIFICATION

K. Kurkinen
University of Kuopio, Kuopio, Finland

Purpose: Traumatic brain injury (TBI) is the major cause for acquired epilepsy in adult humans. The aim of this study was to identify biomarkers for epileptogenesis using proteomic analysis of CSF in rats undergoing post-TBI epileptogenesis.

Method: Adult male rats were subjected to moderate TBI induced by lateral fluid-percussion (30 injured, 10 controls). CSF-cannulas and cortical electrodes were implanted into the brain 11 months later. CSF was collected and video-EEG monitoring was performed in order to detect spontaneous seizures. Pentylenetetrazol test under continuous video-EEG control was carried out to test seizure susceptibility at 12 months after TBI. iTRAQ method was used to examine differential expression of proteins in five pooled control and TBI CSF samples. Prior to isobaric tags for relative and absolute quantification (iTRAQ) labelling the most abundant CSF proteins were removed.

Results: Only one out of five control animals experienced seizures, while 10 out of 14 injured rats had a seizure suggesting lowered seizure threshold after TBI. Altogether 59 proteins were identified, and eight proteins showed difference in expression levels. Four proteins were up-regulated and four proteins were down-regulated in TBI rats as compared to controls.

Conclusions: These preliminary results demonstrate that proteomics using iTRAQ can be used to detect changes in the CSF proteome after TBI. Future research will investigate whether any of the altered proteins in CSF during epileptogenesis will turn out to serve as biomarker for posttraumatic epileptogenesis.

ASSESSMENT OF COGNITIVE FUNCTION – DOES IT REVEAL THE PATIENTS AT RISK?

C. Helmstaedter
University of Bonn, Bonn, Germany

Neuropsychological impairment in epilepsy reflects both, the structural morphological underpinnings of epilepsy as well as the more dynamic seizure and treatment related aspects of the disease. In this regard global intellectual impairment and domain-specific dysfunctions provide information about mental development or retardation, about lateralizing or nonlateralizing impairment, and about focal localized versus diffuse domain over-spanning impairment. By providing disease related information one may well hypothesize that the neuropsychological features of a patient also provide information about risk factors not to become seizure free or to run into mental retardation or decline. At present there is a clear preponderance of studies addressing surgical treatment. Studies addressing pharmacological treatment are rare. A review of surgical studies reveals in part inconsistent results but three aspects appear to be of special interest: 1. particularly in early onset epilepsy, mental retardation can be a marker of a more severe and widespread brain damage. Such lesions often have a developmental background and can result in difficult to treat epilepsies. Poor baseline intelligence additionally indicates poor reserve capacities to cope with additional damage. From a neuropsychological of view point, however, this needs to be differentiated from a dispositional poor intelligence and from circumscribed epileptogenic lesions, which secondarily interfere with adjacent or more distant brain regions and which may well respond to surgery. Point 2 refers to neuropsychological information about the functional adequacy of affected local brain regions. Episodic memory for example is a valid marker for the structural and functional integrity of the temporal lobe structures in temporal lobe epilepsy. Baseline memory performance thus has some predictive value for postoperative seizure and cognitive outcome. 3. As for mental decline, neuropsychology reflects initial damage, acquired damage in uncontrolled epilepsy and, if performed repeatedly, the potential progressive nature of the epilepsy (i.e. limbic encephalitis). However, neuropsychology in epilepsy needs an multidisciplinary implementation and its interpretation requires information from clinical history, electrophysiology as well as structural/functional imaging, which themselves have a predictive value for treatment outcome.

Wednesday 24 September 2008
16:30 – 18:00
Hall 5
Workshop
Genetically determined epilepsy syndromes associated with intellectual disability

MOLECULAR GENETIC ASSOCIATIONS BETWEEN INTELLECTUAL DISABILITY AND EPILEPSY

D. Pilz
Institute of Medical Genetics, University Hospital of Wales, Cardiff, UK

Intellectual disability and epilepsy are commonly associated, and a search on the London Dysmorphology / Neurogenetics Databases, which currently contain 5492 / 4828 known and unknown syndromes respectively, identified 550 / 690 conditions with both a learning disability and

a seizure disorder. Although some of them will be associated with foetal exposure to teratogens or maternal illnesses, many will be due to chromosomal (i.e. Wolf-Hirschhorn syndrome) and single gene disorders (i.e. FraX syndrome; metabolic disorders). Some chromosomal anomalies, like ring chromosome 20 have epilepsy and intellectual difficulties as cardinal features. Technologies like array comparative genomic hybridisation (array CGH) are expected to identify additional small genomic alterations associated with syndromic epilepsy and candidate genes for specific seizure phenotypes. Recent advances in molecular technology and also in neuroimaging have led to the identification of an increasing number of causes for syndromic epilepsy. In this talk I will present examples of this focusing on conditions associated with cortical malformations. Lissencephaly is the paradigm of a neuronal migration disorder, with classical (Type 1) lissencephaly being the most common. Epilepsy and intellectual disability are consistent features. Responsible genes (like the ARX gene) can specifically affect migration of the inhibitory neurons from the ganglionic eminences during cortical development, and conditions associated with ARX mutations are often associated with seizure disorders. The LIS1, DCX and TUBA1A genes associated with classical lissencephaly affect the normal functioning of the cytoskeleton, which can lead to both abnormalities in cell division and cell migration. Polymicrogyria is the most common cortical malformation with a very heterogeneous aetiology. Although familial recurrences suggest single gene disorders, identification of these has so far been limited. A 22q11 deletion is the most common chromosomal anomaly found in this condition; the occasional occurrence of polymicrogyria in 22q11 deletion syndrome has yet to be elucidated.

'IDIOPATHIC' GENETIC EPILEPSY PHENOTYPES ASSOCIATED WITH SEVERE LEARNING DISABILITY OR CHANNELOPATHIES ASSOCIATED WITH EPILEPSY AND SEVERE LEARNING DISABILITY

R. Nabout
Hopital Saint Vincent De Paul, Paris, France

No Abstract Received.

EPILEPSY AND AUTONOMIC DISTURBANCE IN RETT SYNDROME

M. Kerr
Cardiff University, Cardiff, UK

Rett syndrome, a congenital neurodevelopmental disorder seen almost exclusively in females has a prevalence of 1:10000 to 1:15000 and is caused by mutations in the MECP2 gene located at Xq28. There is pronounced autonomic dysfunction and neurdevelopomental regression commencing at the age of 6–18 months. There is considerable phenotypic variability. Seizures have been reported in about 75%–81% of subjects, breath holding in more than 70% and a range of stereotypies, especially hand wringing, in the majority. A wide variety of seizures have been observed in Rett syndrome though an association has been found with early feature of developmental delay there is little information regarding the type of gene mutation and seizure type. The presence of stereotypy, severe developmental delay and autonomic dysfunction including irregular breathing patterns, as many as 13 breathing dysrhythmias have been described in Rett syndrome, can lead to a diagnostic challenge when differentiating these from seizure disorder. In particular the differential diagnosis between epilepsy and nonepileptic vacant spells can lead to confusion. This paper will discuss this differentiation and evidence for the epilepsy phenotype associated with Rett disorder. In addition I will discuss any evidence which points to any association between the Rett genotype and the epilepsy phenotype.

THE EPILEPSY PHENOTYPES OF ANGELMAN'S AND FRAGILE X SYNDROME

M. Elia
Oasi Inst. For Research On Mental Retardation And Brain Aging, Sicily, Italy

Angelman syndrome (AS) is characterized by severe mental retardation, minimal expressive language, ataxia, myoclonic jerks, paroxysmal laughter, and seizures. In more than 70% of cases, a deletion of 15q11–13 of maternal origin is present; in approximately 2–3% of cases a paternal uniparental disomy is recognizable, and in 3–5% of patients a defect of the imprinting center causes the absence of the typical maternal pattern of methylation of DNA. In addition, sporadic and familial cases have been reported (5–10%) with mutations of the UBE3A gene. The typical clinical and EEG pattern is a ''myoclonic status epilepticus.'' Seizures, present in about 90% of cases, usually begin in infancy, and they are rather polymorphous. Epilepsy in AS is relatively benign from later childhood on, and treatment is usually based on valproic acid, also in association with ethosuximide, or benzodiazepines. Fragile-X syndrome (FraXS) is one of the most common causes of inherited mental retardation, with a prevalence of 1:1,500 males. The physical phenotype is characterized by muscle hypotonia, macroorchidism, large ears, narrow face, and other signs related to a connective tissue dysplasia. The gene responsible for the syndrome was identified as the FMR1 gene. In about 40–50% of cases FraXS EEG pattern is characterized by paroxysmal abnormalities, which usually are localized over the central-temporal regions of both hemispheres, appearing around 3–4 years and persisting up to 12–13 years of age. These spikes are markedly activated by non-REM sleep. The prevalence of seizures was estimated to be between 17% and 30. Age at onset was between 2 and 9 years. Seizures were mainly of the complex partial type, and were well controlled by therapy in most of the cases. Drugs used for partial epilepsies, such as carbamazepine, barbiturates, and valproic acid, are effective also in FraXS.

Wednesday 24 September 2008
16:30 – 18:00
Hall 6
Discussion Group
Simultaneous EEG-fMRI recordings in epilepsy: state of the art and critical review

EEG-fMRI IN EPILEPSY: A CRITICAL VIEW ON METHODOLOGY

C. Benar
INSERM U751, La Timone, France

Recording EEG in the MR scanner was introduced in 1993 by Ives and colleagues, and was a breakthrough in the field of imaging techniques for epilepsy. Indeed, it permits to monitor epileptic discharges while scanning, and as a consequence to analyze the fMRI signals based on this information. However, there are many difficult technical issues associated with placing electric wires within high magnetic fields. In particular, movements of the wires and changes in the field from MR gradient switching produce large artefacts on the EEG. We will review these issues and the methods that have been proposed in order to overcome them. Then, we will discuss what can be expected in terms of EEG quality and in terms of information content that can be recovered.

EEG-fMRI STUDIES IN GENERALIZED EPILEPSIES

H. Laufs
Johann Wolfgang Goethe University, Frankfurt Am Main, Germany

No Abstract Received.

EEG-fMRI STUDIES IN FOCAL EPILEPSIES

R. Thorton
The Institute of Neurology, Queen Square, London, UK

One of the initial aims of simultaneous recording of EEG and fMRI was to establish a new, noninvasive technique for localising the seizure onset

zone, a goal which has remained important to the field, although much of the current research focuses rather on attempting to understand the neurobiology of the epileptic network. Initial studies acquired using both the spike-triggered and continuous acquisition techniques focussed on relatively large groups of patients selected for the number of IEDs (inter-ictal discharges) on scalp EEG. More recent work has attempted to characterise the IED correlated BOLD response in specific pathologies and has also assessed the role of negative BOLD signal change within selected patient populations. This session will review the above work and also address the question of the role of simultaneous EEG-fMRI in presurgical evaluation. This topical issue had been raised in recent work and comparison of EEG-fMRI with intracranial data and postoperative outcome will be discussed here. The need for numerous IEDs to be recorded during EEG-fMRI studies has restricted its use to a limited group of subjects. We will also present work which uses data-driven approaches to attempt to overcome this hurdle in focal epilepsy.

SPECIAL ASPECTS OF EEG-FMRI: INFLUENCE OF AGE, MEDICATION, VIGILANCE AND HAEMODYNAMIC RESPONSE

M. Siniatchkin
University Hospital of Paediatric Neurology, Kiel, Germany

No Abstract Received.

Wednesday 24 September 2008
16:30 – 18:00
Hall 7
Workshop
Relevance of interictal discharges in epilepsy

PATHOPHYSIOLOGY OF INTERICTAL DISCHARGE

M. Avoli
La Sapienza University and The Montreal Institute, Montreal, Canada

Interictal discharges are short-lasting asymptomatic events that occur in the EEG of epileptic patients between seizures. To date, the role of interictal discharges in seizure occurrence and in epileptogenesis remain elusive. For instance, while interictal spikes may herald the onset of electrographic seizures in animal models of epilepsy, other data indicate that hippocampus-driven interictal events can prevent seizure precipitation. Specifically, it has been shown that CA3-driven interictal activity can control ictogenesis in several parahippocampal structures as indicated by the ability of cutting the Schaffer collaterals (which connect CA3 to CA1) to (1) abolish interictal spikes in these areas and (2) allow ictal-like activity to be reestablished. In line with this evidence, interictal spiking in the piriform cortex precludes its involvement in seizure-like activity originating from the EC-hippocampus in the in vitro guinea pig brain. However, interictal discharges can shortly precede seizure onset as originally reported in the penicillin-induced focus in vivo. This finding has been confirmed in vitro in brain slices and in the isolated guinea pig brain with the epileptiform activity induced by 4-aminopyridine, Mg2+ free-medium or short-lasting bicuculline treatment. Hence, interictal activity exerts, even in the same experimental model, either protective or precipitating roles with respect to seizure generation. The precise relationship between interictal and ictal activity in patients presenting with temporal lobe epilepsy remains ambiguous as well. Even less clear than the role of interictal events in seizure occurrence is whether and how interictal activity contributes to epileptogenesis. Thus, while plastic changes within limbic neuronal networks may result from ongoing interictal events, experimental evidence supports the view that epileptogenesis is accompanied by a decrease in hippocampus-driven interictal activity.

EFFECTS OF EPILEPTIFORM DISCHARGES ON THE IMMATURE BRAIN

Y. Ben-Ari
Institut De Neurobiologie De La Mediterranee, Marseille, France

No Abstract Received.

EFFECT OF INTERICTAL DISCHARGES ON COGNITION AND BEHAVIOR

R. Pressler
The National Hospital For Neurology and Neurosurgery, London, UK

Interictal discharges are a frequent phenomenon in patients with epilepsy, but are only weakly associated to seizure frequency or severity. Therefore, a principle of treatment is to avoid over-interpretation of epileptiform activity. Yet, there is evidence that sensitive methods of cognitive testing can show brief episodes of impaired cognitive function during such discharges. This phenomenon of Transitory Cognitive Impairment (TCI) has been confirmed in some 60 studies. Specifically it has been shown that TCI is not simple inattention. The effects of interictal discharges are both material and site specific: lateralized discharges are associated with impairment of neuropsychological function located in the affected hemisphere. Conversely, specific tasks may activate or suppress focal discharges over those brain regions that mediate the cognitive ability in question. Lateralized discharges, whether spontaneous or induced by electrical brain stimulation may be accompanied by an enhancement of function located in the contralateral hemisphere. TCI may also interfere with performance of daily tasks such as reading or driving. The clinical relevance of TCI is controversial but uncontrolled case reports and two controlled trial have suggested improved psychological function when discharges where suppressed with antiepileptic medication.

RELEVANCE OF NOCTURNAL DISCHARGES

T. Deonna
Neuropaediatric Unit, University Children's Hospital, Lausanne, Switzerland

Most epilepsies and epileptic syndromes have specific patterns of EEG paroxysms during the waking state and most often, but not always are activated by sleep. The interictal electrographic epileptic activity during sleep, if brief and infrequent, is usually not associated with daytime sleepiness or evident cognitive disturbances and is only the diagnostic marker of the epileptic disorder. Unsuspected electrographic seizures during sleep may occur, not always in cases with already abundant nocturnal interictal discharges, and this should be considered when sleep is disrupted or awakening in the morning is difficult. In some syndromes, for instance West syndrome with hypsarrhytmia, the waking EEG may be free of epileptic discharges which become abundant during sleep. In rolandic epilepsy and variants, Landau-Kleffner syndrome and other partial epilepsies (idiopathic and symptomatic epilepsies, especially if the thalamus is involved) the activation can be marked during sleep amounting to the so-called 'electrical status epilepticus during sleep (ESES)' also named 'continuous spike-wave during non-REM sleep (CSWS)'. This latter EEG pattern is associated with cognitive, language or behavioral regression (or either one or any combination of these and other higher level disturbance, perceptual, praxic, etc.) with improvement and relapse of symptoms showing a close correlation with the intensity, duration, age at onset of CSWS and also with the location of the main epileptic focus. These variables will influence the severity (and nature) of clinical symptoms (which go from subtle and transient to major and persistent) and will dictate how agressively one should attempt to suppress CSWS, which are variably sensitive(or resistant) to various AEDs and steroids. Important new findings on the role of non-REM sleep in learning and memory and their relevance to epilepsy will be discussed.

Wednesday 24 September 2008
16:30 – 18:00
Hall 9
Workshop
The role of aquaporin water channels in pathophysiology of epilepsy

ANATOMY AND PHYSIOLOGY OF AQUAPORINS

E. Nagelhus
University of Oslo, Oslo, Norway

Brain function is inextricably coupled to water homeostasis. The ionic transmembrane shifts that are required to maintain ion homeostasis during neuronal activity are accompanied by water. Aquaporin-4 (AQP4) is the predominant water channel in the neuropil of the central nervous system. It is expressed primarily in astrocytes and a striking feature is its polarized distribution with enrichment in perivascular and subpial astrocytic endfeet. The subcellular compartmentation of AQP4 mimics that of the potassium channel Kir4.1, which is implicated in spatial buffering of K(+). The lecture will review recent data on the structure and function of brain aquaporins.

AQUAPORINS, WATER BALANCE AND EPILEPSY – STUDIES IN ANIMAL MODELS

D. Binder
University of California, Orange, CA, USA

Since recent studies have implicated glial cells in novel physiological roles in the CNS, such as modulation of synaptic transmission, it is plausible that glial cells may have a functional role in the hyperexcitability characteristic of epilepsy. Indeed, alterations in distinct astrocyte membrane channels, receptors and transporters have all been associated with the epileptic state. This talk focuses on the potential roles of the glial water channel aquaporin-4 (AQP4) in modulation of brain excitability and in epilepsy. I will review studies of seizure phenotypes, potassium metabolism and extracellular space physiology of mice lacking AQP4 (AQP4-/- mice) and discuss the available human studies demonstrating alterations of AQP4 in human epilepsy tissue specimens. I will conclude with new studies of AQP4 regulation by seizures and discuss its potential role in the development of epilepsy (epileptogenesis). While many questions remain unanswered, the available data indicate that AQP4 and its molecular partners may represent important new therapeutic targets.

AQUAPORINS AND TEMPORAL LOBE EPILEPSY GENETIC ASPECTS

K. Heuser
Rikshospitalet-Radiumhospitalet, Oslo, Norway

Efforts to find susceptibility genes in common epilepsies and febrile seizures (FS) by means of association studies have not yet lead to convincing results (Tan, 2004). Nevertheless, most promising results derive from studies that investigated mutations in genes encoding ion channel proteins. Ion channels maintain cellular electrical homeostasis and are thus pivotal to neuronal functioning. In the past decade numerous studies have shown that neuronal performance and electrical stability in the brain does not only depend on ion channel functioning, but also on an intact water balance. The glial water channel aquaporin-4 (AQP4) provides bi-directional water flux across plasma membranes in response to osmotic gradients (Agre, 2002). Its distribution in astrocyte endfeet, especially at the blood-brain and brain-cerebrospinal fluid barriers (Nielsen, 1997; Rash, 1998), but also its coexpression with the inwardly rectifying potassium channel kir 4.1 (Nagelhus, 2004) strongly indicates a major function in the maintenance of water- and ion homeostasis. Due to recently published experimental data, it is presumable that functional alterations in these channels may contribute to the etiopathology of Temporal Lobe Epilepsies (TLEs) (Bordey and Sontheimer, 1998; Hinterkeuser, 2000; Hugg, 1999; Amiry-Moghaddam, 2003; Holthoff, 1996; Niermann, 2001; Nagelhus EA 1999; Nagelhus EA 2004). TLEs account for a large number of patients with epilepsy and are of special interest due to frequent pharmacoresistence and a combination of characteristic phenotypical features (Wieser, 2004). This makes TLEs an interesting subject for genetic association studies. We hypothesize that polymorphisms in the genes encoding AQP-4 and the potassium channel kir 4.1 and GIRK 3 may be associated with TLE subgroups, among these Mesial Temporal Lobe Epilepy with Hippocampal Sclerosis (MTLE-HS) and TLE with febrile seizures (TLE-FS), and present data from our association study.

Thursday 25 September 2008
07:30 – 09:00
Hall 3
EUREPA Teaching Session
Status epilepticus: from basic science to prognosis

EPIDEMIOLOGY OF STATUS EPILEPTICUS

G. Logroscino
Harvard School of Public Health, Boston, MA, USA

Status Epilepticus (SE): definition, incidence, and mortality. SE is defined as a seizure persisting for 30 min or two or more seizures without recovery of consciousness over 30 minutes. A more recent definition that has been used only in clinical setting defines five minutes as the time limit. In population based studies, the frequency of SE as assessed by incidence is between 10 and 40 /100000 person year. Incidence is higher in males than in females, with a gender ratio of 1.5–2 to 1. In the only multiethnic study the incidence for whites was lower (20/100,000) than for African American (57/100,000). The mortality after SE varies widely: from 6% to 25% among children and from 11% to 43% in adults. This variability is related to methodological issues including differing definitions of SE, differing distributions of SE aetiology, and variable length of follow-up. In almost all population-based studies, the short term mortality at 30 days is around 20% and almost all early deaths (90%) occur among those with acute symptomatic SE. No deaths occurred in the first 30 days in those with idiopathic SE. Concurrent illness is therefore the most important determinant of early mortality. Among the acute symptomatic cases, cerebrovascular disease and anoxia secondary to cardiac arrest are the two most frequent causes of SE for those dying in the first 30 days. In the only study assessing long-term mortality, more than 40% of those with SE who survived the first 30 days died in the next ten years. The risk of death was increased 3-fold compared with the general population. As in short-term mortality, 3 out of 4 deaths occurred among elderly. In the only study on time trend, SE mortality increased over a fifty- year period. The increase in mortality was due to the occurrence in the last decade of our study of a new emerging condition, myoclonic SE after cardiac arrest.

PATHOPHYSIOLOGY OF STATUS EPILEPTICUS

M. Holtkamp
Charité University, Berlin, Germany

In every third patient, status epilepticus (SE) is refractory to first-line anticonvulsants (lorazepam, phenytoin) und often requires prompt treatment with anaesthetics (barbiturates, midazolam, propofol). However, a considerable number of patients even do not respond to these anaesthetics that all mainly act on the inhibitory gamma-aminobutyric acid (GABA)A receptor. Due to extreme pharmacoresistance and overall poor prognosis, this condition has been termed malignant SE (MSE). The main predictor for MSE is aetiology, in particular encephalitis. Clinical and experimental data indicate that pharmacoresistance in SE is progressive. This may be due to internalisation of GABAA receptors into endocytotic vesicles with ongoing seizure activity. Experimental data show that N-methyl-D-aspartate (NMDA) receptor activation regulates SE refractoriness to benzodiazepines, as NMDA receptor antagonists partially reverse impaired GABAergic inhibition. Furthermore, with ongoing seizure activity

NMDA receptors are overexpressed at the postsynaptic membrane. Therefore, a rational strategy in the pharmacological management of difficult-to-treat forms of SE would be a blockade of the NMDA receptor. In the electrical stimulation model of SE, the NMDA antagonist ketamine did not affect SE within the first 15min after onset, but effectively controlled seizures after 60min when GABAergic phenobarbital had already lost its anticonvulsant potency. Coadministration of diazepam and ketamine in rats has been shown to act synergistically in terminating SE, it was more effective than the additive effects of both substances if given alone. These convincing experimental data on the anticonvulsant properties of ketamine adminstered alone or in combination with GABAergic substances in SE are supported by some rare clinical reports.

TREATMENT OF STATUS EPILEPTICUS

A. Rossetti
Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

When SE is strongly suspected, general measures to maintain stable cardio-circulatory and metabolic parameters have to be accompanied by specific pharmacologic treatment; this consists of three consecutive levels. The first is represented by benzodiazepines, and has the most solid scientific evidence. The second one includes (phos-)phenytoin, valproic acid or phenobarbital; while the rationale supporting the use of these compounds is scarce, the possibility of rapid intravenous administration has favored them over other drugs. The third level, lacking the support of prospective, controlled studies and reserved for refractory SE (i.e., SE resistant to the first two treatment levels), consists of pharmacological coma induction with an appropriate anesthetic, such as barbiturates, propofol, or midazolam. Several other drugs are used at times, including newer antiepileptic compounds and several anesthetics; to date, no comparative assessment of their respective role has been conducted. A treatment protocol using these three levels appears rather simple, but the tuning according to each patient's situation represents the real challenge. The supposed advantages of coma induction should be balanced with the morbidity related to prolonged mechanical ventilation. There is a consensus to treat generalized-convulsive and SE in coma soon and aggressively. Conversely, it remains debatable whether complex-partial and absence SE lead to permanent neuronal damage; it appears therefore advisable not to proceed automatically to coma induction in these cases. Cognitive prognosis has been less well studied than mortality. The latter may be influenced, in either way, by under- or overtreatment. Short-term SE case-fatality has been estimated at 10–20%; etiology is the most important independent predictor, followed by age and extent of consciousness impairment. While absence SE has almost no complication, at the other end of the spectrum, acute-symptomatic SE in coma is linked to significant mortality. Incident SE per se (as compared to a first shorter seizure) increases the risk to develop epilepsy, and probably affects long-term survival. The knowledge of these issues should influence the treatment strategy.

Thursday 25 September 2008
07:30 – 09:00
Hall 5
EUREPA Teaching Session
To treat or not to treat – decisions under uncertainty

DRUG TREATMENT AFTER FIRST SEIZURE?

E. Trinka
Medical University Innsbruck, Innsbruck, Austria

DO WE HAVE TO TREAT ALL CHILDHOOD EPILEPSY SYNDROMES?

G. Bauer
Medical University Innsbruck, Innsbruck, Austria

Do we have to treat all childhood epilepsy syndromes? Gerhard Bauer Neurological Department, Medical University Innsbruck, Austria Two conditions bring up the question to treat or not to treat. 1) The syndrome has an excellent prognosis without antiepileptic drugs (AEDs). 2) The syndrome is resistant to any treatment. Febrile seizures (FS) and the benign childhood epilepsy with centrotemporal spikes (BECTS) are the most frequently encountered examples for the first condition. After a FS a thorough clinical examination is most important. Treatment is directed only against the recurrence of FSs. It is undecided, whether the risks of acute treatment of ongoing seizures outweigh the benefits. After a diagnosis of an uncomplicated FS and after reassuring information to parents a wait and see position seems to be justified. There is a considerable overlap of syndromes with BECTS. Atypical forms exhibit a less benign course. Is the excellent prognosis with more than 99% remission with 18 years of age due to the natural history of the syndrome or due to post hoc exclusion of less benign cases? Emotional and cognitive disturbances are frequently reported with BECTS and might be related to persisting EEG abnormalities. Do these changes improve with AED treatment? Without evidence-based answers to these questions, 81.6% of patients are treated, and a long list of AEDs all had the same result. Should severe epileptic encephalopathies be treated by AEDs despite convincing trials demonstrating pharmacoresistance? No withdrawal studies have been performed. Anectodical reports of improvements after withdrawal should prompt a systematic investigation of this strategy.

DRUG TREATMENT IN CHILDHOOD STATUS EPILEPTICUS – WHEN DO RISKS OF TREATMENT OUTWEIGH THE BENEFITS?

A. Arzimanoglou
Service Epilepsie, Sommeil Et EFNP – HFME – CHU Lyon, Bron Cedex, France

HOW URGENT AND AGGRESSIVE SHOULD WE TREAT NONCONVULSIVE STATUS EPILEPTICUS?

S. Shorvon
National Hospital For Neurology & Neurosurgery, London, UK

The purpose of emergency antiepieptic therapy in status epilepticus (SE) is to control seizures in order to prevent brain damage and improve outcome in terms of (1) mortality, (2) neurological damage, and (3) ongoing seizures). Some categories of nonconvulsive SE are self-limiting and do not cause brain damage (e.g., absence SE) and therefore do not need aggressive emergency therapy. In other categories, the need for aggressive emergency therapy is more contentious. Experimental evidence suggests that complex partial SE causes cerebral damage and ongoing epilepsy, but little clinical evidence that this occurs at least in the great majority of cases. Whether the outcome of the nonconvulsive SE in the epileptic encephalopathies is improved by emergency therapy is also unclear. Myoclonic SE in coma is associated with a poor outcome, but there is little evidence that antiepileptic therapy is helpful. These topics will be discussed and debated.

Thursday 25 September 2008
07:30 – 09:00
Hall 7
Workshop
Seizure or parasomnia? The limits of expertise

THIS IS EPILEPSY! OR IS IT?

W. Van Emde Boas
Epilepsy Clinics 'Meer & Bosch' And 'Heemstaete', Hemstede, The Netherlands

Widespread application of long term EEG-Video and sleep monitoring techniques have greatly advanced the diagnostic possibilities for and hence the clinical interest in manifest or subtle nocturnal paroxysmal events of epileptic and nonepileptic origin. Both, nocturnal epileptic seizures and nonepileptic sleep disturbances or parasomnia's may present in different forms and need correct diagnosis not just as to their basic character but also regarding the exact type of seizure or parasomnia. Age of onset and pattern of persistence of the clinical problem, it's association (or lack of such relation) with time and stage within the sleep cycle, pattern and stereotypy of motor behavior, frequency and duration of the events, associated autonomic signs and symptoms, presence and duration of (post)ictal confusion and other clinical characteristics may provide important clues arguing for specific diagnoses and against others. In most patients thus the differential diagnosis between epileptic seizures or paroxysmal sleep behavior can be made with a fair amount of certainty, including the further diagnosis as to the specific type of disorder. In some cases however the differential diagnosis remains difficult, even for highly qualified experts and in some subjects even the experts fail to establish an unequivocal diagnosis. The objective of this session is to present four clinical cases, adult and pediatric, which, despite analysis by multiple experts, remain in the uncertain borderland between epilepsy and parasomnia and to discuss these, with the arguments for either diagnosis, interactive with the participants. The cases will not represent 'typical' cases, which nevertheless may be misdiagnosed but truly enigmatic cases where uncertainty concerning the diagnosis may remain, even following the discussion during the presentations. The tuition value will be both the increased awareness of differential diagnostic features arguing for either epilepsy or parasomnia and the realization that in clinical medicine diagnosis usually is something which is more likely than something else and certainty is something to strive for but often unattainable, even for experts.

THIS IS SLEEP! OR IS IT? (ADULTS)

A. Kelemen
Nal. Inst. Of Psychiatry And Neurology, Budapest, Hungary

No Abstract Received.

THIS IS SLEEP! OR IS IT? (CHILDREN)

A. De Weerd
SEIN Zwolle, Zwolle, The Netherlands

'Things that go bump in the night' are very common in children and adolescents. In particular in young children the history is often all that is needed for a differentiation between a sleep disorder and epilepsy. For example, extreme motor restlessness lasting for minutes one or two hours after sleep onset combined with amnesia for what happened, in a 6 year old is probably a deep sleep related parasomnia. Unfortunately, things are not always that clear and video/EEG/polysomnography is needed to make the differentiation between sleepdisturbance and epilepsy. Even the use of these techniques is in some cases not enough. Examples of such very difficult cases which are often not clear after many recordings, will be shown during this workshop. As there is no final answer, the audience has a major role in the decision on the final diagnosis.

INTRACRANIAL STUDIES: NEARER TO THE SOURCE, NOT ALWAYS TO THE SOLUTION

L. Nobili
Centre of Sleep Medicine and Epilepsy Surgery C. Munari Niguarda Hospital, Milano, Italy

No Abstract Received.

Thursday 25 September 2008
07:30 – 09:00
Hall 9
Workshop
The effects of epilepsy and its treatment on cognitive functioning: immediate and long-term

NATURAL HISTORY OF COGNITIVE IMPAIRMENT IN CHILDREN WITH EPILEPSY

A. Aldenkamp
Epilepsy Centre Kempenhaegh & Department Of Neurology, Heeze, The Netherlands

No Abstract Received.

IMMEDIATE IMPACT OF EPILEPSY AND ITS TREATMENT IN ADULTS

J. Taylor
University of Liverpool, Liverpool, UK

People with epilepsy commonly report impairments in their cognitive functioning, in particular memory problems, as a result of their epilepsy and its treatment. The main factors that appear to contribute to cognitive dysfunction are the underlying etiology, the effects of recurrent seizures and the side effects of antiepileptic medication. Patients with epilepsy often attribute their impairments to their antiepileptic medication. However, there is a growing body of evidence suggesting that patients with epilepsy are already cognitively compromised before the start of antiepileptic drug treatment and following few seizures. Our current research, as part of the SANAD trial, provides an opportunity to investigate the natural history of cognitive functioning in a group of untreated patients with newly diagnosed epilepsy. Using a comprehensive neuropsychological test battery, we have assessed patients with newly diagnosed epilepsy before the start of antiepileptic drug treatment and after 3 and 12 months. Performance at baseline was compared with a group of healthy volunteers equated for age and sex. Patients with epilepsy performed significantly worse across the majority of measures. On a global battery score, 19.6% of patients were identified as demonstrating mild and moderate impairments compared with 2.6% of healthy volunteers. This implies that at least part of the cognitive impairment may be the result of epileptogenesis rather than the accumulating effects of seizures or treatment. Poorer cognitive functioning can impact on psychological well-being. Patients with epilepsy are already at risk of developing psychosocial problems and reduced quality of life. Therefore, it is important that we are able to identify those patients with cognitive dysfunction at the time of diagnosis, so they can be referred for appropriate intervention and prevent the development of further cognitive decline.

THE LONG-TERM OUTCOME OF EPILEPSY AND ITS TREATMENT ON NEUROPSYCHOLOGICAL FUNCTION

S. Kemp
St. James's University Hospital, Leeds, UK

No Abstract Received.

THE THEORETICAL UNDERPINNINGS OF NEUROPSYCHOLOGICAL FUNCTIONING IN PEOPLE WITH EPILEPSY

R. Kalviainen
Kuopio University Hospital, Kuopio, Finland

Epilepsy is frequently associated with cognitive problems or deficits that may be due to the etiological brain pathology, focal or generalized

epileptiform activity, adverse effects of drug treatment, or epilepsy surgery. Some of the changes caused by epilepsy may be progressive by nature, especially in epileptic encephalopathies, but less severely also in other types of epilepsies. The ecological validity of the neuropsychological impairment is an important issue in the clinical management of the patient. Many patients have subtle discrepancies with normal performance already at the time of diagnosis and do not report them if they respond successfully to drug treatment. In idiopathic epilepsies, cognition is usually only mildly deteriorated or even normal. Localization-related epilepsy disorders are accompanied by focal deficits that mirror the specific functions of the respective areas. Poor cognitive outcome is generally associated with an early onset (< 5 years) and a long duration (> 30 years) of the disease and with poor seizure control or status epilepticus. Epileptic encephalopathies are associated with slowing of cognitive function and evolution of severe behavioral disorders. While an underlying etiology may explain some of this comorbidity, many children have no identifiable etiology found for their seizures. In these cases, recurrent subtle seizures, frequent epileptiform discharge and nonconvulsive status epilepticus probably all play a role in deterioration of cognitive function and evolution of behavior disorders. Cognitive profiles in epilepsy are therefore as heterogenous as the epileptic syndromes themselves; causes, localization of epileptogenic areas, pathogenetic mechanisms, and the clinical course all contribute to the effect on cognition. Sometimes epilepsy can also induces processes of functional reorganisation and thereby compensation of the primary functional loss. Many other factors like primary intelligence, personality and mood, will determine the final effect of cognitive impairment on perceived quality of life.

Thursday 25 September 2008
09:00 – 11:00
Hall 3
The Symposium of Excellence in Epilepsy

THE EPILEPSY BERLIN WALL – THE PAST AND FUTURE ROLE OF THE PRINTED MEDICAL JOURNAL IN THE FIELD OF EPILEPSY

S. Shorvon
National Hospital For Neurology & Neurosurgery, London, UK

There is little point in doing research if it is not communicated to others, and for many years the printed medical journal has been the vehicle for scholarly research publication. Getting an article into a good journal is like scaling the Berlin Wall – it presents a significant hurdle to all researchers. By 2006, there were over 2,000 publishers involved in medicine, 1.2 million articles published annually and 16,000 periodical journals in science, medicine and technology. In 2007, there were 4655 articles on the topic of epilepsy. There are three notable reasons for this growth: the commendable increase in worldwide research activity; the increased importance placed on publishing research for career promotion; and profits from medical publishing, not least those derived from advertising and inflation in journal subscription costs. The previous decade had certainly a time of financial plenty in publishing, as in most other industries. Yet, despite the apparent 'success' of the publishing enterprise, the landscape was rapidly changing, for a number of reasons (1) The US and UK governments announced that publicly funded research should be made publicly available at no cost. How this is to be achieved without critically undermining the viability of the research medical journals is not clear and has engendered considerable discussion; (2) Also, the rapid expansion of the Internet and the ease of on-line access has led some to predict the imminent demise of the print editions of journals; (3) alternative models are being explored which will bypass the peer-review journals; (4) The publishing industry itself is in a period of rapid change; (5) Advertising revenues which fuel the system are failing. What is clear is that the weaker journals will go to the wall, and also that the publishing of epilepsy articles in 10–20 years time will look very different from today.

HOMEOSTATIC PLASTICITY AND GENERATION OF EPILEPSY

U. Heinemann
Johnannes-Muller-Institute of Physiology, Berlin, Germany

Retrospective studies suggest brain trauma, febrile convulsions, tumors stroke and other pathologies as a cause of focal epilepsies. However, prospective studies indicate that epilepsies are relatively rarely the result of such conditions. Following a lesion in the brain the neuronal networks reorganize in order to recover as much function as possible. This regenerative plasticity is like any other plasticity accompanied by homeostatic plasticity. This involves changes in neuronal excitability and efficacy in neuronal synaptic coupling resulting in neuronal activity within physiological ranges. Examples of such homeostatic plasticity involve changes in the function of ion channels and receptors including activity regulated editing of mRNA. Two examples for this type of plasticity will be given in relation to Kv1 channels and glycine receptors. Homeostatic plasticity may also involve heterosynaptic plasticity. An extreme example of homeostatic plasticity may be the upregulation of the GABA synthesising enzyme GAD in glutamatergic granule cells. If homeostatic plasticity accompanies reorganisation in the brain, then epileptogenesis may be due to disturbances in homeostatic plasticity. I suggest that alterations in mitochondrial function, inflammation and an open blood brain barrier may be factors which impair plasticity and particularly homeostatic plasticity.

BLOOD–BRAIN BARRIER IN EPILEPSY: ETIOLOGICAL AND PHARMACOKINETIC ASPECTS

N. Marchi
Cleveland Clinic, Cleveland, OH, USA

The brain is protected by physical and vascular barriers, namely the skull and the blood–brain barrier (BBB). In particular, the BBB controls the exchange of nutrients, drugs and serum-derived factors between the systemic circulation and the brain, thus contributing to brain homeostasis necessary for the proper function of neurons and regulating the passage of drugs into the brain. We have evaluated the effect of acute BBB damage (as induced by osmotic opening) in promoting seizures and affecting the penetration of serum proteins and water into the brain. We have evaluated the pattern of brain penetration of four compounds (including the drugs phenytoin and phenobarbital) chosen according to their lipophilicity and therefore on their varied ability to bind to plasma proteins. Our data suggest loss of brain shielding and homeostatic balance as prodromic events for seizure development (Marchi et al, Epilepsia 2007). Moreover, drastic changes in BBB permeability properties affect drug penetration into the brain and unveil the relevance of intrinsic physical properties (such as lipophilicity) in shaping the pattern of passage across a damaged BBB. The relevance of BBB failure in epilepsy will be critically analyzed also based on important evidence provided by others.

Thursday 25 September 2008
11:30 – 13:00
Hall 5
Discussion Group
Involvement of limbic seizure circuitry in absence epilepsy

CEREBRAL GLUCOSE UTILISATION OF LIMBIC STRUCTURES IN ABSENCE EPILEPSY MODELS

A. Nehlig
Inserm U 666, Strasbourg, France

The expression of absence seizures is characterized by the occurrence of spike-and-wave discharges (SWDs) that occur only in the thalamo-cortical pathway. Cerebral glucose utilization was measured by means of the

quantitative autoradiographic [14C]2-deoxyglucose technique in adult genetic absence epilepsy rats from Strasbourg (GAERS) that all express SWDs. In these rats, glucose utilization rates were increased in all brain structures including cortical and thalamic areas in which SWDs are recorded but also all limbic regions in which SWDs are never recorded. Moreover, when cerebral glucose utilization was measured in 21-day-old GAERS, i.e. before the occurrence of SWDs, functional activity was not increased in the thalamocortical loop but was increased in limbic regions and also in regions belonging to the remote circuit of seizure control. All these data indicate that, although the limbic regions are not directly involved in the expression of absence epilepsy, their activation implies that there is a close relationship between these structures and the thalamo-cortical pathway. The limbic activation could reflect a strong inhibition preventing the spread of the seizures to these highly susceptible structures.

LIMBIC EXCITABILITY IN ABSENCE EPILEPSY MODELS

G. Van Luijtelaar
Nici-Biological Psychology Univ, Nijmegen, The Netherlands

Recent studies in GAERS and WAG/Rij, two well accepted models for absence epilepsy, have established a cortical regional origin for electroencephalographic absence seizures in what has been traditionally described as a generalized type of epilepsy. The role of the thalamus is restricted; it forms a resonance circuit contributing to synchronization of burst firing in the cortico-thalamo-cortical circuit. Other parts of the brain do not play a major role in the theories on absence seizures. Outcomes of recent studies have emphasized that other parts of the brain classically not involved in the generation of the absence seizures, such as the hippocampus and nucleus accumbens exert inhibitory control over cortico-thalamo-cortical oscillations, i.e. the number of SWDs. Local injections with GABA-mimetics in the hippocampus and nucleus accumbens strongly suppress SWDs in WAG/Rij and GAERS. Data from an acute electrical cortical stimulation study in three and six month old but not in younger WAG/Rij rats showed reduced limbic seizure thresholds. Others have found a decreased paired pulse depression of neurons in the dentate gyrus in a model of atypical absence seizures. However, in chronic studies opposite effects were obtained: a resistance to electrical kindling of the amygdala was described in GAERS and WAG/Rij rats, the latter has been interpreted as a decreased limbic excitability. Vinogradova et al. (in press) found in an audiogenic kindling paradigm an increased resistance for audiogenic seizures to become limbic in WAG/Rij vs Wistar control rats. Also these data point towards a decreased excitability of the limbic system in genetic epileptic rats. The outcomes of the studies show opposite effects in acute and chronic stimulation studies. However, they extent the scope and possibilities for intervention and open new vistas for understanding interactions between the cortico-thalamo-cortical circuitry and the limbic system in absence epilepsy.

IS LIMBIC SEIZURE CIRCUITRY INVOLVED IN ABSENCE EPILEPSY MODELS?

F. Onat
Marmara University, Istanbul, Turkey

The clinical observation, that the coexistence of idiopathic generalized typical absence epilepsy and partial temporal lobe epilepsy in the same patient is extremely rare, suggested that one condition might produce changes that made the other less likely. Although limbic structures have been thought not to be involved in the expression and generation of spike-and-wave discharges, and therefore to play no role in typical absence epilepsy, observations in rat models of absence epilepsy point to a possibly important link between typical absence epilepsy and limbic structures. In agreement with this, it has been shown that in rats with genetic absence epilepsy (GAERS and WAG/Rij), there is a reduced capacity for the production of experimental temporal lobe epilepsy by kainic acid and kindling. Studies in GAERS and WAG/Rij animals show that a high level of basal spike-and-wave activity correlates with a resistance to kindling. Additionally this resistance to the secondary generalization of limbic seizures increases with age as the appearance of the spike-and-wave discharges matures. Cerebral blood flow during the production of early stages of kindling (stage 2) in adult GAERS and Wistar control rats show greater increases and more widespread in GAERS than in Wistar control rats in several regions, including the piriform, entorhinal and perirhinal regions of the cortex, the hippocampus and the amygdala, as well as the somatosensory cortex, the ventrobasal and anterior thalamic nuclei. Moreover a significant difference in the density of glutamate immunolabeling in mossy fiber terminals in CA3 and hilar region of the hippocampus has been reported in GAERS. It appears that, even though limbic structures do not play a role in the expression of spike-and-wave discharges, they are a part of absence epilepsy network.

COEXISTENCE OF ABSENCE AND TEMPORAL LOBE EPILEPSIES IN HUMANS

C. Ozkara
Istanbul University, Istanbul, Turkey

No Abstract Received.

Thursday 25 September 2008
11:30 – 13:00
Hall 6
Discussion Group
The ominous effects of epilepsy—avoiding, evading and preventing them

SEIZURE RELATED TRAUMAS AND INJURIES

M. Neufeld
Tel-Aviv Sourasky Medical Centre, Tel-Aviv, Israel

Epilepsy carries with it a risk of injuries. Reports provide conflicting evidence, which may be explained by methodological issues.

Most injuries are seizure-related – and different populations of patients with epilepsy inherently carry different types of risks for injuries and accidents.

Risks are dependent mainly on seizure type and frequency and the presence of an additional disability or disease.

Most injuries occur at home, and mild injuries are the most common type sustained as a result of a seizure.

More severe seizure-related injuries include head trauma, burns, drowning, and those sustained as a result of motor vehicle accidents.

Minimizing the number of seizures a patient has is the most effective factor in reducing seizure-related injuries. Uncontrolled seizures need to be treated aggressively, but overtreatment and drug-related side effects are risks in themselves and need to be kept in mind.

Providing safety information to patients and their caregivers might very well prevent many seizure-related traumas and accidents.

Having epilepsy requires a more cautious lifestyle, but most people with controlled seizures do not face significantly excessive risk of injuries.

STATUS EPILEPTICUS

S. Shorvon
National Hospital For Neurology & Neurosurgery, London, UK

Convulsive status epilepticus (SE) has, in some patients, a significantly poor outcome in terms of: (a) Neurological and intellectual damage; (b) ongoing epilepsy; (c) mortality. The duration of the SE, the age of the patient and the cause of the SE all influence the outcome. Active rapid antiepileptic drug therapy can minimise adverse outcomes, but there are many uncertainties about what constitutes optimal therapy. Attention to

general measures is also important. These topics, in relation to adult SE, will form the basis of the discussion.

SUDDEN UNEXPECTED DEATH IN EPILEPSY

T. Tomson
Karolinska University Hospital, Stockholm, Sweden

Sudden Unexpected Death in Epilepsy (SUDEP) is defined as the sudden, unexpected, witnessed or unwitnessed, nontraumatic, and nondrowning death in patients with epilepsy with or without evidence for a seizure, and excluding documented status epilepticus, in which postmortem examination does not reveal a structural or toxicologic cause for death. It has been estimated that sudden unexpected death is approximately 20 times more common among people with epilepsy than in the general population, but the incidence varies considerably depending on the type of epilepsy population. The rates range from 0.09/1,000 patient-years in newly diagnosed patients up to 9/1,000 in epilepsy surgery candidates, and SUDEP is the leading cause of death in chronic uncontrolled epilepsy. Case-control studies have identified risk factors thereby providing clues to mechanisms and prevention. In most cases, SUDEP is a seizure related event and the risk appears to increase with the frequency of generalized tonic-clonic seizures. Whether the mechanism by which the seizure leads to death is respiratory or cardiac is debated. A European initiative to gather data on SUDEP cases that have occurred during video-EEG monitoring might help to resolve this. Risk profiles have emerged from epidemiological studies, but it is still uncertain to what extent SUDEP can be prevented. One case-control study suggests that night time supervision could reduce the risk of SUDEP. Other studies report comparatively low SUDEP rates among patients rendered seizure free after epilepsy surgery, suggesting that this procedure might prevent SUDEP. However, the effectiveness of these potentially preventive measures is in need of appropriate evaluation.

DEPRESSION AND SUICIDE IN EPILEPSY

B. Elliot
Specialist Registrar, Outpatients Department. The Maudsley Hospital, London, UK

Lifetime prevalence of major depressive disorder, suicidal ideation and completed suicide is significantly increased in patients with epilepsy compared with the general population. There may also be a bidirectional relationship between epilepsy and depression given that in both children and adults depressive episodes and a history of attempted suicide are significantly more common in those who later go on to suffer a first seizure. The diagnosis of depression in epilepsy can be difficult given that 'classic' symptoms may be absent or interpreted as side effects of antiepileptic drugs. The fear of eliciting additional seizures can lead to exaggerated caution in psychotropic drug use. A brief review is provided of this extensive literature followed by a discussion of the recent US-Food & Drug Administration advisory on suicide risk associated with antiepileptic drugs.

Thursday 25 September 2008
11:30 – 13:00
Hall 7
Discussion Group
Neuromodulation and epilepsy: how to match basic research and clinical practice

NEUROGENESIS IN EPILEPSY; WHAT IS THE EVIDENCE?

G. Kuhn
Center For Brain Repair And Rehabilitation, Gothenburg, Sweden

No Abstract Received.

NEUROGENESIS IN EPILEPSY; WHAT IS THE EVIDENCE?

E. Ben-Menachem
Sahlgrenska University Hospital, Goteborg, Sweden

No Abstract Received.

NEUROMODULATION IN EPILEPSY; WHAT IS THE EVIDENCE?

W. Wadman
University of Amsterdam, Amsterdam, The Netherlands

No Abstract Received.

NEUROMODULATORY TREATMENTS IN CLINICAL PRACTICE; WHAT IS THE EVIDENCE?

K. Vonck
Ghent University Hospital, Ghent, Belgium

No Abstract Received.

NEUROMODULATORY TREATMENTS IN THE FUTURE; WHAT CAN WE EXPECT?

P. Boon
Ghent University Hospital, Ghent, Belgium

Neuromodulation and epilepsy, how to match basic research and clinical practice Paul A.J.M. Boon, M.D., Ph.D. Reference Center for Refractory Epilepsy, Department of Neurology, Ghent University Hospital, Belgium Experimental literature supports the rationale for deep brain stimulation (DBS) in epilepsy, although not all available data are congruent. Depending on targets and stimulation parameters, DBS may inhibit or elicit seizures. DBS in areas of the cerebellum, in various (sub-)thalamic nuclei (centromedian nucleus, anterior nucleus, subthalamic nucleus), in medial temporal lobe structures and in a limited number of other CNS structures has been shown to be efficacious in small pilot studies of patients with medically refractory epilepsy. One controlled study on the effects of anterior nucleus stimulation (SANTE) is currently recruiting patients. Only limited data on chronic thalamic and amygdalohippocampal stimulation are available. Chronic DBS in these structures requires resolving many conceptual and technical issues. There is little evidence-based information on rational targets and stimulation parameters. The experience with DBS in temporal lobe epilepsy using quadripolar DBS electrodes bilaterally implanted in the amygdalohippocampal region to identify and subsequently stimulate the ictal onset zone will be described. This work has yielded a significant decrease of seizure counts and interictal EEG abnormalities during long-term follow-up, without major side effects. Various hypotheses on the possible mechanism(s) of action of DBS for epilepsy using EEG, cerebral blood flow and metabolic measures including results from animal experiments have recently been developed. Data from open pilot studies suggests that chronic DBS for epilepsy may be a feasible, effective and safe procedure that reduces interictal EEG abnormalities and seizures. A controlled and randomized trial comparing hippocampal DBS and resective surgery (CoRaStiR) is currently being initiated. Whether DBS may represent an alternative treatment for resective surgery in selected patients or whether it may substitute for chronic antiepileptic drug polytherapy remains to be demonstrated.

Thursday 25 September 2008
11:30 – 13:00
Hall 9
Discussion Group
The role of parahippocampal brain areas in temporal lobe epilepsy

MORPHOLOGICAL AND NEUROCHEMICAL PLASTICITY OF PARAHIPPOCAMPAL AREAS IN THE KAINITE MODEL OF TLE

G. Sperk
University of Innsbruck, Innsbruck, Austria

Plastic changes in parahippocampal areas of rats after kainic acid induced seizures Günther Sperk and Meninrad Drexel Department of Pharmacology, Medical University Innsbruck, Innsbruck, Austria The subiculum is the main output region of the hippocampus receiving input from the CA1 region and projecting to deep layers of the entorhinal cortex (EC), septum, mamillary nuclei, and the amygdala. It remains largely preserved in temporal lobe epilepsy (TLE) and therefore may be importantly involved in the generation of epileptic activity arising from the hippocampus. We characterized neurons of the subicular-EC complex and its projections in the kainic acid (KA) model for TLE using neuropeptides, calcium binding proteins, GAD-67 and the vesicular GABA and glutamate transporters as markers. We observed severe losses of interneurons and principal neurons in layer III of the EC and in the proximal subiculum accompanied by signs of reactive gliosis. The number of parvalbumin-ir interneurons was reduced in the subicular pyramidal cell layer and the deep layers of the EC. After 28 d the number of calretinin-ir neurons was reduced in EC layers III to VI, as was the diffuse calretinin-ir in the subiculum molecular layer and the EC, suggesting degeneration of respective calretinin containing projections. In all parahippocampal areas, increases in NPY mRNA in pyramidal cells and of NPY-ir axons were seen at the late intervals after KA. In the molecular layer and layer I of the EC, diffuse labeling for SOM-ir overlapped with that of NPY. The number of GAD67-ir interneurons was reduced in the inner molecular layer and pyramidal layer of the subiculum and in the EC at late timepoints, but also diffuse labeling for GAD67 and VGAT was enhanced in the molecular and pyramidal cell layers of the subiculum and in EC layer I. Our data indicate losses in neurons projecting from the EC to the subiculum. Similarly, projections from the subiculum to the deep layers of the EC seem to degenerate. Pyramidal neurons of the subiculum become immunoreactive for several neuropeptides. Inhibitory neurons projecting to distal dendrites of subicular principal cells sprout as judged by increased numbers of GAD-67, VGAT, SOM and NPY-ir fibers.

METAPLASTICITY AT CA1-SUBICULUM SYNAPSES IN TEMPORAL LOBE EPILEPSY

J. Behr
Charite, Campus Mitte, Berlin, Germany

Patients with temporal lobe epilepsy suffer from severe problems in the encoding of declarative memory. Declarative memory storage depends on the hippocampus that processes sensory input and relays it to a variety of cortical and subcortical brain regions. The subiculum is the principal target of CA1 pyramidal cells and thus serves as the major relay station for the predominantly unidirectional outgoing information of the hippocampus. Recent work in rats and humans has shown that the subiculum is critically involved in the encoding and retrieval of learned information underpinning its role in hippocampal-cortical interaction. To elucidate disturbances in the consolidation of hippocampal output information, we investigated seizure-induced alterations of synaptic plasticity at hippocampal CA1-subiculum synapses in human and experimental temporal lobe epilepsy. We showed that high frequency synaptic activity as occurs under seizure activity seems to alter the capacity of CA1-subiculum synapses to express long-term potentiation (LTP). Seizure-induced occlusion of LTP at hippocampal output synapses may thus reflect the impaired encoding of declarative information observed in patients suffering from temporal lobe epilepsy.

ACUTE ICTAL DISCHARGES IN THE ENTORHINAL-PERIRHINAL CORTICES

M. De Curtis
Instituto Nazionale Neurologico, Milan, Italy

Intrinsic anatomical connections within the parahippocampal region (PHR) were extensively characterized in different animal species. Associative fibers reciprocally link the main PHR subfields, namely the entorhinal cortex (EC), the perirhinal cortex (PRC) and the postrhinal cortex (PostRC). Neurophysiological studies performed in vitro demonstrated that long-range interactions between these regions are controlled by a powerful control (de Curtis and Paré 2004), possibly mediated by feed-forward inhibitory connections (Apergis et al. 2006). Optical imaging studies performed in the isolated guinea pig brain preparation demonstrated that activity generated within the EC does not propagate to the lateral PRC. We further characterize the functional interactions within the PHR regions in the in vitro isolated guinea pig brain preparation, focusing on the generation of acute epileptiform discharges. Arterial perfusion of the GABAergic receptor antagonist, bicuculline, induced seizures in the EC-hippocamnpus that do not propagate to the PRC, unless sizures were repeated. Still, epileptiform activities in the PRC only occasionally the features of an ictal, seizure-like discharge. Preliminary findings demonstrate that propagation of seizure activity is promoted by local applications of bicuculline in area 35, but not in area 36, suggesting that this region plays a crucial role in the extrahippocampal propagation of epileptiform discharges.

THRESHOLD BEHAVIOR IN THE INITIATION OF HIPPOCAMPAL POPULATION BURSTS

L. De La Prida
Instituto Cajal – CSIC, Madrid, Spain

Temporal lobe epilepsy (TLE), the most common form of pharmacorresistant type of epilepsy, affects extensive hippocampal and parahippocampal regions. Invasive recordings from epileptic patients revealed typical interictal population activity emerging from these regions. However, the cellular and network mechanisms of interictal events are not well understood. In recent years work from our laboratory has explored the mechanisms underlying the initiation and synchronization of epileptiform activities in the hippocampus and the subiculum of normal and epileptic rats. We review these recent findings trying to identify the rules that govern the operation of epileptic microcircuits in vitro and to relate these to the role of the hippocampus and the subiculum in the epileptic brain.

Monday 22 September 2008
11:30 – 13:00
Hall 3
Platform Session
Drug Therapy

001

VARIABILITY IN LAMOTRIGINE CLEARANCE DURING DIFFERENT PHASES OF THE MENSTRUAL CYCLE AND THE INFLUENCE OF ORAL CONTRACEPTIVES

I. Wegner, P. Edelbroek*, J. Segers*, and D. Lindhout†*
**SEIN, Epilepsy Institute In Netherlands, Zwolle,*
The Netherlands and †University Medical Center Utrecht,
Utrecht, The Netherlands

Purpose: Previous studies indicated that lamotrigine (LTG) metabolism increases during pregnancy. A similar kind of pharmacokinetic interaction has been demonstrated between LTG and combined oral contraceptives (OC). This prospective observational study aims to further investigate the interaction between LTG and OC, the effect of endogenous steroid levels during the menstrual cycle and the effect of postmenopausal status.

Method: Group A: Female patients at fertile age with regular menstrual cycles, on monotherapy LTG, without OC (n¬=8). Group B: Female patients at fertile age, on monotherapy LTG using a one-phase combined OC (n=7). Group C: Post menopausal patients on monotherapy LTG

(n=6). The study period covered at least two months (group C) or two menstrual cycles (group A and B) with monitoring trough levels of LTG each other day using a dried blood spot method. Mean relative clearances were calculated.

Results: In Group A, mean (SD; range) Cl was 53.8 (22.8; 21.2–79.8) L/24h. No significant effect of endogenous hormones on LTG clearance was found. In group B mean (SD; range) Cl was 121.4(62.4;48.6–199.6) L/24h. The fluctuation associated with cyclic use of oral contraceptives was rapid and reproducible in successive cycles. In Group C mean (SD; range) CL was 82.2 (41.7; 38.4–122.6) L/24h.

Conclusion: This study confirms previous observations that OC may have a strong effect on LTG clearance. There was no clear effect of endogenous hormones on LTG clearance, whereas, to our surprise, we observed a higher mean LTG clearance in postmenopausal patients in comparison with young females of group A.

002
NEURODEVELOPMENT OF CHILDREN EXPOSED TO ANTIEPILEPTIC MEDICATION IN PREGNANCY

T. Kelly, L. Garwood,* and M. Jackson†*
**Newcastle Primary Care Trust, UK and †Newcastle Acute Hospitals Trust, UK*

Purpose: To investigate the long-term drug effects on cognitive development, social functioning and possible dysmorphic features in school-aged children exposed to antiepileptic drugs in utero (AED).

Method: 85 Women with epilepsy were recruited during pregnancy through a specialist genetics nurse. 85 children with a mean age of 7.6 years completed a follow-up assessment to profile intellect, academic performance, daily living skills and emotional and behavioral levels. Maternal intellect was measured. The assessment was undertaken blind to medication classifications.

Results: Insufficient information led to 9 children being excluded from analysis, thus 76 children's results were used: 31 were exposed to carbamazepine, 26 to sodium valporate, 6 to mixed medication and 13 to no medication (control). Possible effects of social class, as measured by Indices of Multiple Deprivation, were controlled for in the analysis. There were no significant differences found between the four groups on measures of intellect, academic achievement, daily living skills or emotional and behavioral problems.

Conclusion: The results provide no evidence of specific negative drug related effects for children exposed to AEDs in utero. The study does not support the findings of contemporary research reporting detrimental developmental effects of sodium valporate and carbamazepine. Stronger influences on development appear to be the level of deprivation within which the child is living, and to a lesser extent, parental IQ.

003
LEVETIRACETAM THERAPY IN HUMAN PREGNANCY. UPDATED EXPERIENCE FROM THE UK EPILEPSY AND PREGNANCY REGISTER*

S. Hunt, B. Irwin*, R. Waddell*, A.Russell†, W. Smithson‡, L. Parson§, I. Robertson¶, P. Morrison**, J. Morrow*, and J. Craig**
**UK Epilepsy & Pregnancy Register, UK; †Southern General Hospital, Glasgow, UK; ‡The Surgery, Escrick, York, UK; §St Albans City Hospital, Waverley Road, St Albans, UK; ¶Lancashire Teaching Hospitals NHS Trust, Sharoe Green Lane South, Preston, UK and **Belfast City Hospital Trust, Lisburn Road, Belfast, & School Of Biological Sciences, University of Ulster, Coleraine, UK*

*Data through February 29 2008.

Purpose: Levetiracetam is licensed for monotherapy and adjunctive treatment of partial seizures with or without secondary generalisation, and for adjunctive therapy of myoclonic seizures and generalized tonic–clonic seizures. Human pregnancy data are sparse.

Method: This study is part of a 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 antiepileptic 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 263 pregnancies. There were 249 live births. Five of these had an MCM (2.0%; 95% C.I. 0.9–4.6%). No MCMs were observed in 95 monotherapy exposures (0.0%; 95% C.I. 0.0–4.1%). Five cases exposed to levetiracetam as part of a polytherapy regime had an MCM (3.1%; 95% C.I. 1.3–7.1%).

Conclusion: While the absolute number of outcomes of human pregnancies exposed to levetiracetam is low the data we present here are encouraging. Larger numbers are required for statistical analysis; as such it is imperative that practitioners continue to enroll patients into prospective pregnancy registers.

004
INFLUENCE ON SCHOOL RESULTS IN CHILDREN EXPOSED TO ANTIEPILEPTIC DRUGS IN UTERO-EPIDEMIOLOGICAL DATA FROM THE SWEDISH HEALTH REGISTRIES

K. Wide, and L. Forsberg
CLINTEC, Karolinska Institute, Sweden

Purpose: To study if there were any differences in achieving leaving certificate from compulsory school between children exposed to antiepileptic drugs (AED) in utero and unexposed children.

Method: During 1973–1986 1359 children born to mothers with a diagnosis of epilepsy in were identified in the Swedish Medical Birth Registry (MBR), a total of 1 307 080 children were born in Sweden during the time period. All identified children exposed to AED were living in Sweden at the age of 16 and no one had major malformations. The data from the MBR were matched with data from the Statistics Sweden on leaving certificates from compulsory school.

Results: 83/1359 children born to mothers with a diagnosis of epilepsy lacked leaving certificate from school at 16 years of age (OR: 1.83 (95 % CI 1.47–2.29) (adjusting for year of delivery, maternal age, parity and maternal educational level), 3/ 90 study children not exposed to AED (OR: 1.17 95%CI 0.24–3.41), 16/271 (OR:2.27 95% 1.38–3.73) children exposed to AED in monotherapy, and 25/287 (OR: 3.04 95% 2.05–4.51) exposed to polytherapy did not achieve a leaving certificate.

Conclusion: These preliminary results seem to show that exposure to AED during pregnancy may influence the ability to achieve a leaving certificate from compulsory school. The material is being scrutinized and further analyses on drugs and on results for grades for specific core subjects are being performed.

005
CLONALLY EXPANDED MITOCHONDRIAL DNA MUTATIONS IN EPILEPTIC INDIVIDUALS WITH MUTATED DNA POLYMERASE

G. Zsurka, M. Baron, C. Elger, and W. Kunz
University of Bonn, Germany

Purpose: The instability of the mitochondrial genome in individuals harboring pathogenic mutations in the catalytic subunit of mitochondrial DNA polymerase? (POLG) is a well recognized fact, but the underlying molecular mechanisms remain to be elucidated.

Method: We investigated secondary changes of the mitochondrial DNA (mtDNA) in five patients with severe myoclonic epilepsy and valproic acid induced liver failure due to homozygous or compound heterozygous mutations in the POLG gene. Activity of the oxidative phosphorylation was measured with spectrophotometric and histochemical methods. Mitochondrial DNA copy numbers were determined by TaqMan-based quantitative PCR. Point mutations were detected by sequencing and mismatch-PCR RFLP. To quantify low levels of multiple mtDNA deletions, we developed a two-step single-molecule PCR assay.

Results: While muscle biopsies showed rather unremarkable histology in the patients, postmortem liver tissue available from one individual exhibited large cytochrome c oxidase (COX) negative areas. These COX-negative areas contained fourfold less mitochondrial DNA than COX-positive areas. Decreased copy numbers of mtDNA were observed also in skeletal muscle, brain and blood samples from all patients. Furthermore, we observed in different tissues individual-specific patterns of multiple mtDNA deletions, and in two out of five patients clonally expanded mtDNA point mutations. The low amount of deleted mtDNA molecules makes it unlikely that they significantly contribute to the biochemical defect.

Conclusion: The observed clonal expansion of few individual-specific deletions and point mutations indicates an accelerated segregation of early mtDNA mutations, probably as a consequence of low mtDNA copy numbers. Our results suggest a diagnostic approach for identifying mtDNA depletion in patients with myoclonic epilepsy and valproic acid intolerance.

006

THE KOMET STUDY: AN OPEN-LABEL, RANDOMIZED, PARALLEL-GROUP TRIAL COMPARING THE EFFICACY AND SAFETY OF LEVETIRACETAM WITH SODIUM VALPROATE AND CARBAMAZEPINE AS MONOTHERAPY IN SUBJECTS WITH NEWLY DIAGNOSED EPILEPSY

E. Trinka, W. Van Paesschen†, Y. Hallstrom‡, P. Hon§, A. Marson¶, G. Muscas**, R. Kalviainen††, S. Buyle‡‡, J. Marovac‡‡, P. Edrich‡‡, and B. Pohlmann-Eden§§,¶¶*
**Epilepsy Service And EEG Laboratory, University Hospital, Innsbruck, Austria; †University Hospital Gasthuisberg, Leuven, Belgium; ‡Neuro Center, St Gorans Hospital, Stockholm, Sweden; §University Hospital Ostrava, Czech Republic; ¶The University of Liverpool And The Walton Centre For Neurology And Neurosurgery, UK; **Careggi Hospital, Florence, Italy; ††Kuopio Epilepsy Center, Kuopio University Hospital, Kuopio, Finland; ‡‡Global Medical Affairs CNS, UCB Pharma SA, Brussels, Belgium; §§Epilepsy Centre, Bethel-Bielefeld, Germany and ¶¶Division Of Neurology, Dalhousie University, Halifax, Canada*

Purpose: To assess the efficacy and tolerability of levetiracetam (LEV), extended-release sodium valproate (VPA-ER) and controlled-released carbamazepine (CBZ-CR) as monotherapy in patients with newly diagnosed partial or generalized epilepsy.

Method: In this open-label, parallel-group, 52-week trial, patients (>=16y) with >=2 unprovoked seizures in the past 2y and >=1 in the last 6m were stratified to physicians' best recommended treatment (VPA-ER or CBZ-CR). By randomization patients were allocated to best recommended treatment or LEV. The initial target doses were VPA-ER 1000mg/day, CBZ-CR 600mg/day, and LEV 1000mg/day.

Results: 1688 patients (ITT population; mean age 41y; 44% female) with median 3 seizures in the last 2y (62% partial-onset; 32% primary generalized, 6% mix of seizure types) and epilepsy duration of median 0.9y were randomized to LEV (n=841) or standard AEDs (n=847). Completion rates (52-week treatment) were similar between groups (LEV 76.0%; standard AEDs 74.0%). Time to withdrawal (primary endpoint) was not significantly different between groups overall and by strata: hazard ratios (95% CI) (1) LEV/standard AEDs 0.90 (0.74–1.08); (2) LEV/VPA-ER (349/347) 1.02 (0.74–1.41); (3) LEV/CBZ-CR (492/500) 0.84 (0.66–1.07). Discontinuation due to lack of efficacy was 4.2% for LEV and 3.0% for standard AEDs. Discontinuation due to adverse event was 8.4% for LEV and 13.0% for standard AEDs. Similar proportion of patients in all treatment groups experienced >=1 drug-related adverse event (45.6% LEV; 45.9% VPA-ER; 52.3% CBZ-CR).

Conclusion: In this large multicentre study LEV demonstrated similar effectiveness to standard treatment as monotherapy in patients with newly diagnosed partial and generalized epilepsies.

Sponsored by UCB.

Monday 22 September 2008
11:30 – 13:00
Hall 2b
Platform Session
Pediatrics – Epilepsy Surgery

007

PEDIATRIC SURGERY OUTCOMES FOR LOCALIZATION RELATED EPILEPSY

J. Walker, S. Hepner, N. Kadom, M. Santi, A. Yaun, J. Conry, P. Pearl, T. Tsuchida, S. Weinstein, and W. Gaillard
Children's National Medical Center, Washington, DC, USA

Purpose: To determine pediatric temporal and extratemporal lobe epilepsy surgery outcomes.

Method: We reviewed data from 115 pediatric epilepsy surgery patients (47F, mean age at surgery= 10.7) divided into temporal (TL) and extratemporal (ETL) seizure focus groups. We based etiology on MRI and pathology: normal MRI (n=4), dysplasia (n=35), MTS (n=27), tumor (n=38), and vascular lesions (n=11). Postoperative outcome was based on Engel's criteria for greater than one year post surgical follow-up.

Results: Class I and II combined outcomes for TL surgery were 90% (n = 60 CI = 76.0% – 96.0%) and ETL surgery were 87% (n = 55, CI=69.5% – 94.6%). Class I outcome: 68% (n=41) for and 67% (n=37) for ETL. Class II outcome: 22% (n=13) for the TL group and 20% (n=11) for the ETL group. Class III outcome: 3% (n=2) for the TL group and 7% (n=4) for the ETL group. Class IV outcome: 7% (n=4) for TL and 6% (n=3) for ETL. MTS (41.6%, n=25) and tumor (35%, n=21) were the most common diagnoses in patients with TL. Tumor (29%,n=16) and dysplasia (51%, n=28) were the most common diagnoses for the ETL patients. There was no difference in outcome based on the site of resection for tumor or dysplasia. Engle's I and II outcomes based on pathology was: MTS (92%), tumor (89%), and dysplasia (83.7%).

Conclusion: We found no difference in outcome based on the location for pathology substrate. MTS patients have the best outcome. Outcomes for tumor and dysplasia are comparable and independent of location.

008

COGNITIVE OUTCOME AFTER TEMPORAL LOBE SURGERY IN CHILDHOOD: A LONG-TERM FOLLOW-UP STUDY

C. Skirrow,†, J. Cross*,†, F. Cormack*,†, F. Vargha-Khadem*,†, and T. Baldeweg*,†*
**UCL Institute of Child Health, London, UK and †Great Ormond Street Hospital For Children NHS Trust, London, UK*

Purpose: Temporal lobectomy (TL) is a successful surgical treatment for patients with intractable temporal lobe epilepsy. However, little is known about long-term cognitive outcome after TL in children.

Method: 41 TL patients were tested (24 left- and 17 right-sided surgery, 16 with developmental tumors and 25 with hippocampal sclerosis). Mean age at surgery was 13.8 years. In addition we assessed a group of 11 patients with lesional focal epilepsy who underwent the same presurgical evaluation but who did not undergo surgery (non-TL group). Minimum follow-up time was 5 years. General cognitive function was measured using standardized tests of intelligence. Additionally, structural MRI data were used to extract total brain white and grey matter (GM) volumes.

Results: 86% of TL and 36% of non-TL patients were seizure free at follow-up. Surgical and nonsurgical groups were well matched for initial Full Scale IQ (FSIQ). Most surgery patients showed an increase in FSIQ postsurgically, with the most marked change in those with below average preoperative intellect. No change in FSIQ was found in the nonsurgery group. An improvement of >15 IQ points was seen in 10 TL patients and none of the non-TL group. Both left and right TL cases improved in nonverbal intelligence, while the left TL group also showed an improvement in verbal IQ. Change in FSIQ in TL patients was correlated with change in GM volume, regardless of size of the resection.

Conclusion: Temporal lobectomy in childhood results in good seizure control and appears to facilitate intellectual and brain development.

009

CHILDREN WITH LOW IQ BENEFIT FROM RESECTIVE EPILEPSY SURGERY OUTCOME AT TWO-YEAR FOLLOW-UP IN A CONSECUTIVE SERIES FROM GÖTEBORG, SWEDEN, 1987–2004

B. Rydenhag, A. Hedström†, B. Olovson†, P. Uvebrant†, G. Viggedal†, and I. Olsson†*
**Institute of Neuroscience and Physiology, Sweden and †Sahlgrenska University Hospital, Göteborg, Sweden*

Purpose: To present seizure outcome two years after resective epilepsy surgery in a consecutive series of children < 19 years, and to compare outcome in those with normal IQ level and those with cognitive impairment.

Method: All patients are evaluated before surgery and at two-year follow-up. Resective surgery was performed in 80, 35 boys and 45 girls. Mean age at operation was 10.8 (SD 4.9) years, range 0.9–18.6. Preoperative cognitive level was impaired in 44%, IQ < 50 in 28%, IQ 50–69 in 16%.

Results: Outcome after hemispherectomy (n=10) was seizure freedom in 80% and > 75% reduction of seizure frequency in 20%; temporal lobe resections (n=31) 65% and 23% respectively; occipital or parietal lobe resections (n=9) 67% and 11% respectively; multilobe resections (n=12) 42% and 25% respectively; frontal lobe resections (n=18) 28% and 33% respectively. In the group of children with a preoperative IQ level <70, 15/35 became seizure free. The corresponding figure in children with IQ level >70 was 29/45. In the low IQ group 8/35 had >75% reduction of seizure frequency. The corresponding figure in the group with IQ>70 was 10/45. In all, 66% in the low IQ group and 87% in the normal IQ group had benefited from surgery at the two-year follow-up.

Conclusion: Resective epilepsy surgery should be considered also in children with low cognitive level. More than half may obtain > 75 % reduction of seizure frequency.

010

THE EFFECTS OF EPILEPSY SURGERY ON EMOTIONS, BEHAVIOR AND PSYCHOSOCIAL IMPAIRMENT IN CHILDREN AND ADOLESCENTS WITH DRUG RESISTANT EPILEPSY: A PROSPECTIVE STUDY

S. Hannan, H. Cross, R. Scott, W. Harkness, and I. Heyman
Great Ormond Street Hospital, London, UK

Purpose: Children with refractory epilepsy have high rates of emotional and behavioral problems. This study examined change in behavioral disorders and psychosocial impairment following epilepsy surgery, in children and adolescents with drug resistant epilepsy.

Method: Thirteen children with drug resistant focal epilepsy were screened for emotional and behavioral symptoms at four times pre and postoperatively. Qualitative information about the child's emotions, behavior and psychosocial functioning was also obtained 7.5–8.5 years after surgery. Scores on the Strengths and Difficulties Questionnaire (SDQ) preoperatively were compared with postoperative scores. Surgery comprised four hemispherectomies, six temporal lobe resections, two extratemporal resections and one multiple subpial transection.

Results: Scores in emotional and behavioral symptoms (Total Difficulties Scale) were significantly lower after surgery. The mean score reduced from 16.7 (95% confidence interval (CI) 12.7 to 20.8) at Time 1, to 11.2 (95% CI 6.2 to 16.2) ($F(3.12) = 4.72$ $p= 0.015$) at Time 4. A downward trend in total difficulty scores for the group was demonstrated over the 3 postoperative time points. The mean Impact Score showed an initial decrease at the first follow up time point after surgery (5.1 (95% CI 2.9 to 7.2), at Time 1 reducing to 2.8 (95% CI 0.53 to 5.1) at Time 2, with no further improvement subsequently.

Conclusion: Our findings suggest that emotional and behavioral symptoms in children undergoing epilepsy surgery may improve following surgery, with reduction in their functional impact, and that these improvements are maintained in the long-term.

011

VERTICAL PARASAGITTAL HEMISPHEROTOMY FOR RASMUSSEN'S ENCEPHALITIS

G. Dorfmüller,†, C. Bulteau*,†, M. Fohlen*, V. Oliver*, C. Jalin*, I. Jambaque‡, and O. Delalande**
**Fondation Rothschild, Paris, France; †INSERM, U 663, Hopital Necker, Paris, France and ‡Université Paris Descartes, CNRS FRE 2987, Boulogne-Billancourt, France*

Purpose: We present our series of young patients with Rasmussen's encephalitis (RE), operated on for refractory hemispheric epilepsy by the vertical parasagittal hemispherotomy technique.

Method: Forty-two patients with RE were operated on at our institution from 1990 to 2007 by the same surgical technique. Twenty-four were females and 18 males, with a mean age of 10,8 years (3,3 to 22,7). Eighteen patients underwent left and 24 right hemispherotomy, with no significant age difference. The mean age of seizure-onset was at 6,2 years (2,0 to 13,5). Four patients had focal cortical resection prior to hemispherotomy.

Results: Postoperatively, 3 patients developing hydrocephalus had shunt-surgery, progressive subdural hygroma needed surgical treatment in 3 others, and one patient died following shunt-related meningitis. Thirty-nine patients were followed-up more than one year, with 33 (84,6%) being seizure-free, 4 (10,3%) almost seizure-free, and 2 (5,1%) significantly improved. Twenty-six patients had a formal pre- and postoperative neuropsychological assessment, with special emphasis on language skills. No language deterioration was noted in any of the 12 patients following hemispherotomy of their dominant hemisphere. However, an inferior postoperative language improvement was demonstrated in older patients, whereas the younger group reached better language scores.

Conclusion: The vertical parasagittal hemispherotomy represents an effective and relatively safe treatment for patients with RE, with an excellent seizure-outcome in this single-center series. In patients with dominant hemisphere RE, our results confirm a better postoperative language outcome for children operated on at younger age and with shorter preoperative delay.

Monday 22 September 2008
11:30 – 13:00
Hall 5
Platform Session
Pediatrics – Outcome Related Issues

012
DOES SECONDARY EPILEPTOGENESIS IN HYPOTHALAMIC HAMARTOMA EXIST? TWO STEP SURGERY DEMONSTRATION

J. Scholly, M. Valenti, S. Chassagnon, B. Cretin, M. Zimmermann, S. Kremer, P. Kehrli, and E. Hirsch
University Hospital of Strasbourg, France

Purpose: Hypothalamic Hamartoma (HH) related epilepsy manifests with gelastic seizures, behavioral problems, cognitive deterioration and it is usually drug resistant. Other seizure types could be observed. Recent electrophysiological findings suggest that hamartoma itself represents the source of primary ictal discharge in HH-related seizures. This explains previous reports of failure of standard temporal lobectomy. Transcallosal surgery, disconnection, endoscopic or gamma-knife ablation of HH are now considered as standard procedures. However, little is known about seizure recurrence mechanisms in surgical outcome.

Method: We retrospectively studied a HH-related drug-resistant epilepsy case, issue from a series of 10 cases, manifested with gelastic seizures later associated with focal seizures as well as a psychotic disorder. Gamma-knife treatment was unsuccessful. Endoscopic surgical ablation of hamartoma (neuropathologically confirmed) resulted in complete regression of gelastic seizures but not the focal seizures, being still drug-resistant.

Results: Electroclinical features of focal seizures were typical of mesial temporal lobe origin. MRI was normal. Cerebral FDG-PET showed a left temporal hypometabolism. According to these findings, standard temporal lobectomy was performed. Neuropathological study was normal. Seizure outcome corresponded to Engel-IA at one year follow up. Psychiatric outcome was also favorable.

Conclusion: Our data suggest, for the first time, the existence of secondary epileptogenesis with independent nonlesional temporal epileptogenic zone. This dynamics in epileptogenesis should be considered when choosing surgical strategy in HH-patients.

013
CAN CHILDREN WITH EPILEPSY AND THEIR FAMILIES PREDICT THEIR SEIZURES?

A. Papavasiliou, N. Voudouri, G. Niotakis, H. Bazigou, V. Paraskevoulakos, and H. Kotsalis
Pendelis' Childrens' Hospital, Athens, Greece

Purpose: To examine whether patients with pediatric epilepsy themselves or their parents were able to predict seizures using prospectively a seizure diary for one month; to examine whether patients' and/or parents' predictions about their seizures were valid.

Method: Patients 18 years old or younger, with localization-related epilepsy, who had one or more seizures during the past 12 months, were given a 30-day seizure diary asking the question 'Do you think it is possible for you / your child to have a seizure in the next 24 hours?' Answers were as follows: very possible, possible, impossible, highly impossible. A record of the occurrence of seizures for the period under examination was included. Exclusion criterion was the occurrence of 3 or more seizures per day.

Results: Thirty participants returned 900 diary entries; 4 were excluded because they had more than 3 seizures per day and 5 didn't report any seizures. As a result, 21 participants with 630 diary entries were analyzed; 228 seizures were recorded (mean 10.85, range 1–60 seizures). Twelve participants (57.1 %) with 122 seizures reported inability to predict their seizures, whereas 9 (42.8 %) with 106 seizures predicted their seizures. Feeling stressed or nervous, a sense of fear and mood swings were the most commonly reported symptoms (38.4%). A positive prediction of seizures was associated with a 2.117 fold increased risk of seizure.

Conclusion: A significant proportion of the participants (42.8%) were able to predict their seizures. Emotional changes were the most commonly reported preictal symptoms.

014
TREATMENT OF CHILDHOOD CONVULSIVE STATUS EPILEPTICUS THAT HAS BEGUN IN THE COMMUNITY: PROSPECTIVE POPULATION-BASED STUDY

R. Chin, B. Neville, C. Pecham, A. Wade, H. Bedford, and R. Scott
UCL- Institute of Child Health, London, UK

Purpose: Childhood convulsive status epilepticus (CSE) frequently starts in the community. The purpose of emergency treatment is to minimise seizure length and to treat causes to reduce adverse outcomes but there are limited available data on optimum treatment. We report the first systematic population-based data on the treatment of childhood CSE from its onset in the community.

Method: From May 2002 to April 2004 data were prospectively collected on north London children with episodes of CSE (ascertainment 62–84%). Logistic regression was used to examine factors associated with seizure termination after first and second line therapy, CSE lasting > 60 minutes, and respiratory depression. All episodes were included and adjustment made for repeat episodes in individuals.

Results: 240 episodes (182 children, median age 3.24 (0.16–15.98) years) were enrolled. 147 (61%) episodes received prehospital treatment of which 30 (20%) had seizure termination. In multivariable models, in A&E treatment with intravenous lorazepam was associated with a 3.7 times (95%CI 1.7, 7.9) greater likelihood of seizure termination than with rectal diazepam. As second line therapy, treatment with intravenous phenytoin was associated with 9 times (95%CI 3.0, 27.0) greater likelihood of seizure termination compared than with rectal paraldehyde. Lack of prehospital treatment (OR2.4, 95%CI 1.2–4.5) and treatment with > 2 doses of benzodiazepines (OR 3.6 (95%CI 1.9–6.7) were associated with CSE lasting >60 minutes. Treatment with > 2 doses of benzodiazepines was also associated with respiratory depression (OR 2.9, 95%CI 1.4, 6.1).

Conclusion: These findings should be considered in developing treatment guidelines for CSE.

015
LONG-TERM NEURODEVELOPMENTAL OUTCOME OF CRYPTOGENIC WEST SYNDROME

N. Tatishvili, T. Kipiani*, and S. Tatishvili†*
**Childrens Central Hospital, Georgia and †Child Neurology And Neurorehabilitation Centre, Tbilisi, Georgia*

Purpose: To evaluate neurodevelopmental outcome of patients with cryptogenic west syndrome at preschool age and evolution of epilepsy syndrome.

Method: Prospective cohort of 72 patients with cryptogenic West syndrome admitted to Childrens Central Hospital of Tbilisi from 2001–2002

were identified and followed till age 5–6 years. In 2007 67 patients (5 missed) were reevaluated and divided into two groups. I-normal outcome 21 patients, II delayed-46. Epilepsy syndrome and seizure types were identified in both groups. Groups were compared for timing and type of treatment, background EEGs, ictal patterns, seizure types, syndrome evolution.

Results: Duration from onset of spasms till any treatment was longer in group II ($p<0.01$). Persistence of hypsarrythmia was correlated with poor outcome ($p<0.05$). Relapses were more frequent in group II ($p<0.05$). Patients treated with ACTH as first line drug had less relapses of spasms and hypsarrhythmia and better IQ($p<0.005$). Hypsarrhythmia in patients of group II had more asymmetric lateralising features ($p<0.05$). Seizure free patients were only in group I. In group II patients had more seizure types except spasms. Main seizure types were partial seizures in both groups. Myoclonic-astatic and tonic seizures appeared mostly in group II ($p<0.01$). In background activity there was no significant difference in groups, but regional distribution of focal discharges differed. In group I it prevailed in centrotemporal, while in group II more prominently appeared in frontal regions.

Conclusion: Short treatment lag, early cessation of symmetric hypsarrhythmia, ACTH treatment, few seizure types and few relapses are predictors of better neurodevelopmental outcome.

016
'EPILEPSY WITH MYOCLONIC ASTATIC SEIZURES' ELECTROCLINICAL FEATURES OF 51 CASES

B. Dalla Bernardina, L. Giordano†, F. Darra*, E. Fiorini*, S. Gambara†, P. Accorsi†, and E. Fontana**
**University of Verona, Italy and †Hospital Brescia, Italy*

Purpose: According to ILAE Classification MAE is 'a well defined syndrome but its course is variable and many are epileptic encephalopathies'. In order to contribute to a better definition of the electroclinical features characterizing the onset and the evolution of MAE the Authors report the results of an electroclinical study of 51 subjects (39 M, 12 F) aged between 6y 6m and 36y 3m (mean 13y 4m) longitudinally followed from seizure onset.

Method: We considered only subjects more than 6 years old at the last observation without neuropsychological impairment at onset and for which an EEG polygraphic recording was available characterizing the onset period and the evolution.

Results: The age at onset is between 16m and 5y5m (mean: 3y 3m). The seizures characterizing the onset period are: generalized convulsive seizures isolated or in clusters often presenting with a focal onset in nearly 80%, massive myoclonias with generalized PS/W in more than 90%, myoclonic-atonic attacks with drop or head-drop in nearly 90%, brief tonic vibratory seizures mainly nocturnal in more than 50% and atypical absences in almost 50%. 41 subjects (80%) presented a peculiar type of polymorphous long-lasting or brief epileptic status, appearing as the first ictal manifestation or during the first two months from onset in 19(37%). The seizures stopped in 40(78%) often briefly after onset. At follow-up 37 subjects are cognitively normal with learning disabilities in 16, while 14 have a cognitive impairment.

Conclusion: Following a correct clinical and video-EEG polygraphic assessment MAE appears to be a well recognisable idiopathic myoclonic epilepsy often with a stormy onset but having a relatively good prognosis if recognized early and strongly treated.

Monday 22 September 2008
11:30 – 13:00
Hall 6
Platform Session
Experimental Epileptology

017
AGE-DEPENDENT CHANGES IN THE RESPIRATORY CONTROL OF BRAIN PH AND IN THE THRESHOLD OF FEBRILE SEIZURES IN RATS AND MICE

K. Kaila, E. Tolner*, A. Yukin*, J. Voipio*, S. Vanhatalo*, and S. Schuchmann†*
**University of Helsinki, Finland and †Neurowissenschaftliches Forschungszentrum, Charité, Berlin, Germany*

Purpose: Febrile seizures (FS) in humans appear characteristically between the ages of 6 months and 5 years, but the pathophysiological mechanism for this specific time window is unclear. Interestingly, experimental FS as studied in rats and mice can be readily induced at a stage of cortical development that is much more immature than in the human case. These facts point to a noncortical mechanism that is critically involved in the generation of FS. We have previously shown that experimental FS are triggered by a respiratory alkalosis (Schuchmann et al., Nat. Med. 2006, 12: 817–823). Therefore, the maturation of respiratory mechanisms that influence cortical pH regulation may set the developmental time window for the occurrence of FS in rodents and also in children. We studied this question by examining the age-dependence of hyperthermia-induced cortical pH changes in rat and mouse pups.

Method: Experimental FS were induced by raising the body temperature of rat and mice pups (postnatal days 6–18) using a hyperthermic environment. Electrographic recordings were used in freely moving animals to detect seizure onset and threshold. An H+-sensitive electrode was used for simultaneous measurements of cortical pH before and during hyperthermia-induced seizures.

Results: In both rats and mice, we found a linear correlation between age and cortical alkalosis, which showed that the younger animals were more prone to respiratory alkalosis and consequent FS.

Conclusion: Our data suggest that the maturation of mechanisms that control brain pH may be responsible for the characteristic age-dependence of febrile seizures. This study was supported by the Sigrid Jusélius Foundation, the Academy of Finland, and the European Integrated Project EPICURE/EFP6-037315.

018
EVIDENCE FOR A GENERATOR OF SPIKE-AND-WAVE DISCHARGES OF ABSENCE SEIZURES IN THE GENETIC ABSENCE RATS FROM STRASBOURG (GAERS)

I. Guillemain, O. David, C. Deransart, and A. Deapulis
INSERM, U836, Grenoble-Institute of Neurosciences, France

Purpose: Absence epilepsy is a nonconvulsive form of epilepsy characterized by episodes of unresponsiveness and by the presence of bilateral, synchronous and regular spike-and-wave discharges (SWDs) on the EEG. Recently, a new concept has emerged in the physiopathology of this epilepsy supporting that SWDs are initiated in a restricted region of the cortex. The localization of this 'cortical focus' and its functional relationships with other structures were investigated in this work.

Method: In the GAERS model, fMRI/EEG was used to explore the regions involved during spontaneous SWDs. Local field potential (LFP) recordings have enabled to determine the relationships between the different regions.

Results: Seizure-related activations were found in the somatosensory and motor cortex and in the ventrobasal thalamus, structures known to be involved in the generation of absence seizures. Several areas, as the striatum, were found deactivated, supporting the involvement of the basal ganglia in the control of these seizures. Using LFP recordings, we found that SWDs were generated earlier in the somatosensory cortex and then diffuse to the rest of the cortex and to the ventrobasal thalamus.

Time-frequency power analysis of these LFP showed a shift of frequency at the beginning of the seizures.

Conclusion: Altogether these data give new insights to the ictogenesis process of SWDs and their control. They suggest that the facial somatosensory cortex is the trigger zone of SWDs, confirm the involvement of the thalamo-cortical circuit in the generation of SWD and the role of the basal ganglia in their control.

019

ROLE OF INHIBITION-RELATED PARAMETERS IN THE GENERATION OF ICTAL ACTIVITY IN THE ENTORHINAL CORTEX

F. Wendling, L. Uva†, E. Labyt*, and M. de Curtis†*
**Inserm U642, University of Rennes, France and †Istituto Nazionale Neurologico, Milano, Italy*

Purpose: The general purpose of this work is to interpret epileptiform activity (local field potentials – LFPs -) using neurophysiologically-relevant computational models in the context of TLE. In this study, a model of the entorhinal cortex (EC) is described and used to infer information about the evolution of GABAergic inhibition-related parameters during the transition from interictal to ictal activity in an experimental model of ictogenesis.

Method: A combined computational/experimental approach was carried out. A macroscopic (neuronal population level) model of the EC was elaborated. The model accounts for the main sub-populations of neurons and interneurons present in the deep and superficial layers of the EC as well as for their synaptic interactions (glutamatergic and GABAergic). Electrophysiological data were recorded from the EC in the Guinea pig isolated brain. Seizures were induced using bicuculline (GABAa receptor antagonist).

Results and Conclusion: Quantitative comparison between simulated and actual LFPs demonstrated the capacity of the model to generate very realistic signals. A parameter sensitivity analysis and a stability analysis allowed us to identify parameter-related conditions for the emergence of epileptic activity. In particular, insights were gained about the role of GABAa,fast- and GABAb-receptor-mediated inhibition in the generation of ictal fast onset and burst activities, respectively.

References: Labyt, Frogerais, Uva, Bellanger, Wendling (2007) Modeling of entorhinal cortex and simulation of epileptic activity: insights into the role of inhibition-related parameters, IEEE TITB, 11(4):450–61.

Labyt, Uva, de Curtis, Wendling (2006) Realistic modeling of entorhinal cortex field potentials and interpretation of epileptic activity in the guinea pig isolated brain preparation. J Neurophysiol., 96(1):363–377.

020

NEURONAL-ASTROCYTE INTERACTIONS DURING INTERICTAL AND ICTAL DISCHARGES IN THE ISOLATED GUINEA PIG BRAIN PREPARATION

M. de Curtis, L. Uva*, F. Vetri†, M. Brondi‡, S. Sulis Sato†, G. Ratto†, and G. Carmignoto§*
**Fondazione Istituto Neurologico Carlo Besta. Milano, Italy; †Institute of Neuroscience CNR, Pisa, Italy; ‡NEST, Scuola Normale Superiore, Pisa, Italy and §Institute of Neuroscience CNR And Dept. Experimental Biomedical Sciences, University of Padova, Padova, Italy*

Epileptic discharges can organize in interictal patterns and seizure-like (ictal) events. Recent findings from hippocampal slices demonstrated that glutamate released from astroglia generates synchronous activities in pyramidal neurons (Fellin et al., Neuron. 2004; 43:729–43) and suggest that a dysregulation of neuron-astrocyte reciprocal signaling could contribute to epileptiform activities.

Purpose: the aim of our study was to investigate a possible role of astrocytes in generation, maintenance and cessation of epileptiform activities in a close-to-in vivo condition, i.e., the isolated guinea pig brain maintained in vitro by the arterial perfusion.

Method: epileptiform activity characterized by recurrent interictal spikes and ictal discharges was induced in the isolated guinea pig brain maintained in vitro by 3 min arterial perfusion with the GABAergic receptor antagonist bicuculline (50μM) . Field potential recordings and 2-photon imaging of Ca2+ signals from neurons and astrocytes were simultaneously performed in the medial entorhinal cortex, after bulk loading of the Ca2+ sensitive dye Oregon Green BAPTA-1 AM (20 μM).

Results: The analysis of the imaging signal showed that the calcium changes in neurons and neuropile followed with great temporal fidelity the field recordings. Such a strict correlation is not found with the calcium signal measured in astrocytes that are not significantly activated during interictal discharges. In contrast, astrocytes are massively and synchronously recruited during the initial phase of ictal-like discharges.

Conclusion: Our data suggest that astrocytes play distinct roles during the different phases of the neuronal discharges that characterize the epileptiform activity.

021

OSCILLATORY LOCAL FIELD POTENTIAL ACTIVITY IS REDUCED AT HIGH-BETA AND HIGH-GAMMA FREQUENCIES IN BASAL GANGLIA REGIONS OF AMYGDALA-KINDLED RATS

M. Gernert, J. Chiang, and S. Kücker
University of Veterinary Medicine, Hannover, Germany

Purpose: The study aimed to assess whether amygdala-kindling in rats induced alterations in local field potential (LFP) oscillations of basal ganglia regions.

Method: Adult female Wistar rats were fully kindled by daily stimulation of the right amygdala. Sham-kindled and naïve rats served as controls. LFP activities were recorded bilaterally from globus pallidus (GP) and substantia nigra pars reticulata (SNr) in freely moving rats. The recordings were obtained from chronically implanted bipolar electrodes one hour, one day, two weeks, and four weeks after a generalized kindled seizure. Artifact-free sweeps of 1 sec each were analyzed by the Fast Fourier transform in different bands over a broad frequency range.

Results: Preliminary data revealed that synchronization in high frequency bands is suppressed in kindled rats. One day after a kindled seizure, oscillatory LFP activities were significantly reduced at high-beta (20.5–35 Hz) and at high-gamma (60–90 Hz) frequencies in the right SNr in kindled rats versus naïve controls ($p<0.05$; unpaired t-test). Four weeks after a kindled seizure, oscillatory LFP activities were significantly reduced in the left GP at high-gamma frequency (60–90 Hz) in kindled rats versus naïve controls ($p<0.05$).

Conclusion: The data support previous single-unit recordings showing kindling-induced changes in the right SNr one day after a kindled seizure. The basal ganglia motor and limbic loops are thought to be separated anatomically and functionally processed by independent oscillatory frequencies. The data indicate that the motor loops rather than the limbic loops experienced seizure/kindling-induced modulations over time.

Supported by a Fulbright Grant to JC.

022

THE DIURETIC NKCC1 ANTAGONIST BUMETANIDE BLOCKS ONGOING SEIZURES BUT DOES NOT PREVENT THE FORMATION OF AN EPILEPTOGENIC MIRROR FOCUS

I. Khalilov, R. Nardou, and Y. Ben-Ari
Inserm U901-Inmed, Marseille, France

Purpose: In immature neurons, the Na+-K+-2Cl- co-transporter (NKCC1) facilitates the accumulation of Cl- and depolarizing actions of GABA. The NKCC1 diuretic compound bumetanide attenuates acute seizures in neonatal animals but it is not known whether it also operates on secondary epileptogenesis.

Method: We used a triple in vitro chamber that accommodates the two immature intact hippocampi and their connecting commissures in 3 independent compartments (Khalilov et al., 2003. Nature Neurosci., 6, 1079–1085.). Kainate was applied to one hippocampus generating seizures that propagate to the naïve contralateral side. After a determined number of seizures, the connecting axons were severed and the generation of ongoing seizures by the naive side examined. Using single NMDA and GABA (A) channel recordings the resting membrane potential (V rest) and driving force of GABA (DF GABA) were determined.

Results: We report that bumetanide reduced the excitatory actions of GABA and blocked seizures in the epileptic mirror focus. However, continuous application of bumetanide to naïve neurons did not prevent the formation by propagated seizures of an epileptogenic mirror focus. Bumetanide significantly reduced depolarizing DFGABA without affecting resting membrane potential. However, in presence of bumetanide, [Cl –]i remained higher in epileptic than control neurons. Results suggest that seizures augment [Cl -]I partly by a NKCC1 independent mechanism.

Conclusion: Bumetanide is an efficient anticonvulsive agent but not an antiepileptogenic one.

Monday 22 September 2008
11:30 – 13:00
Hall 7
Platform Session
Basic Science – New players and biological markers for epileptogenesis

023
INFLAMMATION, ANGIOGENESIS AND BLOOD–BRAIN BARRIER DAMAGE IN EPILEPTOGENESIS

T. Ravizza, B. Gagliardi*, J. Marcon*, F. Noé*, M. Lerner-Natoli†, and A. Vezzani**
**Mario Negri Inst For Pharm Res, Milano, Italy and †Insitut De La Santé Et De La Recherche Medicale U661, F34094 Montpellier, France*

Purpose: Brain inflammation, angiogenesis and increased blood–brain barrier (BBB) permeability occur in adult rodent and human epileptogenic brain tissue. No information is available if inflammation is responsible for neovascularization and BBB damage; moreover, the contribution of these factors to epileptogenesis is largely unexplored. This study addresses the role of inflammation and putatively-related events in epileptogenesis using a developmental approach since the propensity to develop spontaneous seizures, therefore the induction of epileptogenesis, is age-dependent and increases with brain maturation.

Method: Immunohistochemical analysis of inflammation, angiogenesis and BBB permeability was done in postnatal day (PN)9 and PN21 rats, 4 h, 1 week and 4 months after induction of status epilepticus (SE). Angiogenesis (laminin immunostaining and intraluminal FITC-albumin) and BBB permeability (parenchymal extravasation of albumin and IgG) were spatiotemporally correlated with the extent of inflammation (IL-1 induction and glia activation) in forebrain.

Results: SE in PN9 rats did not induce inflammation, angiogenesis or changes in BBB permeability nor spontaneous seizures in adulthood. SE in PN21 induced inflammation, angiogenesis and changes in BBB permeability in the hippocampus during epileptogenesis, but only in a fraction of rats. Epilepsy was induced in ~80% of adult rats exposed to SE at PN21; these rats showed the three phenomena concomitantly while rats without spontaneous seizures did not. Inflammation preceded the onset of angiogenesis and BBB damage.

Conclusion: There is a close spatiotemporal relationship between inflammation, angiogenesis and BBB damage; these phenomena occur in the rat hippocampus only when epileptogenesis is induced and spontaneous seizures eventually occur. Source of support: DANA Foundation, Negri-Weizmann Programme.

024
ACCUMULATION OF SERUM IGGS IN NEURONS OF EPILEPTIC FOCUS: WHICH IMPACT ON NEURONAL FUNCTION?

A. Lebrun, M. Morin, M. Rousset, G. Alonso, and M. Lerner-Natoli
CNRS-UMR5203, Inserm-U661, UM1, UM2, IGF, Montpellier, France

Purpose: We previously described a blood-brain barrier (BBB) breakdown leading to serum-protein leakage in the hippocampus of patients with intractable temporal lobe epilepsy. An accumulation of immunoglobulin G (IgG) was obvious in parenchyma and also in neurons. We hypothesized that IgGs play a role in hyperexcitability and/or neurotoxicity in the epileptic focus. To investigate the effects of IgGs on neuronal function, we developed different models.

Method: In vivo models: (1) chronic, lesional limbic epilepsy (pilocarpine-induced SE), (2) nonlesional model of hyperexcitability (pentylenetetrazol kindling). By immunohistochemistry and electron microscopy, we checked the localization and morphology of IgG-positive neurons. In vitro, we tested the toxicity of various concentrations of IgG on cultured NG108-15 cell line.

Results: In both in vivo models, we observed IgGs accumulation in pyramidal neurons and interneurons, mainly in the CA3 hippocampal area as soon as the first seizure. These neurons appeared picnotic and eosinophilic. In the chronic phase, they lost synaptic densities and were ensheathed by astrocytes. In vitro, IgGs were taken up by NG108-15 cells and were toxic at the dose of 10µg/ml in 24h.

Conclusion: Therefore, in rat limbic epilepsy, the neuronal accumulation of IgGs following seizure-induced BBB disruption does not depend on the severity of lesions. IgG uptake seems to be deleterious for neurons, suggesting that they are implicated in neuronal dysfunction. The specific effect of IgGs on neurons, in terms of excitability, toxicity or autoimmunity needs to be thoroughly investigated to understand its participation in epileptogenesis.

025
NEUROGENESIS IN THE DENTATE GYRUS: ADAPTIVE ALTERATIONS OF SYNAPTIC DRIVE ON CELLS BORN IN EPILEPTIC AND INFLAMMATORY ENVIRONMENT

M. Kokaia
Lund University Hospital, Wallenberg Neuroscience Center, Sweden

Purpose: Neurogenesis in the dentate gyrus of the hippocampus continues even during the adulthood, and is up-regulated by various stimuli to

the brain, among others, by epileptic seizures. We have previously demonstrated that newly born dentate granule cells in the epileptic hippocampus have decreased excitatory and increased inhibitory synaptic drive, which might mitigate increased excitability in the dentate gyrus (Jakubs et al., Neuron 2006).

Method: Since inflammatory processes are closely associated, and contribute to the pathological environment in the epileptic hippocampus, we asked whether inflammation itself could modify synaptic afferent inputs to the newborn cells in the dentate gyrus. To induce inflammation without associated seizures or cell death, we injected lipopolysaccharide (LPS) into the hippocampus. The newborn cells were labeled by GFP gene-containing retroviral vector injection.

Results: LPS-induced inflammation increased excitatory drive, as measured by sEPSCs, onto both 'pre-LPS' and 'post-LPS' born granule cells, to the same extent. However, the inhibitory drive (sIPSCs) onto the post-LPS born granule cells (i.e., cells born into the inflammatory environment), increased significantly more as compared to those born before LPS treatment (i.e., born in normal environment). This difference in afferent inhibitory drive was no longer observed after blocking action potentials by TTX application.

Conclusion: This would imply that inhibitory synapses formed on the newborn granule cells in the inflammatory environment increase release of GABA in response to action potentials. Our data show for the first time that inflammation alters synaptic excitability of the dentate gyrus, and that new cells born in this environment could modulate their afferent inhibitory synapses to functionally normalize the dentate circuitry.

026

DEFICIENT PROPENSITY OF ADULT HUMAN HIPPOCAMPAL STEM/PRECURSOR CELLS TO BUILD NEURONS CORRELATES STRONGLY WITH MEMORY DYSFUNCTION IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

F. Siebzehnrubl,†, E. Pauli*, R. Coras*, D. Weigel*, M. Buchfelder*, H. Stefan*, and I. Blumcke**
**Univ Erlangen, Germany and †McKnight Brain Institute, Univ Florida, Gainesville, FL, USA*

Purpose: The hippocampal formation is essentially involved in the formation of conscious memories for facts and events and neurological diseases affecting the hippocampus associate with severe memory deficits, i.e. temporal lobe epilepsies. In animal models, the neurobiological substrate to encode memory has been shown to associate with the generation of new neurons in the dentate gyrus (neurogenesis).

Method: Here, we analyzed the differentiation potential of hippocampal precursor cells derived from human epilepsy specimens and found that their ability for neuronal differentiation strikingly correlates with the patients' memory function. Compared to spontaneous neuronal differentiation in 3% of cells, inhibition of histone deacetylation increased this number to 60–71%.

Results: The propensity of hippocampal precursor cells to generate neurons was significantly associated with the patients' learning capacity tested prior to neurosurgical resection by intracerebral amobarbital injection (WADA). No other feature of the respective clinical history could be identified to contribute to hippocampal neurogenesis, i.e. seizure onset and duration or antiepileptic medication. Microscopic examination of the resected hippocampus revealed significant granule cell loss in the internal limb of the dentate gyrus in those patients with compromised learning and memory formation.

Conclusion: Our data experimentally confirm the impact of hippocampal neurogenesis for learning in humans, as previous experiments have successfully proven in animals.

027

AN EARLY MRI BIOMARKER FOR THE EVOLUTION OF HIPPOCAMPAL INJURY FOLLOWING LITHIUM PILOCARPINE-INDUCED CONVULSIVE STATUS EPILEPTICUS

M. Choy, M. Lythgoe*, K. Chueng†, D. Thomas†, D. Gadian*, and R. Scott**
**UCL-Institute of Child Health, London, UK and †UCL, London, UK*

Purpose: Convulsive status epilepticus (CSE) in humans can cause hippocampal injury that may continue to evolve over a period of apparent quiescence to mesial temporal sclerosis associated with epilepsy and cognitive impairment. Identifying a biomarker of hippocampal atrophy will allow early testing of therapeutic strategies. This study investigates whether multiparametric MRI can be used to identify such a biomarker.

Method: Pilocarpine (n=9) or saline (n=7) was administered to adult Sprague-Dawley rats. Quantitative MRI measurements of T1, T2, diffusion and CBF were performed before injection and post-CSE on days 0, 1, 2, 3, 7, 14, 21. Hippocampal volumes were also measured. Statistical analyses were performed using repeated measures ANOVA, principal component analysis (PCA), and regression analysis.

Results: Significant time-dependent differences were observed for hippocampal T1, T2 and CBF and peaked 2 days post-CSE ($p<0.001$). Diffusion decreases were also observed. PCA on the peak changes on day 2 identified a component weighted towards T1, T2 and CBF. Regression analysis of this component with volumes on day 21 indicated a strong relationship between the day 2 changes and volumes on day 21 ($R2=0.899$, $F=44.5$, $p=0.001$).

Conclusion: These data demonstrate that noninvasive multiparametric MRI at 2 days post-CSE can predict the evolution of hippocampal injury on day 21 in the lithium-pilocarpine model. In humans, T2 increases during the early period have been reported post-CSE1. Further studies are required to determine whether early MRI can be used as a biomarker in patients.

Reference:

1. Scott RC et al. (2002) Brain 125:1951–1959.

028

QUANTITATIVE T2 MAPPING AS A POTENTIAL MARKER FOR SEVERITY OF POSTTRAUMATIC DAMAGE AFTER FLUID PERCUSSION BRAIN INJURY IN RATS

I. Kharatishvili, A. Sierra, R. Immonen, O. Grohn, and A. Pitkanen
A.I. Virtanen Institute For Molecular Sciences, University of Kuopio, Finland

Purpose: Occurrence of posttraumatic epilepsy (PTE) positively correlates with severity of traumatic brain injury (TBI). This project aimed to identify reliable markers for severity of posttraumatic tissue damage at an early, seizure free stage in a clinically relevant model of closed head injury, which results in PTE in severe cases.

Method: Lateral fluid-percussion injury was used as a model of TBI. Adult male Sprague-Dawley rats (n=48, 12 controls) were divided into moderate (mTBI) and severe (sTBI) groups according to impact strength. MRI data were acquired 3 days postinjury. Motor deficits were analyzed using neuroscore and beam balance (BB) tests 2 and 3 days postinjury, respectively. Spatial learning and memory was tested in Morris water maze (MWM) 10 days postinjury.

Results: T2 values in the lesion area were higher in injured animals compared to controls ($p<0.01$), and in sTBI compared to mTBI ($p<0.01$). T2 values in the hippocampus ipsilateral to injury were increased in TBI animals compared to controls ($p<0.01$). Latency in MWM correlated positively with the increased T2 values of the lesion ($p<0.001$) and the hippocampus ($p<0.05$). Neuroscore and BB test results showed negative correlations with T2 values of the lesion ($p<0.001$). Also, neuroscore correlated negatively with T2 values of the hippocampus ipsilateral to injury.

Conclusion: Quantitative T2 measurement of the lesion and hippocampus early after TBI can serve as an indicator of the severity of posttraumatic tissue damage and functional impairment and thus, has a potential as a clinical marker for identification of individuals with elevated risk of PTE.

Monday 22 September 2008
11:30 – 13:00
Hall 9
Platform Session
Clinical Neurophysiology

029
AN AUTOMATED SEIZURE DETECTION ALGORITHM FOR LONG-TERM ECoG RECORDINGS: AN EFFICIENT AND FAST SCREENING TOOL FOR PRESURGICAL EVALUATION

R. Hopfengärtner, B. Kasper, F. Kerling, D. Weigel, M. Buchfelder, and H. Stefan
University Hospital Erlangen, Erlangen, Germany

Purpose: To present an efficient algorithm for the offline-detection of epileptic seizures in intracranial EEG recordings providing a high sensitivity and a low rate of false detections without requiring any prior information about the seizure type.

Method: For the detection of rhythmic activity during seizure evolution we have developed an algorithm based on short time Fourier transform (STFT). The integrated and averaged power was computed in different frequency bands (3–12 Hz, 12–18 Hz) for special multi-channel detection montages. All ECoG data (1578 hours) recorded from chronically implanted strip, grid and depth electrodes were analyzed using the same fixed parameters. A total of 15 patients suffering from pharmacoresistant epilepsy displaying 124 seizures of various types were investigated. The seizure detection performance measures sensitivity and number of false-positive events/hour (FPH) were determined.

Results: For the frequency band 3–12 Hz the sensitivity was 85,2% and FPH was 0,12/h. The combination of both frequency bands yielded a higher sensitivity of 90,8% while FPH was 0,4/h.

Conclusion: Using the described fixed parameters the proposed method provides for all patients a high sensitivity while the number of false-positive events is quite low. In addition, the algorithm provides an easy user tuneability of parameters for the detection of patient specific seizures including subclinical events. The algorithm might be capable to make a substantial contribution to the diagnostic gain of long-term ECoG monitoring during presurgical assessment.

030
SOURCE LOCALIZATION OF SCALP-EEG INTERICTAL SPIKES IN POSTERIOR CORTEX EPILEPSIES INVESTIGATED BY HR-EEG AND SEEG.

M. Gavaret,†,‡, A. Trébuchon*,†,‡, F. Bartolomei*,†,‡, P. Marquis*,†, A. McGonigal*,†,‡, F. Wendling§,¶, J. Régis*,†,**, J. Badier*,†, and P. Chauvel*,†,‡*
**INSERM UMR 751, Laboratoire De Neurophysiologie Et Neuropsychologie, France; †Aix Marseille Université, Faculté De Médecine, Marseille, F-13000, France; ‡Assistance Publique Hôpitaux De Marseille, Hôpital De La Timone, Service De Neurophysiologie Clinique, Marseille, F-13000, France; §INSERM, U642, Rennes, F-35000, France; ¶Université De Rennes 1, LTSI, Rennes, F-35000, France; and **Assistance Publique Hôpitaux De Marseille, Hôpital De La Timone, Service De Neurochirurgie Fonctionnelle, Marseille, F-13000, France*

Purpose: To determine the validity of scalp-EEG interictal spike (IIS) source localization in posterior cortex epilepsies (PCE).

Method: 11 patients with drug-resistant PCE were studied with high-resolution EEG (HR-EEG) and SEEG. 64 scalp channels, a realistic head model, and different algorithms (MUSIC and equivalent current dipoles) were used. Results were compared to intracerebral (stereoelectroencephalography (SEEG)) recordings. For SEEG, a semiautomatic detection of intracerebral IIS was used, allowing a classification of intracerebral IIS into one of three groups: Medial, Lateral and Medio-Lateral.

Results: In the Medial group (2 patients), scalp-EEG IIS were usually absent for one patient whereas for the other, scalp-EEG IIS were subcontinuous, predominantly contralateral to the source and accurately localized by HR-EEG. In the Lateral group (2 patients), scalp-EEG IIS were sub-continuous and accurately localized. In the Medio-Lateral group (7 patients), intracerebral interictal distribution was complex and bilateral for 4/7 patients. Source localizations were able to determine only a part, whether lateral or medial, of the intracerebral interictal distribution.

Conclusion: The accuracy of scalp-EEG IIS source localization is dependant on the type of intracerebral interictal distribution. In the most frequent type of PCE, patients proved to have a complex interictal distribution between both medial and lateral cortices and source localizations always underestimated intracerebral IIS. In cases where interictal sources were quite focal, interictal sources were localized with accuracy, even in medial occipital lobe structures.

031
PHOTOSENSITIVITY IN FAMILIES WITH EPILEPTIC PHOTOSENSITIVE PATIENTS

D. Stankovic Jankovic, B. Jocic-Jakubi, M. Jovanovic, and M. Mitic
Medical School Of Nis, Serbia

Purpose: Photosensitivity or photoparoxysmal response (PPR) is a common and highly heritable electroencephalographic trait characterized by an abnormal visual sensitivity of the brain during intermittent photic stimulation (IPS). We investigate the presence of photoparoxysmal response (PPR) in families with photosensitive probands with epilepsy.

Method: Examination of the EEG records in 16 patients aged 8–20 years, who were diagnosed having epilepsy (14 IGE and 2 with focal epilepsy), with PPR and 37 members of their families (both parents and siblings). We looked at response during IPS in both parents and siblings of probands with epilepsy and tried to answer how much PPR is important for having seizures in siblings.

Results: In 62,5% of examined family members we found PPR (43,5% siblings, 19% parents). A half (50%) of siblings is photosensitive, and

majority of them have seizures (57%). All siblings with seizure have shown generalized PPR (Type 3 or 4 Waltz). Thirteen percent (13%) of parents have PPR, 8,6% of them have seizures. Photomyoclonic response was found in 5 parents (21%), and in only 2 siblings. No one parent and only one sibling had photoconvulsive response during PPR.

Conclusion: Most members of family with epileptic photosensitive patients are photosensitive, mainly siblings. A half of photosensitive siblings have seizures, and PPR in them is very important for high risk for having seizures. These results can be explained with age-dependent penetrance of PPR.

032
PROGNOSTICATION OF AWAKENING AFTER POST-ANOXIC STATUS EPILEPTICUS

A. Rossetti, L. Liaudet*, M. Oddo*, and P. Kaplan†*
**CHUV, Lausanne, Switzerland and †Johns Hopkins Bayview Medical Center, Baltimore, MD, USA*

Purpose: Cardiopulmonary arrest (CPA) survivors may develop postanoxic status epilepticus (PSE), often considered an accurate predictor of poor outcome and therefore not treated. However, some exceptions have been sporadically reported. Our aim is to describe characteristics of patients awakening after PSE, in order to define a subgroup that may deserve specific treatment.

Method: Case series of subjects who exhibited consciousness improvement beyond vegetative state. Patients were identified from an ambispective survey at the CHUV, Lausanne, since 1999; one additional patient was recently observed at Johns Hopkins Bayview Medical Center, Baltimore. Clinical and electrophysiological parameters were analyzed. Follow-up was assessed at 3–5 months.

Results: We found 6 patients: 4 men, aged 42–68 years; resuscitation lasted 20–45 minutes; all underwent transitory therapeutic hypothermia. PSE was noted clinically after 1–2 days in 4 patients, and on EEG only after 3–4 days in 2. All had preserved brainstem reflexes and cortical somatosensory evoked potentials (SSEPs; recorded in 4). The first EEG showed preserved background activity reactive to stimuli in all subjects. Treatment consisted of various AEDs including benzodiazepines, and additional propofol in 4 patients. One subject died of pneumonia in minimal conscious state after 17 days; at follow-up, 3 had severe and 2 minimal to moderate cognitive impairment.

Conclusion: Patients with PSE but preserved brainstem reflexes, cortical SSEPs, and reactive EEG background activity may awaken and have a favorable outcome if their condition is treated as status epilepticus. In the prospective CHUV cohort, 2/2 patients with this profile awoke out of 27 with PSE.

033
A COMPARATIVE STUDY OF MYOCLONUS IN SIALIDOSIS AND UNVERRICHT-LUNDBORG DISEASE

L. Canafoglia, S. Franceschetti*, G. Uziel*, R. Guerrini†, E. Visani*, and F. Panzica**
**IRCCS Foundation Carlo Besta Neurological Institute, Milan, Italy and †Meyer Foundation Child Hospital, Florence, Italy*

Purpose: Action myoclonus is the main symptom in adult patients with sialidosis and in patients with Unverricht-Lundborg disease (ULD). It frequently takes a quasi-rhythmic course during posture maintenance. In most patients central fast EEG rhythms are associated with rhythmic jerks. Our study was aimed at detecting the distinctive features of myoclonus recorded in three sialidosis and seven ULD patients.

Method: In each patient, we evaluated the EEG-EMG coherence by means of autoregressive models. Moreover, in each patient we evaluated somatosensory evoked potentials (SSEPs) and long loop reflexes (LLRs).

Results: Myoclonus was more severe in sialidosis patients, while it resulted in a variable motor impairment in ULD patients. All patients had rhythmic myoclonus. In all patients, the coherence spectra showed a main peak in beta band. In sialidosis patients, the relative power of the main coherence peak was significantly higher (45.8±2.5 vs. 34.3±5.4; $p<0.05$) and the band width was significantly narrower (3.3±0.4 vs. 4.5±0.6; $p<0.01$) with respect to those measured in ULD patients. The SSEP amplitude was not significantly different in the two groups, while LLRs had a peculiar shape including well distinct multiple components in sialidosis patients, probably reflecting the especially rhythmic recurrence of the jerks.

Conclusion: We propose that consistently rhythmic myoclonus is a peculiar feature in sialidosis patients and that the rhythmic repetition is responsible for an especially severe motor impairment.

034
WORKING MEMORY PROCESSES IN THE MEDIAL TEMPORAL LOBE

N. Axmacher,†, M. Henseler*,‡, D. Schmitz*,‡, M. Cohen*,†,§, C. Elger*,†, and J. Fell**
**University of Bonn, Bonn, Germany; †Life And Brain Center of Academic Research Bonn, Germany; ‡University of Applied Sciences Remagen, Remagen, Germany and §University of California, Davis, CA, USA*

Purpose: In contrast to classical findings that the medial temporal lobe (MTL) specifically underlies long-term memory, recent data suggest that MTL structures may also contribute to working memory (WM). However, the neural mechanisms by which the MTL supports WM have remained unknown.

Method: We investigated this issue using a serial Sternberg paradigm and a word list learning task both in human epilepsy patients with intracranial EEG (iEEG) electrodes and in healthy subjects using functional MRI (fMRI). Both univariate (DC potentials and cross-frequency coupling in iEEG; BOLD activity in fMRI) and bivariate measures (phase synchronization in iEEG; functional connectivity in fMRI) were calculated.

Results: The iEEG data showed significant negative DC shifts with increasing load (Sternberg task) and for later list positions (word list learning task), reminiscent of an enhancement of sustained activity. BOLD responses were specifically increased in the hippocampus during encoding and maintenance of an increasing number of items. Next, we calculated functional connectivity between category-specific regions in the inferior temporal cortex and MTL regions. We found that phase-synchronization between the IT cortex and the rhinal cortex, and between the rhinal cortex and the hippocampus, increased with WM load, indicative of an enhanced recruitment of medial temporal networks during multi-item WM. The extension of the networks defined by functional connectivity in fMRI decreased with WM load. Finally, we investigated the mechanism of multiitem WM by calculating cross-frequency coupling in the MTL. We found that modulation occurred during a more extended phase range for higher memory load and predicted individual performance.

Conclusion: Taken together, these data indicate that specific neural activity patterns within the human MTL support WM processes.

Tuesday 23 September 2008
11:30 – 13:00
Hall 2b
Platform Session
Pediatrics – Treatment

035

ORAL PREDNISOLONE PULSE THERAPY: A WELL-TOLERATED AND EFFECTIVE TREATMENT REGIME FOR CHILDREN WITH DRUG-RESISTANT EPILEPSIES

M. Wolff, S. Ruf, and I. Kraegeloh-Mann
Children's University Hospital, Tuebingen; Germany

Purpose: For many years ACTH and steroids have been used in the treatment of drug- resistant childhood epilepsies, especially in children with West syndrome. However, severe side effects have been reported using ACTH or continuous treatment with steroids, and frequent hospitalizations are necessary. We propose an alternative treatment scheme using oral high-dose prednisolone pulses in outpatients.

Method: 25 patients with drug-resistant epilepsies aged 2 months to 16 years were selected: West syndrome N=13, Continuous spike and waves during slow sleep (CSWS) N=6 (Landau-Kleffner syndrome N=2, atypical benign focal epilepsy N=4), lesional focal epilepsy with secondary bilateral synchrony N=4, and childhood absence epilepsy N=2. Treatment consisted of 25mg/kg/d oral prednisolone for three days once a week for four weeks followed by a variable tapering phase. Epilepsy, EEG data and adverse effects were documented after four weeks and at the end of the therapy.

Results: From the 13 children with West syndrome, seven became seizure free, and hypsarrhythmia disappeared in six. In two children with CSWS, EEG and cognitive deficits improved markedly. Two children with lesional focal epilepsy became seizure free, and EEG normalized. The two children with absence epilepsy improved markedly after four weeks and became seizure free during follow up. Serious adverse effects did not occur. Serum cortisol levels remained normal between the pulses.

Conclusion: Oral prednisolone pulse therapy was effective in about 50% of these children. Severe adverse effects did not occur. Judging efficacy and adverse effects, a broader use of this treatment regime in drug-resistant childhood epilepsies is suggested.

036

ADJUNCTIVE LEVETIRACETAM IN CHILDREN AGED 1 MONTH TO <4 YEARS WITH REFRACTORY PARTIAL-ONSET SEIZURES: A RANDOMIZED CONTROLLED TRIAL

J. Pina-Garza, D. Rating†, D. Nordli‡, H. Yang§, J. Schiemann-Delgado§, B. Duncan§, C. Romano§, and M. Rasmussen§*
**Children's Hospital At Vanderbilt, Nashville, TN, USA; †Epilepsy Centre Children's Hospital, University of Heidelberg, Heidelberg, Germany; ‡Children's Memorial Hospital, Feinberg School Of Medicine, Northwestern University, Chicago, IL, USA, and §Clinical Development, UCB Inc, Atlanta, GA, USA*

Purpose: To evaluate the efficacy and tolerability of adjunctive levetiracetam in infants and young children (1m to <4y) with refractory partial-onset seizures.

Method: This multicenter, double-blind, randomized, placebo-controlled, inpatient study comprised baseline video-EEG (48h) and evaluation (5d; 1d up-titration; 48h evaluation video-EEG in last 2d). Children with >=2 partial-onset seizures during 48h baseline video-EEG were randomized to levetiracetam oral solution (40 mg/kg/d [age 1-<6m], 50 mg/kg/d [age >=6m-<4y]) or placebo.

Results: 175 patients were screened; 116 randomized (60 levetiracetam; 56 placebo; intent-to-treat [ITT] population); 111 completed study. Responder rate for average daily partial-onset seizure frequency (48h video-EEG; primary variable) was 43.1% for levetiracetam (modified ITT [mITT] =58) vs. 19.6% for placebo (mITT=51; OR 3.1 [95%CI, 1.2–8.3; p=0.013]). Responder rates (levetiracetam vs. placebo) were consistent across all age groups: 54.5% vs. 20.0% for 1m-<12m (n=21; OR 4.8 [95%CI, 0.5–62.3]); 47.4% vs. 25.0% for 12m-<24m (n=35; OR 2.7 [95%CI, 0.5–15.4]); 35.7% vs. 16.0% for 24m-<48m (n=53; OR 2.9 [95%CI, 0.7–14.7]). Median reduction from baseline in average daily partial-onset seizure frequency was 43.6% levetiracetam vs. 7.1% placebo (median difference 39.2% [95% CI, 17.5–62.2; p<0.001]). 15.5% levetiracetam vs. 5.9% placebo patients experienced 100% reduction in partial-onset seizures. Adverse events were reported by 55.0% levetiracetam and 44.6% placebo-treated patients (ITT). Somnolence (13.3% levetiracetam, 1.8% placebo) and irritability (11.7% levetiracetam, 0% placebo) were the most frequently reported adverse events.

Conclusion: Adjunctive levetiracetam is efficacious and well-tolerated in very young children with refractory partial-onset seizures. Efficacy was similar across all age groups.

Study sponsored by UCB.

037

METHYLPHENIDATE TREATMENT OF ADHD IN YOUNG PEOPLE WITH LEARNING DISABILITY AND SEVERE EPILEPSY: A QUALITATIVE STUDY

S. Aylett,†,‡, T. Fosi*,‡, T. Lax-Pericall*,§, R. Scott*,†,‡, and B. Neville*,†,‡*
**National Centre For Young People With Epilepsy (NCYPE), Surrey, UK;†Great Ormond Street Hospital For Children NHS Trust, London, UK; ‡Neurosciences Unit, The Institute of Child Health (UCL), London, UK, and §South London And Maudsley NHS Mental Health Trust, London, UK*

Purpose: To review treatment response to methylphenidate (MPH) in young people with complex epilepsy and attention-deficit hyperactivity disorder (ADHD).

Method: A retrospective case-note review was conducted at a specialist residential center for young epilepsy patients. Mean monthly seizure counts were recorded pretreatment, at 1, 3 and 6 months after starting MPH. Treatment response to MPH was assessed independently by four clinicians using Clinical Global Impressions (CGI) scores. Eighteen patients (6–18 years, 13 male) with epilepsy and learning disability had DSM-IV ADHD diagnosed between 1998–2005. Epilepsy was refractory in 17/18, with median onset at 2.3 years. The median age at diagnosis of ADHD (combined-type in all) was 11.5 years. The median treatment duration and maximum dose of MPH were 12 months and 0.5mg/kg/day (range 0.2 –1.2 mg/kg/day).

Results: CGI ratings agreed closely (type A correlation 0.85). 11/18 patients had clear clinical response, 5/18 no clinical response, and 2/18 were equivocal on CGI. Males were more likely than females to be responders (p=0.049). Responders compared to nonresponders commenced MPH younger, had received a lower cumulative number of AEDs before starting MPH treatment, and were less likely to have severe learning disability (all p<0.0001). Responders were less likely to have MPH discontinued for adverse effects (p= 0.02). One patient had significant increase in monthly seizures, defined as > 25% rise.

Conclusion: ADHD appears to be diagnosed late in children with severe epilepsy and learning disability. A clinical response to methylphenidate is obtainable in almost two-thirds of this patient population without a clinically significant increase in seizure frequency.

038
KETOGENIC DIET IN THE TREATMENT OF ENCEPHALOPATHY WITH CONTINUOUS SPIKE AND WAVES DURING SLOW-SLEEP (CSWS): A PILOT STUDY

M. Miranda, M. Atkins, T. Hoffmann, L. Sahlholdt, H. Nielsen, M. Mortensen, and M. Nikanorova
Danish Epilepsy Centre, Denmark

Purpose: To evaluate the effect of the ketogenic diet (KD) on electroclinical features and cognitive functions in children with encephalopathy with CSWS.

Method: 4 children (3 boys, 1 girl) aged 6–9 years with encephalopathy with CSWS were included. In all cases CSWS was refractory to the conventional antiepileptic drugs (AEDs), levetiracetam and steroids. KD was initiated after our standard protocol (ratio 2.5–4:1). Clinical assessment and 24-hour EEG monitoring have been performed once per 3–6 months, neuropsychological testing – once per 6 month. Ketogenic diet was administered as add-on therapy to AED treatment. The follow-up comprised 14–30 months (mean 24 months).

Results: At the end of the follow-up period no significant improvement of the EEG-characteristics was observed. The spike-wave index during non-REM sleep was unchanged in 3 children and decreased from 95 to 57 % in 1 case. In the same child the appearance of physiological sleep patterns after ketogenic diet treatment was demonstrated. Verbal IQ, performance IQ and full scale WISCIII have been unchanged in 2 patients and progressively decreased in the other 2 patients. The diet had also no positive influence on inattention, hyperactivity and other behavioral disturbances.

Conclusion: Ketogenic diet does not seem to be effective in the treatment of encephalopathy with CSWS. However, further studies with more included patients are needed.

039
UNDERSTANDING HOW DOCTORS AND PATIENTS MAKE ANTIEPILEPTIC DRUG TREATMENT DECISIONS: A QUALITATIVE EXAMINATION

D. McCorry, T. Marson, and A. Jacoby
Liverpool University, UK

Purpose: While there is increasing interest in understanding how doctors and patients make treatment decisions, little previous research has focused on understanding antiepileptic drug (AED) decision making. We undertook a qualitative approach and examined AED decision making from two perspectives.

Method: (1) Semistructured in-depth telephone interviews with 47 patients were conducted shortly after their hospital consultation with an epilepsy specialist. The interviews were recorded and transcribed. Grounded theory, assisted by Nvivo, was used to analyze the data. (2) Sixty consultations between doctor and patient with epilepsy in a hospital outpatient setting were recorded and transcribed. Seven informative case studies were highlighted in detail and interpreted using discourse analysis. Many subjects had both their hospital consultation recorded and an in-depth telephone interview soon after. The findings provided a means of 'data triangulation' to examine and describe decision making from the two methodological perspectives.

Results and Conclusion: (1) Seven major themes immerged from the interviews. Interviewees did not consider specific treatment options prior to their appointment; they used language to imply the doctor made the decision and frequently referred to the role of the doctor as being the decision maker. A deferent-compliant model of decision making dominated. (2) The consultations were highly focused on the treatment decision. The doctor chose the treatment option he considered to be in the best interest of the patient. A model of how decisions were made was devised. The authors interpret the process of decision making as 'paternalistic'.

040
HOW SHOULD WE MANAGE REFRACTORY STATUS EPILEPTICUS FOLLOWED BY DEVASTATING EPILEPSY IN SCHOOL-AGED CHILDREN? OR, IS THE ANSWER REALLY ANOTHER QUESTION: 'WHO SHOULD MANAGE RSE-DESC?'

S. Auvin,†, O. Gozé-Martineau*, M. Lamblin*, J. Cuisset*, J. Cuvellier*, F. Leclerc*, and L. Vallée*,†*
**CHRU De Lille, Lille, France, and †EA1046, Lille School of Medicine, Lille, France*

Purpose: Recent reports accumulate on Refractory Status Epilepticus followed by Devastating Epilepsy in School-aged Children. Under different names, the same condition was described. The data are consistent about the pejorative outcome regarding both epilepsy and cognition.

Method: We report clinical, electroencephalographic, neuroimaging data of five patients. We included all patients with refractory status epilepticus admitted in Pediatric Intensive Care Unit (Lille University hospital) for anesthetic management of SE. We excluded the patient with a condition explaining refractory status epilepticus. We analyze our data comparing to the previous reports. The aims of our study were to identify early characteristics of this clinical presentation and possible pathophysiological mechanisms.

Results: All patients started refractory status epilepticus after a febrile illness. None of them had a previous medical history. The initial seizure was partial in both symptoms and EEG recordings. Biological investigations suggest a prior viral infection in all of them. Viral encephalitis and metabolic disease were rule out. One patient died. All the others have a pharmacoresistant epilepsy and severe cognitive impairement.

Conclusion: As previously reported, the evolution after the initial status epilepticus is pejorative. Our data suggest that a prior viral infection may play a role in the start and/or the refractoriness of the initial status epilepticus. We suggest special interaction with intensive care pediatricians for an early recognition and management. Accumulating data in the acute phase may be a clue to improve our understanding and the outcome.

Tuesday 23 September 2008
11:30 – 13:00
Hall 5
Platform Session
Basic Science – Epileptogenic changes in excitable mechanisms

041
SEROTONIN HYPERINNERVATION ABOLISHES SEIZURE SUSCEPTIBILITY IN OTX2 CONDITIONAL MUTANT MICE

Y. Bozzi, P. Tripathi*, L. Di Giovannantonio†, W. Wurst‡, and A. Simeone†*
**CNR Neuroscience Institute, Pisa, Italy; †CEINGE Biotecnologie Avanzate, Naples, Italy and ‡GSF-Research Center, Munich, Germany*

Purpose: The homeobox-containing transcription factor Otx2 controls fate determination of midbrain neurons. Mutant mice, in which Otx2 was conditionally inactivated by a Cre recombinase expressed under the transcriptional control of the Engrailed1 (En1) gene (En1cre/+; Otx2flox/flox) show a reduced number of dopaminergic neurons and an increased number of serotonergic neurons in the ventral midbrain. Despite these developmental anatomical alterations, En1cre/+; Otx2flox/flox adult

mice display normal motor function. Here, we investigated seizure susceptibility of adult En1cre/+; Otx2flox/flox mice.

Method: Seizures were induced by systemic administration of kainic acid (KA, 20 mg/kg) in control and mutant mice (n = 5 per group). Behavioral seizure scores were determined over a period of 2–3 hours after KA, and c-fos mRNA was detected by in situ hybridization.

Results: KA determined prolonged generalized seizures in control mice, whereas En1cre/+; Otx2flox/flox mice were completely resistant to KA. Immunohistochemistry showed increased serotonin (5-HT) and decreased 5-HT transporter levels in En1cre/+; Otx2flox/flox mice, as compared to controls. 5-HT depletion by prolonged pretreatment with para-chlorophenylalanine (pCPA) fully reestablished KA-seizure susceptibility in En1cre/+; Otx2flox/flox mice. Accordingly, c-fos mRNA induction after KA challenge was restricted to the hippocampus in En1Cre/+; Otx2flox/flox mice, while a widespread c-fos mRNA labeling was observed throughout the brain of En1Cre/+; Otx2flox/flox mice pretreated with pCPA.

Conclusion: Increased serotonin in limbic areas is responsible for seizure resistance in En1cre/+; Otx2flox/flox mice, thus indicating a prominent role of 5-HT in the control of limbic seizures.

042

ROLE OF GABAA RECEPTOR-MODULATING NEUROSTEROIDS IN THE EPILEPTOGENESIS OF THE EPILEPTIC MUTANT EL MOUSE

Y. Murashima, and M. Yoshii
Tokyo Metropolitan University, Graduate School Of Human Health Science, Tokyo, Japan

Purpose: Neurosteroids such as allopregnanolone (THP) act as positive allostelic modulators of GABAA receptors and have exerted anticonvulsant properties. However, their role in the regulation of epileptogenesis is unclear. It has been shown that circulating levels of THP fluctuate during development and seizure episodes. Furthermore, both chronic administrations of THP as well as its withdrawal transiently increase expression of the alpha4 subunit of the GABAA receptor (GABAARa4) in the brain. The steroidogenic enzymes, 5alpha-reductase (5aR) and 3alpha-hydroxy steroid dehydrogenase (3aSDH) have been identified as well, indicating that various cell types are involved in the biosynthesis of neuroactive steroids in the brain. The purpose of the present study is to examine how GABAA receptor-modulating neurosteroids contribute to the epileptogenesis by using epileptic mutant EL mice.

Method: EL mice and their control animal, DDY mice were used. EL mice show secondary generalized seizures, which initiate primarily at the parietal cortex and generalize through the hippocampus. In the interictal period during development, changes of THP, 5aR, 3aSDH and GABAARa4 were investigated by Western blotting in the focus complex (parietal cortex and hippocampus).

Results: In EL mice, levels of the neurosteroid THP and the steroidogenic enzymes 5aR and 3aSDH were significantly decreased during developement. They were predominantly down-regulated before experiencing frequent seizures. In contrast, the expression of GABAAa4 was upregulated in EL mice during development.

Conclusion: In the brain of EL mice, neurosteroids are decreased before experiencing repetitive seizures, which may trigger the ictogenesis. GABAA receptors may become hypersensitive to neurosteroids in compensation.

043

EPILEPSY IN RETT SYNDROME. THE EXPERIENCE OF THE ISRAELI RETT CENTER

A. Nissenkorn, S. Menascu, and B. Ben Zeev Ghidoni
Sheba Medical Center, Tel Hashomer, Israel

Purpose: Rett syndrome, X-linked dominant neurodevelopmental disorder caused by MECP2 mutations, presents with autistic regression, loss of hand usage, hand stereotypies and microcephaly. Epilepsy is frequent, but course and treatment are controversial. Characterizing these features longitudinally in a large cohort contribute to better definitions and management.

Method: Charts, EEG's and v-EEGs retrospective review of 96 patients (18m–42y), followed at the Israeli Rett Clinic.

Results: 73% of patients have epilepsy, divided into three groups: 5 – early epileptic variant (first year of life), 41 – onset at 2–5 years (regression stage), 20 – late onset (after 5 years). Early epileptic variant had severe seizure types in first year of life, followed by typical Rett picture. All were MECP2 negative, 1/4 had CDKL5 mutation. In the second group epileptiform EEG before age 2y was followed by intractable seizures of various types. Nine developed ESES, evolved in 2 to awake NCS. Late onset group had milder epilepsy. V-EEG was crucial in excluding nonepileptic behaviors. Mutation presence, type, head circumference or speech preservation did not influence epilepsy course. Valproate, the most commonly used drug, was relatively effective, controlling seizures and ESES.

Conclusion: Epilepsy appears earlier and is more severe then previously described. ESES is relatively common and has negative clinical impact. Controlling seizures and epileptiform activity may improve alertness and communication. Use of carbamazepine is guarded in young patients due to tendency to spike wave generalization. Valproate, despite putative detrimental role in Rett pathogenesis (HDAC inhibitor), was helpful and did not aggravate symptoms.

044

SUPPRESSION OF CALCIUM SIGNALING AND NEURONAL EXCITABILITY PATHWAYS IN THE REPROGRAMMED TRANSCRIPTIONAL RESPONSE TO STATUS EPILEPTICUS AFTER EPILEPTIC PRECONDITIONING

D. Henshall, G. Mouri*, M. Johnson†, S. Hatazaki*, C. Bellver-Estelles*, J. Prehn*, R. Meller†, R. Simon†, and E. Jimenex-Mateos**
**Royal College Of Surgeons In Ireland, Dublin, Ireland and †Robert S. Dow Neurobiology Laboratories, Legacy Research, Portland, OR, USA*

Purpose: Preconditioning brain with a sub-lethal insult generates a damage-refractory state (tolerance) which may derive from genomic reprogramming of the response to injury. Brief seizures can function to precondition brain but the transcriptional response in epileptic tolerance is unknown.

Method: Presently, we used Affymetrix 430 2.0 microarrays that detect ~39,000 transcripts to compare the transcriptome of mice subject to status epilepticus alone to that of mice given seizure-preconditioning 24 h before status epilepticus.

Results: Microarray analysis of hippocampal CA3 subfields 24 h following status epilepticus detected changes of ≥2 fold to 929 gene transcripts compared to vehicle controls, of which 74% were up-regulated. Epileptic preconditioning reduced hippocampal CA3 damage caused by status epilepticus by > 50%. Preconditioned mice subject to status epilepticus showed changes to 1357 genes, with 54% up-regulated. Among differentially regulated genes, 82% were up-regulated in status epilepticus-only, contrasting 73% down-regulated in tolerance. Gene ontology analysis for differentially suppressed genes in tolerance identified calcium signaling, ion channels, neurotransmitter receptors and long term potentiation and the synaptic component as most over-represented.

Conclusion: The present study reveals epileptic tolerance is defined by selective transcriptional down-regulation which differs from ischemic

tolerance in the contributions of metabolism, synapse-associated signaling and more limited extent of genomic reprogramming.

045
BUILDUP OF HIGH-FREQUENCY ACTIVITY AND SYNCHRONY EXPANSION PRECEDES ONSET OF SEIZURES

P. Jiruska, J. Fox*, W. Chang*, X. Li*, and J. Csicsvari†*
**University of Birmingham, Birmingham, UK, and †University of Oxford, Oxford, UK*

Purpose: The mechanisms responsible for preictal changes and transition to seizures are still not fully understood. In the present work we have identified high-frequency network activity (HFA) in an in vitro model of partial epilepsy and investigated its role in the transition to electrographic seizures.

Method: The experiments were performed on isolated rat hippocampal slices perfused with artificial CSF containing low calcium (0.2 mM). Field potentials from hippocampal CA1 region were recorded using multiple extracellular electrodes. Multiple cell activity was recorded using tetrodes.

Results: In hippocampal CA1 region, periods between seizures are characterized by presence of low-amplitude HFA (185.9±2.1 Hz). This activity is generated by small clusters of pyramidal cells and the HFA is a composite of the low frequency activity of multiple, fluctuating neuronal clusters. During the preictal period, HFA increases in power (10.9 fold increase), due to increased action potential firing of pyramidal cells and the recruitment of 'silent' neurons. Multiple electrode recording showed that HFA build up occurs across the entire CA1 region. However, phase-synchronization analysis revealed that multiple independent areas of local synchrony generate HFA, which expand and coalesce immediately preceding the seizure. The process of synchrony expansion then rapidly progresses until entire CA1 behaves as one hypersynchronous area.

Conclusion: Understanding the spatial expansion of coherent HFA and its underlying mechanisms is a promising approach for improving our understanding of the mechanisms of transition to seizure and perhaps more immediately, for refining seizure prediction techniques.

Supported by Epilepsy Research Foundation UK.

046
FUNCTIONAL ANALYSIS OF NOVEL KCNQ2 GENE VARIANTS IN DUTCH PATIENTS WITH BENIGN FAMILIAL NEONATAL CONVULSIONS (BFNC).

L. Volkers, M. Rook, J. Das, W. Groenewegen, M. van Kempen, D. Lindhout, and B. Koeleman
University Medical Center Utrecht, Utrecht, The Netherlands

Purpose: Benign familial neonatal convulsions (BFNC) is a rare epilepsy disorder with autosomal dominant inheritance. Mutations in the potassium channel genes KCNQ2 and KCNQ3 are linked to BFNC. KCNQ2 and KCNQ3 subunits form tetrameric voltage-gated channels via assembly of conserved si-domains, located in the carboxy-terminus of the proteins. This study reports the biophysical and biochemical properties of p.R588X, p.T359K and p.P410fs11X mutant-KCNQ2 ion channels.

Method: Wild-type (WT) and mutant channel cDNAs were co-expressed in HEK293 cells. Transfection with KCNQ2/3 cDNAs in a 1:1 ratio mimicked WT K+ channel expression in healthy subjects. Transfection with KCNQ2/KCNQ2-mutant and KCNQ3 cDNA in a 0.5:0.5:1 ratio, mimicked K+ channel expression in patients heterozygous for the KCNQ2 mutations. The resulting potassium currents were measured using patch-clamp techniques. Immunofluorescent labeling was performed in CHO cells expressing WT or mutant KCNQ2 and KCNQ3 á-subunits.

Results: Cells expressing WT heteromeric KCNQ2/3 channels revealed large noninactivating, slowly deactivating M-type potassium currents. Cells coexpressing mutant KCNQ2 channel subunits, showed a reduction of ~75% in M-current. The voltage dependence of mutant channel activation was shifted in the depolarizing direction by 6mV. Immunofluorescence of WT KCNQ2/3 combined with membrane staining showed ion channel expression at the plasma membrane. However, mutant KCNQ2/3 ion channels showed more robust staining in the Endoplasmatic Reticulum (ER).

Conclusion: The decreased current density and depolarizing shift in activation mediated by the mutant KCNQ2 channel subunits may be caused by dominant negative trafficking defects. This may result in hyperexcitability and is likely to cause epilepsy in neonates.

Tuesday 23 September 2008
11:30 – 13:00
Hall 6
Platform Session
Neuroimaging

047
FMRI ACTIVATION DURING GENERALIZED EPILEPTIFORM DISCHARGES EVOKED BY PHOTIC STIMULATION

F. Moeller, H. Siebner*, N. Ahlgrimm*, H. Muhle*, S. Wolff*, O. Granert*, R. Boor†, O. Jansen*, U. Stephani*,†, and M. Siniatchkin**
**University Hospital Kiel, Kiel, Germany and †Northern German Epilepsy Center, Kiel-Raisdorf, Germany*

Purpose: Photosensitive individuals respond with epileptiform EEG discharges to intermittent photic stimulation (IPS). The pathogenetic mechanisms underlying this photoparoxysmal response (PPR) remain to be clarified. The present study applied the EEG-fMRI technique to map changes in regional neuronal activity that is associated with PPR.

Method: IPS was performed during simultaneous recordings of EEG (Brain Vision@, MR-compatible EEG amplifier) and fMRI (3-T Philips Achieva scanner) in 14 healthy PPR-positive individuals (mean age: 15ys) and 16 PPR-positive patients with idiopathic generalized epilepsy (IGE) (mean age: 14ys). Online correction of gradient artifacts using RecView software (Brainproducts Co.) enabled visual inspection of PPR throughout the whole recording time.

Results: 3 healthy PPR-positive individuals and 8 PPR-positive patients with IGE showed generalized PPR during IPS. 6 individuals (5 IGE) showed PPR related BOLD signal increases in the thalamus. 7 individuals (4 IGE) displayed an increase in BOLD signal in medial parietal areas. BOLD signal decreases were found in areas of the 'default network' in 6 individuals (5 IGE) and in the caudate nucleus in 4 individuals (3 IGE).

Conclusion: This is the first study showing regional changes in neuronal activity during PPR. PPR shows an involvement of the same striatothalamocortical network that is active in unprovoked generalized spike wave discharges, namely thalamic activation and a deactivation in default mode areas and the caudate nucleus. A novel finding was a consistent activation in medial parietal areas. Whether this area has a specific relevance for pathogenetic mechanisms of PPR has to be evaluated in further studies.

048

FEASIBILITY OF A NOVEL, QUANTITATIVE MAGNETIZATION TRANSFER MAPPING TECHNIQUE IN FOCAL EPILEPSY

N. Focke, F. Klinker*, M. Nitsche*, P. Dechent†, W. Paulus*, and G. Helms†*

**University Hospital Goettingen, Goettingen, Germany, and † University Hospital Goettingen, MR-Research Group, Goettingen, Germany*

Purpose: Magnetization transfer relies on the interaction of macromolecules and water. Recently, an improved (semi-) quantitative MT technique has been devised that accounts for dependencies of relaxation and sequence parameters. It yields the MT effect per repetition (delta) and the T1 relaxation time. In this feasibility study, we assess comparability between subjects and attempt to quantify pathological processes underlying hippocampal sclerosis.

Method: 3D-FLASH datasets with MT-, PD- and T1-weighting were acquired from five healthy volunteers at 3T (Siemens Trio). The SNR was increased by averaging a multi-echo acquisition in high resolution. Maps of the quantitative MT-term (delta in %) and the T1 relaxation time (in ms) were calculated and regions of interest were manually drawn in both hippocampi of all subjects. We also examined a patient with focal, pharmacoresistant epilepsy and known left-sided hippocampal sclerosis (HS).

Results: In the control group mean values (+/−SD) were MT: (left) delta=2.34+/−0.10% (left) / 2.38+/0.06% (right) and T1=2123+/−99ms / 2171+/−178ms. In the patient with HS ipsilateral (left) sided values 2171+were clearly alterated: delta=1.98% and T1=2609ms. Contralateral (right) side values were delta=2.26% and T1=2659ms.

Conclusion: In the control group there was a good between subject's homogeneity with a coefficient of variation of 3.4% for delta and 6.4% for T1. In HS the ipsilateral delta value was more than 3 SD below the control group mean, while the contralateral value was just within 2 SD. This indicates a clear lateralization. T1 values were larger in the patient than in controls but equally on both sides. However T1 values were not bias corrected and are influenced by flip angle inhomogeneities especially at high field strengths. In conclusion we could show in this pilot study the general feasibility of a (semi-)quantitative MT paradigm. Delta values are very stable between subjects and could be useful to identify pathological changes like hippocampus sclerosis.

049

IMPAIRED FUNCTIONAL CONNECTIVITY NETWORKS AND WORD FLUENCY IN PATIENTS WITH NONSYMPTOMATIC LOCALIZATION-RELATED EPILEPSY

M. Vlooswijk, J. Jansen*,†, M. Majoie*,†, P. Hofman*, M. De Krom*, W. Backes*, and A. Aldenkamp*,†*

**University Hospital Maastricht, Maastricht, The Netherlands and †Epilepsy Center Kempenhaeghe, Kempenhaeghe, The Netherlands*

Purpose: Cognitive problems frequently occur in patients with chronic epilepsy. To investigate the neuronal mechanisms underlying cognitive dysfunction, fMRI of silent word generation and functional connectivity were studied in relation with cognitive functioning and word fluency.

Method: Thirty-nine patients with nonsymptomatic localization-related epilepsy (19F, age 39±12y), and 20 healthy controls (11F, age 40±13y) underwent assessment of IQ (WAIS-III) and word fluency (SAN fluency test; naming animals in 2 minutes). Functional MRI was performed with a standard covert word generation paradigm. Connectivity analysis comprised cross-correlation of motion-corrected signal time-series of the most strongly activated regions: left middle frontal gyrus (MFG), left inferior frontal gyrus (IFG), dorsal part of anterior cingulate cortex (ACC), and posterior cingulate cortex (PCC).

Results: Patients with epilepsy displayed lower IQ values (−20, $p<0.01$) and word count in the SAN fluency test (−12, $p<0.01$). Word generation activation maps were not different for patients with epilepsy compared to controls. Patients with epilepsy had significantly lower connectivity values for all connections of the four regions ($p<0.02$). For the patients, the connections ACC-IFG ($p<0.01$), ACC-MFG ($p<0.01$) and IFG-MFG ($p=0.01$) significantly correlated with IQ. The connection ACC-IFG correlated with SAN fluency scores ($p=0.01$). For controls, the connection ACC-MFG was correlated with IQ ($p=0.05$).

Conclusion: A relation between reduced functional connectivity and word fluency performance was demonstrated in patients with nonsymptomatic localization-related epilepsy. Impaired word fluency performance in epilepsy patients could be attributable to reduced functional connectivity in the language system and provides neuronal basis for cognitive decline in chronic epilepsy.

050

WHITE MATTER CHANGES IN POSTSURGICAL TEMPORAL LOBE EPILEPSY

J. Faber,†, J. Schöne-Bake*,†, C. Elger*,†, and B. Weber*,† *University Hospital of Bonn, Bonn, Germany, and †Life & Brain Center, Bonn, Germany*

Purpose: Secondary structural damage has been reported in several studies of temporal lobe epilepsy and unilateral hippocampal sclerosis. We wanted to investigate white matter changes following temporal lobe surgery in patients with medial temporal lobe (MTL) epilepsy applying diffusion tensor imaging (DTI).

Method: We acquired DTI data from 41 patients that underwent surgery for hippocampal sclerosis (right: n=21) between 1996 and 2006 and 39 matched control subjects. DTI images were obtained using a 3T MRI scanner with 60 gradient directions (resolution: 1.7x1.7x2 mm). FMRIB Diffusion Toolkit (FMRIB, Oxford) was used for preprocessing and statistical analysis of DTI data.

Results: Both patients with left- or right-sided surgery exhibit widespread degradation of fractional anisotropy (FA) in main fibre tracts not limited to the respective temporal lobe. Main fiber-tracts as the uncinate fasciculus, the fronto-occipital fasciculus, the corpus callosum and the corticospinal tract on the respective side are also affected. FA is also decreased in the ipsilateral posterior cingulate gyrus. Patients with left-hemispheric surgery additionally show affections of the contralateral temporal lobe, mainly localized in the inferior longitudinal fasciculus.

Conclusion: MTL surgery leads to widespread degradation of fibre tracts consistent with downstream wallerian degeneration. Left-sided surgery has stronger impact on white matter tracts, which is in line with the larger and more widespread neuropsychological effects. Because of the cohort-design of the present study, the side and date of the surgery may not completely explain the results, as the underlying disease itself might also cause part of the white matter changes. Further, longitudinal studies are needed to dissect the influence of the epilepsy and the surgery.

051

DYNAMIC CAUSAL MODELING OF FMRI DATA SUGGESTS A FACILITATING ROLE OF THE PRECUNEUS ON A THALAMOCORTICAL NETWORK DURING GENERALIZED SPIKE-WAVE DISCHARGES

A. Vaudano,†, D. Carmichael†,‡, R. Thornton†, R. Rodionov†, K. Hamandi†, S. Kiebel‡, M. Guye¶, J. Duncan†, H. Laufs†,§, and L. Lemieux†*

**Policlinico Umberto I°, University of Rome 'La Sapienza', Rome, Italy; †UCL Institute of Neurology, Queen Square, London, UK; ‡Wellcome Trust Centre For Neuroimaging, UCL, Queen Square, London, UK; §Johann Wolfgang Goethe-University, Frankfurt Am Main, Germany, and ¶CHU TIMONE Et Université De La Méditerranée, Marseille, France*

Purpose: Absence seizures are characterized clinically by a loss of consciousness and on EEG by generalized spike-wave discharges (GSWD) thought to be sustained by thalamocortical networks. Using dynamic causal modelling (DCM) of EEG/fMRI in 9 patients with frequent GSWD, we examined the causal relationship between GSWD and (sub-) cortical regions including the precuneus, which is known to sustain consciousness.

Method: Patients were selected whom exhibited significant GSWD-correlated haemodynamic signal changes (activation or deactivation) in the thalamus, the frontal cortex and precuneus [K Hamandi et al. Neuroimage 31 (2006); 1700–1710]. Three models were constructed using DCM postulating bidirectional connections between the thalamus, frontal cortex and precuneus to assess the effective connectivity among them. GSWD were used as driving input on the thalamus (model A), frontal cortex (BA10) (model B), and precuneus (model C). Models were compared based on Bayesian information criteria.

Results: Model C (GSWD acting on the precuneus) was the best in 6 patients; model A in 2 patients, while in 1 patient all models were equally likely.

Conclusion: Given the tested models, our results indicate that during GSWD the thalamo-(fronto) cortical network is first influenced by the precuneus. This finding suggests that changes in precuneus activity, which reflects changes of consciousness and awareness [Cavanna AE, Trimble MR. Brain (2006) Mar;129:564–83], may facilitate the generation of GSWD through the thalamic-cortical loop rather than being a mere consequence of GSWD.

052
EXTRAOPERATIVE CORTICAL STIMULATION FOR LANGUAGE MAPPING IN INTRACTABLE FOCAL EPILEPSY: CORRELATIONS WITH TRACTOGRAPHY OF THE ARCUATE FASCICULUS

B. Diehl, Z. Piao*, J. Tkach†, R. Busch*, I. Najm*, W. Bingaman*, and H. Luders†*
**The Cleveland Clinic Foundation, Cleveland, Ohio, USA and † University Hospitals Cleveland, Cleveland, Ohio, USA*

Purpose: Diffusion tensor imaging (DTI) provides information about magnitude (diffusivity) and directionality (anisotropy, FA) of water diffusion and allows reconstruction of tracts. The arcuate fasciculus (AF) connects anterior (Broca) and posterior (Wernicke) language areas. We hypothesized that essential language areas identified through direct cortical stimulation would colocalize with areas revealing subcortical connectivity via the AF.

Method: 14 patients with left hemispheric epilepsy and left hemisphere language dominance underwent invasive evaluations for localization of the epileptogenicity and functional mapping. DTI and T1 volumetric scans were coregistered and the grid electrodes identified, and the AF was reconstructed from a region lateral to the corona radiata on the FA map. Colocalization, defined as less than 1cm between the AF and the electrode positions delineating language cortex, was visually assessed 6 months apart with excellent reliability (Cronbach's alpha =.98).

Results: Grid coverage and areas stimulated varied based upon the clinical indication. A total of 71 grid contacts were overlying language cortex. 19 contacts in eight patients were over Broca's area, 16 of which (84.2%) colocalized with the AF. 52 contacts in 10 patients were on Wernicke's area, 29 of which (55.8%) colocalized. Colocalization was significantly better in anterior regions than in posterior regions [÷2(1)=4.850, p<.05].

Conclusion: The AF, as reconstructed from DTI, colocalized well with anterior language areas, but less so in posterior language areas. This partially supports our hypothesis that fibers defined by DTI as part of the AF tract connect language areas. BD was supported by the Milken Family Foundation.

Tuesday 23 September 2008
11:30 – 13:00
Hall 7
Platform Session
Morphological etiologies and surgery

053
EEG PATTERNS OF ADULT PATIENTS WITH CORTICAL DYSPLASIA

W. Blume, and J. Jiang
University Hospital (London Health Science Centre), The University of Western Ontario, London, ON, Canada

Purpose: Although epileptogenic cortical dysplasias (CD) usually appear as discrete MRI lesions, resective surgery reduces seizures significantly in only 67% (Palmini etal 1991; Bingaman and Catalepe, 2001). To initiate a multipronged investigation into this discrepancy, we review preoperative EEGs of 50 consecutive patients who underwent resective surgery for CD-related intractable focal epilepsy.

Method: The entry criterion was demonstration of one or more type of CD disclosed by histological examination of resected specimens. These specimens were reviewed histologically for confirmation of diagnosis and classification into the different subtypes of CD (Palmini et al 2004). Sufficiently congruent data for seizure localization from semiology, EEG and MRI were required for surgical candidature. Archived EEG reports, categorized according to our classification system (Lemieux etal 1983), were reviewed for localization of epileptiform (ictal and interictal) and nonepileptiform abnormalities occurring during wakefulness or sleep.

Results: Several EEG abnormalities reflected widespread cortical dysfunction 1) independent bi-hemispheric abnormalities (spikes, delta, theta) in 25 (50%) 2) EEGs of 22/25 (88%) had focal spikes in each hemisphere, and 3) 14/50 (28%) had spike-waves (SWs) or other bisynchronous epileptiform patterns. Abnormalities were more widespread in extratemporal than temporal patients: 1) greater average number of lobes with focal spikes (mean= 3.14 vs.2.14; p=0.02), and 2) higher incidence of SWs.

Conclusion: Multifocal and bilateral EEG abnormalities in patients undergoing resective surgery for CD-based intractable epilepsy may underlie less than expected surgical effectiveness.

054
(ARCHI-) CORTICAL LOCALIZATION OF CAVERNOMAS IS ASSOCIATED WITH AN INCREASED RISK FOR EPILEPSY

K. Hattemer, X. Chen*, I. Joanna*, M. Dorothea*, R. Alexander*, P. Axel*, K. Susanne*, B. Helmut†, R. Felix*, and S. Ulrich**
**University of Marburg, Germany and †University of Zürich, Switzerland*

Purpose: Risk factors predicting the occurrence of epileptic seizures in patients with supratentorial cavernomas remain controversial, even though these patients carry an estimated risk to develop seizures of 1.5–2.4%/patient/year.

Method: We analyzed retrospectively the clinical and MRI data of 76 consecutive patients with supratentorial cavernomas confirmed by neuropathology. The influence of the variables sex, age at operation, cortical involvement, archicortical vs. neocortical involvement, side and lobar location of neocortical cavernomas, number of cavernomas, presence of an oedema, maximal diameter of the cavernomas and of the oedema, if present, on the occurrence of seizures was calculated using a univariate logistic regression model.

Results: Cavernomas involving the cortex were more often associated with seizures than subcortical cavernomas (P<0.0001). Furthermore, including only cavernomas with cortical involvement, epilepsy occurred more often in patients with archicortical than in patients with neocortical cavernomas (P<0.05). The lobar location of neocortical cavernomas was not significantly associated with an increased risk for seizures, nor were any of the other variables studied (P>0.05).

Conclusion: The results of the present study suggest, that the epileptogenicity of supratentorial cavernomas depends on cortical, especially archicortical, involvement. Regarding cavernomas with neocortical involvement, lobar location was not significantly associated with epilepsy. This information is helpful in counselling patients with cavernomas regarding their risk of epileptic seizures.

055
THE NEUROPATHOLOGY OF CHRONIC EPILEPSY: WHOLE BRAIN STUDIES IN A LARGE POSTMORTEM COHORT

C. Catarino,†, L. Caboclo*, M. Koepp*,†, M. Yogarajah*,†, L. Martinian*, M. Thom*, and S. Sisodiya*,†*
**Institute of Neurology, University College London, London, UK and †National Society For Epilepsy, Chalfont St. Peter, UK*

Purpose: Clinical histories of epilepsy from onset to death are rarely available, but offer potentially important insights into causes of refractory epilepsy, patterns of evolution of drug resistance, reasons for remission. Examination of the entire brain post mortem is seldom possible, but can reveal further insights into many aspects of epilepsy, including extent of pathology, recovery or changes associated with remission, and molecular underpinnings, such as extent of overexpression of multidrug transporters, and genetic investigation.

Method: Ethics approval was obtained, and informed consent from next-of-kin. We reviewed medical notes, investigation results and neuropathological reports from deceased patients following long-term institutionalization. Further neuropathological analyses were undertaken in selected cases.

Results: Data from 108 patients were reviewed, 44 female. Onset of epilepsy ranged from infancy to 34 years. Median age at death was 69.0 years (range 21–97); median time of follow-up, 33.0 years. Most patients continued to have seizures despite treatment. The range of pathologies included hippocampal sclerosis, brain malformations, DRPLA and familial Alzheimer's disease. We evaluated prevalence of SUDEP, stroke, dementia, and neoplasia in these patients. Fifteen patients with chronic refractory epilepsy went into remission, and this was not always related to AED changes. One patient with polymicrogyria had remission of seizures after a stroke in a cortical region within the malformation. Further several interesting observations open up new opportunities for further research.

Conclusion: Whilst this is a selected cohort, it represents a very valuable resource, which can be explored at both neuropathological and genomic levels, with options for collaborative research.

056
HYPOVENTILATION WITH SEIZURES IN LOCALIZATION-RELATED EPILEPSY

L. Bateman, and M. Seyal
University of California, Davis, CA, USA

Purpose: Both cardiac and respiratory dysfunctions have been implicated as possible precipitating causes of sudden unexpected death in epilepsy (SUDEP). We (Bateman LM and Seyal M. Epilepsia 2007; 48(Suppl 7):62.) have previously demonstrated a high incidence of ictal hypoxemia with partial seizures. In this study we investigated pathophysiological mechanisms that may account for ictal hypoxemia.

Method: We systematically studied 56 consecutive patients with intractable localization-related epilepsy admitted for inpatient video-EEG telemetry. Respiratory parameters including digital pulse oximetry, nasal airflow and abdominal excursions were recorded, synchronized with EEG, video and the electrocardiogram. To determine whether ictal oxygen desaturation is a consequence of alveolar hypoventilation, we simultaneously recorded end-tidal CO2 (ETCO2) in 10 patients.

Results: Oxygen desaturations below 90% were recorded in 101 of 304 total seizures and in 88 of 253 seizures that did not generalize. Severe desaturations (below 80%) occurred in 28 of the 88 seizures without secondary generalization. Thirty-six seizures were recorded in the ten patients who had concurrent ETCO2 monitoring. Oxygen desaturations below 90% occurred in 23 of these 36 seizures, with a median saturation nadir of 79% (range <50% – 86%). All seizures in which desaturations below 90% were recorded had concomitant increases in ETCO2, with a median increase of 13.2 mmHg (range 2.8–77.8 mmHg).

Conclusion: These data provide evidence for ictal alveolar hypoventilation with partial onset seizures. The high levels of ictal hypercarbia and profound oxygen desaturations that occur with some seizures suggest that ictal hypoventilation is a possible mechanism for SUDEP.

057
MORTEMUS (MORTALITY IN EPILEPSY MONITORING UNIT STUDY): PRELIMINARY FINDINGS

P. Ryvlin, T. Tomson†, and *On Behalf of The MORTEMUS Study*
**IDEE, Hospices Civils De Lyon, Lyon, France and †Karolinska University Hospital, Stockholm, Sweden*

Purpose: The MORTEMUS study aims to collect information regarding patients with epilepsy who died during long term video-EEG monitoring (LTVEM), or suffered a near-SUDEP (Sudden Unexpected Death in Epilepsy), that is a cardiac or respiratory arrest that has required a resuscitation procedure for the patient to survive.

Method: This study has been granted by the European branch of the ILAE, and is currently being undertaken in all European Countries. Preliminary data have been collected from all French (N=14) and Scandinavian (N=11) centres performing presurgical evaluation in adult patients. We evaluated the number of LTVEM performed in each centres, both for presurgical and other diagnostic purposes, as well as the average number of in hospital days and hours of video-EEG monitoring. A total of 20106 LTVEM were identified, 60% of which were done for presurgical purpose.

Results: This translated into 321 patients-years of follow-up in-hospital, including 296 for presurgical evaluation, among which 171 patients-years of video-EEG monitoring. Three deaths and four near-SUDEP were identified, including one massive postictal myocardial infarction that resulted into death, and three postictal obstructive apnoea that resolved after ressuscitation. One death occurred at night while the patient was not supervised. Additional information are awaited for the remaining death and near-SUDEP.

Conclusion: The annual risk of seizure related death and SUDEP in this limited sample are respectively 0.93% and 0.62%, figures consistent with those observed in outpatients with drug resistant partial epilepsy. However, the cumulative risk of SUDEP and near-SUDEP raises to 1.9%.

058
DOUBLE CORTEX SYNDROME: EPILEPSY, MENTAL RETARDATION AND PSYCHOPATHOLOGICAL SYMPTOMS

M. Veendrick-Meekes, W. Verhoeven†,‡, W. van Blarikom*, and S. Tuinier†*

**Epilepsy Centre Kempenhaeghe, Netherlands; †Vincent Van Gogh Institute For Psychiatry, Venray, Netherlands and ‡Erasmus University Medical Centre, Rotterdam, Netherlands*

Purpose: This study is performed to provide adequate treatment by obtaining more evidence of the influence of epilepsy on the development of psychiatric symptoms and mental retardation (MR) in patients having Double Cortex Syndrome (DC). Subcortical Band Heterotopia (SBH) or DC is a neuronal migration disorder which has described world wide in at least 110 females. The syndrome is usually associated with mutations in the doublecortin (DCX) (Xq22.3-q23) gene. Reports on psychopathological features in DC patients are scarce.

Method: In this study 3 female patients with DC are described. Symptoms of epilepsy and psychopathology are outlined. The degree of intellectual disability is assessed. Effects of treatment of epilepsy and behavior problems are described.

Results: All three patients have a mutation of the DCX gene and intractable seizures and have used a wide range of anti epileptic drugs. DC was diagnosed at age of 11, 14 and 32 respectively. All patients showed cognitive decline before onset of seizures. IQ ranges 25 –60. Seizures started at age 11, 7 and 1. The patients showed anxieties (n=3), challenging behaviors (aggression: n= 2; self-injurious behavior: n=2), psychotic phenomena (hallucinations: n =2) and mood symptoms (n =1) at ictal, periictal and interictal moments. Psychopathological symptoms were observed before the onset of seizures in 2 patients. Temporary control of seizures resulted in less behavior problems. In 1 patient visual sensations were reported simultaneous with epileptic discharges in EEG that disappeared after administration of 1mg clonazepam intravenously.

Conclusion: DC patients have intractable epilepsy. Behavior abnormalities are hardly to distinguish from epileptic features. Administration of antipsychotics may result in paradoxical effects. In the presented patients, psychiatric symptoms may be related to epileptic activity. The same holds for cognitive decline. The role of brain abnormality is still unclear.

Tuesday 23 September 2008
11:30 – 13:00
Hall 9
Platform Session
Psychiatry and social issues

059
DISTURBED SLEEP IN EPILEPSY: EFFECTS ON COGNITIVE FUNCTION, MOOD, AND QUALITY OF LIFE

C. Huyton, I. Wright†, and R. Nicolson**

**University of Sheffield, UK and †Frenchay Hospital, Bristol, UK*

Purpose: To explore the relationship between self-reported sleep disturbances in epilepsy, and aspects of cognitive functioning, mood, and quality of life.

Method: Self-reported sleep problems were assessed via questionnaire in 99 adults with epilepsy, for comparison with 2986 healthy controls. Patients with epilepsy also completed measures of self-reported cognitive function, mood, and quality of life. The relationship between these variables and sleep disturbance in the epilepsy group was examined.

Results: People with epilepsy reported significantly more disturbances to their sleep, and more problems with daytime sleepiness, than controls ($p < 0.005$). Whilst variables such as seizure frequency, seizure type, and epilepsy duration had little effect on sleep quality, those patients on polytherapy reported significantly more disturbed sleep than those on monotherapy. Regression analyses showed that disturbed sleep in epilepsy is significantly associated with problems in areas of cognitive functioning, and is predictive of poor mood and impaired quality of life.

Conclusion: Results indicate that sleep problems are highly prevalent in patients with epilepsy, when compared with healthy controls. Although epilepsy variables generally had little effect on sleep disturbances, the presence of more than one AED was associated with worse sleep. However it is not clear whether this effect is due to the interactions of multiple medications, or to the profile of patients on polytherapy. Disturbed sleep in epilepsy was also predictive of impaired cognitive function, mood and quality of life. These findings suggest disturbed sleep in epilepsy may have important implications in terms of learning and memory, and should be considered as a factor affecting aspects of psychological functioning.

060
FACTORS CONTRIBUTING TO DEPRESSION IN PATIENTS WITH EPILEPSY

S. Lee, Y. No, and S. Lee

University of Unsan College Of Medicine, Seoul, South Korea

Purpose: Although depression is a powerful predictor of quality of life (QOL) in people with epilepsy (PWE), factors contributing to depression in PWE are not well known. We investigated the effects of the potential variables, including anxiety, stress, coping strategies, self-efficacy, and social support, on depression in PWE.

Method: Data were collected from 150 adult patients, 35 of whom were seizure remission for at least 2 years. Beck Depression Inventory (BDI), Beck Anxiety Inventory, Daily Hassles Scale, Epilepsy Self-Efficacy Scale, Social Support Scale, Stress Coping Style Checklist, and QOLIE-31 were used. In this study, BDI scores significantly predicted QOL.

Results: The mean BDI score was 13.4(SD 9.0). Abnormal BDI scores (>9) were recorded in 93 patients (62%), 25 and 11 of whom were being moderate-to-severe (BDI score >18) and severe (BDI score >29) depression, respectively. In a linear regression including all variables with a $p < 0.10$ in univariate analysis, BDI scores were independently related to employment status ($p=0.019$), anxiety ($p=0.001$), stress ($p<0.001$), self-efficacy ($p<0.001$), and social support ($p=0.042$). In addition, Logistic regression identified that the level of stress ($p=0.001$) and social support ($p=0.029$) were independently related to moderate-to-severe or severe depression. Demographic (age, sex), seizure- or epilepsy-related (onset, duration, localization, lateralization, seizure frequency, type of epilepsy, number of drugs) and social (marriage, education, religion) variables were not related to BDI scores.

Conclusion: PWE are at high risk of depression, which results in poor QOL. Employment status and the level of anxiety, stress, self-efficacy or social support may be the causative factors generating depression in PWE.

061
SERIOUS MENTAL DISTRESS AMONG PERSONS WITH EPILEPSY BASED ON THE CALIFORNIA HEALTH INTERVIEW SURVEY, 2005

L. Moore, J. Elliott, B. Lu, and C. Charyton

The Ohio State University College of Medicine, Columbus, OH, USA

Purpose: Persons with epilepsy (PWE) have been clearly demonstrated to be at higher risk for developing mood disorders than the general population and there are few population based analyses in the literature.

Method: We analyzed data from adults aged ≥18 years (n = 43,020) who participated in the 2005 California Health Interview Survey (CHIS), a geographically stratified, random-digit dialled, cross-sectional, multistage telephone survey of noninstitutionalized persons in the U.S. that tracks the prevalence of key health behaviors and characteristics.

Results: California adults, with a history of epilepsy, reported significantly higher amounts of psychological distress based on the Kessler 6 Scale than did persons without epilepsy. After adjustment for demographics (gender, age, race/ethnicity, income, education and urban/rural residence) and comorbid conditions (asthma, obesity, diabetes, hypertension, heart attack, stroke, high cholesterol and cancer), persons with epilepsy (PWE) reported higher rates of feeling nervous (OR 2.22 adjusted), feeling hopeless (OR 1.35), feeling restless (OR 2.07), feeling depressed (OR 2.28), feeling worthless (OR 2.57) and that everything is an effort (OR 2.57) in the past 30 days. The Kessler 6 total score reveals that serious mental illness is more likely in PWE (OR 2.63) as well.

Conclusion: PWE have significantly higher rates of serious mental distress than the nonepilepsy population based on the Kessler 6 Scale. These co-morbid conditions need to be factored into any comprehensive treatment strategy for managing PWE to achieve optimal quality of life.

062
PREVALENCE OF ANXIETY DISORDERS AMONG PATIENTS WITH REFRACTORY FOCAL EPILEPSY

C. Brandt, M. Schoendienst*, M. Trentowska†, M. Schrecke*, K. Witte-Boelt*, B. Tuschen-Caffier†, T. May‡, and B. Pohlmann-Eden§*

**Epilepsy Centre Bethel, Bielefeld, Germany; †University of Freiburg, Freiburg, Germany; ‡Society For Epilepsy Research, Bielefeld, Germany, and §Dalhousie University, Halifax, NS, Canada*

Purpose: Anxiety disorders have been described in 15–25% of patients with epilepsy including all stages of the disease. The purpose of this study was to evaluate the prevalence of anxiety disorders according to DSM-IV criteria in a group of C otherwise unselected C patients with refractory focal epilepsy.

Method: 96 consecutive out-patients (42.7% male) of the Bethel epilepsy centre, a tertiary referral centre, with focal refractory (≥2 failed drugs) epilepsy were interviewed using the anxiety section of the Structured Clinical Interview for DSM-IV disorders (SCID-I).

Results: 18.8% of patients had a diagnosis of any anxiety disorder (8.3% social phobia, 5.2% panic disorder with/ without agoraphobia, 5.2% specific phobia, 3.1% generalized anxiety disorder and 2.1% anxiety disorder, not further specified). Persons with anxiety disorder were significantly younger than persons without and showed a trend to have shorter epilepsy duration. No relation was found between gender, epilepsy etiology or age at epilepsy onset and anxiety.

Conclusion: The prevalence of anxiety disorders in our patients is considerably higher than in the general population but within the range previously reported for epilepsy patients. The relatively low figure in the stage of refractoriness in our group may reflect continuous adjustment processes during the course of disease. There may also be an underestimation as patients of the specialized neuropsychiatric outpatients department (OPD) were excluded and only patients of the general OPD were examined. This study should lead to further investigations addressing the issue of the time-course of psychiatric comorbidity in epilepsy and also to the development of specific therapeutic strategies.

063
DIMENSIONS OF DISSOCIATION IN PATIENTS WITH NONEPILEPTIC (DISSOCIATIVE) SEIZURES

L. Goldstein,‡, R. Delamont†, and J. Mellers‡*

**King's College London, Institute of Psychiatry, London, UK; †Regional Neurosciences Centre, King's College Hospital NHS Foundation Trust, London, UK, and ‡Maudsley Hospital, South London & Maudsley NHS Foundation Trust, London, UK*

Purpose: We set out to explore whether the Multiscale Dissociation Inventory (MDI) would identify specific dimensions of dissociation that differ between patients with Dissociative Seizures (DS) and partial epilepsy (ES).

Method: Nineteen adults with Video EEG telemetry-confirmed DS and 24 patients with ES completed the MDI and the Hospital Anxiety and Depression scale during their admission to a telemetry unit.

Results: The two groups did not differ in age, gender distribution or educational level. Total MDI scores were higher in the DS group than in the ES group (p=0.006). The DS group had higher scores on the Disengagement (p=0.002), Depersonalisation (p=0.023), Emotional Constriction (p=0.009) and Identity Dissociation (p=0.032) subscales but not on the Derealisation or Memory Disturbance subscales (p>0.05). Since the DS group also had higher anxiety (p=0.009) and depression (p=0.015) scores, the influence of mood on dissociation scores was investigated. Between groups differences in Disengagement scores remained significant using anxiety and depression scores as covariates; differences in Emotional Constriction scores approached significance (p<0.06) when covarying for depression scores.

Conclusion: While DS patients have higher total raw scores on the MDI than ES patients, some aspects of dissociation that differ between the groups appear to be confounded by anxiety and/or depression. However, Disengagement-type symptoms (e.g. absent-mindedness, 'spacing out') and to a lesser extent Emotional Constriction (e.g. knowing that you must be upset but not being able to feel it) may not simply reflect mood and may be more informative in characterising dissociative behavior in DS patients.

064
EFFECTIVENESS OF SPECIALIST EPILEPSY NURSES. EVALUATION OF A PILOT PROJECT

M. Pfaefflin, T. May*, D. Dennig†, S. Urban*, A. Uebelacker‡, H. Kiessling†, and B. Schmitz‡*

**Epilepsy Center Bethel, Bielefeld, Germany; †Private Neurological Practice, Stuttgart, Germany, and ‡University Hospital Charité, Berlin, Germany*

Purpose: To evaluate the effectiveness of specialist epilepsy nurses (EN). Nurses were trained as specialist epilepsy nurses. Primary aim was to improve quality of care of outpatients with epilepsy. The EN provided patients with information, support and counselling 1–3 hours in average per patient.

Method: Controlled, randomized, multicenter, repeated-measures study design. Patients were randomly allocated to either an epilepsy nurse group (intervention) or waiting-list group (control). 203 patients (16 to 78 years) were included: The EN group (n=93) and the control group (n=110) completed the questionnaire twice within 6 months, the EN group before the first consultation (T1) and about 6 months later (T2). Primary outcome measure was the satisfaction of patients with support and information about epilepsy related topics. Secondary measures were epilepsy specific knowledge, satisfaction with the clinic and the staff, coping with epilepsy, restrictions in daily life, epilepsy-related fears, anxiety and depression. Analysis of covariance using the baseline score as covariate was used to test the effects of EN.

Results: The EN group improved significantly in satisfaction with support and information compared to the control group (p=0.035). As expected, the increase in satisfaction was clearly dependent on patient's need for information assessed before consultation (Jonckheere-Terpstra-Test; p=0.006). The EN group improved also in epilepsy specific knowledge (p=0.05). No differences between groups were observed in other measures as well as in regard to seizure frequency and adverse effects reported by the patients.

Conclusion: Epilepsy nurses can improve quality of care and should complement comprehensive care for patients with epilepsy.

Unrestricted grant UCB GmbH, Germany.

Wednesday 24 September 2008
11:30 – 13:00
Hall 2b
Platform Session
Pediatric Epilepsy – Cognitive outcome

065
COGNITIVE DEVELOPMENT IN DRAVET SYNDROME: A RETROSPECTIVE, MULTICENTER STUDY OF TWENTY-SEVEN PATIENTS

F. Ragona, F. Offredi†, M. Morbi*, D. Chieffo‡, S. Cappelletti§, D. Brazzo¶, F. Darra†, I. De Giorgi*, N. Specchio§, R. Gaggero**, A. Toraldo††, and C. Dravet‡*
**IRCSS, Istituto Carlo Besta, Milano, Italy; †Ospedale Policlinico, Università Di Verona, Verona, Italy; ‡Policlinico A. Gemelli, UCSC, Roma, Italy; §IRCSS, Ospedale Bambino Gésù, Roma, Italy; ¶IRCSS C. Mondino, Università Di Pavia, Pavia, Italy; **IRCSS, Istituto G. Gaslini, Genova, Italy, and ††Dipartimento Di Psicologia, Università Di Pavia, Pavia, Italy*

Purpose: According to literature data, in most patients with Dravet syndrome, the psychomotor development is normal before the onset of the seizures and progressively slows down, often associated with behavioral disorders. Only one paper, however, specifically focused on psychomotor development (Wolff et al, Epilepsia 2006; 47 (suppl 2): 45–48). The present study aims to analyze the correlations between the course of epilepsy and the cognitive development, also considering the putative role of the genetic background.

Method: The series include twenty-seven patients from six different centres, observed at the onset of seizures and followed-up to at least the age of four. Serial awake and sleep EEGs, with polygraphy and videorecording, MRI, molecular analysis for SCN1A were obtained in all cases. Serial standardized evaluations included Griffiths or Brunet-Lézine scales, and WIPSSI, according to the age and applicability. Seizure type, mean frequency and frequency variance were reviewed with attention to occurrence of status and myoclonic seizures. The effects of epileptic and genetic variables on cognitive level and development were assessed by various General Linear Models (GLM).

Results: Progressive deterioration of cognitive performance with increasing age was observed in twenty patients, whereas in seven mental developments remain within the low limits of normal range at the age of four.

Conclusion: Our results suggest that, albeit in most patients cognitive evolution is severely impaired in Dravet syndrome, a number of exceptions exist to this rule. The role of epilepsy, genetic background and treatment in determining the final outcome still needs to be elucidated.

Partly supported by a grant from Fondazione Mariani, Milano.

066
COGNITIVE FUNCTIONS IN CHILDREN WITH FRONTAL AND TEMPORAL EPILEPSY

M. Mazurkiewicz-Bedzińska, A. Matheisel, M. Szmuda, and A. Olszewska
Medical University of Gdansk, Gdansk, Poland

Purpose: :In order to compare the cognitive functions in children with newly diagnosed temporal (TLE) versus frontal lobe epilepsy (FLE) and control group which consisted of healthy children the following study was performed.

Method: 39 children with TLE 24 children with FLE and 24 healthy subjects were included in study. Each child had neuropsychology assessment using age-normed and validated instruments. The applied test battery consisted of measures assessing both ntelligence as well as executive and motor skills.

Results: In all epilepsy patients there was no evidence of anatomical brain damage. There were no differences in mean age and gender between the groups. There was no significant difference in global IQ scores between the groups. Children with FLE had significantly lower scores than the other two groups in nonverbal memory tasks, presented higher attention deficit and had slower performance speed. The TLE group performed significantly worse as compared with control group in verbal learning and performance speed with no differences in attention. The correlations between the results of test and the localization of epileptic foci were performed.

Conclusion: The children with new onset FLE present with more severe cognitive and attention problems compared with TLE group, however the TLE group differ significantly in some measures with control group. That can lead to development of school problems. Early recognition of those deficits should lead to appropriate treatment procedures.

067
CAN WE PREDICT LANGUAGE REORGANIZATION IN CHILDREN WITH REFRACTORY LEFT TEMPORAL EPILEPSY?

A. Datta,†,††, I. Jambaqué¶,**, G. Dellatolas§,¶, B. Christine*,**, F. Martine**, D. Olivier**, D. Georg**, D. Olivier**, C. Catherine*,†,‡, and H. Lucie*,†*
**INSERM U663, University Paris V René Descartes, Paris, France; †Frederic Joliot Hospital And Neurospin, CEA, Orsay and Saclay, France; ‡Necker-Enfants Malades Hospital, Paris, France; §INSERM U780, Villejuif, France; ¶Institute For Psychology, René Descartes University, Paris, France; **Rothschild Foundation Hospital, Paris, France, and ††University Children's Hospital (UKBB), Basel, Switzerland*

Purpose: To study the roles of epilepsy and its cofactors in the plasticity of language in children with left temporal lobe epilepsy (LTLE).

Method: 30 LTLE children (mean 12.3 years) with presurgical evaluation (MRI, functional MRI with sentence generation task, neuropsychological testing, EEG), were compared to 18 healthy children (mean 11.4 years). Hemispheric language laterality indices (HLI) were calculated (from +1 (left) to −1 (right)). Uni- and multivariate analyses studied the role of handedness, epilepsy duration, location and type of the lesion.

Results: HLI tended to be lower in patients than controls (0.47 vs 0.69, p=0.085). Handedness provided the most significant contribution to language reorganization (p=0.008): HLI were lower in left-handers than right-handers (0.6 vs 0.1, p=0.02), but, when matched for handedness, patients and controls did not significantly differ (0.6 vs 0.7 in right-handers, 0.1 vs 0.6 in left-handers). The duration of epilepsy also contributed

to reorganization (p=0.048), as well as lesion location (temporal lateral more than mesiopolar, p=0.04). The type of lesion had a more limited contribution (p=0.6), cryptogenic epilepsies more than developmental lesions, themselves more than late lesions.

Conclusion: Handedness greatly contributes to the predictability of language dominance in children with LTLE. Left-handed patients with long lasting cryptogenic epilepsy have a greater tendency to show atypical dominance. Mesiopolar lesions tend to maintain normal left dominance of language in the pediatric age, as opposed to what is observed in adults.

068
PREDICTORS OF THE NEURODEVELOPMENTAL STATUS FOLLOWING EPILEPSY ONSET IN INFANCY

C. Eltze,†, M. De Haan*, A. Whitney‡, A. Merrett*, R. Scott*,†, and J. Cross**

**UCL-Institute of Child Health, London, UK; †Great Ormond Street Hospital For Children, London, UK, and ‡Southampton General Hospital, Southampton, UK*

Purpose: We aimed to determine the predictors of the neurodevelopmental status of children with epilepsy onset under the age of 2 years close to diagnosis and factors that are associated with a change of developmental scores at 12 months.

Method: Infants, recruited through a surveillance study in North London, were evaluated with the Bayley Infant and Toddler Developmental Scales III. Principal component analysis was applied to generate a Developmental Composite Factor (DCF) from language, cognitive and motor scores at initial and follow-up evaluation. Subsequent analyses included multivariable linear regression and repeated measures ANOVA.

Results: 49 children (29 males, seizure onset: mean 6.5 [sd +/−5] months, median time-interval to diagnosis: 9 weeks) were evaluated. Neuroimaging and EEG data were available for 44. Follow-up data were obtained for 30 of 47 eligible children. Significant predictors of lower initial DCF values were abnormal neurology (p= .001), interictal epileptiform activity (p< .001) and abnormal EEG background (p=.034). Although structural brain abnormalities had no significant independent effect there was an important interaction with interictal epileptiform activity (p= .003) and abnormal EEG background (p= .020). There was no significant difference between initial and follow up DCF after adjusting for initial infantile spasms, normal or abnormal initial EEG, seizure status at follow up, structural brain abnormalities, and continued antiepileptic medication.

Conclusion: In this cohort of children with onset of epilepsy in infancy, abnormal EEG and neurological examination independently predict the neurodevelopmental status approximately 3 months after diagnosis. The neurodevelopmental outcome 12 months later is determined by the initial status.

069
DO CHILDREN WITH DRUG RESISTANT EPILEPSY AND LOW IQ ALSO IMPROVE AFTER EPILEPSY SURGERY?

B. Porsche, A. Dressler, G. Groeppel, H. Mayer, B. Plattner, E. Reiter, L. Urak, and M. Feucht

Medical University Vienna, Vienna, Austria

Purpose: To evaluate prospectively pre- and postoperative neuropsychological performance of children with temporal lobe epilepsy (TLE) and low IQ (=85) compared to those with IQ >85.

Method: IQ, concentration, flexibility in thinking, and verbal/nonverbal memory were assessed before, 3 months and once/year after surgery (a.s.). Group and individual changes as well as outcome-predictors were evaluated.

Results: 19 patients with low IQ (6–18 years; 12 right TLE) and 22 age-matched patients with average range intelligence (10 right TLE) were included. 3 months a.s., significantly improved verbal (V-IQ), performance (P-IQ), and full scale IQs (FS-IQ) were identified in low-IQ patients whereas patients with average-range intelligence tend to worsen in their V-IQ. 1 year a.s., improvement of V-IQ, P-IQ and FS-IQ was observed in the whole group. Long-term outcome data (2–6 years a.s.) for 20 children also showed significant improvement in P-IQ and FS-IQ for both groups. Data of individual changes corroborat these findings. Concentration improved for both groups (especially for the low IQ-patients) 3 months a.s. and 1 year a.s. Long term verbal memory outcome showed a significant improvement in both groups, especially for the left TLE. IQ-groups did not differ significantly in age at seizure onset and duration of epilepsy.

Conclusion: Due to our results, epilepsy surgery and surgical intervention is advisable in children with low cognitive function.

Wednesday 24 September 2008
11:30 – 13:00
Hall 5
Platform Session
Basic Science

070
LOCAL ANTIEPILEPTIC THERAPY WITH VALPROATE IN A MOUSE MODEL OF PHARMACORESISTANT TEMPORAL LOBE EPILEPSY

*T. Freiman, D. Altenmueller, M. Mueller, T. Feuerstein, C. Haas, and J. Zentner**

University Hospital, Freiburg, Germany

Purpose: In patients with pharmacoresistant epilepsy caused by an epileptogenic focus in an eloquent brain area, operative resection may result in severe neurological deficits. Therefore we have developed a novel experimental technique by implanting valproate-containing osmotic minipumps with catheter (1) or a gel of controllable release (2) into (1) or on the surface of (2) the hippocampus in an mouse model of pharmacoresistant temporal lobe epilepsy (TLE).

Method: TLE was induced by 50 nL (1 nmol) kainate injected stereotactically into the left dorsal hippocampus Limbic seizures developed within four weeks. Osmotic mini pumps with catheter tips were implanted within the left hippocampus, delivering either saline or 10 mg valproate within 7 days. In a second group (2) valproate gel or placebo was applied on the surface of the hippocampus. Subsequently, intrahippocampal encephalography electrodes were implanted for long term recordings. Anticonvulsant effects were measured by mathematical counting paradigm of high frequency oscillation (fast ripples).

Results: Clear antiepileptic effects of valproate micro pumps and gels, compared to the placebo groups, were observed. Valproate micropumps decreased the fast ripple activity from 100% to 37.7%. Valproate gels decreased the fast ripple activity from 100% to 5% ($p < 0.05$). The antiepileptic effect disappeared after 14 days. After this local antiepileptic treatment, 10 mg valproate was given intraperitoneally in a single dose, but did not decrease fast ripple activity. All hippocampal specimens showed Ammon's horn sclerosis.

Conclusion: We have demonstrated that local, but not systemic application of valproate has antiepileptic effects in a conventionally pharmacoresistant epilepsy model.

071
ICTAL EEG PATTERN OF SECONDARY GENERALIZATION IN SEIZURES OF MESIOTEMPORAL ORIGIN. A SEEG STUDY

I. Rektor, J. Zákopèan, I. Tyrlíkévá, R. Kuba, and M. Brázdil
Ste. Anne Hospital, Masaryk University, Brno, Czech Republic

Purpose and Method: The hypothesis was tested that secondary generalized seizures (SGS) are not truly generalized and may involve selective cortical regions. The spread from focal to generalized seizures was studied in 20 SGS in 15 surgery candidates. Electrode contacts were assigned the following regions: frontal inferior/fronto-orbital; prefrontal lateral; anterior cingulate; temporal lateral; hippocampus; amygdala. A behavioral analysis of the ictal video-recordings was performed by two independent readers in order to ascertain the onset of the SGS. The SGS onset was designated as the moment when the seizure clearly involved the whole body, including the head, face, and all limbs. The EEG recordings were then analyzed and evaluated using the rating scale developed by Blumenfeld et al (2003). Positive ratings were assigned to ictal EEG patterns; negative ratings were assigned to patterns resembling interictal slowing. The seizure ratings in each region were compared with the seizure rating in the hippocampus. The Kruskal-Wallis ANOVA test followed by the Mann-Whitney U test was used.

Results: The ranking significantly differed in the cingulate and fronto-orbital cortex; moreover a trend to significance appeared in the lateral prefrontal cortex. In these regions, the slow activity dominated. It was interesting to note that the slow waves appeared mainly in regions that are critical for regulation of the thalamocortical circuitries. At variance with SGS, in absence seizures, the orbital, dorsolateral and medial frontal cortices are associated with spiking at seizure onset (Holmes et al., 2004).

Conclusion: This may indicate a substantial difference between the mechanisms of seizure spread in primary and secondary generalized seizures. Our data suggest that the secondary generalization involves selective cortical networks. The beginning of SGS does not implicate global cortical involvement.

Supported by MSMT 0021622404.

072
IDENTIFICATION OF THE EPILEPTOGENIC ZONE BY ETOMIDATE IN TEMPORAL LOBE EPILEPSY DURING PRESURGICAL EVALUATION

J. Pastor, R. Wix, M. Meilán, E. De Dios, J. Martínez-Chacón, L. Domínguez-Gadea, and R. Sola
Hospital La Princesa, Madrid, Spain

Purpose: The main object of this work is to analyze the utility of etomidate (Et) in the identification of the onset seizure area (OS) in patients with temporal lobe epilepsy (TLE).

Method: Fifteen patients (10 men and 5 women), ages ranging 22–52 years (35.3 ± 2.5) were evaluated during v-EEG monitoring with foramen ovale electrodes (FOE). Et was i.v. perfused (0.1 mg/kg) meanwhile EEG (scalp and FOE), heart rate, EKG and SaO2 were monitored. Basal activity was defined five minutes prior Et perfusion. The OS zone was defined from v-EEG+FOE results. The frequency (spikes/min) induced by Et in mesial and lateral regions were measured. In mesial recordings, for every minute (n), we defined dif (n) =freqt (n)-freqr (n), basal_sum_dif (n = 5), Et_sum_dif (n = 5) and side = Et_sum_dif-basal_sum_dif, where OS would by in the left if side>0 and in the right if side < 0.

Results: 1) Side effects were mild distal myoclonias (11/15), severe myoclonias of right arm (1/15), pain during infusion (3/15) and euphoric reaction (1/15); 2) Heart rate, breath rate and SaO2 did not change with Et; 3) The frequency of the spikes increased in OS area from the first minute and persisted above the basal level until min =14; 4) The frequency of the spikes followed a simple exponential kinetic; 5) Et lateralized correctly the OS lobe in 15/15 patients with FOE recordings and 3/15 with scalp recordings.

Conclusion: Et perfusion is an easy, safe and accurate method for identify the OS in TLE patients.

073
IS TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) PREDICTIVE FOR VAGUS NERVE STIMULATION (VNS) THERAPY OUTCOME?

I. Orosz, J. Hoffmann†, F. Kerling‡, T. Polster§, M. Hoppe§, I. König¶, H. Stefan‡, and J. Sperner**
**Children's Hospital, University of Lübeck, Lübeck, Germany; †Medical Center University of Bonn, Bonn, Germany; ‡Epilepsy Center, University of Erlangen, Erlangen, Germany; §Epilepsy Center Bethel, Bielefeld, Germany and ¶Institute of Medical Biometry and Statistics, University of Lübeck, Lübeck, Germany*

Purpose: To test the hypothesis of similar effects of VNS and tDCS on seizure reduction and its use as a predictive tool for VNS efficacy in epilepsy patients. VNS is effective in 30–40 % of patients with pharmacoresistant epilepsy. However, up to now, no prediction is possible for VNS therapy outcome. tDCS is a recently developed method to stimulate the cortex noninvasively, without causing significant pain. The cathodal stimulation induces a local hyperpolarization of the cortex and leads to an increase of seizure threshold.

Method: VNS candidates were treated with a CE-certified tDCS device (Neuroconn, Germany) four weeks before VNS-implantation. Seizure frequency as well as epileptic discharges in EEG were compared before and after tDCS and were correlated to VNS-outcome in terms of seizure reduction six months after implantation. tDCS (1mA) was performed with two flat electrodes for 15 minutes. The cathode was placed over the epileptic focus and the anodal electrode to the contralateral hemisphere. EEG results were drawn immediately before and after stimulation.

Results: In 4/14 (28%) VNS-candidates tDCS as well as VNS resulted in seizure reduction (positive correlation). Negative correlation occurred in 8/14 patients. No correlation was found in 2 patients.

Conclusion: According to our preliminary results, short tDCS effects seem to be correlated with VNS outcome. A German (Lübeck, Bethel, Erlangen and Bonn) multicenter study recruiting 70 patients has started to proof the predictive power of tDCS for VNS therapy outcome in order to avoid ineffective VNS implantation surgery. Ethical approval of the universities is confirmed.

074
POST–STATUS EPILEPTICUS CHRONIC EPILEPSY IN RATS: A MODEL OF COMORBIDITY OF EPILEPSY AND DEPRESSION

A. Mazarati, R. Caplan, D. Shin, and R. Sankar
D. Geffen School of Medicine, Univ. of California, Los Angeles, CA, USA

Purpose: To validate an animal model of comorbidity between temporal lobe epilepsy and depression.

Method: Five-week old Wistar rats underwent pilocarpine status epilepticus (SE). Six weeks later, the presence of spontaneous seizures was verified through EEG monitoring. Hippocampal excitability was examined by measuring afterdischarge properties upon electrical stimulation. Behavioral analysis of depression employed forced swim test (FST), in which the immobility time served as a measure of despair, and taste preference, in which reduced consumption of saccharin solution pointed to anhedonia. Serotonin release from, and turnover in the hippocampus were examined using fast cyclic voltammetry and high performance liquid chromatography respectively. Effects of fluoxetine (10 daily injec-

tions, 10 mg/kg) on seizures, behavioral and biochemical markers of depression were also examined.

Results: Post-SE animals developed spontaneous seizures, reduced afterdischarge threshold and prolonged afterdischarge duration. Fluoxetine did not affect spontaneous seizure frequency, but reversed enhanced hippocampal excitability. Compared with controls, epileptic rats showed 2.5-fold increase of the immobility time in FST, and diminished preference towards saccharin. Fluoxetine reduced immobility time in naïve animals; however behavioral impairments in post-SE rats were fluoxetine – resistant. Biochemical assays revealed twofold decrease of serotonin release and turnover in the hippocampus of epileptic rats. Serotonin turnover was inhibited by fluoxetine equally in naïve and post-SE animals.

Conclusion: Post-SE epilepsy in rats is characterized by hallmarks of depression: despair, anhedonia, and compromised serotonergic transmission. Experiments with fluoxetine suggest that depression in epilepsy has underlying mechanisms beyond alterations in serotonergic pathways.

Supported by the NIH research grant NS046516.

075

DIFFERENTIAL EXPRESSION OF MICRORNAS IN HIPPOCAMPUS FROM PATIENTS WITH TEMPORAL LOBE EPILEPSY IN ASSOCIATION WITH HIPPOCAMPUS SCLEROSIS MAY AFFECT THE GLUTAMATE SIGNALING

R. Møller,†, S. Kaalund*, M. Bak*, F. Madsen‡, H. Broholm‡, H. Laursen‡, B. Quistorff§, P. Uldall¶, S. Kauppinen*,**, N. Tommerup*, and Z. Tümer**

**Wilhelm Johannsen Centre For Functional Genome Research, University of Copenhagen, Copenhagen, Denmark; †Danish Epilepsy Centre, Dianalund, Denmark; ‡The Copenhagen Muscle Research Centre, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; §The Panum Institute, University of Copenhagen, Copenhagen, Denmark; ¶National Institute of Public Health, Rigshospitalet, Copenhagen, Denmark, and **Santaris Pharma, Hoersholm, Denmark*

Purpose: Hippocampal sclerosis (HS) is a common feature of temporal lobe epilepsy (TLE). It is found in approximately 50–75% of temporal lobe resections from medically intractable epilepsy and presence of sclerosis is a good indicator for a positive surgical outcome. The underlying molecular mechanism that causes the development of TLE and HS is unknown, but several studies indicate involvement of the glutamate signaling pathway. The aim of the present study is to investigate the role of microRNAs (miRNAs), which are negative regulators of mRNA translation, in the development of TLE and HS, through miRNA expression profiling of sclerotic hippocampus tissues.

Method: Hippocampal biopsies from 10 patients and 2 controls were included in this study. RNA from the biopsies were hybridized to a prespotted miRNA microarray containing probes for all human microRNAs in miRBase version 7.1. The miRNA expression profiles were verified using quantitative RT-PCR.

Results: 44 miRNAs were differentially expressed in the patients; 38 were up-regulated and 6 were down-regulated. 4 of these have been confirmed by qRT-PCR. miR-218 and miR-204 were both down-regulated and both are predicted to target different glutamate receptors and transporters along with other proteins involved in the long-term potentiation (LTP) and depression (LTD) pathways.

Conclusion: In the present study we detected differential expression of 44 microRNAs in HS tissue. Two of these miRNAs, miR-218 and miR-204, potentially regulate the translation of mRNAs encoding proteins involved in glutamate signaling, supporting the role of this pathway in the development of HS.

Wednesday 24 September 2008
11:30 – 13:00
Hall 6
Platform Session
Epilepsy Surgery

076

TYPE II (TAYLOR'S) FOCAL CORTICAL DYSPLASIA: ANATOMO-ELECTRO-CLINICAL ANALYSIS OF 100 PATIENTS

R. Spreafico†, R. Mai, G. Lo Russo*, M. Bramerio*, N. Colombo*, and L. Tassi**

**Centro Chirurgia Epilessia Ospedale Niguarda, Milano,Italy and †IRCCS Fondazione 'C. Besta' – Milano, Italy*

Purpose and Method: One hundred (13%) out of 784 patients, operated on for intractable epilepsy from 1996 at the 'C. Munari' Epilepsy Surgery Centre at Milan, with at least one year of follow-up, were selected with neuropathological diagnosis of Type II (Taylor's) Focal Cortical Dysplasia (FCD). Preoperatory MRI of each patient was retrospectively revised, at the light of the neuropathological findings. Of them 44 were males and 46 females. Mean age at surgery was 24 years (DS 13; 1–53); age at seizure onset 6 years (DS 6; 0–30) and mean duration of epilepsy 19 years (DS 11; 1–46). The mean seizure frequency was 87/month (DS 116; 1–600). Presurgical MRI was normal in 17 patients, positive for a focal lesion in 75, only hippocampal sclerosis was diagnosed in 1, while a double pathology was revealed in 7 cases. Invasive pre surgical procedure (stereo-EEG) was performed in 69 patients in order to exactly define the extent of the Epileptogenic Zone. The site of surgery was located within the Frontal lobe in 48, Temporal in 17, Central and Parietal in 2 and 4 patients respectively. The cortical excision was multilobar in 29 patients and in 10 of them including the temporal lobe.

Results: According to the Engel scale 83 patients are in class I (75 in class Ia + Ic). In 21 patients antiepileptic drugs were completely stopped. Electroclinical and neuroradiological data were further analyzed in two neuropathological defined subgroups: without balloon cells (43 patients; FCD type IIA) and with balloon cells (57 patients; FCD type IIB).

077

THE ASSOCIATION BETWEEN HISTOPATHOLOGICAL FINDINGS FROM DIFFERENT TEMPORAL REGIONS, FEBRILE SEIZURES AND SURGICAL OUTCOME IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY AND HIPPOCAMPAL SCLEROSIS

G. Benbir, M. Uzan, C. Ozkara, B. Oz, O. Ulu, S. Albayram, N. Yeni, and N. Karaagac

Istanbul University Cerrahpasa, Turkey

Purpose: We investigated the relationship between histopathological findings in different temporal regions and surgical outcome, presence of febrile seizures (FS) and other initial precipitating injuries (IPI) in patients with mesial temporal lobe epilepsy and hippocampal sclerosis (MTLE-HS).

Method: We performed anterior temporal lobectomy in a stepwise manner with removal of middle-inferior and superior temporal gyrus, amygdala, uncus, fusiform gyrus, hippocampus and posterior parahippocampus seperately. Histopathological examination was performed from every different region and classified as normal, mild malformation of cortical development (MMCD) and focal cortical dysplasia (FCD). Patients were followed-up for at least 6 months.

Results: In 33 consecutive patients (20 F, 13 M), the mean age was 27.5+8.4 years., 18 patients (54.5%) had FS, and 7(21.2%) had IPI. Only 4 had moderate HS and remaining patients had severe HS. Overall, 81.3% of patients were in Engel 1 at the last follow-up, 12.5% in Engel 2 and 6.2% in Engel 3. The presence of FCD in middle-inferior temporal gyrus (p=0.05), in uncus (p=0.04) and the presence of MMCD in amygdale (p=0.014) were associated with worse outcome. Demographical variables were not significantly related to outcome. FS was present in 88.8% of MMCD, 38.8% of FCD, and in 40% of HS-only patients. The presence of FS was significantly higher in MMCD patients.

Conclusion: The presence of MMCD or FCD in MTLE-HS was high in our study. The stepwise temporal lobectomy led us investigate different temporal regions separately, which demonstrated that the presence of FCD in middle-inferior temporal gyrus or uncus, or the presence of MMCD in amygdala were associated with significantly worse surgical outcome. In addition, febrile seizures were more common in MMCD patients.

078

TRANSSYLVIAN SELECTIVE AMYGDALOHIPPOCAMPECTOMY FOR MESIOTEMPORAL EPILEPSY: EXPERIENCE WITH 151 PROCEDURES

C. Scheiwe, A. Schulze-Bonhage*, C. Elger†, J. Schramm†, and J. Zentner**

**University of Freiburg, Freiburg, Germany and †University of Bonn, Bonn, Germany*

Purpose: Mesial temporal lobe epilepsy (MTLE) is the most common form of epilepsy refractory to medical therapy. Among different surgical approaches available, selective amygdalohippocampectomy (SAH) has gained increasing interest. The aim of this study was to summarize our experience with surgical treatment of MTLE in 151 patients using the transsylvian approach.

Method: Clinical, radiological and histopathological findings of 151 patients with MTLE who were operated between 1993 and 2001 were collected. Postoperative follow-up ranged from 6 to 32 months (mean: 20 months). Epileptological results were available from 140 cases. In 55 patients, postoperative neuroimaging was correlated to seizure outcome and neuropsychological performance.

Results: Overall, 110 (79%) of 141 patients remained completely seizure-free, and 127 (91%) had a worthwile improvement after surgery (>/ = 90% reduction of seizure frequency). Operative complications occurred in 15 patients (9.9%) which were temporary in 14 cases and permanent in one case. There was no perioperative mortality. Postoperative gliosis was observed in 18 (33%) of 55 cases but without significant relation neither to seizure outcome ($p<0.05$) nor to neuropsychological performance (all $p<0.05$).

Conclusion: Transsylvian SAH can be recommended as an adequate procedure for the surgical treatment of mesiotemporal epilepsy in the presence of hippocampal sclerosis, tumorous and nontumorous focal lesions.

079

RUNNING DOWN AND RUNNING UP OF SEIZURES AFTER EPILEPSY SURGERY IN 618 CONSECUTIVE ADULT PATIENTS

A. Elsharkawy,†, A. Hamad*, A. Amar†, H. Pannek*, R. Schulz*, M. Hoppe*, M. Nayel†, A. Issa†, and A. Ebner**

**Bethel Epilepsy Centre, Bethel, Germany and †Cairo University, Cairo, Egypt*

Purpose: To evaluate the factors associated with running down and up of seizures after epilepsy surgery in adults.

Method: we retrospectively reviewed all adult patients operated between 1991 and 2002 in the Bethel Epilepsy Centre. Seizures were considered to running down if seizures decreased over time and finally stopped. If the seizure frequency increased without apparent reasons they were considered running up. There were 618 patients, 339 male. Mean age at epilepsy onset was 12.2 ± 9.3 years, at surgery was 29.5 ± 9.4 years, mean duration of epilepsy was 20 ± 10.9 years and follow-up was 9.3 ± 2.9 years.

Results: Twenty-five (5.4%) of 459 temporal lobectomy and 17 (10.7%) of 159 extratemporal resection patients experienced a running down of seizures. Eleven (2.4%) of temporal and 7 (4.4%) of extratemporal resection patients experienced running up of seizures. Among non–seizure-free patients; 19.5% of temporal and 25.7% of extratemporal had running down of seizures, 8.5% of temporal and 10.6% of extratemporal had running up of the seizures. In all patients, absence of GT-CS was associated with running down of seizures ($p = 0.045$). In the temporal group, running down of seizures was associated with history of febrile seizure ($p=0.004$), and absence of IED in postoperative 2-years EEG. Running up of seizures was associated with a history of head trauma ($p=0.014$), bilateral sharp waves in interictal EEG ($P=0.000$), and presence of postoperative aura ($p=0.000$).

Conclusion: In a substantial number of postoperatively non–seizure-free patients seizure freedom could be reached over time.

080

COMMON MECHANISMS FOR LOCATING THE SELF IN SPACE AND TIME: EVIDENCE FROM INTRACRANIALLY RECORDED EVOKED POTENTIALS

S. Arzy,†, M. Seeck*, and O. Blanke*,†*

**Geneva University Hospital, Geneva, Switzerland, and †Brain Mind Institute, Ecole Polytechnique Fédérale De Lausanne (EPFL), Lausanne, Switzerland*

Purpose: The self is intimately immersed in space and time. It was recently hypothesized that localizing the self in time (re-experience one's own past by subjectively 'locating' the self to a previously experienced place and time, or to preexperience an event by 'locating' the self into the future), and in space (imaging to be within body borders or in different distances from the body), are managed by similar brain mechanisms.

Method: We used a novel behavioral paradigm in combination with intracranially recorded evoked-potentials from electrodes covering the temporal, occipital, and parietal lobe in epileptic patient undergoing presurgical evaluation.

Results: Self-location in time is composed of two different cognitive processes: absolute self-location, which is the location of the self in different points in time (past, present or future), and relative self-location, which is the location of the self with respect to the experienced event (before or after the event). Similarly, self-location in space is composed of absolute self-location to different points in space (different distances from the body), and relative self-location, which is the location of the self with respect to the imagined position in space. Intracranial recordings revealed the presence of five electrodes in posterior temporal and posterior parietal cortex that were active ($V>30\mu V$; t=~350–450ms; $p<0.001$) for absolute self-location in time, and six electrodes in the occipito-temporal cortex that were active ($V>40\mu V$; t=~300–400ms; $p<0.001$) for relative self-location in time and space.

Conclusion: Similar brain mechanisms are coding for the experience of being continuously and intimately embodied through time and space.

081

CHRONIC HIGH-FREQUENCY DEEP-BRAIN STIMULATION IN PROGRESSIVE MYOCLONIC EPILEPSY OF ADULTHOOD. REPORT OF 5 CASES

B. Steinhoff, C. Wille†, D. Altenmüller‡, A. Staack*, S. Bilic*, and J. Vesper†*

**Epilepsy Center Kork, Kork, Germany; †Neurosurgical Clinic, Heinrich-Heine-University, Duesseldorf, Germany, and ‡Epilepsy Center, Albert-Ludwigs University of Freiburg, Freiburg, Germany*

Purpose: To assess systematically efficacy and tolerability of chronic high-frequency deep brain stimulation (DBS) in adult patients with progressive myoclonic epilepsy syndromes (PMES).

Method: Five adult patients (four males, 28–33 years) with PMES underwent chronic high-frequency DBS according to a study protocol that had been approved by the local ethical commission. Electrodes were implanted in the substantia nigra pars reticulata (SNr) / subthalamic nucleus (STN) region in the first patient and additionally in the ventral intermediate nucleus (VIM) bilaterally in the following four cases. The DBS effects were compared with the baseline Video-EEG findings concerning myoclonic jerks and daily life performance eight weeks prior to the implantation and six-monthly afterwards.

Results: No serious complications occurred. The follow-up ranges between 3 and 33 months (median 15 months). The best effects were seen with SNr but not with VIM stimulation in all patients. In the four patients with a sufficient follow-up, the reduction of myoclonic seizures ranged between 30% and 100%. All patients reported clinically relevant improvements of various capabilities such as free standing and walking or significantly improved fine motor abilities. In one patient generalized tonic–clonic seizures increased after 15 months, the best effect was seen in the least impaired patient.

Conclusion: DBS of the SNr/STN may be an effective treatment option for patients with PMES. Less impaired patients may benefit more markedly. The experience in one patient indicates that the beneficial effect may be temporary similarly to the observations in Parkinson's disease.

Wednesday 24 September 2008
11:30 – 13:00
Hall 7
Platform Session
Syndromes and semiology

082

IDIOPATHIC GENERALIZED EPILEPSY OF LATE ONSET (IGELO). A SEPARATE NOSOLOGIC ENTITY?

J. Reichsoellner, J. Larch, I. Unterberger, G. Luef, G. Bauer, J. Ndayisaba, and E. Trinka

Medical University Innsbruck, Innsbruck, Austria

Purpose: Age at onset is a taxonomic criterion in IGE. We aimed to evaluate ages of onset in a large population of IGE and compare the ones with 'classical' with those with a later onset (IGELO).

Method: Patients with IGE treated at the outpatient epilepsy clinic, Medical University Innsbruck, Austria, 1985–2006 (n=798) were screened retrospectively. Inclusion criteria were: IGE according to ILAE-criteria, >2 FU-visits, duration of FU>1yr, normal brain imaging. 306 patients were excluded (130 with <2 visits, FU duration <1yr). We analyzed demographic data, age of onset, seizure phenotypes, syndromic diagnosis, neurological findings, neuroimaging data, EEG-findings, seizure provoking factors, seizure freedom for 1 and 5 years at last FU.

Results: 492 pts (mean age at onset 14.6 yrs, range 0.1–55 yrs, SD 7.9) were included: CAE (n=109, 1–55, 6.5), JAE (n=75, 4–39, 5.1), JME (n=112, 2–39, 5.7), and EGMA (n=196, 1–52, 17.3). Population was stratified into 3 groups: 27 pts with onset >30 yrs, 180 between 15 and 30 yrs and 285 <15 yrs. Distribution of seizure phenotypes and syndromes were different according to the age groups ($p<0.001$); Seizure outcome and other clinical variables did not differ across the groups.

Conclusion: Our data suggest that the age of onset in IGEs has a loose upper limit. The currently accepted narrow borders used in the ILAE classification seem to be too restrictive. IGELO syndromes do not differ from their younger counterparts. Our data do not support the view of IGELO as a separate syndromic or nosologic entity.

083

EVALUATION OF STRUCTURAL AND FUNCTIONAL FRONTAL LOBE PARAMETERS IN JUVENILE MYOCLONIC EPILEPSY.

R. Roebling, N. Scheerer*, I. Uttner*, O. Gruber†, E. Kraft‡, and H. Lerche**

**University of Ulm, Ulm, Germany; †University of Goettingen, Goettingen, Germany, and ‡University of Munich, Munich, Germany*

Purpose: Although MRI scans of patients with idiopathic generalized epilepsy (IGE) in general and juvenile myoclonic epilepsy (JME) in particular are normal on visual inspection, previous studies using advanced imaging techniques have suggested subtle structural and functional changes in JME patients, mostly localized to. In addition, it has been reported that these patients show neuropsychological deficits best attributed to frontal lobe function.

Method: We studied 18 JME patients and 20 age-, sex- and education-matched controls using a battery of standardized neuropsychological tests, optimized voxel based morphometry (VBM) to evaluate structural differences and two working memory paradigms combined with functional magnetic resonance imaging (fMRI) to assess an important functional aspect of the frontal lobe.

Results: Our investigations did not reveal statistically significant differences between the groups of JME patients and normal controls in both the VBM and the fMRI study for working memory. The neuropsychological examination showed a slightly worse performance for the JME patients across most tests used, reaching statistical significance for semantic and verbal fluency. These changes were correlated with the antiepileptic medication. In our cohort, we could not reproduce results from previous studies showing any changes in frontal gray matter in JME patients and we could not detect an fMRI correlate of previously reported differences in working memory in JME.

Conclusion: We conclude that structural and functional frontal lobe deficits are a questionable phenomenon in JME. The neuropsychological deficits may be attributed to antiepileptic medication.

084

CORRELATIONS OF MYOCLONUS SEVERITY ASSESSED WITH UNIFIED MYOCLONUS RATING SCALE WITH CLINICAL PHENOTYPE CHARACTERISTICS IN PATIENTS WITH UNVERRICHT-LUNDBORG DISEASE (EPM1)

J. Khyuppenen, M. Alikia*, P. Koskenkorva†, R. Vanninen†, E. Mervaala†, K. Eriksson‡, A. Lehesjoki§, and R. Kalviainen**

**University of Kuopio And Kuopio University Hospital, Kuopio, Finland; †Kuopio University Hospital, Kuopio, Finland; ‡Tampere University Hospital and University of Tampere, Tampere, Finland, and §University of Helsinki, Helsinki, Finland*

Purpose: Unverricht-Lundborg disease (EPM1, OMIM254800) is an autosomal recessively inherited neurodegenerative disorder characterized by stimulus-sensitive myoclonus and epileptic seizures. Severity and progression of EPM1 are known to vary from patient to patient even within the same family. We aim to provide additional characterization of the clinical disease phenotype and identify possible factors influencing patient-to-patient variations.

Method: Medical histories of 36 genetically verified EPM1 patients (31 expansion homozygotes and 5 compound heterozygotes) were collected retrospectively from hospital records. Myoclonus severity was assessed using standard protocol from video recordings of patients performing tests from the Unified Myoclonus Rating Scale (UMRS) panel. Verbal (VIQ) and Performance (PIQ) intellectual functioning were evaluated with three verbal and three performance subtests of the Wechsler Adult Intelligence Scale Revised. All patients underwent MRI and voxel-based morphometry (VBM).

Results: UMRS scores negatively correlated with the age of EPM1 onset ($P < 0.01$). Intellectual functioning, especially PIQ, of the EPM1 patients was found to be at the low average level and negatively correlate with myoclonus severity scores. Compared to age-matched controls, VBM showed gray matter volume loss in frontal premotor and supplementary motor areas, cuneus and thalamus bilaterally.

Conclusion: We present clinical results of the ongoing study aiming to unravel the disease mechanisms in EPM1. Age at EPM1 onset appears to be a significant predictor of the disease progression. Finally, intellectual functioning seems to be significantly affected in the course of the disease.

The study has been funded by the Academy of Finland, the NEURO Research Programme and UCB Pharma.

085
NEUROPSYCHOLOGICAL PROFILE IN PATIENTS WITH UNVERRICHT-LUNDBORG DISEASE

E. Ferlazzo, A. Magaudda†, A. Gagliano†, T. Calarese†, P. Striano‡, L. Cortese†, C. Cedro†, P. Bramanti*, P. Di Bella*, V. Laguitton§, M. Carbonaro‡, A. Albachiara‡, N. Fragrassi‡, A. Coppola‡, and P. Genton§*
**IRCCS Centro Neurolesi 'Bonino Pulejo', Messina, Italy; †University of Messina, Messina, Italy; ‡Federico II University, Naples, Italy, and §Centre Saint-Paul, Hôpital Henri Gastaut, Marseille, France*

Purpose: Unverricht-Lundborg disease (ULD) is characterized by action myoclonus, rare seizures and mild ataxia. Aim of this study was to evaluate neuropsychological profile of patients with ULD.

Method: We evaluated 20 ULD patients (13 M, 7 F) with diagnosis of ULD genetically confirmed and an average age of 35 years. Patients underwent a wide neuropsychological battery exploring intelligence (WAIS), executive functions (WCST, Stroop test, and verbal fluency), visuospatial and verbal short-term memory (Corsi test, 15 words of Rey). To examine association with anxiety and depression we used Hamilton Rating Scales. The same protocol was applied to 20 healthy matched controls.

Results: 11/20 patients with ULD presented a mild to moderate mental retardation and they had lower performances in all WAIS subtests, particularly coding, digit span, block design and arithmetic. ULD patients reported lower scores in all short-term memory and executive functions tasks, compared with controls. Moreover three patients presented a moderate to severe depression, while only 2 referred anxiety symptoms. A significant association between impaired performance to memory tests and duration of disease was observed trough linear regression analysis. On the contrary, no association was found between severity of myoclonus and all neuropsychological variables.

Conclusion: Most patients with ULD present a mild to moderate cognitive impairment. The mostly affected cognitive domain is short-term memory, while long-term memory is less impaired. Our findings are consistent with a decline of adaptive capacity related not only to motor symptoms, but also to a progressive cognitive impairment.

086
ICTAL HYPERSOMNOLENCE

M. Cenusa, I. Mothersill, and G. Krämer
Swiss Epilepsy Centre, Zurich, Switzerland

Purpose: Diagnostic reevaluation of patients presenting with unusual seizure semiology.

Method: Radio-Telemetry Video-EEG recordings of spontaneously occurring events.

Results: Ictal recordings showed in 3 patients seizures in which the sole clinical symptomatology was a hypersomnolent state. EEG findings were in two cases focal (left temporoparietooccipital and right temporo parietal), in the other bifrontal.

Conclusion: A single case of episodic hypersomnolence in conjunction with complex partial seizures or immediately following seizure discharges in the EEG has been reported (Wszolek et al., Epilepsia, 36:108–110, 1995).

Hypersomnolence as the sole clinical manifestation of an epileptic seizure has until now to our knowledge not been described. We describe three patients with therapy refractory epilepsy who were referred for diagnostic reevaluation implementing combined radio-telemetry/video-EEG. Ictal recordings showed in all patients seizures in which the sole clinical symptomatology was a hypersomnolent state. Ictal EEG findings were in two cases focal (left temporoparietooccipital and right temporo parietal), in the other bifrontal. Electrical stimulation has been used as an aid to the understanding of both the pathogenesis of epileptic seizures and the basic mechanisms of sleep. It has been shown that stimulation of thalamic, frontal and brainstem structures can elicit both sleep reactions or epileptic seizures, and perhaps more importantly epileptiform discharges in the EEG. This experimental evidence in conjunction with the clinical and ictal EEG findings in our patients suggests a subcortical involvement in the pathogenesis of this unusual seizure type.

087
A VIDEO-POLYGRAPHIC ANALYSIS OF ICTAL ORO-ALIMENTARY AUTOMATISMS

E. Gardella, E. Zambrelli*, S. Francione†, V. Chiesa*, L. Tassi†, A. Piazzini*, K. Turner*, A. Vignoli*, R. Canger*, G. Lo Russo†, and M. Canevini**
**Epilepsy Center – S. Paolo Hospital – Milan – Italy and †Epilepsy Surgery Center 'C. Munari'- Niguarda Hospital – Milan – Italy*

Purpose: to investigate the clinical and polygraphic features of different types of ictal oro-alimentary behaviors and to attempt to describe their localizing value.

Method: Among the series of patients selected for presurgical investigation in the last decade at S. Paolo Hospital and Niguarda Hospital, Milan, two independent observers analyzed seizures with oro-alimentary (OA) manifestations. A study of video-EMG-EEG/SEEG correlations has been attempted, in order to subdivide and classify clinical subgroups and to investigate their possible localizing value. The study of neuropsychological functions, in particular memory functions, has been compared in different clinical subgroups.

Results: We observed two main clinical-polygraphic subgroups of OA behaviors: (1) a chewing pattern and (2) an masticatory-deglutitory pattern. Most patients had a widespread ictal discharge in the temporal region concomitant with OA behaviors of type 1, while OA automatisms of type 2 could be related also with extratemporal involvement. The same pattern of chewing has been observed comparing ictal and postictal auto-

matisms and voluntary mastication in the same patient, while eating. Despite the lacking of a significant difference in memory scores in two OA subgroups, patients with ictal chewing behavior more frequently refer memory disturbances.

Conclusion: we propose a clinical division in subgroups of oro-alimentary ictal patterns, possibly involving different motor circuits. The polygraphic analogies between ictal and postictal chewing and voluntary mastication support the hypothesis that a releasing mechanism of the physiological central pattern generator for mastication is subtending ictal OA automatisms, probably resulting from inactivation of cerebral modulations of the motor control.

Wednesday 24 September 2008
11:30 – 13:00
Hall 9
Platform Session
Drug Therapy

088
TITRATION INFLUENCES INITIAL EFFICACY OF MONOTHERAPY IN NEWLY DIAGNOSED EPILEPSY

G. Sills, J. Leach‡, E. Wilson†, P. Parker†, K. Kelly†, I. Hamill‡, S. Yule‡, J. Greene‡, R. Duncan*,‡, and M. Brodie‡*
**University of Liverpool, Liverpool, UK; †Western Infirmary, Glasgow, UK, and ‡Southern General Hospital, Glasgow, UK*

Purpose: We have investigated the influence of titration schedules on short-term efficacy of levetiracetam (LEV), topiramate (TPM) and lamotrigine (LTG) in newly diagnosed epilepsy as part of an ongoing, long-term follow-up study.

Method: A total of 251 patients (143 male; median age = 35, range 16 to 99) with new-onset epilepsy were randomized to receive open-label LEV (n=81), TPM (n=85) or LTG (n=85), irrespective of seizure type or epilepsy syndrome. Daily target doses were 1000mg LEV, 100mg TPM, and 150mg LTG, achieved by titration over two, four, and six weeks, respectively. The primary outcome measure was seizure-freedom, determined at six weeks and three months after commencing treatment.

Results: Intention-to-treat analysis revealed that 63.0% of patients receiving LEV were seizure-free at six weeks after starting treatment, compared with 41.2% on TPM ($x2=7.89$, $p<0.01$) and 40.0% on LTG ($x2=8.75$, $p<0.005$). At three months, 49.4% of LEV patients were seizure-free, compared with 32.9% on TPM ($x2=4.64$, $p<0.05$) and 34.1% on LTG ($x2=3.98$, $p<0.05$). Median daily doses at six weeks were 1000 mg LEV, 100 mg TPM, and 100 mg LTG, with an increase to 150 mg LTG at three months. There were no significant differences among treatment groups in multiple demographic variables at baseline, including gender, age, epilepsy type, and total number of pretreatment seizures.

Conclusion: The ability to reach therapeutic doses of LEV within two weeks of starting treatment may confer an early advantage over TPM and LTG in comparable populations of patients with new-onset epilepsy and have implications for initial drug selection.

Disclosure: Supported by an unrestricted grant from UCB Pharma.

089
RETIGABINE AS ADJUNCTIVE THERAPY IN ADULTS WITH REFRACTORY PARTIAL-ONSET SEIZURES

J. French, and H. Mansbach†*
**New York University Comprehensive Epilepsy Center, New York, NY, USA and †Valeant Pharmaceuticals International, Aliso Viejo, CA, USA On Behalf of the RESTORE 1 Investigators*

Purpose: To determine the efficacy and safety of 1200 mg/day retigabine (RTG) as adjunctive therapy in adults with refractory partial-onset seizures.

Method: Multicenter, randomized, double-blind, placebo-controlled Phase 3 trial with 6-wk titration period and 12-wk maintenance phase. Patients with =4 partial-onset seizures/mo despite 1–3 AEDs during prospective baseline were randomized to placebo or RTG. Study drug was force-titrated to 1200 mg/d (400 mg tid), which was maintained for the duration of double-blind treatment (minimum maintenance dosage, 1050 mg).

Results: Of 306 patients randomized (placebo, n=152; RTG, n=154), 301 (placebo, n=150; RTG, n=151) received >1 dose of study medication and underwent >1 efficacy evaluation (intent to treat). Baseline demographics: mean age, 37 yrs; female, 54%; epilepsy duration, 23 yrs; >2 background AEDs, 84%. Median monthly seizure reduction during double-blind phase: RTG, 44.3%; placebo, 17.5% ($p<0.0001$); responder rate (=50% seizure reduction): RTG, 45%; placebo, 18% ($p<0.0001$). Differences in seizure reduction with RTG were also significant vs placebo during both titration and maintenance phases ($p<0.0001$). Discontinuations due to adverse events: RTG, 27%; placebo, 9%, with most occurring during forced titration. Adverse events with >10% incidence: dizziness, somnolence, fatigue, confusion, dysarthria, headache, urinary tract infection, ataxia, blurred vision, tremor and nausea.

Conclusion: Retigabine 1200 mg is effective and generally well-tolerated in adults with refractory partial-onset seizures, confirming findings from a Phase 2 dose-ranging study. These results validate the therapeutic usefulness of neuron-specific potassium (KCNQ/M-current) channel openers.

Funded by Valeant Pharmaceuticals International.

090
A HEAD-TO-HEAD COMPARISON OF PREGABALIN AND LAMOTRIGINE, INCLUDING A THIRD PLACEBO ARM, AS ADJUNCTIVE THERAPY IN PATIENTS WITH REFRACTORY PARTIAL ONSET SEIZURES

M. Baulac, T. Leon†, E. Whalen†, and J. Barrett†*
**University of Paris-APHP, Paris, France, and †Pfizer Global Pharmaceuticals, New York, NY, USA*

Purpose: Evaluate comparative efficacy of pregabalin as add-on treatment for reducing frequency of partial seizures compared with placebo and lamotrigine.

Method: 434 patients were randomized to pregabalin 300/600 mg/d, lamotrigine 300/400 mg/d, or placebo for 17 weeks of double-blind (DB) treatment. Phase 1: 11 weeks DB treatment, starting with titration period (pregabalin, 1 week; lamotrigine, 5 weeks). Dosage fixed for both at 300 mg/d after titration. Phase 2: additional 6 weeks DB treatment. Inclusion criteria: males and females ≥18 years old; diagnosis of epilepsy with partial seizures; minimum 4 seizures during 6-week baseline period; no 28-day seizure-free period. Primary efficacy measure was reduction in seizure frequency (RRatio).

Results: During Phase 1, RRatio between pregabalin (300 mg/d) and placebo groups did not reach statistical significance (−12.0, 95% CI: −19.8, −4.2, p=0.052), nor lamotrigine group versus placebo (−4.0, 95% CI: −11.9, 4.0, p=0.5) or versus pregabalin (−8.1, 95% CI: −15.9, −0.3, p=0.13). During Phases 1 and 2, difference in RRatio between pregabalin and lamotrigine was −8.2 (95% CI: −16.0, −0.4, p=0.0825) in favor of pregabalin. Responder rate (≥50% reduction in seizure frequency) was 36% pregabalin vs placebo (21%, p=0.007) and lamotrigine (24%, p=0.041). There was no significant treatment by cluster interaction during Phase 1 alone or Phases 1 and 2 combined. No new or unexpected AEs were reported.

Conclusion: This is the first head-to-head, placebo-controlled comparison of two newer AEDs in an adjunctive therapy setting. Based on

percent reduction in seizure frequency, pregabalin 300/600 mg/d was not superior to lamotrigine 300/400 mg/d.

Study funded by Pfizer Inc.

091

EFFICACY AND SAFETY OF ESLICARBAZEPINE ACETATE AS ADD-ON TREATMENT IN ADULTS WITH REFRACTORY PARTIAL-ONSET SEIZURES: BIA-2093-301 STUDY

C. Elger, P. Halasz†, J. Maia‡, L. Almeida‡, and P. Soares-da-Silva‡*

**University of Bonn, Bonn, Germany; †National Institute of Psychiatry And Neurology, Budapest, Hungary, and ‡BIAL – Portela & Co, SA, S Mamede Do Coronado, Portugal*

Purpose: To investigate the efficacy and safety of eslicarbazepine acetate (ESL) as adjunctive therapy in adult patients with ≥4 partial-onset seizures per 4 weeks despite treatment with 1–2 AEDs.

Method: During this multicentre, double-blind, parallel-group, placebo-controlled study, patients were randomized to placebo (n=102) or ESL 400 mg (n=100), 800 mg (n=98) or 1200 mg (n=102) once-daily after a 8-week baseline period. ESL was titrated at 400 mg weekly increments over 2 weeks and maintained for 12 weeks.

Results: The most frequently administered concomitant AEDs were carbamazepine (56%–62% of patients), followed by lamotrigine (24%–28%) and valproic acid (22%–28%). Primary analysis (ANCOVA of log-transformed seizure frequency in the intent-to-treat population) showed a significantly lower seizure frequency relative to placebo over the 12-week maintenance period in the 1200 mg (p=0.0003) and 800 mg (p=0.0028) groups. Median relative reduction in seizure frequency was 45% (1200 mg), 36% (800 mg), 26% (400 mg) and 16% (placebo). The responder rate was 43% (1200 mg), 34% (800 mg), 23% (400 mg) and 20% (placebo). Similar efficacy results were obtained in patients administered ESL with or without carbamazepine. Discontinuation rates due to treatment-emergent adverse events (TEAEs) were 3.9% (placebo), 4.0% (400 mg), 8.2% (800 mg) and 19.6% (1200 mg). TEAEs occurring in >10% in any group were dizziness, headache and diplopia. Most TEAEs were mild or moderate in severity.

Conclusion: ESL 800 mg and 1200 mg once-daily adjunctive therapy was well tolerated and effective in reducing partial-onset seizures in patients refractory to treatment with 1 or 2 concomitant AEDs. Efficacy of ESL was not altered when given concomitantly with carbamazepine.

Supported by BIAL- Portela & Co, SA.

092

A RANDOMIZED CONTROLLED STUDY OF AN IMPLEMENTATION INTENTION INTERVENTION TO ENHANCE ADHERENCE WITH ANTIEPILEPTIC DRUG TREATMENT

I. Brown, P. Sheeran, and M. Reuber

University of Sheffield, Sheffield, UK

Purpose: Suboptimal adherence with antiepileptic drug (AED) treatment is commonplace, and constitutes an important risk factor for status epilepticus and sudden unexplained death in epilepsy. Effective and easy-to-administer interventions to improve tablet-taking behavior therefore are needed. Implementation intention interventions (III), a simple planning technique, have proven effective in promoting behavior change. A prospective randomized controlled trial was used to evaluate the effects of III on AED adherence.

Method: 81 patients receiving AEDs for epilepsy (74% focal, 12% idiopathic generalized, 14% unclassifiable) were randomized. The mean duration of epilepsy was 20.1 years, 46% were taking AED monotherapy, 79% reported seizures within the previous year. 69 completed the objective adherence measure (electronic registration of pill-bottle openings, Medication Event Monitoring System, MEMS®) over a one-month observation period and completed self-report measures identifying moderating factors (Theory of Planned Behavior, Brief Illness Perception Questionnaire, Multiple Ability Self-Report Questionnaire, Hospital Anxiety and Depression Scale, Liverpool Seizure Severity Scale, Prospective and Retrospective Memory Questionnaire).

Results: Intervention participants showed improved adherence relative to controls on all outcomes: total doses taken (93.4% vs. 79.1%), days correct dose taken (88.7% vs. 65.3%), and on-schedule doses (78.8% vs. 55.3%), $p < .01$. Intervention effects were pronounced in participants who were at greatest risk of poor adherence (i.e., exhibiting poor understanding of epilepsy, emotional maladjustment to epilepsy, higher self-estimated missed doses, poor prospective memory scores).

Conclusion: III are an easy-to-administer and promising means of promoting AED adherence. Future studies should confirm the longer term effectiveness of the intervention.

093

THE IMPACT OF ADVERSE EFFECTS ON HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH PHARMACORESISTANT EPILEPSY: THE SOPHIE (STUDY OF PHARMACORESISTANCE IN EPILEPSY) STUDY

V. Alexandre Jr, S. De Fazio†, C. Fattore*, V. Franco*, B. Frassine‡, F. La Briola§, M. Ladogana¶, A. La Neve¶, L. Licchetta**, A. Papantonio††, S. Pellacani‡‡, E. Rosati§§, P. Striano¶¶, and E. Perucca**

**University of Pavia And Institute of Neurology IRCCS C. Mondino Foundation, Pavia, Italy; †Magna Graecia University, Catanzaro, Italy; ‡Epilepsy Center, C. Poma Hospital, University of Brescia, Brescia, Italy; §Epilepsy Center, San Paolo Hospital, Milan, Italy; ¶Epilepsy Center, University of Bari, Bari, Italy; **Institute of Neurology, University of Bologna, Bologna, Italy; ††Epilepsy Center, University of Foggia, Foggia, Italy; ‡‡Children's Hospital A. Meyer, Florence, Italy; §§Epilepsy Center, Careggi Hospital, Florence, Italy, and ¶¶Epilepsy Center, Federico II University, Napoli, Italy*

Purpose: In drug resistant epilepsy, treatment should aim at the best compromise between seizure suppression and adverse drug effects (AEs). We investigated the relative contribution of seizures and AEs to health-related quality of life (HRQOL) in adults with refractory epilepsy.

Method: A cross-sectional baseline evaluation was conducted in adults with refractory epilepsy included in a large multicentre prospective study. Patients enrolled consecutively at 11 tertiary centres were assessed for medical history, types and frequency of seizures, epilepsy diagnosis, comorbidities, previous and current treatments, AEs by clinical examination and unstructured interview, and results of Quality of Life in Epilepsy (QOLIE-31) and Adverse Events Profile (AEP) questionnaires.

Results: This analysis refers to the first 881 adults enrolled (mean age 41 years, range 16–86), 79% of whom were on polytherapy. Epilepsy was classified as focal in 755, generalized in 118 and undetermined in 8. Median number of seizures in the previous 6 months was 16 (range 1–3960). QOLIE-31 and AEP were completed by 791 patients and 224 had an AEP score ≥45. Spontaneously reported AEs were recorded in 303 patients. QOLIE-31 scores showed a strong inverse correlation with AEP scores ($r=-0.689$, $p<0.0001$) and a modest inverse correlation with seizure frequency ($r=-0.123$, $p<0.0005$).

Conclusion: In refractory patients seen at tertiary centres, HRQOL is influenced more by the AEs of treatment than by the frequency of seizures.

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Alexandre V Jr was supported by CAPES Foundation, Brazil.

Monday 22 – Wednesday 24 September 2008
Traditional Poster Session
Adult Epileptology

T094
THE RELATIONSHIP OF EPILEPSY AND INTELLECTUAL DISABILITIES IN AUTISM SPECTRUM DISORDERS AND ATTENTION – DEFICIT / HYPERACTIVITY DISORDER

M. Igor, M. Volodymyr†, M. Inna*, and B. Jana**
**Ukrainian Research Institutes Social Psychiatry and Drug Abuse, Kiev, Ukraine and †National Medical Academy Postgraduate Education, Kiev, Ukraine*

Purpose: Data regarding the presence of epilepsy in children with autism spectrum disorders (ASD) and attention-deficit / hyperactivity disorder (ADHD) were analyzed to explore the relationship among epilepsy, intellectual disabilities (ID), autistic and conduct behaviors.

Method: We studied 205 patients (ages 12–18) from a well-characterized longitudinal sample collected by Ukrainian Research Institutes Social Psychiatry and Drug Abuse who were referred for either ASD or ADHD. Verbal IQ (VIQ) and nonverbal IQ, ASD and ADHD diagnostic testing (ADI-R, CARS, Cohen's RS) scores from age 7–12 were analyzed. Presence / absence of epilepsy (>1 unprovoked seizure) was determined by chart review confirmed with interview. ASD and ADHD subjects with and without epilepsy were compared on IQ and measures of behaviors.

Results: The prevalence of epilepsy was greater in group ASD than in group ADHD (14% vs 10%). 21% of the ASD and 8% of the ASD patients with epilepsy had significant brain malformations. Epilepsy was associated with lower VIQ and NVIQ in both the ASD and ADHD groups. Epilepsy was not associated with more prevalent behaviors, but a trend for increased conduct behaviors in the ADHD epilepsy group was seen. The only notable difference between the ASD and ADHD groups with epilepsy. The number of ADHD epilepsy patients with VIQ<70 was no significantly higher than the ASD epilepsy group. All children with VIQ<50 have been concentrated in the ASD epilepsy group.

Conclusion: Epilepsy is associated with lower IQ scores both in ASD and ADHD groups. However, the increased number of patients with low VIQ scores in the ASD group and accumulation in this group of children with heavy forms of an ID has more of an impact on verbal function in ADHD, verbal and nonverbal function in autism.

T095
EPILEPSY AND COMORBIDITY

V. Duca
National Scientific Practical Center For Emergency Medicine, Moldova

Purpose: To determine the incidence of different comorbidities in epilepsy in women of childbearing age.

Method: The observational, randomized, prospective study was realized in Neurology Department of National Scientific Practical Center of Emergencies. Were investigated 80 women of childbearing age with different types of epileptic seizures, with range of ages 11 and 40. The investigation included the general and neurological women's examination and analyzed the medical history of every patient, special women's medical card and seizure diary.

Results: Among 69 women with simple partial seizures and complex partial seizures, 12 (17.3%) of them suffer from renal disorders, 13 (18.8%) – autoimmune thyroiditis, 4 (5.7%) – rheumatisms, 7 (10.1%) – menstrual dysfunction, 4 (5.7%) – head trauma, 2 (2.8%) – arachnoidian cyst and 27 (39.1) of unknown etiology (cryptogenic) epileptic seizures. In another group, which consist of 11 women with secondary generalized tonic-clonic seizures have been described 3 (27.2%) cases of menstrual dysfunction (a prolonged length of menstrual cycle, from 36 up to 43 days, persistence of polycystic ovaries), 3 (27.2%) cases of rheumatisms and 5 (45.4%) of unknown etiology.

Conclusion: The distribution among seizures and different diseases give us the following dates: most of the patients emphasized renal diseases and rheumatisms, which were determined by streptococcus, the second disease was autoimmune thyroiditis and only 10 (12.5%) cases with menstrual disturbances. The study suggests that the infection may play a more harmful role in evolution of epilepsy than we were expected. It is recommended to eradicate the infection and to observe its influence in the course of epilepsy.

T096
PREGNANCY AND BIRTH OUTCOMES IN FEMALES OF CHILD BEARING AGE IN MALTA

J. Mifsud, T. Camilleri*, and R. Galea†*
**University of Malta, Malta and †Mater Dei Hospital, Malta*

Purpose: Epilepsy in females of child bearing age belongs to a special population that require specific interventions, since pregnancy can result in high obstetric risks. The aim of the study was the evaluation of the outcomes in pregnancy in Maltese women with epilepsy.

Method: The medical and obstetric data records of mothers with epilepsy (PWE) who gave birth were reviewed from the 120 Monthly Birth Registers, 1996–2005. Data obtained was statistically analyzed and compared to that of the whole population.

Results: The data obtained was analyzed using student t-tests at the 5% significant level. In total, 58 birth outcomes in 46 PEW were documented. CBZ (n = 29) and PHT (n = 21) were the two most widely prescribed AEDs i: 60% were on monotherapy, 22% on two drugs, 9% on 3 drugs and 9% on no treatment. Birth weight, AGPAR scores and incidence of congenital anomalies fitted in with the general population, but there was a higher incidence of obstetric intervention in PWE (normal vaginal delivery 50% vs 74.8%).

Conclusion: The study population was too small to draw more statistically significant conclusions. Further studies to assess the level of risk of adverse outcomes over a longer follow up period are necessary. Setting up local prospective ongoing studies amongst PWE in a pregnancy registry in a small population can contribute to the pooling of data to larger international data centres and may change current practice in the management of epilepsy in women of childbearing potential.

T097
ALTERATIONS IN KCNJ4 POTASSIUM ION CHANNEL GENE EXPRESSION IN HUMAN TEMPORAL LOBE EPILEPSY

X. Wu, Z. Hong, G. Zhu, X. Gao, G. Zuo, and P. Yu
Huashan Hospital of Fudan University, Shanghai, China

Purpose: To evaluate the possible molecular pathogenesis of intractable temporal lobe epilepsy. 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 the function or expression of this gene would cause disturbance of ionic concentrations, thus leading to seizure activity.

Method: Reverse transcription polymerase chain reaction (RT-PCR) and western blot analysis were used 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 for intractable epilepsy (n=12). Tissue from 10 subjects who did not have epilepsy served as controls.

Results: The expression of KCNJ4 mRNA and its protein Kir2.3 were significantly decreased in epileptic brain compared with the controls (P<0.05).

Conclusion: The variation in KCNJ4 expression might be a potential etiological agent for TLE that may offer a novel target for anticonvulsant therapy.

T098
RESULTS OF VNS THERAPY IN PATIENTS WITH REFLEX EATING SEIZURES

A. Cukiert,†, J. Burattini*,†, P. Mariani*,†, C. Cukiert*,†, C. Baise-Zung*,†, C. Forster*,†, M. Argentoni-Baldochi*,†, and V. Mello**

**Epilepsy Surgery Program, Hospital Brigadeiro, São Paulo, Brazil and †Clinica de Epilepsia De São Paulo, São Paulo, Brazil*

Purpose: VNS therapy is stimulating the vagus nerve, which has extensive projections to gastrointestinal organs, to reach the central nervous system. Some patients have eating reflex seizures, alone or in combination with nonreflex seizures. We hypothesized that VNS therapy would have a differential effect in this subset of patients.

Case Reports: Patient 1: This 23 year-old, very thin man had daily refractory epigastric simple partial and complex partial seizures since the age of 8 years. Ninety percent of the seizures occurred during meals. His MRI showed bilateral perysilvian polimicrogiria and his interictal EEG showed independent bitemporal spiking. He was submitted VNS: final parameters were 2.0mA, 500Usec and 30Hz. All his reflex seizures disappeared. He remained with nonreflex complex partial seizures (once a month). He gained weight and has been able to adequately feed after VNS. Patient 2: This 34 year old woman had daily refractory complex partial seizures since the age of 6.

Seventy percent of her seizures occurred during meals. Her MRI was normal. She had been previously submitted to right temporooccipital resection at other institution. Postresection video-EEG recording at our institution recording showed that her seizures were coming from the left brain side. She was submitted VNS: final parameters were 2.5mA, 500Usec and 30Hz. Ninety percent of her reflex seizures disappeared. She remained with nonreflex complex partial seizures (once every 15 days).

Discussion: Eating reflex seizures responded extremely well to VNS. The improvement in seizure frequency was much higher in these 2 patients then usually expected for patients with complex partial seizures. We postulated that this differential seizure frequency outcome was related to both VNS antiepileptic activity and modulation of neural signaling from/to the gastrointestinal organs. VNS might prove to be the therapy of choice in patients with refractory eating epilepsy that are not amenable for resective surgery.

T099
VALPROATE-ASSOCIATED HYPERAMMONEMIC ENCEPHALOPATHY

C. Forster,†, A. Cukiert*,†, J. Burattini*,†, P. Mariani*,†, C. Cukiert*,†, M. Argentoni-Baldochi*,†, C. Baise-Zung*,†, and V. Mello**

**Hospital Brigadeiro, Sao Paulo, Brazil and †Clinica De Epilepsia De Sao Paulo, Sao Paulo, Brazil*

Purpose: Valproate is the drug of choice for patients with a variety of primary and secondary generalized epileptic syndromes. We describe 3 patients under this condition.

Case Reports: Patient 1: This 53-year-old woman presented with refractory generalized epilepsy. Her MRI was normal. In 2 attempts of introducing valproate she developed hyperammonemic encephalopathy characterized by impairment of consciousness and vomiting (ammonia higher then 200 micromol/l; normal range lower then 30 micromol/l) at very low (250mg/day) dosage of the drug. She responded rapidly to drug withdrawal in both circumstances. Patient 2: This 7-year-old boy presented with Lennox-Gastaut syndrome. He was taking valproate, topiramate and clobazan. He underwent an uneventful callosal section. After surgery, his level of consciousness was impaired. There was no surgical or systemic abnormality. Hyperammonemia was documented by the second postoperative day (ammonia levels higher then 250 micromol/l). After valproate withdrawal ammonia levels got to the normal range after 10 days. Six months postoperatively, we were able to reintroduce valproate in this kid regimen. Patient 3: This 10-year-old boy presented with refractory frontal lobe epilepsy. He was taking valproate and lamotrigine. He underwent an uneventful right frontal lobe resection. After surgery, his level of consciousness was impaired. There was no surgical or systemic abnormality. Hyperammonemia was documented by the third postoperative day (ammonia levels higher then350 micromol/l). After valproate withdrawal ammonia levels got to the normal range after 14 days. Eight months postoperatively, valproate was reintroduced in this kid drug regimen. Patients 2 and 3 anesthetic procedure made use of propofol and fentanil.

Discussion: There are probably two types of valproate related hyperammonemic syndromes. The first one (patient 1) is very likely related to patient unique metabolic profile. The second one (patients 2 and 3) is very likely related to an interaction between valproate and anesthetic agents.

T100
LEVETIRACETAM IN NEWLY DIAGNOSED LATE-ONSET POSTSTROKE SEIZURES: A PROSPECTIVE OBSERVATIONAL STUDY

V. Belcastro, C. Costa*, F. Galletti*, A. Autuori*, F. Pisani†, P. Calabresi*, and L. Parnetti**

**Clinica Neurologica, Università di Perugia, Perugia, Italy and †Clinica Neurologica, Università di Messina, Messina, Italy*

Purpose: Stroke is the most common causes of symptomatic epilepsy in the elderly. Most first-generation AEDs, exhibit important negative effects on cognition, behavior, bone health and motor function. Levetiracetam (LEV), one of the newer AEDs, has a favorable tolerability profile, no drug-drug interaction and may therefore be a valuable treatment in patients with poststroke seizures. This study was aimed at investigating the safety and efficacy of LEV monotherapy in patients with poststroke seizures.

Method: LEV monotherapy was investigated in 35 patients (pts) (16M/19F, 71.9+ 7.3 years of age) with late-onset poststroke seizures (i.e. seizures occurring at least 2 weeks after an ischemic stroke) in a prospective open-label study.

Results: Overall, 27 pts (77.1%) achieved a condition of seizure freedom (defined as one year without seizures): 19 (54.3%) at a daily LEV dose of 1000 mg, 7 (20.0%) at 1500 mg, 1 (2.8%) at 2000 mg. Four pts (11.4%) discontinued the drug because of intolerable side effects (drowsiness associated to gait disturbance in 1 pt, and aggressive behavior in the remaining 3 pts); 3 pts were unresponsive at a dose of 3000 mg, and 1 pt was lost to follow-up.

Conclusion: These observations suggest that LEV exhibits safety and efficacy profiles which make it an optimal candidate as a first-choice drug against poststroke seizures.

T101
ATYPICAL VALPROATE ENCEPHALOPATHY

I. Novotná, and M. Brázdil
St. Anne's University Hospital, Brno, Czech Republic

Purpose: The aim of this work was to find reasons of various ambiguous problems of a patient. Finally, valproate encephalopathy (typical symptoms: confusion, ataxia, focal neurological symptoms, more seizures, hepatopathy, hyperammonemia), an occasional complication of treatment of epilepsy, was determined.

Method: A 39-year-old man, from age of three observed and neurologically treated for cerebral tumor in tectum mesencephali; installation of Torkildsen shunt and radiotherapy in 1971. Histological type of tumor not known. Since 1991, he started having partial complex seizures (about one minute lasting), in the beginnings once a month. Progressively higher frequency of PCS. For intractable epilepsy since 2003 carbamazepine 900 mg/day, topiramate 200mg/day, valproate 1500 mg/day. Since 2006 bradypsychia, apraxia, ataxia, worsening of cognitive functions, weight loss. Suspections: tumor progression, nonconvulsive status epilepticus, influence of medication, which makes cognitive functions worse. Higher levels of valproate lead to worsening of the symptoms.

Results: MRI without progression of tumor, EEG in acute status: basal activity theta, frequent slow waves, without traces of nonconvulsion status. Ammonia 231 µmol/l. Speculations about valproate-induced encephalopathy. Valproate stopped: decrease of ammonia to 42,5 µmol/l., improvement of cognitive functions, other symptoms and EEG foundings, decrease in frequency of PCS.

Conclusion: The problems of the patient were determined, even without accomplishing of all criteria of valproate encephalopathy (high valproate and ammonia level, hepatopathy etc.). No other cause was found (tumor progression, shunt disfunction). After change of medication high improvement, nowadays carbamazepine and topiramate, less seizures, better EEG and neurological foundings.

T102
EPILEPSY IN THE ELDERLY—ETIOLOGY AND COMPLEXITY OF THE THERAPY

R. Corina, R. Ciprian*, R. Adina†, and B. Ovidiu†*
**Lucian Blaga University, Sibiu, Romania, and †University Emergency Hospital, Bucharest, Romania*

Purpose: Epilepsy is common in old age. Management of epilepsy in the elderly can be a challenging exercise and is an important clinical problem. The increasing awareness of this phenomenon has led to a better understanding of the etiology of seizures and complexity of pharmacokinetics in the elderly.

Method: We retrospectively analyzed data of elderly patients with epilepsy admitted in our Department from January 2005 until December 2007.

Results: The study included 157 patients with epilepsy older than 60; 95 M (60,5%),62 F (39,5%) 114 patients (72,6%) had newly diagnosed epilepsy. Aetiology of seizures included cerebrovascular diseases in 95(60.5%), degenerative diseases in 28 (17,8%), tumors in 13(8,2%), trauma in 12 (17,8%), alcoholism in 6(3,8%), meningoencephalitis in 3(1,9%). The initial antiepileptic drug (AED), was Carbamazepine in 82 (52,2%), Valproic acid in 31 (19,7%), Oxcarbazepine in 20 (12,7%), Carbamazepine plus Phenobarbital in 10 (6,3%), Lamotrigine in 7 (4,4%), Gabapentin in 1(0,6%). Lamotrigine was introduced as add-on therapy in 4 patients and Topiramate in 2 patients.

Conclusion: Cerebrovascular disease is the most common cause of new onset epilepsy in the elderly. Treatment is complicated by age related drug-drug and drug-disease interactions. Carbamazepin was preferred for focal seizures and valproic acid was the first choice agent for generalized tonic-clonic seizures. The newer AEDs oxcarbazepin, lamotrigine, topiramate also warrant some consideration as first line agents because of their efficacy and favourable side effect profiles.

T103
COMBINATION OF PARTIAL EPILEPSY WITH ABSENCES

V. Karlov, and V. Gnezdizky†*
**Moscow State Medico-Stomatological University, Moscow, Russia, and †Scientific Neurological Centre of Russian Medical Academy of Sciences, Moscow, Russia*

Our past clinical-neurophysiological (EEG, evoked potentials) epilepsy investigation has revealed same patients with medio-basal epileptogenic foci and hypomotor seizures, which turned out absences (Karlov VA et al. 1987) (Epilepsia 38:S214).

Purpose: Study of epileptic patients, who has shown the electrographic pattern of absence activity in EEG in order to analyze clinical display of this phenomenon in basic epilepsy forms and make clear its source.

Method: the EEG, EEG monitoring of night sleep and multistage dipole localization (MDL), Brainloc program were used.

Results: 100 patients age from 4 to 50 years were studied with electrographic pattern of absences in EEG: 54 had GIE (47- absence epilepsy forms), 7-PIE, and 39 symptomatic/probably symptomatic epilepsy with hypomotor sizures (S/PSE). After EEG and MDL investigation, clinical inhibitory motor seizures were qualified as absences in all patients with IE, but only in 9 among 39 with S/PSE. The highest rate of interictal spike localization in IE was registered in mediobasal frontal cortex (41 among 54) while in S/PSE- medial temporal and temporofrontal cortex. Postspike wave was registered in 81 patients in mediobasal frontal cortex and frontal pole independently of epilepsy forms.

Conclusion: 1. Electrographic manifestation of absence activity is revealed not only in IE, but also in S/PSE. About 8% patients with S/PSE and correlates of absence in EEG have clinical combination of partial seizures with absences. 2. Spike is originated in the 2/3 IE patients in the mediobasal frontal cortex, in S/PSE patients as a rule in medial temporal and temporofrontal cortex.

T104
PAROXYSMAL EXERTION-INDUCED DYSKINESIA, HEMOLYTIC ANEMIA AND EPILEPSY: ENERGY DEFICIT AND ELECTROLYTE SHIFT

A. Storch†, Y. Weber, T. Wuttke*, K. Brockmann‡, A. Pekrun§, J. Kempfle*, F. Lehmann-Horn*, and H. Lerche**
**University of Ulm, Ulm, Germany; †University of Dresden, Dresden, Germany; ‡University of Goettingen, Germany and §Prof. Hess Kliniken, Bremen, Germany*

Purpose: Paroxysmal dyskinesias are characterized by attacks of involuntary movements classified as kinesiogenic, nonkinesiogenic or exertion-induced. The pathophysiology of these syndromes is still unclear. We describe a novel autosomal dominant syndrome in a four-generation family with four affected individuals presenting with a combination of a paroxysmal exertion-induced dyskinesia, hemolytic anemia and epilepsy.

Method: The syndrome was characterized by extensive clinical, genetic and experimental studies.

Results: Three individuals suffer from attacks of involuntary movements with dystonic and choreoathetotic components after heavy workload since early childhood. The two sons of the index case show mild neuropsychological deficits, mild permanent motor problems and a focal epilepsy with myoclonic and atonic seizures with status epilepticus in fasting state. A good response of the symptoms to glucose infusion and

long term ketogenic diet was observed. Affected individuals presented with decreased CSF glucose, hemolytic anaemia, and increased intracellular sodium and decreased potassium concentrations in red blood cells, which showed an increased percentage of echinocytes. Genetic analysis of SLC2A1 encoding the glucose transporter type 1 (Glut1) revealed a mutation in the pore region. Functional analysis in Xenopus oocytes revealed a decreased glucose uptake and a cation leak of the mutant transporter compared to the wild type.

Conclusion: We propose that the dyskinesias are caused by an electrolyte shift in glial cells expressing the transporter which is due to the cation leak decompensating during prolonged exercise when not enough glucose as an energy source can be delivered across the blood–brain barrier.

T105
CLINICAL FEATURES OF CONVULSIVE STATUS EPILEPTICUS IN A CHINESE POPULATION

L. Chen, B. Zhou*, J. Li*, Y. Zhu*, J. Sander†, and D. Zhou**
**West China Hospital, Sichuan University, Chengdu, Sichuan, China, and †UCL Institute of Neurology, and The National Hospital For Neurology And Neurosurgery, Queen Square, London, UK*

Purpose: To understand the clinical features of convulsive status epilepticus (CSE) in a Chinese population, identify factors affecting prognosis, and to provide a basis for future CSE prevention and treatment.

Method: Patients with CSE hospitalized from January 1996 to October 2007 were prospectively observed. Demographic information, causes of disease, attack types and treatment methods were collected and compared data from with the United States and Europe. Logistic regression was used to identify the predictors of prognosis.

Results: The average age of the CSE patients (n=220) was 37.5 (SD 20.31) years, 46.4% of them were rural inhabitants, and 50% had a history of epilepsy. The primary cause of CSE was central nervous system (CNS) infection (32.7%), followed by discontinuation or decrease in the use of antiepileptic drugs (AEDs) (15.5%). The median duration of CSE before treatment was 2 hours and was longer in rural patients than in city patients ($P<0.05$). The fatality rate was 15.9%. Logistical regression analysis showed that the duration of CSE (OR 1.049, 95%CI 1.028~1.071), a history of epilepsy (OR 0.347, 95%CI 0.136~0.885), and respiratory depression (OR 5.956, 95%CI 2.490~14.244) were independent predictors of the prognosis of CSE.

Conclusion: In this population, the majority were from rural areas and had a history of epilepsy. CNS infection and the discontinuation or decrease of AEDs in the epilepsy patients were important causes of CSE. There exists a large gap between antiepileptic therapy in China and the European status epilepticus (SE) guidelines.

T106
IS THE CPAP THERAPY CAUSE TO SEIZURE REDUCTION AT THE EPILEPTIC PATIENTS WITH OSAS?

H. Yilmaz, K. Gunhan, and M. Demet
Celal Bayar University School of Medicine, Manisa, Turkey

Purpose: To investigate whether the severity of obstructive sleep apnea syndrome (OSAS) is associated with seizure exacerbation in the epileptic patients with OSAS and to investigate relationship between continuous positive airway pressure (CPAP) therapy and seizure frequency in the epileptic patients with OSAS.

Method: We retrospectively reviewed the database of our sleep centre to identify patients with both OSAS and epilepsy. Recordings were done using an Embla Recording Systems with somnologica software (Medcare, Reykjavik, Iceland) which was included continuous video-EEG monitoring and polysomnography. The effect of CPAP on seizure reduction was prospectively analyzed after a median interval of 17 months (range: 2–33 months) from the diagnosis of OSAS.

Results: OSAS was found in 57 epilepsy patients (35 men and 22 women) with a median age of 54 years (range: 21–79). The median apnea hypopnea index was 23 (range: 10–64), and 56% of the patients had an Epworth Sleepiness Scale (ESS) score >10. In 27 patients, epilepsy appeared 1 month to 44 years prior to the diagnosis of OSA. In 21 patients, the appearance of OSAS symptoms coincided with a clear increase in seizure frequency or severity of seizures. Treatment with CPAP was continued with good compliance in 33 patients and led to a significant reduction of both ESS scores and seizure frequency in 24 patients.

Conclusion: Our data to show that CPAP therapy reduce the seizures at the epileptic patients with OSAS and CPAP therapy is very important for the reduction of the seizures at the epileptic patients with OSAS.

T107
THE FUNCTIONAL ANATOMY OF HYPERKINETIC SEIZURES FROM TEMPORAL LOBE ORIGIN

L. Vaugier†, A. Mac Gonigal†, A. Trébuchon, S. Aubert†, M. Gavaret*, M. Guye*, J. Régis*, F. Wendling‡, P. Chauvel*, and F. Bartolomei**
**Université Aix Marseille 2, Marseille, France; †Assitance Publique Hôpitaux de Marseille, Marseille, France and ‡Université Rennes 1 & INSERM, Rennes, France*

Purpose: Hyperkinetic seizures are most often considered to originate from prefrontal cortex. Recently it has been suggested that this clinical picture can be found in patients with temporal epilepsy (Nobili et al, Neurology. 2004 Feb 10; 62(3):482–5) The objective of this study was to determine the features of temporal epilepsy with hyperkinetic seizures and the functional anatomy of involved brain networks.

Method: We have retrospectively searched from our database (2000–2008), patients in whom hyperkinetic manifestations were proved to be linked to an initial temporal lobe involvement. We have reviewed the data from 130 consecutive drug-resistant patients that benefited from intracerebral recordings (Stereoelectroencephalography, SEEG). Anatomy of seizures was determined according to visual analysis and to signal analysis aiming at determining the initial involved brain networks as well as the networks involved during clinical manifestations.

Results: We found 7 patients among 130 SEEG investigations that full-filled the inclusion criteria. Most of the patients presented with seizures occurring (or predominating) during sleep. Behavioral modifications were found to occur rapidly after seizure onset, often marked by emotional facial changes. Motor changes included axial rotation, bimanual/bipedal activity, axial and pelvic movements with sexual connotation. SEEG analysis demonstrated a common temporofrontal network in which the temporal pole played a central role. Rapid involvement of medial 'limbic' prefrontal structures was also a particular feature of these seizures.

Conclusion: Temporofrontal seizures must be recognized as an important cause of hyperkinetic seizures. The temporal pole and its connexions with mediobasal prefrontal cortex represent the main structures involved in epileptogenic networks.

T108
INSULIN-DEPENDENT DIABETES MELLITUS, ANTI-GAD ANTIBODIES AND WELL-CONTROLLED TEMPORAL LOBE EPILEPSY OF ADULT ONSET

M. Falip, M. Carreño†, M. Aiguabella*, A. Donaire†, I. Maestro†, and S. Fernández†*
**Hospital General Universitari Bellvitge, Hospitalet De LLobregat, Spain and †Hospital Clínic I Provincial, Barcelona, Spain*

Introduction: Previous reports have observed an association between focal drug resistant epilepsy and antibodies to glutamic acid decarboxylase (antiGAD) in insulin-dependent diabetes mellitus (IDDM) patients.

Purpose: To present three patients with IDDM and antiGAD antibodies diagnosed of well-controlled temporal lobe epilepsy.

Method: Patient 1. 60-year-old woman with IDDM since childhood whose epilepsy started at 51. She suffered complex partial seizures without aura (1seizure/3 months) and the EEG showed focal spikes over the right frontotemporal region. Cranial magnetic resonance (MR) was normal. AntiGAD antibodies titles were 77UI/ml (<1UI/ml) and antithyroid antibodies were also high. After initiation of antiepileptic drug treatment (AED) she was completely seizure free, although she suffered important memory decline. Patient 2. 36-year-old woman who was diagnosed of temporal lobe epilepsy and IDDM at 30. Her seizures started with psychic aura (dejà-vú) and were always related with mild hypoglycemia (>40 mgr/dl). MR was normal and antiGAD antibodies titles were 22.7 UI/ml. After controlling episodes of hypoglycemia the epilepsy was also controlled. Patient 3. 53-year-old woman whose epilepsy started at 46. She referred no aura followed by complex partial seizures with ictal speech. The MR showed bilateral hippocampal sclerosis. Late onset IDDM was diagnosed at 50. AntiGAD antibodies titles were 79.9 UI/ml. The epilepsy was completely controlled after introducing AED but she referred progressive memory decline since the epilepsy onset.

Conclusion: AntiGAD antibodies can be observed not only in focal drug resistant epilepsy. All IDDM patients who start seizing should be tested for antiGAD antibodies.

T109

MAGNETIC RESONANCE TOMOGRAPHY (MRI) IN PATIENTS WITH VAGUS NERVE STIMULATOR (VNS)

Y. Weber, R. Roebling, and H. Lerche
University of Ulm, Ulm, Germany

Purpose: In general, it is possible to perform a cranial MRI in patients with VNS. The VNS should be switched off and a head coil in a magnetic field of 1.5 Tesla or lower used. In other parts of the body, an unpredictable risk for adverse events is present such as dislocations, heating of the tissue surrounding the stimulator or a change of the parameters.

Method: We describe the performance of a cervical MRI in a 72-year-old patient in an emergency situation.

Results: The patient suffered from a focal epilepsy with frequent complex partial and generalized tonic–clonic seizures and a depression since many years. The VNS was implanted 5 years ago. Since the VNS therapy, she had only a slight reduction in seizure frequency, but improved in the depression. Before hospitalization, she suffered from an initially stable fracture of the sixth cervical spine after a generalized tonic–clonic seizure. Several days later, a fast progressive paraparesis up to paraplegia was observed.

Without any complications, a MRI was performed using a neck array in a 1.5 Tesla machine. The MRI showed a nearly complete compression of the spinal cord in the distal cervical spines. The region was then stabilized ventrally. After the operation, the paraplegia of the patient ameliorated to a light proximal paraparesis up to date.

Conclusion: We would propose here that, in emergency cases, a MRI of other regions than the skull is possible in patients with VNS.

T110

10-YEAR FOLLOW-UP AFTER TEMPORAL LOBE RESECTION

H. Meencke, D. Meinken-Jäggi*, T. Lehmann†, and F. Schmitt**
**Epilepsy Center Berlin Brandenburg at Ev. Krankenhaus Königin Elisabeth Herzberge, Germany, and †Charité Campus Virchow-Klinikum Clinic For Neurosurgery Berlin, Berlin, Germany*

Purpose: Epilepsy surgery is a wide established measure in pharmacoresistant focal epilepsy. There is a rate of seizure free patients after one year of 66,6%. There is very little data about long term seizure outcome exceeding two years.

We have analyzed seizure outcome ten years after epilepsy surgery of pharmacoresistant temporal lobe epilepsy.

Method: We analyzed the records of all consecutively operated patients with temporal lobe epilepsy operated on before May 1997 with a minimum follow up of ten years. The outcome was defined by the Engel Outcome Classification and has been prospectively documented in the patient records.

The surgical approach was a modified very restricted temporal pol resection and amygdalohippocampectomy.

Results: Age range of 50 patients was between 9.98 and 58.2 years. 60% had a left sided, 40%, a right sided temporal lobe epilepsy. The class I outcome over ten years was changed year by year between 78% and 74%. Completely seizure free since operation were 48% of the patients (Class IA). Never seizure free were 6 patients (12.5%). After ten years 20 patients were seizure free with out antiepileptic drugs (40%).

From 9 patients having seizures in the first two weeks after surgery, two became completely seizure free. From 11 patients suffering from seizures within the first six month after surgery five patients became completely seizure free.

Conclusion: We report about an excellent seizure outcome ten years after surgery of temporal lobe epilepsy. Half of the patients are completely seizure free since surgery. The year by year analysis shows class I outcome between 74% and 78%. 40% of the patients which are seizure free without antiepileptic drugs can be aspected as cured. This excellent outcome is due to a careful patient selection.

T111

MORTALITY AND NATURAL HISTORY AND OF EPILEPSY IN A POPULATION BASED PREVALENT COHORT OF PWE IN RURAL BOLIVIA: A TEN-YEAR FOLLOW-UP STUDY

V. Sofia, A. Nicoletti*, M. Zappia*, A. Bartoloni†, F. Bartalesi†, P. Preux‡, D. Tran‡, V. Bejarano§, S. Bonelli†, G. Vitale*, and E. Bruno**
**University di Catania, Catania, Italy; †Infectious and Tropical Diseases Unit, University of Florence, Florence, Italy; ‡Institute of Neuroepidemiology and Tropical Neurology (EA 3174)2, Limoges, France, and §Health District of The Cordillera Province, Camiri, Bolivia*

Purpose: To evaluate mortality and natural history in a population-based prevalent cohort of PWE, in the rural area of Bolivia.

Method: During 1994–1996 we carried out a two phase door-to-door epidemiological survey in a sample of 9,995 subjects living in 55 rural communities of the Cordillera province. At the end of the prevalence survey we identified 130 PWE who fulfilled the diagnostic criteria proposed by ILAE on 1993. Of these 130 subjects, 118 were classified as 'active epilepsy' (66 were classified as having partial seizures and 52 as generalized seizures); 33 of the 118 PWE (28%) were affected by NCC. We carried out a follow-up of this prevalent cohort of 118 'active' PWE about 10 years after the prevalent survey.

Results: During the follow-up survey we traced 103 (87.3%) of the 118 active PWE previously identified. Ten of the 103 subjects died during the follow-up period giving a mortality rate of 9.7/1000 (95%CI 5.3–16.6); three died due to causes possibly related with epilepsy. Five (50%) of the 10 died subjects were affected by NCC. Out of the 93 traced PWE still alive, adequate information on the occurrence of seizures was available for 68 subjects of whom 31 (45.6%) were seizures free for more than five years (not active epilepsy).

Conclusion: Mortality risk at 10 years in this well defined population based cohort of PWE was 9.7/1 000. Highest mortality risk was found in PWE affected by NCC; 50% of PWE who died were in fact affected by NCC.

T112
LONG-TERM TREATMENT WITH TOPIRAMATE MONOTHERAPY IN EPILEPSY

A. Schreiner†, B. Schauble, and K. Rettig‡*
**Medical & Scientific Affairs, Janssen-Cilag, Neuss, Germany; †Medical & Scientific Affairs, Janssen-Cilag EMEA, Neuss, Germany and ‡GEM mbH, Meerbusch, Germany*

Purpose: To describe long-term outcomes of topiramate treatment in epilepsy (TOP-GER-11).

Method: Subjects with a diagnosis of epilepsy (ILAE, 1989) who had completed one of two recent trials with topiramate (TOP-GER-5 and TOP-GER-12) were eligible for this 12-month prospective, noninterventional trial. Patients were evaluated during their previous trial and after 3, 6, 9, and 12 months during this trial (seizure frequency, AEs). A post hoc gender-based analysis was added.

Results: Median follow up was 19 months (ITT = 102 patients, 51% male, mean age 43±17). Mean duration of epilepsy in men vs. women was 54 months (SD±96) vs 68 months (SD±138.2). Generalized epileptic syndromes were more frequent in women than men (66% vs 48%). More women switched due to side effects (50% vs 35%) or lack of efficacy (48% vs 25%). Initial TPM monotherapy was more frequent in men (52% vs 36%). Median dose of TPM was 100mg/day for both genders unchanged from previous trials. 73% of patients were seizure free for at least 12 months with no gender differences. There was no difference in response between final visits. 5% of patients discontinued the long-term study prematurely due to an AE, 3% due to lack of efficacy. Treatment related AEs were paresthesias (12%), nausea (6%), somnolence (5%), decreased appetite (5%) and memory-/concentration- disturbances (6%).

Conclusion: Long-term monotherapy with topiramate resulted in sustained seizure reduction in both men and women. In addition topiramate doses remained generally unchanged and topiramate was well tolerated in both genders.

T113
SEVERE EARLY ONSET OSTEOPOROSIS IN FIVE YOUNG MEN WITH AN INTELLECTUAL DISABILITY, EPILEPSY AND LONG-TERM ANTIEPILEPTIC DRUG USE

K. Beerhorst, M. de Krom*, B. Aldenkamp†, and F. Tan†*
**University Hospital Maastricht, Maastricht, The Netherlands and †Epilepsy Centre Kempenhaeghe, Kempenhaeghe, The Netherlands*

Purpose: We report 5 men diagnosed with early onset osteoporosis after use of antiepileptic drugs (AEDs) to draw attention to the lack of official guidelines on osteoporosis in people with epilepsy.

Method: Case reports.

Results: In five young males with an intellectual disability, aged between 19 and 38 years with epilepsy and long-term AED use (mean number AEDs 4, range 1–5, range AED use 14–34 year), all sustained one or more fractures, osteoporosis (range DEXA T-score -3.3 – -2.4) was diagnosed. One patient was nonambulant, two patients were treated with cyproterone because of hypersexualism, which drug is also associated with the development of osteoporosis (1). In all patients antiresorptive bone therapy was started.

Conclusion: These case reports draw attention to the possibly underestimated effect of AEDs on the development and osteoporosis with consequently increased fracture risk, not only in postmenopausal women, but also in children (2) and as reported here also in young males. Furthermore the combination of cyproterone and AEDs is an additional risk factor. Screening for osteoporosis is in our opinion compulsory in this patient class. However European or AAN guidelines on the management of osteoporosis in people with epilepsy with or without intellectual disability are still lacking. Further investigations on this subject should result in protocols for surveillance and treatment of osteoporosis in people with epilepsy.

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T114
ABNORMAL FINDINGS OF EEG IN PATIENTS WITH POST TRAUMATIC HEADACHE

R. Susak, D. Janculjak, S. Juric, and S. Soldo Butkovic
Clinical Hospital Osijek, Osijek, Croatia

Purpose: The modern view of posttraumatic symptoms is that they have a biological or organic basis even in mild concussion. In general patients with posttraumatic syndrome do not show objective signs of evidence of morphological changes in the CNS using usual instrumental procedures, including cranial tomography and magnetic resonance.

Results of neuroelectrophysiological studies in patients with acute posttraumatic headache are inconsistent and electroencephalography (EEG) is generally not accepted as an assessing tool for its prognosis. In this study we evaluated the EEG findings and clinical features of patients presenting with posttraumatic headache in the outpatient clinic setting.

Method: The study group consisted of 79 outpatients (40 males and 39 females, mean age 38 years, range 12 to 79 years) with posttraumatic headache who had attended our neurological outpatient clinic during one calendar year. Standard EEG was performed in all patients as a routine assessment tool. In a selected subgroup of patients EEG was repeated to monitor abnormal changes.

Results: 23 out of 79 patients with posttraumatic headache have changed EEG. 3/23 have neurological deficit. None of them have epileptic seizures. 12 (23) patients have psyhological changes.

Mild head injury: 40% patological changes, Celebral concussion: 25% patological changes, Severe brain injury: 30% patological changes, Abnormal findings in first EEG recording: Slight dysrhytmia: 15/23 patients, Paroxismal dysrhytmia: 4/23, Focal changes: 3/23, Diffuse dysrhytmia: 1/23 Repeated EEG showed 50% same changes, 30% was better and 20% was worse.

Conclusion: Abnormal findings of EEG were found in significant proporcion of patients presenting with posttraumatic headache, most notably after mild head injury. First indication of repeated EEG findings suggests that such changes may disappear after a shorter period of observation. A larger follow-up study is needed to evaluate clinical relevance of those phenomena.

T115
TO SKIP OR NOT TO SKIP THE MORNING ANTI-EPILEPTIC DRUG DOSE PRIOR TO EEG?

S. Kipervasser, T. Vishne†, and M. Neufeld**
**Tel Aviv Sourasky Medical Center, Sackler Medical School, Tel Aviv University, Tel Aviv, Israel, and †Ness Ziona Mental Health Center, Beer Yaacov, Israel*

Purpose: To determine the effect of postponing the morning dose of antiepileptic drug (AED) prior to an EEG on the likelihood of obtaining increased epileptiform activity in the recording.

Method: This prospective study was conducted on patients undergoing video EEG monitoring. On the first full day of recording, each patient received the usual AED dosage at 8 a.m; the following day, the medication was postponed until 11 a.m. Using this 3-hour time frame, we counted the interictal spikes in one-hour intervals and compared the corresponding hour's epileptiform activity for each day.

Results: There were 50 patients. M/F = 28/22. Mean age 32 years (range 16–62 years). Three patients had generalized epilepsy and 47 had focal epilepsy. Comparing the number of spikes with and without medication yielded no significant differences either in the 1st, 2nd or 3rd hour: 1st hour: 5.5±15.8 vs. 5.1±9.4 spikes, p=.814; 2nd hour: 8.1±26.6 vs. 7.7±13.9 spikes, p=.901; 3rd hour: 6.0±19.7 vs. 4.6±10.4 spikes, p=.540. Age, gender, type of epilepsy, disease duration, seizure frequency and type of AED did not influence the change in number of spikes.

Conclusion: Skipping the morning dose of AED prior to EEG offers no additional information regarding the appearance of epileptiform activity.

T116
OPINION OF BELGIAN NEUROLOGISTS ON ANTIEPILEPTIC DRUGS IN 2006: BELGIAN STUDY ON EPILEPSY TREATMENT-2 (BESET-2)

B. Legros, D. Peter†, S. Bernard‡, S. Eric§, V. Kenou¶, and B. Paul***
**ULB-Hôpital Erasme, Brussels, Belgium; †Universitair Ziekenhuis, Antwerpen, Belgium; ‡CHU Sart-Tilman, Liège, Belgium; §VUB-Academisch Ziekenhuis, Brussels, Belgium; ¶Centre Neurologique William Lennox, Ottignies, Belgium, and **Universitair Ziekenhuis, Gent, Belgium*

Purpose: To describe the choice of treatment in adult patients with epilepsy in Belgium in 2006 and to detect the presence or absence of consensus among neurologists in epilepsy treatment.

Method: In December 2006, a sample of 100 neurologists, representative of the entire neurological community in Belgium, practicing both in teaching and academical hospitals and in regional hospitals were personally interviewed with a structured questionnaire, based on ordinal 4-point scales. The questionnaire contained questions on treatment choices and strategies in adult patients with epilepsy.

Results: Initial monotherapy was the preferred treatment strategy. Valproate was first choice in idiopathic generalized epilepsy for all seizure types (tonic–clonic, absence and myoclonic seizures). Carbamazepine and oxcarbazepine were first choice in focal epilepsy with simple and complex partial seizures. Both drugs and valproate were first choice in focal epilepsy with secondarily generalized seizures. The new AEDs were usually recommended in second-line. However, in special treatment situations, they were considered first-line, e.g. lamotrigine in case of women in childbearing age.

Conclusion: Neurologists reached consensus for most questions on epilepsy treatment. In end 2006, old drugs like carbamazepine and valproate and the newer drug oxcarbazepine were considered to be first choice drugs, whereas other newer drug, like lamotrigine, levetiracetam and topiramate were predominantly prescribed in second-line. Belgian neurologists, except for some special situations still prefer old drugs as first line.

T117
NOCTURNAL SYNCOPES OFTEN MISDIAGNOSED AS EPILEPSY

M. Aiguabella, M. Falip, M. Veciana, and X. Sabaté
Hospital de Bellvitge, Barcelona, Spain

Purpose: Nocturnal paroxistic events and transitory loss of consciousness have a large differencial diagnosis. They occur in supine position while the patient is sleeping, and most of the times a nocturnal syncope is never considered in the differential diagnosis. We present five cases diagnosed initially as epilepsy, in whose further evaluations demostrated a vagal or cardiogenic origin.

Method: We included all patients with exclusively paroxistic nocturnal events first diagnosed and treated as epilepsy. During the reevaluation in our center—a tertiary hospital with monographic epilepsy consultation- this diagnosis was ruled out. Vagal, cardiac or cerebral hypoperfusion origin was proved. In all patients antiepileptic treatment was discontinued, and after a minimum follow-up of one year the evolution was excellent.

Results: Five patients (three men and two women) were included, mean age was 49. Four patients developed loss of consciousness, and in three of them followed by clonic movements of the limbs. A positive tilt test gave us a concluent diagnosis of vasovagal syncopes in three patients. The other one had a cardiogenic syncope because of a pacemaker dysfunction. The fifth suffered from frequent nocturnal confusional episodes with abnormal movements of superior limbs. These episodes disappeared after a surgical treatment of a severe aortic stenosis, being diagnosed as episodes of cerebral hypoperfusion.

Conclusion: Supine nocturnal paroxistic events have a varied aethiology, among which we should include cardiogenic as well as vasovagal syncopes and cerebral hypoperfusion events.

T118
PREGABALIN AS ADJUNCTIVE THERAPY FOR PARTIAL EPILEPSY: AN AUDIT STUDY IN 101 PATIENTS FROM THE SOUTHEAST OF ENGLAND

A. Valentin, N. Moran†, *, R. Hadden*,‡, A. Oakes§, R. Elwes¶, S. Delamont*,‡, N. Mullatti¶, and L. Nashef**
**King's College London, London, UK; †Kent and Canterbury Hospital, Canterbury, UK; ‡Maidstone and Tunbridge Wells NHS Trust, Maidstone, UK; §Dartford and Gravesham NHS Trust, Dartforth, UK, and ¶King's College Hospital, London, UK*

Purpose: Pregabalin is a recently licensed new antiepileptic drug used as adjunctive therapy in focal epilepsy, neuropathic pain and generalized anxiety in adults.

Method: We performed an audit on 101 consecutive patients (45 male) prescribed with pregabalin for refractory epilepsy.

Outcome was determined in relation to seizure freedom, reduction in seizures, seizure pattern, retention rate and side-effect profile. Mean follow-up, for those who remained on pregabalin was 21 months (range 3–39).

Results: Fifty-five patients remain on pregabalin, 41 of whom reported clear improvement in seizure frequency. Among these 41 patients, 2 became seizure free (mean duration 11 months), 31 had a seizure reduction of >50%, and 8 improved by <50%. Nine patients reported improvement due to less severe seizure pattern, without change in seizure frequency. Eleven patients reported an improvement in anxiety or mood/well-being. Side effects were reported by 26 patients out of the 55 patients still on treatment: 12 reported drowsiness or tiredness, 8 weight gain, 7 dizziness, 2 headache, 1 irritability, 1 itchiness, 1 anxiety, 1 nausea feelings, and 1 transient rash. Among the 45 patients who discontinued treatment, 9 had worsening of seizure frequency, 27 showed lack of efficacy and 8 had intolerable side effects (4 dizziness or drowsiness, 2 weight gain, 1 peripheral edema, 1 pain in arms and legs). One patient had a seizure related death within one month of starting pregabalin.

Conclusion: Pregabalin seems an effective and well tolerated antiepileptic drug when used as add-on treatment in patients with refractory partial epilepsy.

T119
EPILEPTIC SEIZURES AND ANTIEPILEPTIC TREATMENT IN PATIENTS WITH HIV

M. Fischera, K. Anneken, K. Christoph, H. Ingo Wilhelm, and E. Stefan
University Münster, Münster, Germany

Purpose: Seizures are a common manifestation in HIV-positive patients as they often suffer from disorders of the central nervous system (CNS).

Method: In our study we enrolled patient charts of all HIV-infected patients with epileptic seizures who presented to the neurological inpatient clinic of the University Hospital of Münster, Germany, between 2004 and 2007. Additional seizure type was classified and seizure frequency as well as seizure cause was determined.

Results: 15 HIV-infected patients (10 male, 5 female) had at least one epileptic seizure. Seizure etiology was progressive multifocal leucencephalopathy (PML) in five (33%), encephalitis in four patients (27%), AIDS dementia complex in one, CNS toxoplasmosis in one, cerebral cryptococcosis in one patient and concurrent etiology in three patients (20%).

Seizures were generalized tonic–clonic in four (27%), partial motor in seven (47%) and partial motor with secondary generalization in four patients (27%). Antiepileptic drug (AED) treatment was gabapentine in six cases (40%), carbamezepine in one, clonazepame in one case and AED polytherapy in seven cases (47%). After HAART therapy three patients (20%) had a seizure reduction, nine patients (60%) had a seizure increase – after AED treatment only two patients (13%) complained of seizure increase, nine patients had a seizure reduction (60%).

Conclusion: The majority of patients with HIV infection and seizures have secondary brain lesions as seizure etiology. As 60% had a seizure reduction after AED treatment an anticonvulsant therapy after the first seizure has been recommended.

T120
EFFECTIVENESS AND TOLERABILITY OF TOPIRAMATE IN THE TREATMENT OF EPILEPSY IN ELDERLY PATIENTS WITH NEW ONSET VERSUS LONGER DURATION EPILEPSY

H. Stefan, F. Kerling*, B. Kasper*, A. Schreiner†, J. Krimmer‡, and B. Schauble§*
**Center of Epilepsy, University of Erlangen, Germany; †Medical & Scientific Affairs EMEA, Janssen-Cilag, Neuss, Germany; ‡ClinAssess, Leverkusen, Germany, and §Medical & Scientific Affairs, Janssen-Cilag, Neuss, Germany*

Purpose: To explore seizure outcomes and tolerability of topiramate (TPM) in mono- or combination therapy in elderly patients with epilepsy with either new onset (NOE) or longer duration epilepsy (LDE).

Method: Prospective, multicenter phase IV clinical trial enrolling patients ≥60 years for 12 months. Doses of TPM and concomitant antiepileptic drugs could be adjusted individually. Seizure frequency and adverse events were documented at each visit.

Results: 107 patients (53% male, mean age 69±7 years) enrolled. 52 patients had NOE (disease duration <1 year) with a median baseline seizure frequency of 0.83/4 weeks (interquartile range (IQR) 0.67–1.83) and 1.33/4 weeks (IQR 0.67–2.33) in patients with LDE (≥1 year). At endpoint, mean TPM monotherapy dose was 98 mg/day and 153 mg/day as add-on. Median seizure frequency / 4 weeks decreased to 0 in NOE (IQR 0–0.47) and 0.14 in LDE (IQR 0–0.84); both p<0.0001 versus baseline. Differences in baseline and absolute seizure frequency change between groups (NOE vs LDE) were nonsignificant (p>0.05). However, 58.8% of patients with NOE were seizure free throughout the trial which contrasts to 29.4% of patients being seizure free in the LDE group (p=0.005, Fisher's exact-test). 43% had at least one treatment-emergent adverse event (TEAE). TEAEs >=5% were somnolence (9.4%), dizziness (7.5%), paraesthesia (5.6%), memory disturbance (5.6%) and depression (5.6%).

Conclusion: In elderly patients with epilepsy, TPM was well tolerated and associated with a high number of seizure free patients which was highest among patients with recent onset epilepsy.

T121
INITIAL TREATMENT WITH TOPIRAMATE IN HOSPITALIZED PATIENTS – A PROSPECTIVE, OBSERVATIONAL STUDY

B. Schauble, A. Schreiner†, and K. Rettig‡*
**Medical & Scientific Affairs, Janssen-Cilag, Neuss, Germany; †Medcial & Scientific Affaris EMEA, Janssen-Cilag, Neuss, Germany, and ‡GEM, Meerbusch, Germany*

Purpose: To explore effectiveness outcomes of hospitalized patients with epileptic seizures treated with topiramate (TPM).

Method: Prospective observational study in hospitalized patients >12 years with epilepsy being evaluated in-house (visits V1-V3) and during an optional follow up visit. Seizure frequency, AEs were documented.

Results: 154 patients (53% male; mean age 61 years±19) were selected. 84% were treatment naive. 81% with data from V4 continued on TPM. Mean age in treatment naive patients was higher than in pretreated patients (63 years vs. 50 years, p<0.002). Therapy naive patients were older at first diagnosis and epilepsy duration was shorter (p<0.0001). Reasons for hospitalization were acute epileptic seizures (73%), diagnostic workup (29%). Reasons to initiate TPM were comorbidities (66%), concomitant medication (42%) or advanced age (39%). Median dose of TPM at V3 was 50mg/day. At V4 (median 103 days) median maximum daily dose was 75mg/day. Seizure frequency decreased from 11±70 /4 weeks during the retrospective baseline to 3±11 (p<0.001) at end point (V3). 82% were seizure free during the hospitalisation. 58 treatment related AE were reported. AE ≥ 3%: headaches (3%), aggressiveness (3%), weight reduction (4%), paresthesias (7%), and dizziness (12%).

Conclusion: This explorative study suggests that in hospitalized patients TPM is well tolerated given the low discontinuation rate due to adverse events. Even doses below the recommended initial target dose are associated with a significant seizure reduction.

T122
RHYTHMICITY OF EPILEPTIC SEIZURES OVER A 24-HOUR DAY, DETECTED BY INTRACRANIAL EEG-ELECTRODES

R. Van Regteren, B. Grootemarsink, W. Hofstra, and A. De Weerd
SEIN, Zwolle, The Netherlands

Purpose: Knowledge that the occurrence of seizures is influenced by the circadian rhythm is limited. In a previous study we differentiated more precisely the occurrence of seizures within 24 hours using superficial EEG recording. The current study aims to describe the rhythmicity of epileptic seizures over 24 hours using intracranial EEG recording.

Method: In 25 patients data was obtained after placing intracranial grid electrodes. Seizures were documented during longterm video and intracranial EEG registration (for at least 40 hours). A seizure was defined as an epileptic event when a clinical and electroencephalographic change occurred over at least 5 seconds. We noted the classification of the epileptic seizure, the moment of the day on which the seizure occurred and whether the patient was awake or asleep before the seizure.

Results: In total 316 seizures were assessed, of which most seizures occurred during the period of 2–8h (26%) and 14–20h (32%). of all documented seizures 37% was of frontal origin, 38% of temporal origin, and 13% of other origin and the rest of unknown origin. Complex partial seizures were documented mainly in the period from 14–20h (35%). The partial seizure with secondarily generalisation occurred mainly in the night from 2 to 8h (37%).

Conclusion: Most epileptic seizures were documented in the periods 2–8h and 14–20 h. Nearly half of the epileptic seizures occurred in wake in the period 14–20h. There seems to be a relation between seizures and circadian rhythm.

T123

MEMORY PERFORMANCE IS RELATED TO LANGUAGE DOMINANCE AS DETERMINED BY THE INTRACAROTID AMOBARBITAL PROCEDURE

S. Kovac,†, G. Moddel*,†, J. Reinholz†, A. Alexopoulos*, and T. Loddenkemper**

**Neurological Institute, Cleveland Clinic, Cleveland, OH, USA and †Klinik Und Poliklinik Für Neurologie, Universitätsklinikum Münster, Münster, Germany*

Purpose: The goal of our study was to explore the relationship between language and memory lateralization in a large cohort of epilepsy patients with or without MRI-identifiable lesions undergoing intracarotid amobarbital procedure (IAP).

Method: 386 consecutive patients with IAP and MRI results were reviewed. Language and memory lateralization as determined by laterality index were calculated and correlated to MRI lesion. Pearsons correlation coefficient, chi-square test and z-statistics were used for statistical analysis.

Results: 138 patients had hippocampal sclerosis, 51 neoplasms, 41 cortical dysplasia, 66 had rare etiologies (13 subgroups) and 90 patients had a normal MRI. There was a significant correlation between memory and language lateralization ($r=0.344$, $p<0.01$). Subgroup analysis showed that the degree of correlation differed depending on the presence, type and localization of lesion (greatest correlation with cortical dysplasia followed by hippocampal sclerosis and tumor; no correlation in nonlesional patients). Post hoc tests revealed that laterality scores correlated significantly higher ($p<0.01$) in patients with cortical dysplasia ($n=41$; $r=0.614$, $p<0.01$) compared to the nonlesional group ($n=91$; $r=0.157$, $p>0.05$.). Furthermore, in these groups the pattern of language lateralization differed significantly ($p<0.05$).

Conclusion: We found that the correlation between language and memory lateralization is more pronounced in patients with structural lesions as compared to patients with nonlesional MRI. Although our results are limited due to retrospective analysis these findings are in-line with the notion that type, location and timing of the lesion play a role in the determination of lateralization.

T124

HOW IS ORGANIZED THE EPILEPTOGENIC ZONE IN PARTIAL EPILEPSIES? A QUANTIFIED STUDY FROM SEEG SIGNALS

S. Aubert,†, P. Chauvel*,†,‡, J. Régis§, F. Wendling¶, D. Branger-Figarella**, and F. Bartolomei*,†,‡*

**Service de Neurophysiologie Clinique, Hopital Timone Adultes, Marseille, France; †Université de la Méditerranée, LNN, Marseille, France; ‡INSERM, U751, Marseille, France; §CHU Timone, Service de Neurochirurgie Fonctionnelle, Marseille, France; ¶Université De Rennes 1, LTSI, Rennes, France, and **Service D'Anatomo-Pathologie, Hopital Timone Adultes, France*

Purpose: In most cases of focal pharmacoresistant epilepsy investigated by intracerebral EEG a key problem is the assessment of the extent of the epileptogenic zone (EZ) and its organization. Indeed, the EZ may disclose features that may range from a simple focal organization corresponding to the site of a lesion to a more complex facet commonly described as a 'epileptogenic network' extending out of the lesional site. This distinction is particularly relevant in developmental lesions as focal cortical dysplasias (FCD), dysembryoplastic neuroepithelial tumors (DNET) and may be determining for surgical strategy and prognosis.

Method: To gain insight into the EZ organization we have developed a new tool, which is able to quantify the epileptogenicity of each anatomical structure explored by SEEG electrodes. We computed an 'Epileptogenicity Index' (EI) that combines both spectral and temporal parameters respectively related to the propensity of a brain area to generate rapid discharges and the time for this area to get involved into the seizure process. We determined this EI from signals recorded in distinct brain structures including the lesional site in patients investigated by SEEG (stereoelectroencephalography) and suffering from focal pharmaco-resistant epilepsy associated with FCD or DNET.

Results: We studied the type of EZ organization (focal versus network) and looked for a correlation with clinical data and postsurgical outcome. We could demonstrate that the number of structures displaying a high EI score is a significant prognostic factor for a worse postoperative outcome with a higher probability of persistant seizures after surgery. The determination of EI in several brain structures throughout SEEG technique is a new and usefull tool for quantification of the EZ and its extent, and could help for more accurate surgical resection.

T125

EPI PARTIALIS CONTINUA AS THE FIRST PRESENTATION OF ANTIPHOSPHOLIPID SYNDROME

S. Bacvanin

General Hospital, S. Mitrovica, Serbia

Purpose: A case report of antiphospholipid syndrom (APS) initially presented with focal myoclonic status. The purpose was to find the cause of these prolonged focal status.

Method: A 52-year-old woman presented with involuntary movements of the right upper limb and face, permanently day and night, during ten days. These involuntary movements were labelled as faciobrachial myoclonia at the beginning during first admission, and after second admission the diagnosis was of APS, bilateral brachiofacial myoclonia. These prolonged myoclonic seizures were partially ameliorated by a complex of medications: anticonvulsants and immunosuppressants.

Results: Increased titers of anticardiolipin antibodies (aCL-a) (IgG 52 GPLU/ml; IgM 14,9 MPLU/ml) were detected. EEG showed background 8/s alfa activity with excessive bifrontocentral slow wave and spikes discharges. Cranial NMR was normal.

Conclusion: The presence high titers of aCL-a strongly suggests that the immune system contributed to focal prolonged seizures, in this patient.

T126

AGENESIS OF CORPUS CALLOSUM: REPORT OF 4 CASES

G. Gul, O. Uzunkaya- Ethemoglu†, D. Yandým Kuscu*, and C. Keskinkilic**

**Bakýrkoy Hospital For Psychiatric And Neurological Diseases, Istanbul, Turkey, and †Bagcilar State Hospital, Neurology Clinic, Istanbul, Turkey*

Purpose: The aim of this study is to investigate clinical profile, EEG features, cranial MRI and neuropsychological evaluations of 4 patients with total agenesis of corpus callosum.

Method: Four patients with epilepsy who have total agenesis of corpus callosum in their MRI are reported. Clinical features of epileptic seizures were analyzed. EEG investigations and neuropsychological test battery were performed.

Results: The seizure onset was at 3 months in one case and after 10 years old in 3 cases. All of the 4 cases have total agenesis of the corpus callosum with involvement of other brain areas in their MRI's. The seizures types and EEG patterns were nonspecific. Two of the patients were intellectually impaired and could not cooperate with the neuropsychological tests. The other 2 cases showed disconnection syndrome.

Conclusion: Cases with corpus callosum agenesis show a variable clinical spectrum. They exhibit deficits on tasks requiring interhemisferic integration.

T127
INCIDENCE OF GENERALIZED CONVULSIVE STATUS EPILEPTICUS IN CENTRAL SERBIA

P. Nikic, S. Jotic†, D. Denic†, and S. Djurdjevic†*
**Special Hospital for Cerebrovascular Diseases 'Sveti Sava', Belgrade, Serbia, and †Community Hospital, Krusevac, Serbia*

Purpose: Generalized convulsive status epilepticus (GCSE) is a medical emergency that always requires immediate identification and prompt management. Our objective is to determine the incidence, case fatality and duration of GCSE in Central Serbia.

Method: We carried out a prospective one-year study of all cases of GCSE in the population of the Rasinski district, that is located in the central part of the Republic Serbia. It encompasses six municipalities and has a population of 259 441 to the last census. We were using the district hospital database and information was obtained on age, etiology, duration and mortality of GCSE.

Results: Overall annual incidence rate of GCSE was 8.09/100,000 (95% CI=4, 6–11, 5). The highest incidence was in the age group 0–14 year (28, 52/100,000, 95% CI=11, 62–45, 35). The most frequent etiologic factors were febrile convulsions in children and cerebrovascular disease and cerebral tumors in adults. The mean duration of convulsive status was 84, 2±57, 6 minutes. Over half of the patients (61, 9%) had a diagnosis of epilepsy and 23, 8% had generalized convulsive status previously. The case fatality was 4, 7%.

Conclusion: We found higher incidence of GCSE than reported in population studies from developed countries. The generalized convulsive status epilepticus has a predilection for the young, with the highest occurrence in children under age 14 year. The mortality directly caused by GCSE itself was lower than previously reported. The most frequent causes were infectious in children and destructive lesions of brain in adults.

T128
RECURRENT FORM OF COMPLEX PARTIAL STATUS EPILEPTICUS WITH FRONTAL LOBE ORIGIN: TWO CASE REPORTS WITH LONG-TERM FOLLOW-UP

F. Ýlgen Uslu, N. Bebek, C. Gürses, B. Baykan, and A. Gökyiðit
Istanbul University, Istanbul, Turkey

Purpose: In spite of the increasing reports in regard to all possible aspects of CPSE, its recurring nature in some patients has very rarely been stressed. We report two cases of recurrent CPSE probably with frontal lobe origin to draw attention to this unusual feature.

Method: Two female adult patients have had seizures consisting of versive-rotatory and asymmetric tonic components with secondary generalisation. They both described some behavioral or mood disturbances beginning many hours before the appearance of focal motor symptoms. These attacks recurred regularly every month and lasted several hours sometimes more than a day since more than a decade.

Results: Their ictal EEGs revealed continuous, 2–3Hz rhythmic, generalized spike and wave activity dominating in one of the frontal regions. MRI studies for both patients were normal. There were no known risk factors for epilepsy, ring Chromosome 20 was not found. One of them showed no marked cognitive deterioration during follow up of 13 years, combined antiepileptic medication was only partially effective. The second patient's seizures had worsened and psychotic behavior developed during attacks, her cognitive tests deteriorated. She did not respond to antiepileptic drugs and even to resective epilepsy surgery performed after invazive monitorization.

Conclusion: Patients presented here showed a recurrent form of CPSE of frontal lobe origin. These episodes occurred at regular intervals over many years in spite of appropriate antiepileptic treatment. We suggest that this recurrent form of CPSE could be included in the classifications of nonconvulsive status epilepticus as a separate subdivision.

T129
PATTERNS OF RELAPSE AND REMISSION IN CHRONIC EPILEPSY

A. Neligan, J. Sander, and S. Shorvon
UCL Institute of Neurology, Queen Square, London, UK

Purpose: Despite recent advances in the therapeutic options for the treatment of epilepsy, chronic epilepsy still represents 20–30% of the total (1). Several small studies (2,3) have looked at different patterns of seizure frequency in chronic epilepsy. We sought to determine the relative frequency of different seizure patterns in a cohort of patients attending a tertiary referral centre and to determine whether epileptic syndrome or aetiology was predictive of any particular seizure pattern.

Method: All participants had by definition chronic active epilepsy. Data was obtained by administration of a patient questionnaire and chart review. Seizure pattern was defined as 1) continuous frequent seizures, 2) intermittent burst pattern and 3) infrequent intermittent seizures. Seizure type and epileptic syndrome were noted in addition to all relevant investigations.

Results: A pattern of continuous frequent seizures was found in 50% (50% male), 40% had at least one period of remission (> 2 years) since onset and 10% had an infrequent intermittent pattern. MRI Brain was abnormal in 25% but the association with any particular epileptic syndrome or aetiology and particular seizure pattern was not statistically significant. Investigations and seizure pattern was disconcordant in 5%.

Conclusion: A higher proportion then expected of those with chronic epilepsy, had a significant period of remission then as previously been reported. Detailed results will be discussed.

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T130
PREPARING FOR PREGNANCY: THE EXPERIENCE OF WOMEN WITH EPILEPSY

J. Winterbottom, A. Jacoby, and G. Baker
University of Liverpool, Liverpool, UK

Purpose: Women with epilepsy (WWE) require the timely delivery of information to enable them to make informed decisions during their reproductive lives. Information presented during routine epilepsy review often details potential risks of adverse pregnancy outcome. While some women request additional information and counselling, others present during pregnancy unaware of possible risks. There is an urgent need to

understand the potential barriers and influences of providing counselling interventions, upon decisions made by WWE who are pregnant or preparing for pregnancy, and to direct future service development.

Method: A purposive sample of WWE of child-bearing age (16–45yrs) were recruited from epilepsy clinics across the North West of England (n=41), and invited to attend one of eight focus groups. Focus groups were structured by a topic guide, and the data was audiotaped and transcribed. Analysis has followed a phenomenological approach.

Results: The main themes arising from the analysis demonstrate the multi-directional influence of information, with WWE reporting a range of experiences including; misplaced optimism, fear and worry. The results highlight the complexity of experiences' for WWE; expressed as difficulty preparing for pregnancy, becoming fearful of risk, and bewildered by a perceived conflict of information from sources including professionals, lay organizations and the internet.

Conclusion: Interpretive phenomenology has facilitated exploration of the experience of being a WWE during their childbearing years. This study offers the potential to extend our understanding of the needs of WWE, and directs the preconception counseling agenda to promote the best possible outcomes for WWE and their offspring.

T131
EPILEPTIC SEIZURES AS A ORIMARY CAUSE FOR ADMISSION TO NEUROLOGY INTENSIVE CARE UNIT (ICU)

D. Vyskocilova, S. Klimosova, D. Hlinovsky, and M. Brzak
Faculty Thomayer's Hospital Prague, Prague, Czech Republic

Purpose: To determine the incidence and specific features of epileptic seizures as a primary cause for admission to Neurology ICU.

Method: Retrospective analyses of medical records – medical history, neurological, laboratory, EEG findings and therapeutic measures.

Results: Among 231 patients hospitalized from January 1, 2006 to December 31, 2007 we have identified 49 patients, 33 men and 16 women, 18 to 86 years old, admitted to our NICU because of epileptic seizures with complicated course. Generalized seizures were observed in 96%. 15 patiens (30,6%) had convulsive status epilepticus, 2 patients (4%) had partial motor status epilepticus. Etiological factors were represented by alcohol withdrawal in 24,5% cases, cerebrovascular pathology in 22,3% cases, head trauma in 12,4% cases. Combined etiology of alcohol withdrawal and head trauma was found in 16,4%. 18,4% of cases were patients with known history of epilepsy. Tumor, AV malformation and metabolic disorder represent 6% of our cohort. 36,7% of patients were treated by one antiepileptic drug (AED), 40,8% of patients were treated by two and 20,4% of patients by three AEDs, one patient (2%) with four AEDs.

Conclusion: Patients with epileptic seizures represent 21% of patients hospitalized in the Neurology ICU during 24 month. Majority of them (67,3%) were men. Most frequent type of seizures was primary or secondary generalized (GTCS).

Dominant etiological factors were alcohol withdrawal alone or in combination with head trauma (41%) and cerebrovascular patology (22,3%).

T132
PROGNOSTIC FACTORS OF POSTSTROKE EPILEPSY ACCORDING TO 'TRIAL OF ORG 10172 IN ACUTE STROKE TREATMENT (TOAST)' CLASSIFICATION

H. Bozdemir, K. Aslan, F. Over, A. Özeren, and Y. Saryca
Çukuroba University Medicine Fac., Adana, Turkey

Purpose: Cerebrovascular diseases are one of the most etiologic factor of the adult epilepsy. The aim of this study is to evaluate the prognosis of epileptic patients with stroke according to TOAST classification.

Method: 34 female and 47 men with a mean age of 55,98,16,35 (18–80) years included in this study. The seizure begun in the first week at 40,7%, between 8–30 days in 13.6% and after one month in 45,7% of the patients. According to TOAST classification; there was large arterial involvement (LAE) in 35.8%, small arterial involvement in 23,5%, cardioembolic stroke in 11.1%, other reasons in 8,6% (Pro S deficiency, SVT etc), intracerebral hemorrhage (ICH) in 17,3%, subarachnoid hemorrhage in 3.7% of the patients. All of the seizure type were partial type and 9,9% of the patients resorted to the hospital with status epilepticus.

Results: Of the patients, the seizures were totally under control in 70.4% with monotheraphy and partial controlled in 22.2% with polytherapy. Of the remaining patients (n:6) prognosis was bad in spite of 3 antiepileptic drug and 4 of them died.

Conclusion: There was no statistical significant correlation between duration of seizure onset and seizure frequency at the begining (p: 0,742; 0,843) but there was correlation between prognosis and TOAST classification (p: 0,43). So the prognosis was bad in patients with ICH, LAE, and cortical involvement according to TOAST classification.

T133
ETIOLOGY AND PROGNOSIS AT ACUTE SYMPTOMATIC SEIZURES

K. Aslan, H. Bozdemir, G. Özer, and Y. Saryca
Çukurova University, Balcali, Turkey

Purpose: It is known that the cases applied with acute seizure have wide etiologic spectrum, besides to approach to the patients correctly and on time will affect the prognosis favourably.

Method: The data of 49 cases with acute seizure were assessed. Thirty female, 19 men with a mean age of 52, 29, 19, 34 were included in our study.

Results: of the patients, 28,6% on status, 53.1% having seizure 2–3 times a day, 10.2% having only one seizure. The seizure etiology revealed; acute stroke in 26,5%, old stroke history in 24.5%, silent infarct in 22.2%, sinus thrombosis in 8,2%, metastatic tumor in 10.2%, metabolic disorder 10.2%, epilepsy diagnosis in 4.1%, encephalitis in 4.1%. EEG revealed; diffuse slow activity in 16,3%, lateralized epileptic activiy in 22.4%, lateralized slow activity in 55.1%, bitemporosentral paroksysmal disorder in 4.1% and normal only in one. At the clinical follow-up, 6.1% of the patients were dead. of the remaining patients, seizures were totally under control in 71.4% and partially controlled in 22.4%. Two of the cases whose seizure was in control died due to malignancy. Diabetic non-ketotic hyperglycemia detected in two of the patients whose seizure etiology was metabolic disorder and the seizure could be controlled after metabolic correction.

Conclusion: In conclusion, in the cases applied with acute seizure, it was detected that the stroke was the most common reason and the prognosis was the worst in malignancy and CNS infection.

T134
LEVETIRACETAM: SAFETY AND EFFICACY IN ELDERLY PATIENTS WITH FOCAL EPILEPSY – A ONE-YEAR OBSERVATIONAL STUDY IN 484 SUBJECTS

K. Werhahn, S. Klimpe*, F. Hummel†, S. Glogau†, E. Trinka‡, and G. Krämer§*
**University of Mainz, Germany; †UCB GmbH, Monheim, Germany; ‡Medical University Innsbruck, Innsbruck, Austria; and §Swiss Epilepsy Centre, Zurich, Switzerland*

Purpose: Preliminary evaluation of long-term safety and efficacy of levetiracetam (LEV) as add-on therapy in patients with focal epilepsies aged > 65 years who failed a first monotherapy.

Method: Multicentre observational study in 484 patients aged > 65 yrs (72 + 5.6; mean + SD), 46.5% women, epilepsy duration 13.1 + 17 yrs). Previous monotherapies: VPA (47.3%), CBZ (42.4%), PHT (9.1%). Aetiology: cerebrovascular (41.5%), trauma (9.9%), tumor (7.2%), dementia (6.6%), metabolic (1.9%), toxic or infectious (1.7% each), 29.5% unknown. Initial dose 500 mg LEV bid, increase in steps of 500 mg every 14 to 28 days to a maximum of 3000 mg/day. Follow-up visits at 3, 6, 12 months.

Results: LEV add-on therapy significantly (p< 0.01) reduced seizure frequency already at 3 months follow-up compared to baseline. Seizure control remained unchanged throughout until last follow-up at 12 months. Only 7.8% of patients took more than 1000 mg LEV per day at last visit, 37.6% were on 750 mg LEV per day or less. Adverse events (AE) occurred in 22.9% of patients, 9.3% serious (unrelated death in 75%), 11.4% related to LEV (i.e. somnolence, dizziness, aggression). A proportion of 3.7% dropped out due to AE.

Conclusion: Levetiracetam is an efficient and safe add-on therapy in elderly epilepsy patients who do not respond to a first antiepileptic drug. Addendum: This post authorization safety study was sponsored by UCB GmbH, Germany.

T135
THE FACTORS INFLUENCING THE PROGNOSIS IN JME; THE ROLE OF FOCAL EEG CHANGES

K. Niedzielska, A. Wierzbicka, M. Barañska-Gieruszczak, L. Wokow, and J. Lêcka
Institute of Psychiatry and Neurology, Warsaw, Poland

Purpose: In juvenile myoclonic epilepsy (JME) the remission can be obtained in 75–80% of cases with first monotherapy, usually with valproate. However, in some patients seizures persist even despite polytherapy. The aim of this study was to investigate various factors determining the prognosis of JME, especially the presence of focal EEG features.

Method: We studied 49 JME patients from the outpatient clinic (25 women and 24 men; mean age 29.6+/− 10.6 yrs; mean duration of disease 14.9+/−10.5 years). In all the patients routine EEG, Video-EEG after sleep deprivation and MRI/CT were performed. The group of patients with seizure remission for at least 3 years (RE, n=17) was compared to the group with drug resistant seizures (DR, n=32). Fisher's exact test was used for statistical analysis.

Results: At present 15 patients from the DR group and only 4 subjects from RE group are on polytherapy. The focal features in EEG were found in 68.7% of DR patients and 35.3% RE patients. These differences occurred statistically significant (p<0,05). However, the differences in incidence of brain lesions between the groups were not significant. Other examined factors, such as age of JME onset, positive family history or compliance were not important for the prognosis.

Conclusion: Our study revealed the presence of focal changes in EEG as the unfavourable factor for the prognosis in JME. Localized changes in EEG have been so far considered as the cause of the delayed diagnosis of JME, but their relationship to the prognosis has not been actually examined.

T136
NOCTURNAL FRONTAL LOBE EPILEPSY (NFLE): A FOLLOW-UP STUDY OF 81 PATIENTS

L. Licchetta, L. Di Vito, F. Bisulli, I. Naldi, F. Pittau, F. Provini, J. Fares, L. Vignatelli, P. Montagna, and P. Tinuper
University of Bologna, Bologna, Italy

Purpose: To analyze the clinical and prognostic features of 81 patients with NFLE and a long follow-up.

Method: We analyzed 81 NFLE patients (49 males) with a follow-up ranging 5–25 years (12.7 years ±6.8). All patients underwent a full clinical, neuroradiological and neurophysiological examination. At the end of the follow-up we considered 2 groups: patients with negative evolution (NE-seizure frequency varying from daily to pluriyearly: 44 patients, 54.3%) and with positive evolution (PE-seizure-free for at least 1 year or with sporadic seizure: 37 patients, 45.7%).

Results: At disease onset, seizures were daily in most patients in both NE (36%) and PE (35%) groups. At the last visit, most NE patients presented plurimonthly (31%) pluriweekly (22%) or pluriyearly seizures (20%) and only 17.8% still had daily seizures. Among NE patients the mean age at onset of epilepsy was lower than in PE patients (PE 15.5 years vs NE 11.1 years; p=0.02); a family history of febrile seizures (FS) was found only in the PE group (13.5%). No significant differences were observed between the 2 groups in seizure type, history of FS, status epilepticus, family history of epilepsy (PE 35.1% vs NE 36.4%) and parasomnias (PE 37.8%vs NE 38.6%), secondary generalisation, seizures also in wakefulness, interictal epileptiform abnormalities.

Conclusion: The only 2 significant differences between NE and PE group are an earlier age at onset in the NE group, that seems to be a negative prognostic factor, and a positive family history for FC reported only in the PE group.

T137
MESIAL TEMPORAL LOBE EPILEPSY (MTLE): PROGNOSTIC FACTORS

F. Pittau, F. Bisulli*, R. Mai†, J. Fares*, L. Vignatelli*, A. Labate‡, I. Naldi*, D. Capannelli*, P. Avoni*, A. Parmeggiani*, M. Santucci*, A. Gambardella‡, A. Baruzzi*, and P. Tinuper**
**University of Bologna, Italy; †Center for Epilepsy Surgery, Niguarda Hospital, Milan, Italy; and ‡University of Catanzaro, Catanzaro, Italy*

Purpose: To disclose familial, clinical, anamnestic, electrophysiological and neuroradiological factors correlated to prognosis in patients with mesial temporal lobe epilepsy (MTLE).

Method: 136 MTLE patients were studied for family history, clinical findings, neuropsychological and instrumental data (EEG, video-EEG, neuroimaging) and outcome. This population was divided into drug-resistant (DR: 108 pts, 79.4%) and non–drug-resistant (NDR: 28 pts, 20.6%) groups; all variables were studied in the two groups.

Results: Comparing DR and NDR groups, the DR group had a higher frequency of: febrile seizure (FS) history (43.5% vs. 17.8%, p:0.008), presence of MTS (64.8% vs. 32.1%, p:0.0025), age at seizure onset before 3 years (23.1% vs. 3.6% p:0.0160) and persistence of epileptiform interictal abnormalities after medical treatment (89.7% vs. 68%, p:0.010). Familial cases were equally present in DR and NDR groups. Febrile seizures were more common in patients with MTS than in patients without (46.28% vs. 26,3%, p:0.0199). Sixty-nine patients underwent surgery and 85.3% had a good outcome.

Conclusion: MTLE is a heterogeneous syndrome.
Establishing the factors responsible for and associated with drug resistance is important for therapeutic purposes, as prompt diagnosis of drug resistance will lead to an early surgical approach. Febrile seizures, MTS, early age at seizure onset, and the persistence of epileptiform interictal abnormalities after medical treatment are negative prognostic factors and that FS are related to MTS.

T138
THE EFFECT OF LAMOTRIGINE, CARBAMAZEPINE AND VALPROATE ON THE LEVELS OF FREE AND CONJUGATED STEROIDS IN THE SERUM OF PREMENOPAUSAL WOMEN WITH EPILEPSY

J. Zarubova, and M. Hill†*
**Thomayer's Teaching Hospital, Prague, Czech Republic and*
†Institute of Endocrinology, Prague, Czech Republic

Purpose: Antiepileptic drugs (AEDs) may affect the steroid metabolism. To evaluate the differences in the effect of lamotrigine (LTG), carbamazepine (CBZ) and valproate (VPA) on the steroid biosynthesis and catabolism, 54 steroids and steroid conjugates were measured in the serum from 12 women with epilepsy in both phases of menstrual cycle (PMS) using GC-MS and RIA. We followed the steroids in the 5-ene and 4-ene metabolic pathway including 7a-, 7ß-, 7-oxo and 16a-hydroxy-metabolites, polar conjugates of the 3a- and 3ß-hydroxy-steroids and active hormones as sex hormones, cortisol and neuroactive metabolites of progesterone, testosterone and androstenedione.

Method: The effect of AEDs on steroid profiles was evaluated using repeated measures ANOVA consisting of subject factor, drug as the between-subject factor, PMS as the within-subject factor and between-factor interaction. Significant decrease was found in conjugated DHEA in the sequence LTG, CBZ and VPA ($p<0.0001$). The levels did not differ between LTG and CBZ groups but were depressed in VPA for conjugated pregnenolone and 5a-androstane-3a, 17ß-diol ($p<0.0001$ and $p<0.05$, respectively). In conjugates of allopregnanolone, isopregnanolone, pregnanolone, and epipregnanolone the LTG group showed higher levels when compared to the remaining groups ($p<0.01$, 0.001, 0.01 and 0.05, respectively). The levels of conjugated androsterone, epiandrosterone, etiocholanolone and epietiocholanolone showed a decreasing trend in the sequence LTG, VPA and CBZ ($p<0.0001$).

Results: The results indicate that lamotrigine may promote the sulfation of 3ß-hydroxy-5-ene steroids, androgens and neuroinhibiting progesterone metabolites. Alternatively, the valproate hyperandrogenic effect may be partly ascribed to relatively higher proportion of unconjugated precursors that are available for androgen synthesis.

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T139
ETIOLOGY AND CLINICAL SYMPTOMS AS A SHORT-TERM PREDICTORS OF STATUS EPILEPTICUS

K. Pierzchala, M. Adamczyk-Sowa, K. Kumor, and P. Sowa
Medical University of Silesia, Katowice, Poland

Purpose: The aim of the study was to analyze clinical symptoms, causes, complications and predictors of mortality in status epilepticus patients.

Method: This retrospective study included 25 patients, 14 men and 11 women (aged 53+/−14 yrs) with status epilepticus (SE) treated in our Department between the year 1997 and 2007.

Results: Preexisting epilepsy was found in 54% and previous SE in 15% of patients. In anamnesi, 44% of individuals were chronic alcoholics and 24% have cerebrovascular disease. The most common cause of SE were alcohol-related seizures (8 cases – 33%), followed by cerebrovascular incidence (4 cases – 17%) and brain tumors (3 cases – 12.5%). Unidentified cause of SE was in 30% of patients. About 85% of SE type seizures in our study were primarily or secondarily generalized. Markers of infections or initial increased body temperature (>38°C) were present in 33% and 20% of patients, respectively. Respiratory and cardiovascular complications were the most common complications of SE. During treatment, after previous diazepam application intravenous phenytoin in 56% of patients was given. Moreover 33% of patients required thiopental and 12.5% needed propofol for controlling the seizure activity. In about half of cases intubation and mechanical ventilation were required. Patient's mortality was about 37.5%, among which 44% were chronic alcoholics.

Conclusion: Chronic alcohol dependence or/and alcohol withdrawal was the most common cause of SE in our series (33%) and was related with increased markers of infection, respiratory and cardiovascular complicances and high mortality.

T140
TODD'S PARESIS AND INTRAVENOUS THROMBOLYSIS

C. Silar, R. Herzig, and P. Kanovsky
University Hospital and Palacky University Medical School, Czech Republic

Purpose: Differentiation of Todd's paresis (postictal paralysis) presents a difficult problem in patients with acute stroke considered for intravenous thrombolytic therapy (IVT). Main bjective of this study was finding the incidence of Todd's paresis in this patient population.

Method: A total of 138 patients with stroke were hospitalized between 11/2006 to 11/2007 at Stroke Unit, Department of Neurology, University Hospital in Olomouc. Based on history and clinical examination, IVT was considered in a subgroup of 52 patients (31 male, 21 female; age 23–86, mean 64.9 ± 13.6 years). These patients underwent laboratory investigation and brain imaging (MRI-stroke protocol in 41, CT in 11 patients with MRI contraindication). For patients with normal MRI or MRI findings unrelated to the acute neurological deficit, an EEG study was completed.

Results: IVT was performed in 25 patients. Out of the 27 patients non-indicated for IVT, Todd's paresis was found in 8 patients, 3 patients had history of epilepsy and 5 patients had newly diagnosed epilepsy or a single epileptic seizure. In patients with Todd's paresis, left-sided impairment (62.5%) dominated over right-sided (37.5%) and postictal paralysis persisted for 3 to 24 hours (mean 12.4 ± 7.9 hours). Average NIHSS score was 14.0 in the IVT group and 9.4 in patients with Todd's paresis.

Conclusion: Brain imaging with the MRI-stroke protocol permits better definition of patients presenting as acute stroke, in whom IVT is not indicated. This selection decreases the risk of iatrogenic impairment and treatment costs.

T141
PALINACOUSIS-AUDITORY PERSEVERATION: CLINICAL MANIFESTATION OF SEIZURE PHENOMENA?

D. Campos, E. Marin, M. Peñas, S. Herrero, R. Fernández, and M. Toledano
University Hospital, University of Valladolid, Spain

Purpose: Palinacousis is an auditory illusion in which external auditory stimuli such speech, music and other noises perseverated internally in a paroxysmal way. Only few cases in the literature have been reported. We would like to describe the EEG changes during the phenomena and its correlation with an ictal event.

Method: A 43 year old woman with a history of inmunosupresion secondary to pharmacological treatment related to an allogenic transplant was admitted to hospital because of a tonic–clonic seizure. Three days before she started episodes of palinacousis in her left ear, with intercalated extremely acute paroxysmal headaches. Neurological examination and cerebrospinal fluid studies showed anything remarkable. Cranial MR discovered white matter lesions specially periventricular and in right temporal region.

Results: EEG: over a normal background activity a continuous irregular right temporal delta activity and 4 seizures were registered. Electrically the seizures started with a pseudorhythmic 4–5Hz activity over centro-parietal and right midtemporal regions, with increasing amplitude and 10 seconds latter, a spike component appeared associated, with tendency to spread to left hemisphere. Clinically palinacousis in left ear was present continuously during the recording and clinical manifestation of

electrical seizure was an intense headache. Auditory illusions did not change related to electrical seizures. The patient was treated with levetiracetam and a month latter, symptoms disappeared and EEG was normal.

Conclusion: Palinacousis seem to be related to seizure activity but at least in this case is not clearly associated with electrical seizures. The phenomena disappeared when seizures were controlled.

T142
SEMIOLOGICAL ASPECTS OF EPILEPTIC SEIZURES IN 31 PATIENTS WITH HYPOTHALAMIC HAMARTOMA

B. Oehl, D. Altenmüller*, A. Brandt*, T. Bast†, S. Biethahn*, S. Fauser*, M. Trippel*, V. van Velthoven*, and A. Schulze-Bonhage**
**University Hospital Freiburg, Germany, and †Childrens Epilepsy Center Heidelberg, Heidelberg, Germany*

Purpose: To investigate age-dependence of seizure semiology in patients with hypothalamic hamartoma (HH).

Method: Retrospective video-EEG analysis of 31 patients with HH before surgical or radiosurgical treatment. The group comprised five children, four adolescents and 22 adults. Mean duration of epilepsy in the children was 4 (vs. 20) years.

Results: Gelastic seizures occurred in all patients, in 23/31 in the beginning of epilepsy, rarely (2/31) with a feeling of mirth. Laughter varied in all groups from facial grinning to intense contractions of the diaphragm and body shaking. 31/41 (75%) seizures recorded in children were simple partial gelastic, 5/41 (12%) complex partial gelastic. In adolescents and adults, 58/212 (27%) seizure were simple partial gelastic and 47/212 (22%) were complex partial gelastic. Other seizure types were simple partial, complex partial and generalized tonic–clonic without gelastic component. Children had the gelastic component as initial clinical sign in 87% (36/41) vs. 35% (74/212) in adolescents and adults. The mean duration of the gelastic component vs. total seizure duration in children was 11.2 seconds / 15.2 s, in adolescents and adults 6.7 s / 45,8 s.

Conclusion: Results show differences in the quantity and positioning of the gelastic seizure component depending on patient age. The percentage of gelastic seizures, the number of seizures in which the gelastic component was the initial sign, and the duration of the gelastic component decreased with higher age and duration of epilepsy. This may reflect changes in propagation or secondary changes in epileptogenic networks in the course of time.

T143
STATUS EPILEPTICUS (SE) AS AN INITIAL SIGN OF INTRACRANIAL HEMORRHAGE FROM ANGIOMA CAVERNOSUM: A CASE REPORT

S. Ristic, D. Ristic†, and M. Zivkovic**
**University Clinical Centre Nis, Serbia, and †Institute of Pulmonary Diseases, Nis, Serbia*

Introduction: Vascular malformations are congenital local agenesis of the capillary web which appear in 1–1,4% of all intracranial process. They appear more often in men. Localization is in 85% supratentoriel, cortical or subcortical. Progression of the disease is often asymptomatic. Symptoms of the disease are: epileptic seizures, headache, mental disorders, neurological difunctions, intracranial hanemorrhagiae- intracereral and subarachnoidal.

Case report: A 33- year man, without earlier disease. After a time spent on a sun he had short lose of conscience without convulsions when he was in high school, but no further testing was done. The disease started suddenly during the afternoon nap as a loss of conscience with epileptic seizures of generalized tonic–clonic seizures type. The neurological status showed right hemiparesis. After the admission the generalized, tonic–clonic SE is developed. SE was stopped by infusion of midazolam, with adding of continuated antiepileptic therapy (AET). Brain CT and MRI examination, 3D TOF angiography and digital subtraction angiography, brain MSCT, MSCT brain angiography: Mentioned analysis showed angioma cavernosum of the orbital gyrus of the left frontal lobe. In the interhaemispheric fissure zone of the fresh blood signal was spotted. Brain surgeon was consulted but he wasn't for radical treatment but for the continuation of the conservative treatment. EEG: focal nonspecific dysfunction on the left side F-T with epileptiformous changes. After the treatment patient was left to go home recovered, he was included in his professional activities bit by bit with regular AET.

Discussion: cavernous cerebral angiomas often are asymptomatic. Appearance of SE in adult period is often caused by other diseases', so further testing is always indicated.

T144
A EUROPEAN DATABASE FOR SEIZURE PREDICTION

A. Schulze-Bonhage, B. Schelter†, M. LeVanQuien‡, F. Sales§, and A. Dourado¶*
**University Hospital Freiburg, Germany; †FDM, Albert-Ludwigs-Universität Freiburg, Germany; ‡CNRS Paris, France; §Hospitais De Universidade De Coimbra, Portugal; and ¶Faculdade de Ciências e Tecnologia da Universidade de Coimbra, Portugal*

Purpose: For the evaluation of seizure prediction algorithms, continuous long term EEG data containing a sufficient number of seizures are necessary. This project is a European multi centre effort supported by the European Union (www.epilepsiae.eu) aiming at an extended database for prediction purposes.

Method: A relational database is established containing long term EEG data of at least 5 days duration each from a total of 175 patients from centres of Freiburg, Paris and Coimbra. Data content will comprise raw EEG data, derived univariate and multivariate features for prediction algorithms and clinical metadata of patients. Metadata will contain imaging findings, neuropsychological data, data on seizure spread, and semiological signs relevant to an interpretation of seizure dynamics. Access will be restricted to participating research groups from the prediction groups for the first three years but is planned to be open from 2011 for further groups working on basic mechanisms of epilepsies and of electroencephalography.

Conclusion: This multi centre approach opens up a new standard for application of algorithms on continuous long-term EEG data. Close interactions with a planned NIH project will take place to allow for mutual access for research groups from a wide range of countries.

T145
PILOMOTOR SEIZURES ARISING FROM A LESION IN THE ANTERIOR CINGULATE GYRUS

S. Biethahn, B. Oehl, D. Altenmüller, J. Zentner, and A. Schulze-Bonhage
University Hospital Freiburg, Freiberg, Germany

Introduction: Ictal piloerection is a rare epileptic symptom, usually associated with ipsilateral temporal lobe epilepsy.

Case report: A patient with a lesion in the left anterior cingulate gyrus, which was histologically classified as low grade astrocytoma, initially developed hypermotoric secondary generalized tonic–clonic seizures (SGTCS). After stereotactic radiotherapy the patient suffered from simple partial pilomotor seizures (SPPS) starting in the left face with a march to the left arm and sometimes left leg. This was sometimes accompanied by a weakness of the right arm;

however, there were no other autonomic features. Furthermore, he suffered from complex partial seizures with hypermotoric features in the right shoulder (CPS), and SGTCS, sometimes with a preceeding SPPS. On video-EEG-Monitoring 3/33 SPPS and all CPS and SGTCS demonstrated a rhythmic activity bifrontally accentuated over the left frontal lobe at the onset, compatible with the lesion in the left anterior cingulate gyrus.

Discussion: Up to now, only few cases with pilomotor seizures arising extratemporally have been described, among them one case with an isolated origin in the anterior cingulate gyrus (Seo DW et al. Seizure. 2003;12:241–244), and another with a nonparaneoplastic limbic encephalitis (Wieser S et al. Epileptic Disord. 2005;7:205–211). From animal experiments it has long been known that piloerection can be generated in different parts of the limbic system. Our case supports the assumption that ictal piloerection might be a localizing sign not only for temporal lobe seizures, but also for parts of the limbic system, such as the anterior cingulate gyrus.

T146

ASTROCYTIC POTASSIUM AND GLUTAMATE BUFFERING CONTROLS SYNAPTIC RESPONSES IN A FREQUENCY-DEPENDENT MANNER

Y. David, L. P. Flores†, S. Ivens‡, U. Heinemann†, D. Kaufer†,§, and A. Friedman*,‡*

**Zlotowski Center For Neuroscience, Ben-Gurion University of The Negev, Beer-Sheva 84105, Israel; †Helen Wills Neuroscience Institute, UC Berkeley, Berkeley 94720–3140, USA; ‡Charité University Medicine, Berlin, Germany; and §Berkeley, USA*

Purpose: We have recently shown that in the rat neocortex long-lasting BBB opening or exposure to serum-derived albumin leads to a rapid upregulation of the astrocytic marker, glial fibrillary acidic protein (GFAP), followed by a gradual development (within 4–7 days) of an epileptic focus. The purpose of the present study was to explore the role of astrocytic activation in epileptogenesis.

Method: We studied three models of lesion-induced neocortical epilepsy, previously described in our laboratory: Rats were anaesthetized, a bone window was opened and the neocortex was exposed to either artificial cerebrospinal fluid (aCSF) in the sham-operated animals or aCSF containing deoxycholate (2 mM), serum bovine albumin (BSA, 0.2 mM) or TGF-? (10 ng/ml). Gene expression was studied during epileptogenesis (8–48 hrs after treatment) using gene array technology and qRT-PCR. A NEURON model was developed to simulate the outcome of astrocytic-related changes in extracellular buffering on excitatory synaptic potentials (EPSPs). Extracellular recordings were obtained from neocortical slices maintained in vitro.

Results: A similar, fast (within hours) robust change in astrocytic gene expression was found in all treatments predicting reduced buffering capacity for both extracellular potassium and glutamate. The computational model indicates increased amplitude and duration of a single EPSP during the accumulation of synaptic glutamate. However, potassium accumulation was associated with frequency-dependent (maximal at 20Hz) facilitation of EPSPs. Electrophysiological experiments in neocortical slices exposed to albumin confirmed synaptic facilitation at 10–20Hz.

Conclusion: Our data suggest rapid astrocytic activation during epileptogenesis leading to reduced potassium buffering as the critical cause for neuronal hyper-excitability.

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T147

USING OF CRANIOCEREBRAL HYPOTHERMIA IN PATIENTS WITH REFRACTORY PARTIAL EPILEPSY

A. Dubenko, A. Bachericov, G. Cherevatenko, and O. Vasylieva

Institute of Neurology, Psychiatry and Narcology of AMS of Ukraine

Purpose: Prospective controlled observational open study was done for investigation possibility of using cranocerebral hypothermia (CCH) in patients with refractory epilepsy.

Method: 79 patients were included. All patients had diagnosed epilepsy with refractory partial seizures with or without secondary generalisation, frequency of seizure was 6 and more during 1 month of screening period.43 patients had symptomatic epilepsy, 36 – cryptogenic. All patients took 1–3 AED and had in past two or more treatment failure with adequate AED. 40 patients 2 or 3 CCH procedures were done with EEG monitoring control. 39 patients were observed as control group. Patients were observed during 6 month's. All this period doses of AEDs were not changed. Control of seizures and decrease of seizure frequency more then 50% were estimated.

Results: In group after CCH during 6 month's seizure control had 4 patients (10%) and 50% decreasing seizure frequency – 4 patients (10%). In control group seizure control had 1 patients (26%) and 50% decreasing – 2 patients (5,1%). These dates significantly lower that in main group. Worsening of EEG during CCH, increasing of seizure frequency after CCH and clinical significant adverse events, which were correlated with CCH were absent.

Conclusion: CCH using is effective in patients with refractory partial seizures with and without secondary generalisation. The dates are reason for further investigations off efficiency and safety of CCH in epilepsy patients.

T148

A RANDOMIZED TRIAL OF CLASSICAL AND MEDIUM-CHAIN TRIGLYCERIDE KETOGENIC DIETS IN THE TREATMENT OF CHILDHOOD EPILEPSY – EFFICACY AND TOLERABILITY AFTER 12 MONTHS

E. Neal, H. Chaffe*,†, G. Fitzsimmons*, N. Edwards*, M. Lawson*, R. Schwartz‡, and H. Cross*,†*

**Institute of Child Health & Great Ormond St Hospital, London, UK; †National Centre for Young People with Epilepsy, Lingfield, UK; and ‡Central Middlesex Hospital, London, UK*

Purpose: To conduct a randomized trial comparing the efficacy and tolerability of classical and medium chain triglyceride (MCT) ketogenic diets in the treatment of children with intractable epilepsy.

Method: 145 children were randomized to receive either the classical or MCT ketogenic diet. Children continuing on the diets were followed up for 12 months. Efficacy and tolerability of the two protocols were compared, and blood ketone levels measured.

Results: 61 children started treatment with the classical and 64 the MCT diet. 12-month seizure data is available for 47 children who continued on a diet (22 classical, 25 MCT). There was no difference between the classical or MCT diet in mean percentage of baseline seizures (41% and 53% respectively, $p>0.05$), or numbers achieving greater than 50% reduction in seizure frequency (13 classical (21%), 16 MCT (25%), $p>0.05$). Mean α-hydroxybutyrate and acetoacetate levels were higher in children following the classical protocol; this was significant for acetoacetate only ($p<0.01$). There was no correlation between either ketone level and seizure control ($p>0.05$). Side effects reported after 12 months included vomiting (45% classical, 13% MCT, $p<0.05$), diarrhea (10% classical, 17% MCT, $p>0.05$), abdominal pain (10% classical, 17% MCT, $p>0.05$), constipation (45% classical, 39% MCT, $p>0.05$) and lack of energy (10% classical, 13% MCT, $p>0.05$).

Conclusion: Results from the first randomized trial of the ketogenic diet show classical and MCT dietary protocols to be comparable in efficacy after 12 months. There were no significant tolerability differences except increased vomiting in the classical group.

This work was supported in part by funding from SHS International, HSA, The Smith Charity and the Milk Development Council.

T149

WHAT DO EPILEPSY SPECIALIST NURSES TELL PATIENTS ABOUT SUDDEN UNEXPLAINED DEATH IN EPILEPSY? A SURVEY OF NURSES IN THE UNITED KINGDOM

M. Goodwin, S. Lewis, and S. Higgins*
**Northampton General Hospital, Northampton, UK*

Purpose: Sudden unexplained death in epilepsy (SUDEP) has been identified as the principle cause of epilepsy related death in people with epilepsy in the UK, and has been estimated to account for approximately 500 deaths each year (NICE 2002).

The purpose of this study was to identify how, what and when information surrounding this subject was discussed with patients and their families.

Method: A postal questionnaire was sent to 250 members of the Epilepsy Nurses Association (ESNA). The questionnaire had been modified from that developed by Morton et al (2006).

Results: A total of 103 (71%) ESNs completed and returned their questionnaires. Forty-five (44%) ESNs discussed SUDEP at diagnosis and 17 (17%) when therapy was commenced. Sudden unexpected death was discussed in the context of nonconcordance (14%), safety risks (14%), nocturnal seizures (12%), alcohol/drug use (12%) and a history of status epilepticus (12%). The main patient responses observed were improved concordance (25%), avoidance of risk (24%) and anxiety (19%).

Conclusion: There is much that can be done to minimize the risks of epilepsy. However the timing and information given must be appropriate and relevant to the individual and their family to ensure that the patient is enabled to continue to lead an 'ordinary life'.

T150

HIPPOCAMPAL HIGH FREQUENCY DEEP BRAIN STIMULATION REDUCES SEIZURE FREQUENCY IN THE KAINIC ACID MODEL

T. Wyckhuys, R. Raedt*, K. Vonck*, W. Wadman†, and P. Boon**
**Ghent University Hospital, Ghent, Belgium; and †University of Amsterdam, Amsterdam, The Netherlands*

Purpose: Deep brain stimulation of the hippocampus is an experimental treatment for medically refractory epilepsy. This study evaluates the effect of high frequency deep brain stimulation (HFS – 130Hz) in the hippocampus in a validated rat model for spontaneous seizures. Seizure frequency was compared before, during and after continuous unilateral HFS.

Method: Rats were intraperitoneally injected with kainic acid (5mg/kg, 2–5 administrations), resulting in a status epilepticus (SE). More than 50 days following SE, 11 rats were implanted with hippocampal HFS- and recording electrodes. After 15 days of continuous baseline EEG monitoring, HFS was started for 10 days during which EEG was continuously monitored. After termination of the HFS, rats were monitored for 30 days to determine the outlasting effect.

Results: Seizure frequency was decreased from 37.5 (±1.6) seizures/24h baseline to 19.4 (±0.8) seizures/24h during ten days of hippocampal HFS ($p<0.005$) in 5 out of 11 rats (45.5%). The seizure frequency in 6 out of 11 rats did not decrease significantly. When HFS was stopped, seizure frequency remained decreased in the responder rats (20.4 (±0.9) seizures/24h) for the length of the experiment.

Conclusion: Continuous deep brain stimulation with a frequency of 130Hz in the hippocampus of kainic acid treated rats is able to significantly decrease the frequency of the spontaneous seizures in 45.5% of rats. When stimulation is stopped, the effects of HFS remain present for at least 30 days.

T151

EFFECTS OF LOW-POWER LASER IRRADIATION ON THE THRESHOLD OF PAROXYSMAL DISCHARGE IN THE RABBIT HIPPOCAMPUS

S. Kogure, N. Saito, K. Kozuka, and Y. Matsuda
Soka University, Tokyo, Japan

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. In frog sciatic nerves, low-power laser irradiation (LLI) blocked the generation of anode break excitation, which was consistent with the result when applying ZD7288 instead of LLI. Thus we examined the effect of LLI (Nd:YVO4, 532 nm) on PADT in the rabbit hippocampus CA1.

Method: Fifty-three adult male rabbits were used. A pair of concentric electrodes was implanted into each side of the dorsal hippocampal CA1 region: the right anterior electrode was used for stimulating as well as LLI. The stimulus train for paroxysmal discharge was 1-ms pulses of 50 Hz for 1 s. The laser was introduced into the same site with an optical fibre (125 μm) through a fibre-coupler. We measured the PADT before and after the LLI.

Results: The averaged PADT was 3.7±0.2 V (mean±SE; n=18) before LLI, whereas after 10 min LLI of 50 mW, 75 mW, and 100 mW, it changed to 4.1±0.5 V (n=8), 5.1±0.7 V (n=9, $p<0.05$) and 7.2±0.9 V (n=11, $p<0.01$), respectively.

The PADT increment was maintained at least for 16.3 hrs. The temperature near the right anterior electrode increased 1.0–2.6 °C during 10 min LLI, whereas the histological damage was microscopically confirmed to be ranged 0.69–1.44 mm.

Conclusion: We conclude that LLI with a specific wavelength and an average power has a potential to suppress the generation of paroxysmal discharge in the rabbit hippocampus CA1.

T152

SLOW REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION FOR SENSORIMOTOR EPILEPSY: EFFECT ON CORTICAL EXCITABILITY AND INDUCED NEUROPLASTICITY

C. Benjamin, B. Arnaud, T. Pierre, H. Edouard, and C. Serge
Hôpital Civil De Strasbourg, France

Purpose: Drug resistant sensorimotor epilepsy (SME) is a therapeutic challenge due to high risks of postoperative neurological deficit in case of resective surgery. According to previous studies, slow repetitive Transcranial Magnetic Simulation (rTMS) can decrease the cortical excitability and be effective in patients with refractory epilepsy. We aimed to understand the underlying mechanisms of this therapeutic effect.

Method: We first identified 6 patients with refractory SME and previously responders to primary motor cortex rTMS versus placebo

(≥ 50% reduction on seizure frequency). Cortical excitability (by evaluating Active Motor Threshold [AMT], Intracortical Inhibition [ICI] and Silent Period [SP]) were repetitively assessed before and after (immediately, 4h and 24h later) three different sessions of rtTMS (0,5 Hz) at 100% AMT intensity : 1/25 minutes; 2/50 minutes; 3/Priming (= 10 minutes preconditionning with 6 Hz rTMS at 100% AMT followed by session 1).

Results: The major result was the consistent SP lenghtening by slow rTMS without differences between sessions. The mean SP enhancement was + 22,3%. Moreover, only the Priming session led to a consistent 24h-lasting SP reinforcement (+ 15,9%). AMT was not modified and mean ICI variation was poor (-6,63%).

Conclusion: Slow rTMS improves SP, which is considered to reflect cortical inhibition. We hypothetize that this effect explains, at least, partially the clinical efficacity of rTMS on SME. The long lasting effect of Priming could furthermore be useful in clinical practice.

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T153
RETIGABINE INHIBITS RAPID KINDLING EPILEPTOGENESIS IN RATS THROUGH THE ACTIVATION OF KV7.2/7.3 CHANNELS

R. Sankar, J. Wu†, D. Shin*, and A. Mazarati**
**D. Geffen School of Medicine, Univ. of California, Los Angeles, CA, USA and †Valeant Pharmaceuticals International*

Purpose: To study the effects of retigabine under conditions of rapid kindling, and to examine the role of KV7.2/7.3 channels in mediating antiepileptic effects of retigabine.

Method: Two-, three-, and five- week old Wistar rats underwent rapid kindling: sixty 10 -seconds stimulations delivered every 5 minutes at the threshold current through the intrahippocampal electrode. Electrographic responses were recorded from cortical electrode. In the acquisition studies, retigabine (2.5 mg/kg in two-week old; 5 mg/kg in three- and five- week old rats) was administered intraperitoneally 20 minutes prior to the start of the kindling procedure. In retention studies, retigabine was administered to previously kindled animals. Retigabine was given either alone, or in a combination with a KV7.2/7.3 blocker XE991.

Results: In the applied doses retigabine induced no or mild motor impairments, raised after-discharge threshold, shortened after-discharge duration and prevented the development of full kindling seizures (stage 4–5) at all three ages; in addition in two-week old subjects retigabine delayed the occurrence of focal (stage 1) convulsions. In previously kindled animals, retigabine significantly attenuated the severity of seizures induced by the test stimulation. XE-991 at doses that affected neither ambient excitability, nor kindling (0.5 mg/kg in two-week old; 5 mg/kg in 5-week old rats) completely abolished antiepileptic effects of retigabine.

Conclusion: Retigabine inhibited both kindling acquisition and retention during postneonatal, early childhood and adolescent stages of development. Antiepileptic effects of retigabine depend on the activation of KV7.2/7.3 channels. Supported by Valeant Pharmaceuticals International, and by NIH research grants NS059505 and NS046516.

T154
EFFECTS OF SSRIS ON GABAERGIC INHIBITION IN THE HIPPOCAMPUS OF NORMAL AND PILOCARPINE INDUCED EPILEPSY RATS

H. Song, H. Choi*, T. Kang*, D. Shin†, B. Kim‡, and Y. Kim§*
**Hallym University, Gangwon, Korea; †Gacheon University, Korea; ‡Eulgi University, Korea; and §Catholic University of Seoul, Korea*

Purpose: Selective serotonin reuptake inhibitor (SSRI)s may influence on the serotonin(5-HT) receptors, mainly 5-HT1A, 5-HT1B and 5-HT2C sub-types, and also act on aminobutyric acid(GABA)-ergic transmission. The role of 5-HT in the epileptic hippocampus is still controversial since 5-HT has both convulsive and anticonvulsive effects.

Method: We investigated the effects of SSRIs such as fluoxetine, paroxetine and citalopram on the GABAergic transmission in the normal and pilocarpine-induced epileptic rat hippocampus by using electroencephalogram (EEG), paired pulse inhibition(PPI) and vesicular GABA transporter(VGAT) immunoreactivity.

Results: In normal rats treated with citalopram, fluoxetine, and paroxetine, EEG showed spontaneous spike activities. PPIs in normal rats treated with citalopram, and fluoxetine were reduced, and especially, prominent in the citalopram group of normal rats. PPIs in epilepsy rat after citalopram treatments were markedly reduced but not in the paroxetine group of epilepsy rats. In VGAT immunohistochemistry in the hippocampi of normal rats, the citalopram and paroxetine group showed more reduced relative density than that of normal control group. In VGAT in the hippocampi of epilepsy rats, the citalopram and fluoxetine group showed more reduced relative density than that of epilepsy control group.

Conclusion: These findings suggested that GABAergic transmission in the hippocampus was slightly different from each other after SSRI treatment. SSRI treatment may increase seizure susceptibility in the normal hippocampus and increase the frequency and intensity of seizure in the epileptic hippocampus. However, whether these different effects are resulted from direct effect on the GABAergic interneuron or via other 5-HT subtype receptors remains to be elucidated.

T155
A NEW TRANSCRIPTION-INDEPENDENT INTRACELLULAR PATHWAY MEDIATES IL-1BETA PROCONVULSANT ACTIONS IN THE RODENT HIPPOCAMPUS

S. Balosso, M. Maroso*, M. Sanchez-Alavez†, T. Ravizza*, T. Bartfai†, and A. Vezzani**
**Mario Negri Inst For Pharm Res, Milan, Italy; and †The Scripps Research Institute, La Jolla, CA, USA*

Purpose: IL-1beta was identified as an endogenous brain molecule with proconvulsant activity upon its overproduction in epileptic conditions. IL-1beta prolongs seizures after its brain application, while pharmacological prevention of its endogenous synthesis, or IL-1 receptor blockade, and mediates powerful anticonvulsant actions. We report here on the in vivo activation of a novel, transcription-independent intracellular signaling pathway activated by IL-1beta during seizures.

Method: EEG seizures were induced by intrahippocampal injection of kainic acid (KA) in C57BL6 adult male mice. IL-1 mediated activation of sphingomyelinase and Src-kinase were investigated pharmacologically using drugs selectively blocking the activity of these enzymes. Src kinase and NMDA-NR2B subunit phosphorylation were measured in hippocampal homogenates by western blot (WB) analysis.

Results: C2-ceramide, a cell permeable analog of ceramide, mimicked the proconvulsant effects of IL-1beta upon intrahippocampal injection. 3-O-methylsphingomyelin, a selective inhibitor of sphingomyelinase, or

CGP076030, a c-Src kinase inhibitor, or ifenprodil, an NR2B-selective NMDA antagonist fully prevented the proconvulsant effect of IL-1beta without affecting seizures per se. CGP076030 reduced by 50% kainate seizures upon its intracerebroventricular injection. IL-1beta or KA increased by 20% and 50% the phosphorylated form of NR2B and Src kinase respectively and these effects were more than additive in IL-1beta+KA-treated mice.

Conclusion: A sphingomyelinase-dependent pathway activated by IL-1beta during seizures leads to the production of ceramide which in turn induces Src kinase-dependent phosphorylation of NR2B subunit. This novel pathway mediates the proconvulsive effects of IL-1beta, thus representing a crucial mechanism of ictogenesis which may be targeted to attain fast antiinflammatory effects and seizure inhibition.

T156
EFFECT OF U-92032 ON GENETIC ABSENCE EPILEPSY RATS FROM STRASBOURG

H. Yananli, D. Akin, R. Aker, and F. Onat
Marmara University, School of Medicine, Turkey

Purpose: Absence epilepsy is characterized by generalized nonconvulsive seizures with loss of consciousness and spike-and-wave discharges (SWDs) in the EEG. Low-threshold Ca2+ potentials have been suggested to underlie the firing of thalamocortical neurons during SWDs in absence epilepsy. Genetic Absence Epilepsy Rats from Strasbourg (GAERS) is a well defined animal model of absence epilepsy. The present study aims to investigate the effect of U-92032, which is a novel Ca2+ channel blocker, in GAERS.

Method: Experiments were carried out GAERS animals. U-92032 was injected (0.25, 1, 5 mg/kg; intraperitoneally) to GAERS. The EEG in the nonepileptic Wistar control and GAERS groups were recorded continuously for 1 hour before and 5 hours after i.p. U-92032 injections. The cumulative total duration of SWDs, the number of SWDs, the mean duration of SWD complexes were analyzed over 20-min periods.

Results: In GAERS, no changes in SWD were detected after saline injection. The cumulative duration of SWD significantly decreased after 1 mgkg-1 and 5 mgkg-1 U-92032 injections. 0.25 mg.kg-1 U-92032 did not produce any significant change in the number of SWD and mean duration of SWD in any time period, but 1 and 5 mg.kg-1 U-92032 injection caused a significant decrease in the number of SWD compared to the baseline values. 1 and 5 mg.kg-1 U-92032 injection also caused a significant decrease in the mean duration of SWD.

Conclusion: A dose-dependent decrease in duration and number of SWDs with systemic administration of U-92032 in GAERS shows that U-92032 is of value as an antiabsence agent.

T157
SYNAPTIC VESICLE PROTEIN 2A (SV2A) EXPRESSION IN EPILEPSY-ASSOCIATED BRAIN TUMORS AND IN THE PERILESIONAL EPILEPTIC CORTEX

E. Aronica, S. Toering, K. Boer, J. Heimans, and J. Reijneveld
VU University Medical Centre, The Netherlands

Purpose: To identify the cellular distribution of synaptic vesicle protein 2A (SV2A) which is the binding site for the antiepileptic drug levetiracetam.

Method: We compared the expression and cellular distribution of SV2A in surgical specimens of patients with glial (30 glioblastoma multiforme, 5 anaplastic and 2 low-grade astrocytoma, 8 anaplastic and 4 low-grade oligodendroglioma, 1 low-grade oligoastrocytoma) and glioneuronal (6 gangliogliomа (GG), 6 dysembryoplastic neuroepithelial tumors (DNT)) tumors with or without epilepsy, with perilesional cortex from nontumor patients with or without epilepsy.

Results: Immunohistochemical analysis in control neocortical tissue specimens demonstrated strong and diffuse SV2A immunoreactivity of the neuropil, with punctuate labeling of neurons throughout all cortical layers. SV2A was colocalized with the presynaptic marker synaptophysin. Similar distribution was observed in the peritumoural cortical specimens from patients with or without epilepsy. Modest SV2A immunoreactivity was observed within the tumor area, particularly within glial tumors. There was little evidence of SV2A expression in glial tumor cells. In GG strong SV2A-immunoreactivity was present along the dysplastic neuronal cell borders and processes (perisomatic synapses). In both GG and DNT SV2A immunoreactivity was occasionally observed within the neuronal perikarya.

Conclusion: The pattern of SV2A immunoreactivity in the peritumoural regions of glial tumor patients with chronic epilepsy suggests that treatment with levetiracetam could be effective in case of epilepsy refractory to traditional AEDs. The distinct pattern of SV2A immunoreactivity in glioneural tumors suggests a redistribution of the SV2A protein. How this may affect the epileptogenicity and/or the effectiveness of levetiracetam needs to be further investigated.

T158
CELECOXIB PREVENTS SEIZURE-INDUCED UP-REGULATION OF ENDOTHELIAL P-GLYCOPROTEIN IN THE BLOOD–BRAIN BARRIER

G. Zibell, B. Unkrüer*, A. Pekcec*, B. Bauer†, A. Hartz†, D. Miller‡, and H. Potschka**
**Institute For Pharmacology, Toxicology and Pharmacy, Ludwig-Maximilians-University, Munich, Germany; †University of Minnesota, MN, USA; and ‡Laboratory of Pharmacology and Chemistry, NIH/NIEHS, NC, USA*

Purpose: In up to 40% of all epileptic patients pharmacoresistance is a major problem. Seizure-induced overexpression of the blood–brain barrier efflux transporter P-glycoprotein (Pgp) has been hypothesized to limit the penetration of antiepileptic agents into the brain in pharmacoresistant epilepsy. Thus, the prevention of Pgp up-regulation would offer an option to overcome pharmacoresistance. Based on recent data from in vitro studies and preliminary in vivo studies with a nonselective cyclooxygenase (COX)-inhibitor, we hypothesized that selective COX-2 inhibition will prevent seizure-associated Pgp-upregulation in an effective manner in vivo.

Method: On 4 consecutive days study adult female Wistar rats received celecoxib or vehicle twice daily for a in vivo study. A status epilepticus (SE) was induced by administration of pilocarpine on the second day of treatment (10 mg/kg fractionated at 30 min intervals). The effect of celecoxib on Pgp-expression was investigated by immunohistochemistry two days following SE.

Results: Celecoxib but not sc-560 inhibits the glutamate-induced increase of Pgp in vitro indicated by Western blot analysis. In vivo the up-regulation of Pgp following pilocarpine-induced SE was prevented by celecoxib.

Conclusion: The data convincingly substantiate the hypothesis that seizure-induced up-regulation of BBB Pgp expression can be prevented by selective COX-2 inhibition. Targeting COX-2 is therefore suggested as a new therapeutic strategy to prevent seizure-induced up-regulation of Pgp and associated pharmacoresistance.

The study was supported by the grant DFG PO 681/4-1 from the German Research Foundation.

T159
INCREASED EXPRESSION OF P-GLYCOPROTEIN AFTER CLUSTER SEIZURES OR STATUS EPILEPTICUS IN THE CANINE BRAIN

B. Unkrueer, A. Pekcec*, V. Stein†, J. Bankstahl‡, W. Baumgaertner‡, A. Tipold†, and H. Potschka**
**Institute of Pharmacology, Toxicology, And Pharmacy, Ludwig-Maximilians-University, Munich, Germany; †Department of Small Animal Medicine and Surgery, University of Veterinary Medicine, Hannover, Germany and ‡University of Veterinary Medicine, Hannover, Germany*

Purpose: Pharmacoresistance of epilepsy remains a major problem despite considerable innovations in the pharmacotherapy of epilepsy. There is cumulating evidence that increased expression of multidrug-transporters, such as P-glycoprotein (Pgp) contributes to drug resistance of epilepsy. For proof of the multidrug transporter hypothesis, we studied the effect of spontaneous cluster seizures and status epilepticus on Pgp expression in the canine brain.

Method: We obtained tissue from 29 nonlaboratory dogs and compared animals with cluster seizures or status epilepticus with control animals that did not show any evidence of CNS diseases. Pgp expression was quantified in different brain regions by Pgp-immunohistochemistry using a monoclonal mouse anti-Pgp antibody (C 219).

Results: We demonstrated a significant up-regulation of Pgp in the canine brain following spontaneous status epilepticus compared to control animals. Seizure activity was due to several different aethiopathologies. In dogs with virus encephalitis or brain tumors Pgp expression was increased compared to control animals, in contrast to dogs with hydrocephalus (n=2), where Pgp labeled area seemed to be lower than in control animals, despite prolonged seizure activity.

Conclusion: Our present data give evidence that Pgp expression is up-regulated as a consequence of spontaneous prologed seizure activity without any bias of electrical or chemical stimulation. Differences in Pgp expression in dogs with hydrocephalus, virus encephalitis, and tumors indicate that the up-regulation of Pgp by seizure activity is influenced by the underlying pathology.

The study was supported by the grant DFG PO 681/4-1 from the German Research Foundation.

T160
IMPACT OF THE NCAM-DERIVED PEPTIDE PLANNEXIN ON NEUROGENESIS IN A STATUS EPILEPTICUS MODEL

C. Fuest, A. Pekcec*, E. Bock†, V. Berezin†, and H. Potschka**
**Inst. of Pharmacology, Toxicology, and Pharmacy, LMU, Munich, Germany and †Protein Laboratory, Institute of Molecular Pathology, School of Medicine, Copenhagen, Denmark*

Purpose: A series of mimetic peptides derived from the neural cell adhesion molecule (NCAM)-have been shown to influence neuronal plasticity and to exert neuroprotective effects in different animal models of CNS diseases. Therefore, we studied the effect of the recently developed NCAM-mimetic plannexin in the pilocarpine model of temporal lobe epilepsy. We concentrated on seizure-induced hippocampal cell loss and alterations of hippocampal neurogenesis which have been hypothesized to contribute to the development and progression of epilepsy.

Method: Adult female Wistar rats received either plannexin or vehicle-injections (10 mg/kg s.c.) twice daily for 4 consecutive days. A status epilepticus (SE) was induced by administration of pilocarpine on the third day of treatment. The effect of plannexin on neuronal progenitor cells and neurodegeneration was investigated by doublecortin (DCX)- and neural specific nuclear protein (NeuN)-immunohistochemistry two days following SE and compared with control animals which had not experienced a SE.

Results: Status epilepticus decreased the number of NeuN-positive and DCX-labelled cells in the dentate gyrus and enhanced the number of persistent basal dendrites 48 h post–pilocarpine administration. Even though SE-induced reduction of the number of DCX-labeled cells was not completely suppressed by plannexin, the number of DCX-immunoreactive cells was significantly increased as compared to the vehicle-injected pilocarpine-treated rats. In addition, plannexin significantly reduced the number of persistent basal dendrites. There was no effect of plannexin treatment on SE-induced hippocampal neuronal cell loss.

Conclusion: The results indicate that neuronal progenitor cells and mature neurons are vulnerable to SE. Plannexin partially protects neuronal progenitor cells but not mature neurons from SE-induced degeneration and decreases seizure-associated alteration of hippocampal neurogenesis such as the generation of persistent basal dendrites.

T161
MODULATION OF P-GLYCOPROTEIN EXPRESSION BY RNA INTERFERENCE IN VIVO

P. Winter, C. Fuest*, M. Czapp*, M. Uhr†, C. MacLean‡, M. Helm‡, G. Fricker‡, A. Pekcec*, and H. Potschka**
**Ludwig-Maximilians-University, Munich, Germany; †Max Planck Institute of Psychiatry, Munich, Germany; and ‡University of Heidelberg, Heidelberg, Germany*

Purpose: Resistance to drug treatment remains a major problem in the pharmacotherapy of many CNS diseases, including epilepsy. Overexpression of multidrug-transporters (MDTs), such as P-glycoprotein (Pgp) is thought to contribute to drug resistance by limiting the penetration of various therapeutic drugs into the brain. Inhibition of MDTs may constitute a new strategy to overcome transporter-based pharmacoresistance. Therefore, we tested whether Pgp expression encoded by mdr1a/1b gene can be downregulated based on RNA interference (RNAi) through administration of small interfering RNAs (siRNAs) targeting the mdr1a gene in mice.

Method: Several putative sequences for silencing mdr1a specifically were examined in an in vitro study using a rat brain endothelial (RBE4) cell line. Cells were transfected with OligofectamineTM and harvested for mRNA isolation at 24 h and 48 h after transfection. For in vivo studies male BALB/c mice received hydrodynamic intravenous tail vein injections of either 'naked' siRNA or vehicle solution (~ 3125 µg/kg) once daily for four consecutive days. Pgp expression was quantified for different brain regions by Pgp-immunohistochemistry.

Results: The targeted sequence for silencing mdr1a was successfully tested in vitro. Among several targeted sequences, the most effective one was used for in vivo studies. Hydrodynamic injections of 'naked' siRNA targeting the mdr1a gene for four consecutive days significantly decreased the Pgp-labeled area in the parietal cortex and in the hippocampus compared to vehicle-treated mice.

Conclusion: Our data indicate that hydrodynamic intravenous administration of 'naked' siRNA targeted the mdr1a gene down regulates the expression of the multidrug transporter Pgp in different brain regions. Thus, we hypothesize that silencing the mdr1a gene by RNAi renders a new strategy to enhance the penetration of many therapeutic drugs into the brain Supported by the grant DFG PO 681/4-1 (German Research Foundation). We thank Bayer HealthCare and the FAZit-Stiftung by providing a scholarship (to C. F.).

T162
PUMA DEFICIENCY PROTECTS AGAINST SEIZURE-INDUCED NEURONAL DEATH AND SUPPRESSES THE EMERGENT EPILEPTIC PHENOTYPE IN MICE

T. Engel, G. Mouri, S. Hatazaki, I. Woods, E. Jimenez-Mateos, J. Prehn, and D. Henshall
Royal College of Surgeons in Ireland, Ireland

Purpose: Neuronal death is a consequence of prolonged seizures but its contribution to epileptogenesis remains incompletely understood. Studies of clinical material and animal models of epilepsy suggest a role for apoptosis-associated signalling pathways and in particular, members of the Bcl-2 family. PUMA (p53-upregulated mediator of apoptosis) is one of the most potent pro-apoptotic proteins of the Bcl-2 family. In this study, we examined the role of PUMA in seizure-induced neuronal death.

Method: Adult (20–22 g) male C57Bl/6 and puma-/-, puma+/− and puma+/+ mice were subjected to prolonged seizures via intraamygdala microinjection of kainic acid (KA). Mice were killed and brains harvested at different time points and Western blotting and Immunofloures-cence performed. Cell death was assessed by DNA fragmentation assay (TUNEL) and Flourojade B positive cell counts. Long term studies of the emergent epilepsy phenotype were performed by using EEG telemetry.

Results: Protein levels of p53 and PUMA were up-regulated shortly after induction of prolonged seizures within the hippocampus. Puma-/- mice displayed significantly less neuronal death in hippocampal CA3 when compared to wild-type and heterozygous mice. Video-EEG recordings beginning 3 days after KA injection determined that while both puma+/− and puma-/- mice developed chronic recurrent seizures, the incidence of epileptic seizures was significantly lower in puma-/- mice.

Conclusion: The present data suggest that PUMA contributes to seizure-induced neuronal death. In addition, mice protected against hippocampal damage by PUMA deficiency develop fewer chronic recurrent seizures.

T163
OLFACTORY SYSTEM PARTICIPATES IN MECHANISMS OF THE SPIKE-WAVE DISCHARGES GENERATION IN WAG/RIJ RATS.

K. Abbasova, S. Chepurnov*, N. Chepurnova*, M. Belousova*, V. Blik*, and G. van Luijtelaar†*
**Lomonosov Moscow State University, Russia; and †NICI, Radboud Nijmegen University, The Netherlands*

Purpose: The aim of the present experiment was to evaluate the role of olfactory system in the generation of the spike-and-wave discharges (SWDs) in WAG/Rij rats.

Method: Before surgery WAG/Rij rats were anesthetized by Nembutal in a dose of 47 mg/kg. EEG electrodes were chronically implanted into frontal cortex. The mean duration and number of SWDs were calculated. CONAN EEG recording software was used. The deafferentation of olfactory bulbs was induced by i.p. injection of the olfactory epithelial toxin 3-methyl indole (3 MI) in a dose of 200 mg/kg.

Results: Significant increase in number of SWDs ($p<0.01$, by means of Wilcoxon matched pairs test) was found for the treatment group compared to the control rats. Analysis of duration of SWDs showed no significant effects.

Conclusion: According to our results we can suggest that olfactory system is include to the mechanisms of generation of the SWDs. I.p. injection of the olfactory epithelial toxin 3-methyl indole (3 MI) induced the increase of the number of the SWDs.

T164
INSULIN-REGULATED AMINOPEPTIDASE: A POTENTIAL TARGET FOR ALTERNATIVE ANTIEPILEPTIC THERAPIES

D. De Bundel, F. Kiagadaki†, K. Thermos†, Y. Michotte*, and I. Smolders**
**Research Group Experimental Pharmacology: Department of Pharmaceutical Chemistry and Drug Analysis, Vrije Universiteit Brussel, Brussels, Belgium; and †University of Crete, Heraklion, Crete, Greece*

Purpose: Angiotensin IV (Ang IV) and LVV-hemorphin 7 (LVV-H7) are competitive inhibitors of insulin-regulated aminopeptidase (IRAP). IRAP catalyzes the degradation of the antiepileptic neuropeptide somatostatin (SRIF) in vitro. We previously demonstrated that intracerebroventricular administration of Ang IV increases hippocampal dopamine and serotonin levels to anticonvulsive concentrations and protects against pilocarpine-induced limbic seizures via a somatostatin SST2 receptor dependent mechanism. We hypothesized that Ang IV exerts its effects through inhibition of IRAP and augmentation of the extracellular concentration of SRIF. The present study further investigates the mechanism of action behind the anticonvulsant effects of IRAP ligands.

Method: Using the microdialysis technique in freely moving rats, Ang IV and LVV-H7 were administered into the hippocampus and hippocampal dopamine, serotonin and SRIF levels were monitored. A behavioral scoring system was applied to determine seizure intensity in the focal pilocarpine model.

Results: Intrahippocampal administration of both Ang IV or LVV-H7 protected against pilocarpine-induced limbic seizures suggesting the participation of IRAP in the observed effects. In contrast to intracerebroventricular administration, intrahippocampal administration of Ang IV or LVV-H7 did not alter hippocampal dopamine and serotonin levels. Our preliminary data showed no effects on hippocampal SRIF.

Conclusion: These results suggest that in the hippocampus, IRAP is the target site for the anticonvulsive effects of Ang IV and LVV-H7, but dopamine, serotonin and SRIF may not be involved in the observed effects. Further research is needed to decipher the anticonvulsant mechanism of action of Ang IV and LVV-H7.

T165
ALTERED CHOLINERGIC GENE EXPRESSION FOLLOWING STATUS EPILEPTICUS AND ITS ROLE IN EPILEPTOGENESIS

Y. Gnatek, N. Najami, and A. Friedman
Soroka Medical Center, Ben-Gurion University, Israel

Purpose: We have recently showed changes in cholinergic gene expression in temporal lobes of the epileptic brain (Zimmerman et al., EJN, 2008). However, their role in the pathogenesis of epilepsy is not known. The aim of the present study was to study changes in cholinergic-expression and their role in status epilepticus (SE)-induced epileptogenesis.

Method: Real time RT-PCR and In-situ hybridization for the acetylcholine hydrolyzing enzyme, acetylcholinesterase (AChE) were used 2 days following pilocarpine-induced SE. Activity gel and Karnovski staining were used to examine AChE protein activity. Continuous video recordings were made in wild type (WT) and transgenic mice over expressing ACHE to monitor spontaneous seizures.

Results: Most (82%) WT mice injected with pilocarpine (280–340mg/Kg) showed spontaneous seizures 4–8 weeks following SE (n=11). mRNA levels of both the synaptic (S) and read through (R) alternatively spliced transcripts of the ACHE gene were increased. ACHE upregula-

tion was found at 48 hours following SE, correlated with an increase enzyme activity and lasted for more than two weeks. In situ hybridizations and immunostanings confirmed that AChE is expressed in all regions of the hippocampus, in both principal pyramidal and GABAergic neurons, but only rarely in astrocytes. Transgenic mice over-expressing AChE-S showed higher rate of spontaneous seizures 5 weeks post SE.

Conclusion: Our findings support the notion that the upregulation of AChE during the latent period has a role in epileptogenesis.

T166
AGE-DEPENDENT CORTICAL PLASTICITY IN SYNAPSIN KNOCKOUT EPILEPTIC MICE

M. Ketzef,†, A. Friedman*,†, and D. Gitler†*
**Ben Gurion University, Israel; and †Ben Gurion University of The Negev, Beer Sheva, Israel*

Purpose: Synapsins are phosphoproteins associated with the surface of synaptic vesicles that regulate neurotransmission and participate in short-term synaptic plasticity. In mammals they are the product of three related genes. A deletion mutation in one of the synapsin genes (SYN1) was found to account for a type of human familial epilepsy, motivating our research into a potential role for synapsin dysfunction in epilepsy.

Method: The phenotype of mice in which all three synapsin genes had been knocked-out (TKO mice) was characterized and compared to wild type (WT) aged-matched controls by continuous video monitoring. Network electrophysiological activity was recorded in acute hippocampal-cortical slices.

Results: TKO mice older than 2 months, but never younger animals, suffered from recurrent generalized seizures. Recording of network activity in temporal cortical structures revealed significantly larger evoked field potentials in slices from TKO mice in comparison to WT slices. In slices from TKO mice older than one year, robust, all-or-none, hypersynchronous epileptiform activity was often observed in temporal and entorhinal regions of the cortex but not in the hippocampus. Reducing inhibitory synaptic transmission by adding the GABA-A receptor antagonist bicuculline (10 uM) to the perfusion solution revealed a significantly larger glutamatergic-mediated network response in TKO compared to WT slices. Furthermore, slices from TKO mice were significantly more resistant than WT slices to the epileptogenic effect of 4-Aminopyridine (50 uM).

Conclusion: Our results suggest that induction of age-dependent homeostatic plasticity contributes to the control of an otherwise hyperexcitable cortical network in mice rendered epileptic by genetic intervention.

T167
THE CHANGE OF FDG-PET AND MRI AFTER LITHIUM-PILOCARPINE INDUCED STATUS EPILEPTICUS IN RATS

G. Park,‡, Y. Kim†, E. Lee*, Y. No*, J. Kim*, K. Kim*, K. Im*, S. Park‡, S. Kim‡, S. Lee*, and J. Kang**
**University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea; †Catholic University College of Medicine, KangNam St. Mary's Hospital, Seoul, South Korea; and ‡The Asian Institute For Life Science, Seoul, South Korea*

Purpose: Fluorine-18-fluordeoxyglucose([18F]-FDG) micro positron emission tomography (FDG-PET) and MRI have been useful as non-invasive methods to demonstrate the metabolic and morphologic changes of brain structure after lithium-pilocarpine induced status epilepticus (SE) in rats. The aim of this study was to investigate the imaging changes on FDG-PET and MRI before and after SE to reveal the mechanism of developing chronic epileptogenesis.

Method: Eleven-male Spraque-Dawley rats weighing 290–300g were used. All rats performed with baseline FDG-PET and 4.7 T MRI with T2- and diffusion-weighted image. SE was induced with intraperitoneal injection of lithium and pilocarpine. After SE terminated with antiepileptic drugs, rats were scanned with PET and MRI from acute (1–2 days and 1–2 weeks), subacute (3–4 weeks) and chronic period (8 weeks later).

Results: Statistical parametric mapping of FDG-PET at acute period showed severe diffuse hypometabolism in all cortical areas, especially on the hippocampus with slow recovery at subacute and chronic period. MRI findings at 1 day after SE showed high signal on bilateral hippocampal area, basal ganglia, and pyriform cortex with most prominent on the hippocampus, but high signal at pyriform cortex recovered at subacute and chronic period.

Conclusion: MRI and PET can be useful for monitoring the changes from the acute phase of SE to the chronic phase of spontaneous recurrent seizures. Brain areas which changed may be important sites for the neurobiological changes that contribute to epileptogenesis in this model. This study was supported by a grant (08–338) from the Asian Institute for Life Sciences, Seoul, Korea.

T168
LONGITUDINAL IN VIVO MAGNETIC RESONANCE SPECTROSCOPY VERIFIED BY IMMUNOHISTOCHEMISTRY IN A JUVENILE MODEL OF TEMPORAL LOBE EPILEPSY

W. van der Hel, P. van Eijsden*, I. Bos*, R. de Graaf†, K. Behar†, O. van Nieuwenhuizen*, K. Braun*, and P. de Graan**
**Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht, The Netherlands; and †Magnetic Resonance Research Center, Yale School of Medicine, New Haven, CT, USA*

Purpose: The pathophysiology of temporal lobe epilepsy (TLE) is poorly understood. Proposedly, early events, e.g. status epilepticus (SE), initiate an epileptogenic process, characterized by hippocampal injury and imbalance between excitatory (glutamate) and inhibitory (GABA) neurotransmission. We aim to both noninvasively and invasively study glutamatergic and GABAergic cell populations and neurotransmitter concentrations during epileptogenesis in rats.

Method: Neurochemical concentrations were measured in the rat hippocampus during the latent phase of epileptogenesis, at four and eight weeks after pilocarpine-induced SE at P21 with spatially localized 1H MRS at 9.4 Tesla and compared with control animals. Ex vivo (immuno)histochemistry was performed at the same time-points to verify MRS findings.

Results: During epileptogenesis, N-Acetyl-aspartate (NAA) levels decreased, while choline increased, indicating neuronal death and gliosis, which was confirmed by FluoroJade and vimentin stainings. Glutamate and particularly GABA concentrations decreased over time. GABAergic cell death was confirmed by decreased parvalbumin-immunoreactivity. Glutamine concentrations increased significantly after four weeks, but returned to control levels at eight weeks. Immunoreactivity of glutamine synthetase (GS), the enzyme that converts glutamate into glutamine, decreased in time.

Conclusion: We propose that neuron loss leads to decreased glutamate/GABA synthesis and thus to accumulation of their precursor glutamine, with a subsequent reduction of GS to normalize glutamine levels. The loss of particularly GABAergic neurons may create a hyperexcitable state and concomitant, possibly epileptogenic, changes in GS expression. These changes occur before spontaneous seizures appear and may be early markers of imminent epilepsy, indicating the potential of MRS in early diagnosis of TLE.

T169
INFLUENCE OF ORPHENADRINE UPON THE PROTECTIVE ACTIVITY OF ANTIEPILEPTICS IN THE MAXIMAL LECTROSHOCK-INDUCED CONVULSIONS IN MICE

W. Turski,†, J. Cieszczyk†, K. Czuczwar*, M. Czuczwar†, and J. Kis†*

**Institute of Agricultural Medicine, Lublin, Poland; and †Medical University, Lublin, Poland*

Purpose: Orphenadrine, a low affinity antagonist of muscarinic receptors and an uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist, is used as an antiparkinsonian, antispastic and analgesic drug. In this study influence of orphenadrine on the seizure threshold and the anticonvulsant activity of various antiepileptic drugs was assessed.

Method: Male Swiss mice, weighing 20–24 g were used. The convulsive threshold was evaluated as CS50, which is the current strength (in mA), necessary to produce tonic hindlimb extension in 50% of the animals tested. In order to estimate the anticonvulsant ED50 values (50% effective anticonvulsant dose) of orphenadrine and studied antiepileptics (given alone or in combination) mice were pretreated with different doses of drugs and then challenged with maximal electroshock (25 mA).

Results: Orphenadrine significantly elevated the electric seizure threshold at the dose of 5.65 mg/kg. Orphenadrine at the subthreshold dose of 2.8 mg/kg significantly enhanced the anticonvulsant activity of valproate in the maximal electroshock test, yet it failed to affect the protective activity of carbamazepine, diphenylhydantoin, phenobarbital, lamotrigine, topiramate and oxcarbazepine. Administration of orphenadrine at doses exceeding 20 mg/kg resulted in the seizure like-activity.

Conclusion: Summing up, we may conclude that orphenadrine possesses weak anticonvulsant properties and that it may enhance the anticonvulsant activity of valproate in epileptic patients.

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T170
EFFECT OF ACUTE AND LONG-TERM VAGUS NERVE STIMULATION IN FULLY KINDLED RATS

R. Raedt, L. Waterschoot*, T. Wyckhuys*, V. De Herdt*, R. El Tahry*, J. Delbeke†, K. Vonck*, W. Wadman‡, and P. Boon**

**Ghent University Hospital, Ghent, Belgium; †Université Catholique De Louvain, Brussels, Belgium; and ‡University of Amsterdam, Amsterdam, Netherlands*

Purpose: Vagus nerve stimulation (VNS) is a widely used treatment option for patients with refractory partial or generalized epilepsy. The precise mechanism of VNS-induced seizure suppression is still unknown and optimal stimulation parameters remain to be identified. Currently, a reliable animal model to further investigate these VNS-related issues is unavailable. This study evaluates the effect of VNS in the alternate day rapid kindling (ADRK-) model.

Method: Nineteen rats were implanted with a stimulation/recording electrode in the hippocampus, two epidural recording electrodes and a cuff-electrode around the vagus nerve. After recovery, the rats were fully kindled according to the ADRK-protocol. Fully kindled rats were randomly assigned to a control (SHAM group, n=6) or treatment group (VNS group, n=13). Two VNS experiments were performed. In experiment I, acute VNS was applied in combination with kindling stimulation. In experiment II, chronic VNS was administrated continuously during 6 weeks while rats received 12 kindling stimulations/day on alternate days. Outcome parameters were afterdischarge threshold (ADT), after discharge duration (ADD) and seizure severity.

Results: Experiment I showed that acute VNS did not affect ADD and seizure severity. Experiment II showed that chronic VNS did not significantly affect ADT and ADD but reduced seizure severity.

Conclusion: Acute VNS has no obvious effects on excitability in fully kindled rats. Chronic VNS, if applied long enough, can induce neuromodulatory changes which result in a subtle reduction of seizure severity.

T171
STATUS EPILEPTICUS-INDUCED ALTERATIONS IN THE RAT BRAIN AFTER PILOCARPINE ADMINISTRATION: NEW EVIDENCES ABOUT THE INVOLVEMENT OF CEREBRAL CORTEX AND THALAMUS

L. Zanetti, G. Navarro Mora*, A. Chakir*, F. Schio*, P. Farace*, C. Nanni†, S. Trespidi†, D. D'Ambrosio†, A. Spinelli†, C. Quarta†, V. Ambrosini†, A. Sbarbati*, and P. Fabene**

**Section of Anatomy And Histology, Department of Morphological and Biomedical Sciences, University of Verona, Italy; and †Mecina Nucleare, Azienda Ospedaliero-Universitaria Di Bologna Policlinico S. Orsola-Malpighi, Bologna, Italy.*

Purpose: Pilocarpine injections elicit in laboratory rodents sustained seizure activity that develops into SE, followed by a silent period for an average period of 2 weeks; animals then develops chronic epilepsy characterized by spontaneous recurrent seizures without remission. Pilocarpine-induced epilepsy has been widely used as a model of temporal lobe epilepsy, the most frequent epilepsy in humans. For this reason, hippocampal alterations represent the most common focus in experimental studies. However, recent evidences seem to indicate that structural and functional alterations are present widespread in rodent brain after SE, and are not limited to temporal lobe structures.

Method: We investigated pilocarpine-induced SE in Wistar rats, in order to evaluate metabolic alterations in different limbic areas, using as intravenous contrast agent the 18F-fluorodeoxyglucose (18F-FDG), by the mean of microPET acquisition, at different time points: baseline, and 5, 30, 60, 120 min after SE-onset.

Results: Immediately (5 min) after seizures-onset, evident alterations were detected in the cingulate and parietal cortices, thalamus and basal forebrain nuclei, whereas hippocampal formation was almost on basal levels. Hippocampal formation showed 18F-FDG uptake only 1–2 h after SE-onset.

Conclusion: These preliminary data arise questions about the hippocampal origin of the alterations induced by pilocarpine. Further study will be performed with angiography in order to evaluate the vessel diameters that could be changed after epileptogenic insults. In order to ameliorating the mechanisms involved in structural and functional alterations, in the first steps of pilocarpine-induced epileptogenic mechanisms, further analyses will be performed with perfusion-MRI and EEG-MRI techniques.

T172
HIPPOCAMPAL NEURONAL GABA TRANSPORTER EXPRESSION IN PATIENTS WITH MESIAL TEMPORAL SCLEROSIS-ASSOCIATED TEMPORAL LOBE EPILEPSY

O. Schijns, U. Karaca*, E. Lemmens*,†,¶, H. Pannek‡, R. Lahl‡, A. Ebner‡, M. van Kroonenburgh*, K. Herscheid§, and G. Hoogland*,†,¶*

**University Hospital Maastricht, The Netherlands; †School for Mental Health and Neuroscience, Maastricht University, Maastricht, The Netherlands; ‡Epilepsy Center Bethel, Bielefeld, Germany; §VU University Medical Center, Amsterdam, The Netherlands and ¶European Graduate School of Neurosciences, University Maastricht, Maastricht, The Netherlands*

Purpose: GABA-Transporters (GATs) indirectly modulate synaptic neurotransmission. The purpose of this study was to compare the neuronal GAT (GAT-1) immunoreactivity (IR) in the hippocampal hilus and dentate granule cell layer of temporal lobe epilepsy (TLE) patients with mild mesial temporal sclerosis (MTS) with that of TLE patients with severe MTS.

Method: Hippocampal specimens were intraoperatively obtained during surgical treatment of TLE patients. The biopsies were fixed in 4% paraformaldehyde, embedded in paraffin, and histopathologically evaluated as mild (i.e. Wyler1 grade 1–2; n=6–8) or severe (i.e. Wyler grade 3–4; n=13–16) MTS. In addition, we obtained hippocampal biopsies from three nonneurological controls upon autopsy. For GAT-1 IR, the paraffin embedded tissue was cut into 4 µm sections and immunohistochemically stained with polyclonal GAT-1 antibodies. The hilar and dentate granule cell layer was delineated and the IR was quantified by optical density measurements using a microscope-CCD camera-CellP software setup (Olympus). To test possible group differences we applied a one-way ANOVA test with a post hoc Bonferroni test.

Results: A significant group difference was detected for the hilus but not for the dentate granule cell layer. The hilus of patients with severe MTS had significantly less GAT-1 IR than that of patients with mild MTS or controls ($p<0.01$), whereas the GAT-1 IR of controls was comparable to that of mild MTS.

Conclusion: These data support the hypothesis that GATs play a role in the pathophysiology of seizure generation. The different GAT-1 IR between mild and severe MTS suggests a difference in the population of GABAergic neurons between the two patient groups.

Reference:

1. Wyler AR, Curtis Dohan F, Schweitzer JB, Berry III AD. A grading system for mesial temporal pathology (Hippocampel sclerosis) from anterior temporal lobectomy. J Epilepsy 1992;5(4):220–225.

T173

PLASMA ALBUMIN INDUCES INCREASE IN CYTOSOLIC CALCIUM IN HUMAN ASTROCYTES FROM EPILEPTIC PATIENTS

H. Ivan, W. Rivel, R. J. Sola, and P. Jesús
Hospital Universitario de La Princesa, Madrid, Spain

Purpose: The main goal of this job is to characterize the effect of plasma albumin (BPA) on human astrocytes in culture obtained from epileptic patients.

Method: Human astrocytes were obtained from resected hippocampus of patients operated by temporal lobe epilepsy. The tissue was subjected to enzymatic and mechanical dissociation; the resultant cell suspension was plated to obtain separate astrocyte culture. Astrocytes were loaded with the fluorescence Ca2+ probe fura-2 AM, and cytosolic calcium concentration [Ca2+]c was measured by epifluorescence microscopy (Olympus), the frequency recording was 0.77 Hz Analysis was performed with the software Cell-R (Olympus), The BPA was purchased from Sigma-Aldrich (Madrid, Spain). All experiments were performed at room temperature (22°–24°C).

Results: Astrocyte cultures were viable for 3 to 4 weeks and experiments were performed during the 4th week. BPA induced an increase of [Ca2+]c in a dose-dependent manner between 1–40 mg/ml. Increase in [Ca2+]c was not modified by ryanodine (Ca2+-dependent Ca2+ release blocker). Nevertheless, the application of 2-APB (IP3 receptor blocker) abolished the response induced by BPA. Albumin induced an increase in [Ca2+]c in 0 mM Ca2+ solution.

Conclusion: BPA increase [Ca2+]c in human astrocytes from epileptic patients by mobilising Ca2+ from intracellular stores using IP3 as a second messenger, in a manner almost exactly similar as previously reported in animal models [1] where BPA also induces astrocyte proliferation. [1] Plasma Albumin is a potent trigger of calcium signals an DNA synthesis in astrocytes.

Nadal A, Fuentes E, Pastor J, McNaughton P. PNAS USA, 1995; 92: 1426–1430.

T174

COMPARISON OF PROLONGED TREATMENT WITH VALPROATE OR THE HDAC INHIBITOR TRICHOSTATIN A IN THE PENTYLENETETRAZOLE SEIZURE THRESHOLD MODEL IN MICE

M. Czapp, K. Hoffmann, and W. Löscher
University of Veterinary Medicine Hannover, Hannover, Germany

Purpose: In both epilepsy models and patients with epilepsy, anticonvulsant activity of valproate (VPA) increases during prolonged treatment, although therapeutic levels in plasma and brain are reached shortly after onset of treatment. The mechanism of this increase in anticonvulsant efficacy during prolonged treatment with VPA is not known. We hypothesized that the known inhibitory effect of VPA on histone deacetylases (HDACs) may be involved. This hypothesis was tested by comparing the effects of prolonged treatment with VPA and the selective HDAC inhibitor trichostatin A (TSA) in the pentylenetetrazole (PTZ) seizure threshold model in mice.

Method: NMRI mice were treated twice daily either with VPA (200 mg/kg), a low (0.5 mg/kg) or a high (5 mg/kg) dosage of TSA. Intravenous PTZ administration was performed to evaluate the anticonvulsant efficacy of VPA and TSA at time points from 5 minutes to 6 days after onset of treatment.

Results: Prolonged VPA administration led to significantly increased anticonvulsant activity for most evaluated seizure parameters. No anticonvulsant effect was determined after treatment with TSA.

Conclusion: The results substantiate that the anticonvulsant effect of VPA increases during prolonged treatment in mice. However, the lack of anticonvulsant activity of TSA argues against the possibility that inhibition of HDACs is involved in the increase of anticonvulsant efficacy upon prolonged treatment with VPA.

T175

FK506 AGGRAVATES DEVELOPMENT AND SEVERITY OF DISEASE IN THE RAT MODEL OF TEMPORAL LOBE EPILEPSY

K. Lukasiuk, and A. Sliwa
The Nencki Institute of Experimental Biology, Warsaw, Poland

Purpose: FK506 is an immunosuppressive drug which has neuroprotective properties and prevents microglia activation in experimental models of traumatic brain injury and ischemia. In this work we tested the hypothesis that FK506 modifies the development and/or severity of temporal lobe epilepsy.

Method: In our experiments we used the amygdala stimulation model of temporal lobe epilepsy. To detect spontaneous seizures, continuous video-EEG monitoring was performed every other day starting from the stimulation until the end of the experiment. FK506 (0.5 mg/kg, i.p.) or vehicle was injected 24 hours after induction of status epilepticus and than every day for 2 weeks. Thereafter the animals were observed for 1 more month and perfused.

Results: Fifty percent of control animals and 78% of FK506 treated animals developed epilepsy. Chronic application of FK506 decreased duration of the latency period to the first spontaneous seizure (26 ± 8.7 days in control vs. 6 ± 5,4 days in FK506 treated animals, $p<0,01$) and increased number of seizures in epileptic animals (2,3 ± 0.6 vs. 64.7 ± 99.5, $p<0.01$). Number of seizures in FK506 treated animals did not alter during the 1 month washout period following cessation of FK506 applications.

Conclusion: Chronic application of FK506 accelerated development and worsened the course of epilepsy. Supported by The Polish Ministry of Science and Higher Education grant no. K 138/P01/2006.

T176
POTENTIAL EPILEPSY TARGET GENES IDENTIFIED THROUGH 14-3-3 PROTEOMICS

M. Heverin, I. Woods, C. Koehler, A. Treumann, J. Prehn, and D. Henshall
Royal College of Surgeons in Ireland, Ireland

Purpose: 14-3-3 proteins are highly expressed in the neurons of the hippocampus and are involved in the regulation of signal transduction, apoptosis and the cell cycle through chaperone and protein-protein interactions. We have previously shown that prolonged experimental seizures cause a selective degradation of 14-3-3 isoforms within the hippocampus, while in human hippocampus 14-3-3 expression is regulated in an isoform and subcellular compartment-specific manner.

Method: This study endeavored to find potentially novel interactors of 14-3-3 in the hippocampus in order to establish what cellular systems might contribute to survival in the neuron following seizure. To identify novel interacting proteins, recombinant His-tagged 14-3-3 zeta was incubated with mouse hippocampal lysate and associated proteins were eluted with imidazole and separated by 1-D SDS PAGE. The protein bands were trypsin digested and analyzed by LS/MSMS. Proteins were identified by searching the mouse ensemble database using X Tandem. Novel interactions were confirmed using immunoprecipitation experiments.

Results: The pull down was duplicated and 32 proteins were found to bind to 14-3-3 zeta in both experiments. 8 of these were known 14-3-3 interactors while previously no 14-3-3 interactions have been reported for any of the remaining 26 proteins. These proteins are involved in a number of different processes including ubiquitinylation, intracellular transport and ATP regulation.

Conclusion: We have identified new, hippocampus-specific 14-3-3 zeta binding partners. They will lead to the unravelling of new mechanisms of action of 14-3-3 proteins, which could explain their involvement in the protection of neurons against seizure induced damage.

T177
THE ROLE OF NEUROINFLAMMATION IN PILOCARPINE-INDUCED EPILEPTOGENESIS

G. Navarro-Mora, F. Schio, M. Pellitteri, A. Chakir, L. Zanetti, A. Sbarbati, and P. Fabene
University of Verona, Verona, Italy

Purpose: The systemic administration of a single dose of pilocarpine can lead to status epilepticus (SE), which could result in wide brain lesions. In contrast to the human pathology, pilocarpine-induced SE (1h) has been reported to be mandatory in order to develop the chronic condition. However, preliminary data obtained in our lab, suggest that chronic phase can evolve even in absence of SE. Furthermore, recent literature suggests a link between vascular inflammation and pro-epileptogenic events.

Method: We have investigated the effect of chronic (three/week, 1 mg/kg/0.5 ml) and acute (twice/month, 30 mg/kg/0.5 ml) i.p administration of LPS for 40 days in saline-injected rats (control) and pilocarpine-injected animals (pilo) without SE (3–4 weeks after pilo), to verify whether inflammation influences the epileptogenic process in this model. Telemetric EEG, body temperature and circadian rhythms were recorded for up to 2 months. After sacrifice, microarray on inflammatory cytokine, chemokine & receptors and adhesion molecules were performed.

Results: Preliminary results suggest that: A) even in absence of SE, pilocarpine-injected animals exhibit a significant higher frequency of seizures during both acute and chronic LPS administration. B) In control rats, acute LPS administration triggers early (5–8 days) seizure activity. C) Pilo show acutely a late (>10 days) temporal pattern. D) Chronic LPS subclinical injections result in a higher number of seizures.

Conclusion: Pilocarpine injections without SE result in a seizure priming during LPS inflammatory insults. We are currently investigating whether such priming is only a facilitating factor or is related to epileptic condition.

T178
PET IMAGING OF BRAIN METABOLISM INDUCED BY 4-AMINOPYRIDINE IN WISTAR RAT

F. Schio, Zanetti*, Navarro Mora*, Chakir*, Farace*, Nanni†, Trespidi†, D'Ambrosio†, Spinelli†, Quarta†, Ambrosini†, Sbarbati*, and P. Fabene**
**University of Verona, Verona, Italy; and †Hospital-Universitary Unit of Bologna, Policlinico S. Orsola-Malpighi, Bologna, Italy*

Purpose: In the present microPET study, we investigated the metabolic modifications occurring in rat brain after single injection of 4-aminopyridine (4-AP), a K+ channel antagonist that produces brief behavioral seizures in experimental animals.

Method: We used [18F]-fluorodeoxyglucose (FDG) as the radiotracer, which maps cerebral glucose uptake and metabolism in male Wistar rats (200–225 g). The effects of 4-AP include delayed presynaptic repolarization and increased transmitter release and result in neuronal hyperactivity and paroxysmal depolarization shifts in cerebrocortical neurons. We thus decided to better characterize such alterations analyzing the metabolic modifications induced by convulsions. Changes were studied 5 min, 30 min, 1h and 2h after 4-AP-induced seizures.

Results: [18F]-FDG-PET has demonstrated that at the initial phase (5 min) of 4-AP-induced convulsion, cerebellum is the area with the higher metabolic activity (increase of neuronal activity). Thirty min after convulsion onset, a marked increase of [18F]-FDG uptake results in hippocampus, somatosensory cortex, thalamus and cingulate, to higher values than cerebellum. Sixty min after convulsion onset, in all the structures investigated the metabolic activity return to baseline values.

Conclusion: In conclusion, we observed hypermetabolism in cerebellum just after 4-AP seizure onset, differently to other brain areas, such as limbic structures reported to be involved in seizures. Late activation of limbic structures can be explained as a secondary activation process. Further analyses will be done using [11C]-methionine, which allow the analysis of protein metabolism and [11C]-choline, for the metabolism study of the membrane's phospholipids and thus of brain injury.

T179
THE EFFECT OF GLUTATHIONE ON BRAIN NITRIC OXIDE LEVELS IN EXPERIMENTAL EPILEPSY

A. Akcali, S. Pence*, N. Kurtul†, M. Bosnak*, and M. Neyal**
**Gaziantep University, School of Medicine, Turkey; and †Sutcu Imam University, Kahramanmaras, Turkey*

Purpose: Glutathione (GSH) is a major antioxidant, with primary role in protecting against reactive oxygen species produced by the mitochondrial respiratory chain. We aimed to investigate the effects of GSH on nitric oxide levels in the different brain regions after pentylenetetrazole (PTZ) induced epilepsy in the mice.

Method: Experiments were carried out on 80 mice in 8 groups consisting of 10 mice. The groups were the sham, control, PTZ (convulsive dose), convulsive dose PTZ plus single dose GSH, five dose GSH, single dose GSH, kindling, and kindling plus single dose GSH groups. 200 mg/kg GSH was administered at each time. In all groups brains were divided into 5 parts as right hemisphere, left hemisphere, right brain stem, left

brain stem and cerebellum under microscopy. Nitric oxide levels were measured spectrophotometrically on wet tissue. Nitric oxide levels of each brain region were compared both with the other regions in the same group and with homologous regions within the other groups. Values of $p<0.05$ were accepted as statistically significant.

Results: NO levels of 4th and 7th groups in all brain regions were significantly higher than those of the other groups; while highest values were found in brain stems, lowest values were in the cerebral hemispheres. NO levels of in all brain regions decreased markedly in the groups which were given kindling plus GSH compared to kindling group.

Conclusion: We demonstrated that administration of GSH decreased NO levels in an experimental epilepsy model which may confirm a neuroprotective effect of GSH.

T180
RELATION BETWEEN THE EXTENT OF NEUROGENESIS AND THE SPREAD OF EPILEPTIFORM ACTIVITY IN THE HIPPOCAMPUS IN A MOUSE MODEL FOR MESIAL TEMPORAL LOBE EPILEPSY

U. Häussler, L. Bielefeld*, M. Müller*, R. Meier†, and C. Haas**

**Experimental Epilepsy, University of Freiburg, Freiburg, Germany and †Bernstein Center For Computational Neuroscience, Freiburg, Germany*

Purpose: Hippocampal sclerosis in mesial temporal lobe epilepsy (TLE) is associated with pronounced granule cell dispersion (GCD). We have shown that GCD is not caused by increased neurogenesis but by a displacement of adult neurons in patients and in the intrahippocampal kainate model in mice (Heinrich et al., JNS 2006;26(17):4701–13; Fahrner et al., Exp. Neurol. 2007;203(2):320–32). In contrast, increased neurogenesis has been proposed to underlie the network changes in TLE (Scharfman et al., JNS 2000;20(16):6144–58). Here, we want to clarify whether excessive excitatory activity during seizures has a depressing or stimulating effect on neurogenesis, separated from the effects of kainate.

Method: We recorded epileptiform activity with implanted electrodes in the granule cell layer at several positions along the hippocampal septo-temporal axis of intrahippocampally kainate-injected mice. In parallel, we performed bromodeoxyuridin (BrdU) injections and doublecortin (DCX) stainings to characterize neurogenesis along this axis.

Results: We show that the loss of BrdU and DCX staining, as well as GCD in the dentate gyrus is limited to a focal area surrounding the kainate injection site. At distance, the number of DCX-positive cells in the subgranular zone of the ventral hippocampus is increased compared to controls, indicating increased neurogenesis. Accordingly, epileptic spikes are not limited to the area of strongest sclerosis surrounding the injection site but spread along the septo-temporal axis of the hippocampus from the first days after injection until at least four weeks later.

Conclusion: Epileptiform activity does not disturb, but most likely stimulate neurogenesis which in turn may contribute to the development of epileptic seizures.

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T181
NETWORK EXCITABILITY CRITICALLY DEPENDS ON SK-DEPENDENT AHP-CURRENTS IN A MODEL OF CHRONIC TLE

T. Kirschstein, R. Schulz, and R. Köhling

University of Rostock, Institute of Physiology, Germany

Cellular excitability changes are thought to underly epilepsies.

Among the currents shaping this excitability, after-hyperpolarizing currents are important candidates, to which small conductance Ca2+-activated K+ currents (SK) contribute substantially. Here, the functional expression of SK was investigated in isolated hippocampal CA1 pyramidal neurones from chronically epileptic (pilocarpine-treated) and control animals. In addition, the functional importance of SK in the generation of epileptiform activity was tested in hippocampal slices by blockade of SK in the 0-Mg2+ model. The experiments show that, in chronic epilepsy, (a) SK currents are downregulated, that (b) this downregulation causes a decrease in AHP and reduces spike frequency adaptation and that (c) an SK-blockade dramatically potentiates 0-Mg2+ -induced epileptiform activity in tissue from chronically epileptic rats and significantly less so in controls. We conclude that SK channel activity is critically dampened in chronic epilepsy, resulting in exacerbation of epileptic activity when SK function is further challenged.

T182
PREDICTORS OF PHARMACORESISITENT EPILEPSY: PHARMACORESISTANT RATS DIFFER FROM PHARMACORESPONSIVE RATS IN BEHAVIOR, COGNITION AND SEIZURE FREQUENCY

C. Brandt, A. Gastens†, and W. Löscher**

**University of Veterinary Medicine, Hannover, Germany; and † University Heidelberg, Heidelberg, Germany*

Purpose: About 20 to 40% of patients with epilepsy are resistant to pharmacological treatment. Identifying predictors for pharmacoresistant epilepsy may be important to decide on the further treatment of the patient. Potential predictors of pharmacoresistant epilepsy include high seizure frequency and psychiatric comorbidity (Hitiris N et al. Epilepsy Res. 2007; 75: 192–196). Animal models of epilepsy which allow the selection of pharmacoresistant and -responsive rats may be valuable tools to identify predictors of drug resistance.

Method: In the present study, we investigated whether phenobarbital (PB)-resistant rats differ from PB-responsive rats in seizure frequency and behavior. Chronic epileptic female Sprague Dawley rats were selected according to their response to PB treatment. Before PB treatment, baseline seizure frequency was determined over 2 weeks. Six to seven month after the drug experiment rats were evaluated in different behavioral tests (elevated-plus maze (EPM), open field (OF) and Morris water maze (MWM)).

Results: From the 33 treated rats 20 PB-responders and 13 PB-nonresponders were selected. A very high seizure frequency (>3 seizures/day) was determined in six of these rats, which all were in the nonresponder group. Eleven responders and 4 nonresponders could be tested in behavior tests. The nonresponders differed markedly from responders in anxiety tests (EPM, OF) and the learning and memory test (MWM).

Conclusion: In the rat model used, we identified high seizure frequency and behavioral abnormalities as phenotypic markers that seem to predict pharmacoresistance. Our data substantiate that rodent models of epilepsy are useful in the search for predictors and mechanisms of pharmacoresistance.

T183
MICROARRAY ANALYSIS CORRELATED TO STRUCTURAL AND FUNCTIONAL MRI IN WAG/RIJ RATS

M. Pellitteri, Nicolato*, Boschi*, Navarro Mora*, Chakir*, Galiè*, Merigo*, Marzola*, Sbarbati*, van Luijtelaar†, and P. Fabene**

**University of Verona, Verona, Italy; and †Radboud Nijmegen University, Nijmegen, The Netherlands*

Purpose: Absence seizures are considered the most pure form of generalized epilepsy characterized in the EEG by widespread bilaterally synchronous spike-wave discharges (SWDs) caused by thalamocortical

oscillations. Latest Cortical Focus theory suggests a consistent cortical 'focus' within the perioral region of the somatosensory cortex.

Method: MRI data were correlated with gene-array analysis for cell signaling pathways involved in spindles generation and propagation in different cerebral areas. Four-months-old WAG/Rij rats were used as control (no SWDs). Nine-months-old rats (daily SWDs) were referred as experimental group. In order to exacerbate SWDs episodes, rats were treated with Vigabatrin.

Results: MRI data revealed a significant T2-values decrement in the lateral thalamus (LT), somatosensory (SS) and motor cortices (Mo) in 9-months-old WAG/Rij rats versus controls. Interesting enough, in the Mo cortex and in the LT, Vigabatrin treatment results in a moderate return to 4-months levels in experimental animals. DWI analysis revealed a significant effect in the Mo cortex due to treatment with Vigabatrin and in the LT, SS, Mo and Hippocampus related to time. Perfusion-MRI changes are still in progress. Microarray analysis suggests that genes belong to inflammatory and proliferative pathways can be modulated by Vigabatrin treatment, characterized by a partial return to 4-months levels.

Conclusion: Our preliminary data seems to indicate that, in parallel to structural and molecular modification observable in the thalamo-cortical circuitry, some focal cortical events can be detected. However, the study of the biological meaning of these variations is currently in progress.

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Clinical Neurophysiology

T184
FRONTOPARIETAL INTERACTIONS BETWEEN HEMISPHERES AT THE MODEL OF EPILEPSY

V. S. Gennady, and D. S. Natalia
Moscow State University of Medicine and Dentistry, Russia

Purpose: The aim of the study was to analyze the functional associations of frontal areas with parietal, temporal and occipital areas of contralateral hemispheres in patients with symptomatic epilepsy.

Method: The changes of higher integrative (mental) functions were evaluated in separated groups with different lateralization and localization of epileptic focus (58 patients, 35 women, 23 men, mean age of 33 years, S.D. 5.7). 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 behavioral 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 parietotemporal 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 reorganization of integrative activity.

T185
ASYMMETRIC FEATURES OF EEG AND RESPONSE TO TREATMENT IN JUVENILE MYOCLONIC EPILEPSY

K. Létourneau, C. Deacon, and C. Cieuta Walti
Centre Hospitalier Universitaire De Sherbrooke, Sherbrooke, Canada

Purpose: Juvenile myoclonic epilepsy (JME) is a common type of idiopathic generalized epilepsy and is distinctively characterized by myoclonic jerks often associated to generalized tonic–clonic seizures and typical absence seizures. EEG asymmetries are not uncommon in JME and can contribute to the misdiagnosis of this syndrome. The objective of this study is to further characterize patients with focal electroencephalographic abnormalities and specifically in terms of response to treatment.

Method: We retrospectively revised clinical and EEG data of a group of consecutive JME patients followed at our Epilepsy Service. The first EEG available for each patient was reviewed by two independent electroencephalographers.

Results: Twenty-eight patients with JME were identified: 11 (39.3%) were resistant to at least one antiepileptic drug (AED), including valproic acid, lamotrigine, topiramate or levetiracetam. All patients except two had generalized epileptiform abnormalities. In our group, EEG asymmetries were detected in 57.1% of the cases. In the AED-resistant group, 63.6% had asymmetries versus 52.9% in the AED-sensitive group but the difference wasn't statistically significant. Concordance between examiners was good. Analysis of patients with and without asymmetries showed no statistically significant differences in comparisons of age, familial history of seizure, presence of polyspike and slow wave, photosensitivity and timing of EEG related to onset of treatment.

Conclusion: Focal electroencephalographic abnormalities are frequent in patients with JME. These features should not be misinterpreted as being indicative of partial epilepsy. In our group, asymmetries were not associated with resistance to treatment.

T186
FOCAL POLYSPIKES IN ADOLESCENTS WITH IDIOPATHIC GENERALIZED EPILEPSY

Z. Ahmed, A. Akhter*, M. Mobin*, A. Malik*, F. Khan*, and K. Siddiqui†*
**Liaquat National Hospital, Karachi, Pakistan; and*
†Neuroscience Center, King Fahad Medical City, Riyadh, Kingdom of Sauid Arabia

Purpose: Polyspike discharges have been reported in patients with myoclonic epilepsies, especially juvenile myoclonic epilepsy (JME). We wanted to look at frequency of focal polyspike discharges in adolescents with Idiopathic Generalized Epilepsy (IGE).

Method: We looked at digital EEG data done over a period of three months from October-December 2007. We identified all adolescent patients who presented to us with a generalized seizure, diagnosed IGE, and had polyspike discharges, in addition to generalized spike and wave discharges. We looked at their demographics, reason for EEG referral, confirmation of presence of generalized epileptiform discharges and frequency and site of focal and generalized polyspikes discharges.

Results: We found 12 adolescent patients diagnosed with IGE as per, above criteria and had polyspike discharges. We found 9 males and 3 females. Mean age 14.5 years (SD+2.7). We confirmed the presence of generalized spike and wave discharge in various parts of recording, and reason for referral was a generalized seizure. We found 75%(n=9) had focal polyspikes and 25%(n=3) had generalized polyspikes seen, in addition to generalized spike and wave discharge. Most frequent sites for focal polyspikes were left frontotemporal and right centroparietal.

Conclusion: We conclude that in our adolescent patients focal polyspikes were seen in 75% of patients. This confirms the possibility of higher frequency of JME in patients with IGE, in this age. Focal polyspikes usually represents the semiologic evidence of asymmetric and focal myoclonic jerks that has been reported frequently in patients with JME.

T187

ELECTROENCEPHALOGRAPHIC FINDINGS IN POST–CABG ENCEPHALOPATHY

K. Siddiqui, A. Benito, M. Marasigan, M. ElMubarak, R. Bunyan, and S. Sinha

Neuroscience Center, King Fahad Medical City, Riyadh, Kingdom of Saudi Arabia

Purpose: Post CABG encephalopathy (PCE) occurs in about 7% of patients and can be due to varied etiologies. EEG may ascertain degree of encephalopathy, identify regional dysfunction and may points towards underlying etiology. We aim to determine the EEG findings associated with PCE.

Method: We reviewed EEG in all patients with diagnosis of PCE (diagnosed as per DSM -IV) b/w 2006 to 2008. In addition, we looked at demographics and neuroimaging findings.

Results: We identified 10 (9 males and 1 female) patients with PCE. Mean age (+ SD) was 64.9 (+ 9.1) years. PCE was diagnosed 5.6 (range 1–20) days post CABG. Seven patients had agitation and altered level of consciousness, and 3 presented with confused and acute seizures. EEG patterns observed were: a) Generalized theta + intermixed diffuse delta in 4 (40%); b) generalized theta + lateralized delta in 3 (30%); c) generalized theta with PLEDs and BIPLEDs in 2(20%); and d) One patient with electrographic seizure. Patients with generalized theta + intermixed delta had normal imaging. EEGs which showed generalized theta + lateralized delta, electrographic seizure and PLEDs had fresh infarcts. Patient with BIPLEDS had unremarkable imaging, but history of hypoxic insult.

Conclusion: Focal and epileptiform EEG patterns with acute cerebral insults was seen in 60% of patients with PCE. Nonconvulsive seizure detected by EEG may clinically present as PCE. Agitation and altered level of consciousness were commonest symptomatology in our cohort.

T188

SUPPRESSION OF CORTICAL EPILEPTIC ACTIVITY IN RATS AND HUMANS BY CARBON DIOXIDE

E. Tolner, J. Otahal‡, P. Hassinen†, G. Tsenov‡, E. Gaily†, L. Metsahonkala†, S. Schuchmann§, H. Kubova‡, S. Vanhatalo†, and K. Kaila**

**University of Helsinki, Finland; †Helsinki University Central Hospital, Finland; ‡Institute of Physiology, Academy of Sciences of The Czech Republic, Prague, Czech Republic; and §Neuroscience Research Center, Charitè, Berlin, Germany*

Purpose: We recently showed that experimental febrile seizures in neonatal rats are triggered by a respiratory alkalosis, and blocked by 5% CO2 applied in the ambient air (Schuchmann et al., Nat Med 2006; 12: 817–823). Since changes in acid-base balance are known to have significant effects on neuronal excitability also in the mature brain, we set out to study the effects of CO2 on cortical epileptic activity both in adult rats and humans.

Method: A rat model for myoclonic seizures was used in which electrical stimulation of the sensorimotor cortex elicits bilateral epileptiform afterdischarges in the EEG that are paralleled by clonic seizures of face and forelimb muscles. Studies in humans were performed on epileptic patients undergoing video-EEG monitoring for prospective epilepsy surgery. Gas mixtures consisted of 5% or 10% CO2 in air in rats, and 5% CO2 in oxygen in humans (medical carbogen). They were applied for 3 minutes before stimulation in rats, and in humans for a period of 20–30 seconds shortly after the start of generalized seizure activity.

Results: In rats, 10% CO2 application dramatically reduced or completely blocked the stimulation-evoked epileptiform afterdischarges. In the epileptic patients, 5% CO2 application significantly reduced the duration of generalized seizures.

Conclusion: Our data suggest that application of CO2 may be effective in the acute treatment of epileptic seizures not only in neonates but also in adults. This study was supported by the Academy of Finland, the European Integrated Project EPICURE/EFP6-037315, and grant #1QS501210509 from the Academy of Sciences of the Czech Republic.

T189

EVENT-RELATED POTENTIALS (ERPS) IN THE EVALUATION OF THE EFFECT OF LEVETIRACETAM AND CARBAMAZEPINE ON COGNITIVE FUNCTIONS IN ADULT NEWLY DIAGNOSED EPILEPTIC PATIENTS. PRELIMINARY RESULTS OF A RANDOMIZED OPEN TRIAL

L. Specchio, R. Goffredo*, O. Castriota*, M. de Tommaso†, A. La Neve†, A. de Palo†, T. Di Claudio*, and M. Guido**

**Clinic of Nervous System Diseases, University of Foggia, Italy; and †Clinic of Nervous System Diseases, University of Bari, Bari, Italy*

Purpose: To evaluate effect of levetiracetam (LEV) and controlled-release carbamazepine (CBZ-CR) on cognitive functions of newly diagnosed focal cryptogenic epilepsy patients by ERPs in a randomized open trial.

Method: Patients were randomized to LEV or CBZ-CR. P300 and contingent negative variation (CNV) were performed with an oddball acoustic paradigm before (T0) and after 12 (T1) and 24 (T2) weeks. At same times patients underwent neuropsychological tests. P300 amplitude and latency and CNV amplitude were considered for analysis that was performed by ANOVA and Spearman correlation test.

Results: Twenty-seven patients were recruited (13 LEV, aged 42 -17; 14 CBZ-CR, aged 35 -14). Three patients on CBZ-CR dropped out (2 lost during follow-up, 1 for skin rash). All patients were seizure-free at 12th week. P300 showed a tendency to decrease in amplitude and increase in latency in CBZ-CR patients, but no changes were found in LEV group [mean amplitude±SD: LEV (T0) 11.6+6.8, (T1) 11.2+6.4, (T2) 11.3+7 mVs; CBZ-CR (T0) 11.9+8.3, (T1) 11.8+9.4, (T2) 9.9+6.5 mVs; mean latency±SD: LEV (T0) 297.7+29.3, (T1) 289.1+26.2, (T2) 290.5+28.4 msec; CBZ-CR (T0) 289+49.2, (T1) 298.2+42.2, (T2) 305.2+43.9 msec]. These variations were not significant. No variations were found in CNV amplitude [LEV (T0) 9.6+2.9, (T1) 9.4+2.1, (T2) 9.1+1.5 mVs; CBZ-CR (T0) 8+1.9, (T1) 9.4+2.2, (T2) 7+1.8 mVs]. No differences emerged in neuropsychological scores.

Conclusion: Results show a trend of impairment of P300 in CBZ-CR patients indicating a possible effect of drug on attention and working memory. The lack of significativity requires caution and could be explained with scarse numerosity of patients.

T190

ACCURACY OF INDIVIDUAL MRI BASED ELECTRIC SOURCE IMAGING OF EPILEPTIC SPIKES IN PATIENTS WITH EXTENSIVE BRAIN LESIONS

V. Brodbeck, L. Spinelli†, M. Seeck†, and C. Michel**

**Functional Brain Mapping Laboratory, University Hospital and Department of Fundamental Neuroscience, University Medical School Geneva, Switzerland; and †Presurgical Epilepsy Unit, University Hospital Geneva, Switzerland*

Purpose: To evaluate the accuracy of electric source imaging (ESI) in localizing epileptogenic cortical areas in patients with symptomatic epilepsy and large brain lesions where conductivity inhomogeneity could interfere with the localization precision.

Method: We recorded high-density (128–256 channel) spontaneous EEG containing numerous spikes in eight patients with symptomatic focal epilepsy and extensive brain lesions. offline analysis comprised visual identification of spikes, and ESI analysis using a distributed linear inverse solution constrained on the gray matter of the individual MRI. Paired t-tests compared each time point of the spike period with a pre-spike baseline for each voxel. All 8 patients underwent surgical intervention and had a favourable postoperative outcome (Engel's Classification I) providing reliable confirmation of the goodness of identification of the epileptogenic region.

Results: In all patients the statistical analysis showed first significant active voxels well before the peak of the spike, correctly localized within the epileptogenic zone. Sources at the maximal negativity of the spike already included propagated areas or even located falsely only propagated regions. The need of the individual MRI as head model was evident.

Conclusion: ESI of epileptic activity is a useful tool in presurgical evaluation of epilepsy patients even in cases with extensive brain lesions. Eventual changes in conductivity values due to the lesions do not seem to impede correct source identification. Our data also confirm again that the rising phase of the spike provides more accurate information than the spike maximum because of rapid propagation of interictal activity.

T191

ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) AND ITS ELECTROENCEPHALOGRAPHIC (EEG) FINDINGS

S. Bakhtadze, N. Geladze, N. Khachapuridze, and M. Megrelishvili
Tbilisi State Medical University, Tbilisi, Georgia

Purpose: ADHD is one of the most frequent disorders of childhood. The prevalence of ADHD among children with epilepsy estimated between 12 and 39%, is much higher than in the general population. Less is known about EEG parameters of nonepileptic ADHD children and their practical importance. Thus, the aim of our research was to assess the EEG of seizure free ADHD children and their significance for improving the pharmacological management of ADHD.

Method: We've conducted prospective study of 76 seizure-free children with ADHD, between 6–12 years (42 boys, 34 girls), which meet ADHD criteria by DSM-IV.

Results: In 23 children (30%) EEG was normal. 35 had focal spikes (28 presented by spike-wave activity); 18-bilateral (generalized) spikes. In the group with normal EEG (30%) cognitive impairment was minimal. Another 70% showed various cognitive problems. Attention and concentration was affected in both group with bilateral spikes and with focal discharges. Learning disability was significantly related to focal epileptiform activity.

Conclusion: According to results, it is evident that only 30% of ADHD children have normal EEG, another 70% have subclinical epileptiform EEG events affected cognitive functions and educational attainments by different way. Suppression of such discharges by antiepileptic therapy must be discussed, which in combination with stimulants may be more effective in correction of behavioral problems occurring in ADHD.

T192

DISTRIBUTION, DURATION AND SPECTRAL CHARACTERISTICS OF INTERICTAL HIGH-FREQUENCY EPILEPTIC OSCILLATIONS RECORDED USING STANDARD DEPTH MACROELECTRODES IN PATIENT WITH CORTICAL DYSPLASIA

M. Brazdil, J. Halámek†, P. Jurak†, P. Daniel*, R. Kuba*, J. Chrastina*, Z. Novak*, and I. Rektor**
**Brno Epilepsy Center, St. Anne's University Hospital And Medical Faculty of Masaryk University, Brno, Czech Republic; and †Institute of Scientific Instruments, Academy of Sciences of The Czech Republic, Brno, Czech Republic*

Purpose: Interictal high-frequency oscillations (ripples /R/ and fast ripples /FR/) have been recently reported in recordings from depth macroelectrodes in epileptic patients. FR mostly differentiated between the seizure onset zone (SOZ) and remote areas, whereas R did not. FR clearly predominated in the SOZ in the majority of patients. Surprisingly, FR was more frequent outside the SOZ in the only published patient with cortical dysplasia investigation. This finding suggests different electrophysiological properties for this specific pathological condition.

Method: In this study, we report high-frequency epileptic oscillations in signals from standard depth macroelectrodes implanted during long-term preoperative evaluation in a patient with cortical dysplasia and intractable focal epilepsy. SEEG recordings were obtained interictally during wakefulness. They were low-pass filtered at 450 Hz and sampled at 1024 Hz. The characteristics of ripples (80–200 Hz) and fast ripples (200–450 Hz) within and outside the SOZ were analyzed.

Results: R and FR occurred in recordings from both within and outside the SOZ, mostly at the same time as interictal spikes. This association was stronger in the SOZ. The rate of FR occurrence was significantly higher in recordings from within the SOZ (median, 540/min versus 370/min), whilst the rate of R occurrence was higher from outside the SOZ (238/min versus 160/min). The duration of R and FR was approximately double within the SOZ compared to recordings from outside the SOZ. The mean power of R was significantly higher within the SOZ than outside the SOZ, whilst the mean power of FR was comparable within and outside the SOZ.

Conclusion: The limitations of standard analysis of R and FR are discussed and new methods of mathematical analysis will be suggested.

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T193

INTERICTAL SPIKING RATE IN RELATION WITH SEIZURE OCCURRENCE AND SLEEP STAGES: A STEREO-EEG STUDY

I. Merlet, F. Bartolomei†, P. Chauvel†, and F. Wendling**
**INSERM U642, University of Rennes, France; and †INSERM, U751, Marseille, France*

Purpose: On one hand, preictal modification in the spiking rate remains a matter of debate. On the other, variable changes of the spike frequency have been observed during sleep stages yet their topographical relationship to the epileptogenic zone (EZ) remains unclear. In this study we concomitantly explored the relationship between spike frequency and 1) the occurrence of seizures and 2) sleep stages in depth EEG signals.

Method: For each patient, interictal spikes were automatically detected for each intracerebral contact where spikes occurred to estimate the average spike rate per minute over the Stereo-EEG exploration (several days). At each minute we defined both the vigilance state (wakefulness, light sleep, deep sleep, REM-like sleep) and the 'distance to seizures' (interictal, preictal and postictal). The EZ was determined by visual inspection of EEG traces at seizure onset.

Results: Patients with mesiotemporal ictal onsets had seizures mostly during wakefulness, when the spike rate was low, conversely to patients with temporal neocortical ictal onset for whom seizures occurred during light sleep. EZ regions showed specific patterns of variations between interictal, preictal and postictal periods. In particular, the spike rate initially decreased and then increased just before seizure. Results also revealed reproducible changes of interictal vs. postictal spike frequency in the EZ.

Conclusion: These preliminary results suggest that in the EZ, specific changes might be observed in the transition between sleep stages as well as between interictal and ictal states. Current work aims at processing data from a larger cohort of patients, including extratemporal EZ.

T194
EPILEPSY IN RETT SYNDROME WITH MECP-2 MUTATIONS: A CLINICAL AND VIDEO-POLYGRAPHIC STUDY

G. d'Orsi, V. Demaio*, M. Minervini*, A. La Neve†, D. Galeone‡, V. Sciruicchio‡, T. Calvario§, and L. La Selva¶*
**Epilepsy Center – Casa Divina Provvidenza, Opera Don Uva – Bisceglie Bari, Italy; †Epilepsy Center, University of Bari, Italy; ‡Giovanni XXIII Hospital, Bari, Italy; §Neurological Rehabilitation, 'Quarto Di Palo' – Andria Bari, Italy; and ¶Epilepsy Center, San Paolo Hospital, Bari, Italy*

Purpose: To investigate the clinico-polygraphic features of seven girls with epilepsy and stage 2 to 4 Rett syndrome (RTT) with a proven MECP2 mutation.

Method: All patients underwent a full clinical and neurophysiological examination with long-term video-polygraphic monitoring.

Results: Many events classified as seizures weren't epileptic and usually included episodes of motor activity as well as of breathing abnormality; spells identified by parents as nonepileptic manifestations were contrary epileptic (i.e. myoclonic seizures). The mean age at seizure onset was 4,5 years (range 1–10 years). Seizure types were focal in two patients, focal with secondary generalization in three; two patients were affected by myoclonic seizures (M) and recurrent myoclonic status (MS). During the course of epilepsy, seizures remained rare in frequency and responded to therapy; in particular, Levetiracetam improved dramatically M and MS. Only three patients proved to be drug-resistant. EEG showed multifocal and bilateral abnormalities, increased in sleep, in all stages of disease. Multifocal and arrhythmic myoclonus appeared in six patients. Jerk-locked back-averaging of EEG activity showed a cortical origin in all patients. Apnea and hyperventilation were reported almost entirely during wakefulness. In one patient, central apnea was evident during sleep. Tachycardia and cardiac arrhythmias were documented in five patients.

Conclusion: Epileptic seizures may be overestimated, but also underestimated in RTT. Although EEG abnormalities appeared in all stages of disease, the relatively benign course of epilepsy emerged in 4 of 7 patients. Breathing disturbances, cortical myoclonus and tachycardia were present in most patients.

T195
THE EPILEPSY DIAGNOSIS BY ECHOENCEPHALOGRAPHY AND INTERNET

V. Andreev
Moscow State Medical Stomatology University, Moscow, Russia

Purpose: The aim of the present work is to study the echo-spikes at the focal and general epileptic ictus. This work was directed to find the method epilepsy diagnosis at general practice.

Method: This method was realized with an A-mode BIOSS Ultrasound scanner Angiodin-ECHO. A 1.5 mega Hz ultrasound transducer was fixed to an area about the root of the ear. We examined patients with 14 focal epileptic seizures, 17 patients with epileptic hemiclonic seizures and patients with 9 hemiclonic psychogenic seizures. The age range was 17–49 years. For clinical diagnosics we used the search engines of the Internet.

Results: The 4–5 mm midline spike shift at ictus was strong evidence of a focal epileptic seizure. At generalized seizures multiple echoencephalography spikes (MES) were observed. During psychogenic seizures there were no visible midline spike shift and MES. We took patient's two strong evidential signs as for example 'myoclonic epileptic seizure' and 'eye fundus macula red spot'. The results of the search give us few references about sialidosis and one reference with Tay-Sachs disease. Taken together all received references we can get a moment diagnostic database. Using the third sign 'age adolescent' we receive the exact diagnosis – sialidosis.

Conclusion: A-mode midline spike shift and MES may be strong evidence of the increase in the cerebral regional blood flow. This method of application is covered by patent [1]2182463 (2001) registered in Russian Federation. The knowledge from Internet can be used as a database for the diagnostics in general practice.

T196
INTERICTAL MAGNETOENCEPHALOGRAPHY (MEG) SPIKES REVEAL FOCAL CORTICAL DYSPLASIA TYPE 2B

R. Paetau,‡, L. Valanne†, A. Paetau‡, L. Metsähonkala*, G. Blomstedt*, M. Medvedovsky†, L. Lauronen‡, E. Kirveskari‡, J. Mäkelä‡, and E. Gaily**
**Helsinki University Central Hospital, Helsinki, Finland; †University of Helsinki, Finland; and ‡Huslab, Hospital District of Helsinki and Uusimaa, Finland*

Purpose: Focal cortical dysplasias (FCDs) are highly epileptogenic, but challenging targets for surgery, because they may be poorly visible on MRI, and often have extra-temporal and sulcal location. We studied the sensitivity of magnetoencephalography (MEG) to identify the epileptogenic FCD2b (with balloon cells).

Method: We included 11 operated patients whose pathologico-anatomical examination revealed FCD2b and who had been studied with MEG preoperatively. The presurgical workup also included structural 1.5 and / or 3-Tesla magnetic resonance imaging (MRI) and long-term video-EEG. The extent of resection was based on preoperative findings and extraoperative subdural grid recordings, including direct cortical stimulation mapping. Ten patients were seizure-free after surgery during follow-up ranging from 3 months to 8 years.

Results: MRI revealed FCD lesions in nine patients: four in the superior frontal sulcus, one in the medial frontal cortex, and four in the sulci adjacent to the primary sensorimotor (SM1) cortex. In eight patients, MEG spikes were generated at the epileptogenic cortex; two of these patients had normal 3-T MRI, but microscopic FCD2b in the right SM1 (one patient) and in the right temporo-parietal cortex (one patient). Three patients with MRI lesion showed no MEG spikes (one baby and two with rare spikes), and two patients generated sylvian spikes outside the epileptogenic lesion.

Conclusion: MEG spikes appear sensitive in localizing the epileptogenic FDC2b region, sometimes even in patients whose FCD2b is beyond MRI resolution. This may be due to the typical sulcal location and abundant electrical activity of FCD2b.

T197
ROLE OF VIDEO EEG POLYSOMNOGRAPHY IN DIFFERENTIAL DIAGNOSE OF PAROXYSMAL MOTOR ACTIVITY

E. Feketeová, M. Tormašiová, J. Janèo, and J. Dragašek
Safarik University, Kosice, Slovak Republic

Introduction: Paroxysmal motor activity during night and on certain occasions during wakefulness has to be considered for primary sleep disorder (disorders of arousal, parasomnias associated with REM sleep, other parasomnias,), epileptic seizure, and psychiatric disorder. The differential diagnosis between these conditions is based on clinical manifestation (stereotyped motor activity, onset, recurrence of the episodes and their duration) and EEG recording. Missing objective history with precise description of the motor activity and the fact, that even ictal EEG can fail to disclose paroxysmal epileptiform abnormalities produce clinical uncertainty. The role of video EEG polysomnography for the clinical diagnosis by documenting epileptiform activity or typical changes in hypnogram accompanying motor activity is presented on four cases. Two cases with frontal lobe epilepsy misinterpreted as somnambulism because of missing ictal epileptiform activity are described. The third case with frequent transient focal neck and facial muscle weakness accompanied by periorbital muscle twitches was diagnosed as pharmacoresistant partial epilepsy in mistake of status cataplecticus in narcolepsy. A man (4th) with paroxysmal psychosis was treated as epilepsy due to EEG abnormalities (connected with thyreotoxicosis), in error of recurrent hypersomnia.

Conclusion: Video EEG polysomnography analysis provides effective and sensitive diagnostic tool for evaluation of the patient with paroxysmal motor activity in cases being resistant on standard treatment or having atypical clinical course.

Monday 22 – Wednesday 24 September 2008
Traditional Poster Session
Drug Therapy

T198
ANTIEPILEPTIC DRUG WITHDRAWAL AFTER ANTERIOR TEMPORAL LOBECTOMY IN PATIENT WITH TEMPORAL LOBE EPILEPSY

V. Fedotov
Kharkov State Medical University, Ukraine

Purpose: To assess the rate of successful antiepileptic drug (AED) discontinuation, prognostic factors and proper time of AED withdrawal after surgery for medial temporal lobe epilepsy (MTLE).

Method: We reviewed 82 consecutive patients who underwent resective surgery for MTLE. All patients were followed up for more than two postoperative years. AEDs were slowly tapered with an individualized schedule for each patient. Outcome status was determined from medical records and telephone interviews.

Results: 37.8% of patients experienced no seizure recurrence. 31.7% discontinued medication without seizure recurrence for more than 2 years at final assessment. Multivariate analysis revealed that an age greater than 10 years at surgery and postoperative AED reduction before 10 months increased the risk of recurrence [hazard ratio (HR) 2.4, 95% confidence interval (CI) 1.7–4.2 and HR 2.5, CI 1.1–5.6].

Conclusion: Resective surgery for MTLE brings seizure remission without AED to one-third of patients. Postoperative AED tapering is recommended after at least 12 months. Younger age at surgery is a good predictive factor of remission after MTLE surgery.

T199
EFFECTS OF LEVETIRACETAM, PHENOBARBITAL AND LAMOTRIGINE ON NEUROPSYCHOLOGICAL PERFORMANCE AND MOOD IN PATIENTS WITH ALZHEIMER'S DISEASE AND EPILEPSY

E. Cumbo
A.U.S.L.2 Caltanissetta, Italy

Purpose: To evaluate cognitive performance and mood changes in elderly patients with mild to moderate Alzheimer's disease (AD) and epilepsy during one year antiepileptic drug (AED) treatment.

Method: 80 patients (65–80 years) were randomized to receive either LEV (mean dose 955.88 mg/day), LTG (mean dose 57.2 mg/day) or PB (mean dose 90 mg/day), as monotherapy. Neuropsychological test included MMSE, ADAS-Cog and Cornell scale for depression. All subjects were evaluated at baseline and after 6 and 12 months. All groups were compared with a group of control (63 subjects). All subjects have been taking a colinesterase inhibitor for dementia.

Results: Out of 80, 11 subjects withdrew from the study. Analysis PP (69 patients) at 12 months LEV group: the mean change in MMSE scores was + 0.41; in ADAS-Cog score was – 0.32. PB group: the mean change in MMSE scores was – 1.61; in ADAS-Cog score was -1.78 scores. LTG group the mean change in MMSE score was -0.70; in ADAS-Cog score was -0.39. Subjects treated with LTG scored better for measures of mood (-0.52) respect to LEV (+0.20) and PB (+1.74). Control group (60 subjects) 3 points improvement in MMSE; 5.92 points decrease in ADAS-Cog score; 0.12 points worsening in Cornell score.

Conclusion: LEV shows a good neuropsychological and tolerability profile in epileptic patients with cognitive impairment. LTG had a better influence on mood than other AED. PB shows persistent negative cognitive side effects.

T200
THE EFFECT ON COMPLIANCE AFTER SWITCH FROM LIQUID TO CHRONOSPHERE FORMULATION OF VALPROATE

M. Mazurkiewicz-Beldzinska, A. Matheisel*, and R. Roczeñ†*
**Medical University of Gdansk, Poland and †Sanofi-Aventis, Poland*

Purpose: One of the very important elements that influence the efficacy of antiepileptic therapy is compliance. The aim of the study was to find out if the type of formulation of valproate (and connected with it numbers of day doses) effect on compliance.

Method: That was the multicenter questionnaire research. The questionnaires that were distributed to the pediatric neurologists included 20 questions about the preferable type of drug formulation. The design of the study was submitted to the Independent Bioethical Committee and the approval was obtained. The parents or caregivers signed informed consent form before they were asked the questions from the questionnaire.

Results: There were 543 questionnaires completed. The patients age ranged from 11 months to 17 years (mean 5,86 years). There were 264 girls and 279 boys. All the patients were treated with valproate and switched from liquid to chronosphere formulation more than four weeks before the data were collected. The percentage of patients that did not follow the dosage instructions was 3,8% during the therapy of chronosphere, and 56,55% on liquid formulation. 96,5% of parents or caregivers were more satisfied with the chronosphere formulation, which one of the advantages is the possibility of administering only once daily (98% of responders preferred this mode of administration).

Conclusion: The new formulation of valproate – chronosphere, is a valuable treatment option which significantly improves the compliance.

T201
EFFECT OF GERMANIUM DYPHOSPHONATE COMPOUND ON THE ANTICONVULSANT ACTIVITY OF CONVENTIONAL ANTIEPILEPTIC DRUGS IN MICE

O. Kashchenko, V. Godovan*, V. Kresyun*, and P. Shandra†*
**Odessa State Medical University, Ukraine; and †Odessa National University, Ukraine*

Purpose: The aim of the study was to evaluate the influence of germanium dyphosphonate compound with nicotinamide (MIGU-5) on the antiseizure activity of conventional antiepileptic drugs (AEDs): carbamazepine (CBZ), phenitoin (PHT), valproate (VPA), diazepam (DZP) and lamotrigine (LTG).

Method: the anticonvulsant effects of MIGU-5 and its combination with AEDs at fixed drug-dose rations of 1:3, 1:1 and 3:1 were determined in maximal electroshock (MES) and 6 Hz-induced seizures in mice.

Results: combination of MIGU-5 with CBZ, PHT, LTG et the fixed ratio of 1:3, 1:1, 3:1 produced supra-additive (synergistic) interactions in two experimental models. All other MIGU-5/AED combinations displayed additive effects. Futhermore, no enhanced adverse effects were induced by combinations of MIGU-5 with these AEDs as assessed in the rotarod test.

Conclusion: The isobolographic analysis revealed that combinations of MIGU-5 with CBZ, PHT and LTG seem to be favourable from preclinical viewpoint due to synergistic (supraadditive) interactions in two experimental models of epilepsy.

T202
EFFICACY AND TOLERABILITY OF LEVETIRACETAM MONOTHERAPY IN PARTIAL AND GENERALIZED SEIZURES

P. Palumbo, P. Forleo, A. Caruso, and R. Campostrini
Epilepsy Center, Neurology Unit, Prato City Hospital, Italy

Purpose: To retrospectively evaluate the efficacy and tolerability of Levetiracetam (LEV) monotherapy in an outpatient series.

Method: We have identified 23 patients (10 female, 13 male; mean age 65.6+/−22.31 SD years) with a confirmed diagnosis of epilepsy, receiving LEV monotherapy. Four patients had generalized idiopathic epilepsy, 13 partial symptomatic epilepsy, and 6 cryptogenic epilepsy with partial seizures, with or without secondary generalization. Five patients began LEV as first line therapy. Seventeen patients were converted to LEV monotherapy after failing of previous AEDs (VPA, PHT, PB, CBZ, OXC, and TPM) for adverse events despite good seizure control (11) and for lack of efficacy (6). Patients were evaluated every three months, for a mean follow-up of 23.5 months (range 12–41).

Seizure frequency changes and side effects were observed.

Results: LEV was increased with a rapid titration, the dose individualized over the range of 1000–3000 mg/die (mean 1956,5 mg/day). Three patients (13%) interrupted LEV monotherapy: 2 for lack of efficacy, 1 for adverse events. Among patients who continued LEV monotherapy: All 9 (39%) seizure free patients maintained the seizure control achieved with previous AEDs. 8 (35%) became seizure free. 2 (9%) had more than a 50% seizure reduction. 1 (4%) had no significant change in seizure frequency. Seven (30%) developed mild adverse effects. One patient (4%) discontinued LEV because of gastric upset.

Conclusion: Our data confirm that LEV monotherapy has high tolerability and effectiveness. The safe profile of LEV could be useful particularly in the elderly.

T203
EFFICACY AND TOLERABILITY OF PREGABALIN IN PATIENTS WITH DIFFICULT-TO-TREAT EPILEPSY AND INTELLECTUAL DISABILITY

*B. Huber, M. Bocchicchio, E. Feuerbaum, T. May, T. Meinert, E. Robertson, H. Schorlemmer, W. Wagner, E. Wilking, and M. Seidel**
VBA Bethel, Bielefeld, Germany

Purpose: In a retrospective evaluation of 32 in-patients with therapy-resistant epilepsy and intellectual disability, the efficacy of PGB treatment was assessed after 6 and 12 months.

Method: In order to refine the usual 50% reduction criterion, a combined efficacy measure was used which also included the Clinical Global Impression (CGI) scale. Tolerability was assessed using a list of the ten adverse effects most frequently observed in the regulatory studies, and also by the CGI scale.

Results: After 6 months, the retention rate was 75%. 6 patients (18.75%) were responders (50% seizure reduction and/or 'good' or 'very good' effect on CGI scale). 7 patients had adverse effects that were not impairing. 8 patients had side effects that impaired essentially. Half of the patients reported no side effects at all. Weight gain, somnolence, asthenia and ataxia were the most frequent adverse effects. Rare adverse events were severe mental slowing and loss of daily life capacities on a low dose of PGB in one patient and an increase of auto-aggression in another. After 12 months, the retention rate was 40.6% and the responder rate was 25%.

Conclusion: Statistical analysis did not identify any predictor of outcome (seizure type, epilepsy syndrome, comedication, degree of intellectual disability). In this highly selected population the efficacy of PGB was only moderate.

T204
ZONISAMIDE IN CHILDREN AND ADOLESCENTS WITH REFRACTORY EPILEPSY: AN OPEN-LABEL, MULTICENTER EXPERIENCE

G. Coppola, S. Grosso†, A. Verrotti‡, P. Parisi§, A. Luchetti§, E. Franzoni¶, S. Mangano**, A. Pelliccia§, F. Operto*, P. Iannetti§, P. Curatolo††, P. Balestri†, and A. Pascotto**
*Seconda Università Degli Studi Di Napoli, Italy; †University of Siena, Siena, Italy; ‡University of Chieti, Italy; §La Sapienza II University, Rome, Italy; ¶University of Bologna, Italy; **University of Palermo, Italy; and ††Tor Vergata University of Rome, Italy*

Purpose: To report the first multicenter Italian experience of zonisamide as adjunctive therapy for refractory generalized or partial epilepsy in children and adolescents.

Method: Patients were recruited into this open-label study from eight Italian centres. Eighty-two patients (45 males, 37 females) aged 3–34 years (mean 13.1 years) with partial (n=47) or generalized (n=35) refractory epilepsy, were enrolled into the study. Twice daily zonisamide was added to baseline therapy at a starting dose of 1 mg/kg/day. This dose was increased in increments of 2 mg/kg every 1–2 weeks over a period of up to 3 months, adjusted at the investigator's discretion according to response and tolerability, to a maximum dose initially set at 12 mg/kg/day.

Results: Zonisamide was administered at a mean daily dose of 5.7 mg/kg/day (range 1–12 mg/kg/day). Nine patients (11.0%) were seizure free after a mean follow-up period of 11.9 months (range 2–64 months). Seizure frequency was reduced by 50–99% in 31 patients (37.8%), and by 25–49% in 5 patients (6.1%). Seizure frequency remained unchanged in 29 patients (35.4%), and increased in 8 patients (9.8%). After 15 months of follow-up, 61 patients (74.4%) were still receiving zonisamide, while 21 (25.6%) had withdrawn from the study. Twenty-two patients (26.8%) reported adverse events (AEs) while taking zonisamide. AEs generally appeared during the early stages of treatment, and were mild to moderate in severity. The most common AEs were irritability and decreased appetite.

Conclusion: Zonisamide was well tolerated and reduced seizure frequency in pediatric patients with refractory partial and generalized epilepsy.

T205
EFFICIENCY OF ADD-ON ZONISAMIDE IN ADULTS: A 3-YEAR FOLLOW-UP

M. Bacher, and B. Steinhoff
Epilepsiezentrum Kork, Kehl-Kork, Germany

Purpose: To assess the long-term efficacy and tolerability of zonisamide (ZNS) based on clinical retention rates.

Method: A prospective, year-by-year, ongoing assessment of clinical data files of all adult epilepsy patients who were treated with add-on ZNS between June and December 2005.

Results: In total, 57 adult patients, most of who were suffering from intractable focal epilepsy syndromes, have been prospectively followed since 2005. The most recent retention rate is 39%, compared with the previously reported 1- and 2-year retention rates of 75% and 45%, respectively. In most cases the tolerability of ZNS was good and the efficacy profile was satisfactory. We did not identify any new late-onset long-term adverse events.

Conclusion: Based on our experience, ZNS is a favourable addition to our antiepileptic drug treatment options.

T206
ZONISAMIDE FOR PARTIAL ONSET SEIZURES: AN OPEN-LABEL STUDY (ZEUS)

S. Dupont, S. Striano†, E. Trinka‡, J. Springub§, A. Giallonardo¶, P. Smith**, S. Ellis††, A. Yeates‡‡, and G. Baker§§*
**Hôpital Pitié-Salpêtrière AP-HP, Paris, France; †Federico II University, Napoli, Italy; ‡Medical University, Innsbruck, Austria; §Joint Practice for Neurology and Psychiatry, Westerstede, Germany; ¶University of Rome La Sapienza, Rome, Italy; **Welsh Epilepsy Research Network (WERN), University Hospital of Wales, Cardiff, UK; ††North Staffordshire Royal Infirmary, Staffordshire University, Stoke-On-Trent, UK; ‡‡Eisai Europe Ltd, Hatfield, UK; and §§University of Liverpool, Liverpool, UK*

Purpose: ZEUS (EudraCT reference 2005-001982-33) assessed the efficacy and safety of zonisamide in a diverse adult patient population.

Method: ZEUS was an open-label, flexible-dosing study of adjunctive zonisamide in patients with refractory partial epilepsy, receiving ¡Ü2 concomitant AEDs. The primary efficacy end point was change in seizure frequency from baseline to Week 19. Secondary end points included 50% responder rate, seizure severity and quality of life (QoL).

Results: of 317 patients enrolled, 207 completed the study; 43 (15.3%) were withdrawn due to AEs, 13 (4.6%) due to lack of therapeutic benefit and 8 (2.8%) due to protocol deviation. The most common seizure types at baseline were any complex partial (193 patients), any partial leading to generalized tonic–clonic (155 patients) and complex partial with automatisms (115 patients). At the end of Week 19, patients demonstrated a significant median reduction in monthly seizure frequency of 41.1% (95% CI C50.0, C30.4), and a responder rate of 44.2% (95% CI 0.37, 0.51) [observed cases]. 15.9% of patients achieved total freedom from seizures. Significant improvements were also observed in seizure severity and QoL. The most commonly reported AEs were fatigue, somnolence and headache. Somnolence was the most common AE leading to discontinuation (3.2%). 182 patients (64.8%) experienced AEs suspected to be related to zonisamide. The most common AEs suspected to be related to zonisamide were somnolence (14.9%), fatigue (14.9%), asthenia (8.2%), nausea (6.0%) and headache (6.0%).

Conclusion: Zonisamide was effective and well tolerated in refractory partial epilepsy in a naturalistic setting with clinically relevant dosing.

T207
EFFICACY AND TOLERABILITY OF ZONISAMIDE IN IDIOPATHIC GENERALIZED EPILEPSY

J. Serratosa, A. Marinas*, B. Giráldez*, A. Molins†, J. Salas-Puig‡, and V. Villanueva§*
**Fundación Jiménez Díaz, Madrid, Spain; †Hospital Josep Trueta, Gerona, Spain; ‡Hospital Central de Asturias, Oviedo, Spain; and §Hospital La Fe, Valencia, Spain*

Purpose: The objective of this study was to evaluate the efficacy and safety of zonisamide (ZNS) in the treatment of idiopathic generalized epilepsy.

Method: Thirteen patients with idiopathic generalized epilepsy who were treated with ZNS between the years 2006 and 2008 were identified. Efficacy and tolerability were assessed at months 6 and 12. Efficacy was assessed by comparing monthly seizure frequency during the last 3 (6 month follow-up group, n=13) and 9 months (12 month follow-up group, n=12) with the 1 year pre-ZNS seizure frequency. Response was defined as >50% reduction in seizure frequency.

Results: Two patients had childhood absence epilepsy, 2 juvenile absence epilepsy, 6 juvenile myoclonic epilepsy and 3 idiopathic generalized epilepsy with generalized tonic–clonic seizures only. Twelve patients continued on ZNS at month 6 (92%), and 10 (76.9%) at month 12. Mean daily dose was 319 mg (range 100–500 mg/d). At month 6, 8 of the 12 patients (66.6%) were responders and 7 (58.3%) were seizure free. At month 12, 7/10(70%) patients were responders and 6/10(60%) were seizure free. For absences, response was observed in 3/5(60%) at month 6 and 4/5(80%) at month 12; for generalized tonic–clonic seizures in 7/10(70%) at month 6 and in 6/9(66.6%) at month 12; for myoclonic seizures in 3/5(60%) at month 6 and in 2/4(50%) at month 12. Four patients out of 13 (30.7%) experienced adverse events. In 2, (15.3%), these led to withdrawal.

Conclusion: In this retrospective and open-label study, ZNS showed efficacy in 66.6% (month 6) and 70% (month 12) of patients with idiopathic generalized epilepsy. Absences and generalized tonic–clonic seizures responded better.

T208
SURVEILLANCE OF CROATIAN PREGNANT WOMEN WITH EPILEPSY – NEURODEVELOPMENTAL AND TERATOGENIC EFFECTS OF ANTIEPILEPTIC DRUGS EXPOSURE

S. Miskov, R. Gjergja Juraski, I. Mikula, L. Cvitanovic-Sojat, J. Bosnjak, and V. Demarin
University Hospital 'Sestre Milosrdnice, Zagreb, Croatia

Purpose: The teratogenic effects of antiepileptic drugs (AED) exposure in pregnancy have been recognized but the relative risks of new antiepileptic drugs and its long-term neurodevelopmental effects remain poorly understood.

Method: To follow up pregnancies exposed to AED and their offspring in order to assess teratogenic and neurodevelopmental effect of particular AED of newer generation.

Results: During 4.5 years we have surveyed 47 pregnancies and analyzed it according to woman's age, duration of epilepsy, frequency of seizures, exposure to specific AED, pregnancy planning and periconceptional folic acid intake, complications during pregnancy/delivery and pregnancy outcome. About 80% of pregnancies (39/47) were exposed to monotherapy: 23 to LTG, 7 to CBZ, 1 to PHT, 1 to PB, 1 to GBP, 4 to VP and 2 to MPB. Six pregnancies were exposed to polytherapy: 3 to TMP/VP, 1 to CBZ/PB, 1 to TMP/CBZ/PHT and 1 to VPA/clonazepam. Two women with epilepsy were without AED.

Conclusion: We have surveyed pregnancies exposed to LTG, VP, PHT, PB, GBP, TMP, CBZ, MPB and clonazepam. Besides 4 spontaneous abortions, 2 stillbirths, 2 premature deliveries we have also noted 1 evidence of intrauterine AED effect (intrauterine growth retardation and craniofacial dysmorphism) and 1 premature live-birth with ASD, psychomotor delay and epilepsy. Further follow up of live-births till school age will be also provided in order to assess the potential neurodevelopmental effect of AED in the offspring.

T209

EFFICACY AND SAFETY OF ESLICARBAZEPINE ACETATE AS ADD-ON TREATMENT IN ADULTS WITH REFRACTORY PARTIAL-ONSET SEIZURES: BIA-2093-302 STUDY

A. Hufnagel, E. Ben-Menachem†, A. Gabbai‡, J. Maia§, L. Almeida§, and P. Soares-da-Silva§*

**University of Essen, Essen, Germany; †Sahlgren University Hospital, Göteborg, Sweden; ‡Federal University of S. Paulo, S. Paulo, Brazil; and §BIAL – Portela & Co, SA, S Mamede Do Coronado, Portugal*

Purpose: To investigate the efficacy and safety of eslicarbazepine acetate (ESL) when used as adjunctive therapy in adult patients with 4 partial-onset seizures per 4 weeks despite treatment with 1–3 AEDs.

Method: Multicenter, double-blind, parallel-group, placebo-controlled study. After a 8-week baseline period, patients were randomized to placebo (n=100) or ESL 400 mg (n=96), 800 mg (n=100) or 1200 mg (n=97) once-daily. Treatment duration was 14 weeks. Patients in the 1200 mg group received 800 mg in the first 2 weeks. The other groups had no titration.

Results: The most frequent concomitant AEDs were carbamazepine (60% of patients), followed by valproic acid (22%) and lamotrigine (21%). Primary analysis was an ANCOVA of log-transformed seizure frequency in the intent-to-treat population. The difference to placebo was significant for both ESL 800 mg and 1200 mg during the 12-week maintenance period ($p<0.002$) and the overall 14-week treatment ($p<0.001$). Median relative reduction in seizure frequency was 33% (1200 mg), 33% (800 mg), 21% (400 mg) and 5% (placebo). The responder rate was 35% (1200 mg), 32% (800 mg), 20% (400 mg) and 18% (placebo). Discontinuation rates due to treatment-emergent adverse events (TEAEs) were 3.0% (placebo), 12.5% (400 mg), 18.8% (800 mg) and 26.5% (1200 mg). TEAEs occurring in >10% in total population were dizziness, somnolence and headache. Most TEAEs were mild or moderate in severity.

Conclusion: ESL 800 mg and 1200 mg once-daily adjunctive therapy was well tolerated and effective in reducing partial-onset seizures in patients' refractory to treatment with 1–3 concomitant AEDs. Supported by BIAL- Portela & Co, SA.

T210

A RANDOMIZED, DOUBLE-BLIND, PLACEBO- AND MOXIFLOXACIN-CONTROLLED, 4 PERIOD CROSSOVER TRIAL TO EVALUATE THE EFFECT OF ESLICARBAZEPINE ACETATE ON CARDIAC REPOLARIZATION IN HEALTHY SUBJECTS

L. Almeida, T. Nunes*, M. Gutierrez†, J. Litwin‡, and P. Soares-da-Silva**

**BIAL – Portela & Co, SA, S Mamede Do Coronado, Portugal; †Comprehensive PhaseOne, Miramar, FL, USA; and ‡ERT – EResearchTechnology, Inc, Philadelphia, PA, USA*

Purpose: To evaluate the effect of eslicarbazepine acetate (ESL) on the placebo corrected time-matched change from baseline using individually corrected QT (QTcI) interval durations in adult healthy volunteers.

Method: Randomized, double-blind, placebo-controlled, open-label active-controlled, 4 period crossover study. In 3 periods subjects were administered 1200 mg QD, 2400 mg QD and placebo QD for 5 days; in one period placebo was administered on days 1–4 and a 400 mg moxifloxacin dose was administered on day 5. In each treatment period, 24 hour 12-lead Holter ECG monitoring was performed on Day -1 (baseline) and Day 5. From each recording, triplicate ECGs of 13 time-points were extracted corresponding to predefined times.

Results: There was no evidence of any effect of ESL 1200 mg and 2400 mg on atrioventricular conduction, depolarization, or cardiac repolarisation as measured by the PR, QRS or QTc interval. There was no effect on mean heart rate with ESL or with the active control moxifloxacin. Mean changes from baseline in the individually corrected QT interval (QTcI) were mostly decreases in the ESL and placebo groups (time-averaged mean change from baseline QTcI duration: -5.8 msec for the 1200 mg dose of ESL and -4.7 msec for the 2400 mg of ESL). Moxifloxacin demonstrated the expected increases in QTcI (+5.5 msec change in time-averaged placebo-corrected QTcI). No treatment-related differences were observed for the maximum values at each time point.

Conclusion: ESL 1200 mg and 2400 mg once-daily doses had no effect on ECG intervals or morphology. Supported by BIAL – Portela & Co, SA.

T211

EVALUATION OF A SELF-REPORT QUESTIONNAIRE FOR THE ASSESSMENT OF ADVERSE EFFECTS OF ANTIEPILEPTIC DRUGS

T. May, C. Brandt†, and J. Kassel**

**Epilepsy Research Foundation, Germany; and †Epilepsy Center Bethel, Bielefeld, Germany*

Purpose: To investigate the psychometric properties (reliability, validity) of a new self-report questionnaire for the assessment of patient-perceived present and chronic side effects of antiepileptic drugs (AED).

Method: The self-report questionnaire FENAT (Fragebogen zur Erfassung von Nebenwirkungen unter Antiepileptika-Therapie) comprises two scales, one for 'current' (16 items) and another for 'chronic' adverse effects (25 items). The scales cover physical as well as cognitive/mental adverse effects of AED often reported in clinical studies. Furthermore, the patients should specify the degree of impairment by these adverse effects, the most impairing adverse effects, time of the occurrence and overall impairment by adverse effects. In total, 188 adult patients (> 16 yr.) with epilepsy treated with AED were included in the study. Reliability of the FENAT scales (internal consistency, Cronbach's alpha) was examined as well as their validity investigated by principal component analysis and by comparison with the AEP (Adverse Event Profile), the POMS (Profile of Mood States; psychic and mental symptoms), and the GBB (Gießener Beschwerdebogen, physical symptoms). Furthermore, the relationship between type and severity of adverse effects and quality of life in epilepsy (QOLIE-31) was investigated.

Results: The internal consistency of FENAT scales (current and chronic adverse effects) was high (Cronbach's alpha=0.89 and 0.92). The scales were significantly correlated with the AEP (r=0.59, r=0.69) as well as with the POMS tiredness subscale (r=0.40, r=0.45) and GBB subscales (r=0.37–0.61). Furthermore, the two FENAT subscales were significantly related with the total score of QOLIE-31 (r=−0.58, r=−0.64) as well as with its subscales (e.g. medications effects, well-being, energy).

Conclusion: Our study indicates that the FENAT scales are reliable and valid self-report questionnaires for the assessment of current and chronic adverse effects of AED. Supported by an unrestricted grant from UCB GmbH Germany.

T212
EFFECT OF ZONISAMIDE ON MYOCLONUS IN PROGRESSIVE MYOCLONIC EPILEPSY

L. Bongiovanni, G. Rubboli†, R. Michelucci†, M. Avesani*, F. Rossini*, M. Vedovello*, and P. Manganotti**
**University of Verona, Italy and †'Bellaria' Hospital, Bologna, Italy*

Purpose: There is no specific treatment for Progressive Myoclonic Epilepsy. For seizures and myoclonus control valproic acid, clonazepam, levetiracetam and zonisamide have been used. We analyzed the effect of zonisamide on two patients with Progressive Myoclonic Epilepsy type 1 after a long period of treatment with different combined drugs.

Method: We studied two patients a 34 years old man and a 52 years old woman. Generalized seizures were the presenting symptoms in both patients. Stimulus sensitive myoclonic jerks and bilateral massive myoclonus, with frequent status epilepticus, gradually in the years caused both impairment of activity of daily living and inability to walk. The EEG became abnormal with mild slowing of back ground activity with generalized high voltage spike and wave and polyspike and wave, ranging from 2.5 to 4.5 Hz. EEG and fMRI coregistration has been performed. Different combination of clonazepam, valproic acid, levetiracetam, lamotrigine and phenobarbital reduced the seizures, but were unable to control the myoclonus.

Results: Zonisamide, given at doses of 350 mg/ die, had a dramatic beneficial effect on both paroxysismal activity and stimulus – sensitive and action – induced myoclonus without side effects. The large bold activation observed in EEG-fMRI was reduced. The patients were able to walk assisted after being wheel chair bound. And clonazepam, lamotrigine and phenobarbital were stopped.

Conclusion: Even if the pathophysiolgy of myoclonus is not well understood, the adjunctive therapy with zonisamide appears to be effective against a variety of seizure types and reflex and spontaneous myoclonus in these neurodegenerative disorders.

T213
SYNERGISM OF LACOSAMIDE WITH ESTABLISHED ANTIEPILEPTIC DRUGS IN THE 6 HZ SEIZURE MODEL IN MICE

A. Shandra, P. Shandra†, O. Kaschenko*, and T. Stoehr‡*
**Odessa State Medical University, Ukraine; †Odessa National University, Ukraine; and ‡Schwarz Biosciences, Inc., A Member of The UCB Group*

Purpose: Lacosamide (LCM) is a functionalized amino acid with a novel dual mode of action: enhancement of sodium channel slow inactivation and modulation of collapsin response mediator protein 2. Due to this novel mode of action lacosamide has the potential to act additively or even synergistically with other antiepileptic drugs (AEDs). New AEDs are initially licensed as add-on treatment, often with no evidence to suggest which existing drugs they should be employed with. The objective of this study was the evaluation of the interaction between LCM and a number of other AEDs by isobolographic analysis.

Method: The anticonvulsant effect of LCM with other AEDs (carbamazepine (CBZ), phenytoin (PHT), valproate (VPA), lamotrigine (LTG), topiramate (TPM), gabapentin (GBP) and levetiracetam (LEV)) at fixed ratios of 1:3, 1:1 and 3:1 was evaluated in the 6Hz-induced seizure model in mice. The protective action of an AED was defined as the absence of seizure.

Results: All studied AEDs produced dose-dependent anticonvulsant effects against 6 Hz induced seizures. Combinations of LCM with CBZ, LTG, TPM, GBP or LEV were supraadditive (synergistic). All other LCM/AED combinations displayed additive effects with a tendency towards supraadditivity. Furthermore, no enhanced adverse effects were induced by combinations of LCM with these AEDs as assessed in the rotarod test.

Conclusion: The isobolographic analysis revealed that combinations of LCM with first-generation (CBZ) or novel AEDs (TPM, GBP, LTG or LEV) are associated with synergistic anticonvulsant effects. Similar but less profound synergistic effects were seen with LCM in combination with PHT or VPA.

T214
THE ANTICONVULSANT AND ANTIEPILEPTOGENIC EFFECTS OF LACOSAMIDE IN AN EXPERIMENTAL MODEL OF STATUS EPILEPTICUS

T. Stoehr, and C. Wasterlain†*
**Schwarz Biosciences GmbH, A Member of The UCB Group; and †UCLA School of Medicine, Los Angeles, CA, USA*

Purpose: Lacosamide is an investigational anticonvulsant with effects in a large variety of animal models and is currently being evaluated in Phase 3 clinical trials. The current experiments aimed at evaluating its long-term effects in an animal model for status epilepticus.

Method: Male rats were implanted with stimulating and recording electrodes in the perforant path. Self-sustaining status epilepticus was induced by stimulation with 10s 20 Hz trains of 1ms / 30V pulses delivered every 1min over 30min. Seizure frequency was assessed following an at least 6 week waiting period by continuous EEG and video monitoring. Lacosamide was administered either 10 min (early treatment) or 40 min (late treatment) following onset of self-sustaining status epilepticus.

Results: All untreated rats developed spontaneous recurrent seizures as assessed at least 6 weeks following induction of status epilepticus. Early treatment with lacosamide resulted in a dose dependent reduction of the number of spontaneous recurrent seizures with a maximum of 70% reduction at the highest dose tested (50 mg/kg). There was also a significant reduction in the number of spikes and the cumulative time spent in seizures by lacosamide. Late treatment with lacosamide resulted in a 50% reduction in the frequency of spontaneous recurrent seizures in the highest dose groups (30 and 50 mg/kg). At the same time, the number of seizure free animals increased from 0% in the untreated group to 65% in the highest dose groups.

Conclusion: Lacosamide showed a potential for disease modification in this rat model of self-sustaining status epilepticus.

T215
LACOSAMIDE: SAFETY ASSESSMENT IN JUVENILE ANIMALS TO SUPPORT PEDIATRIC CLINICAL DEVELOPMENT IN EPILEPSY

N. Krebsfaenger, and T. Stoehr
Schwarz Biosciences GmbH, A Member of The UCB Group

Purpose: Lacosamide is a functionalized amino acid which showed anticonvulsant as well as analgesic effects in a large variety of animal models and is currently being evaluated for marketing approvals. The objective of the present experiments was to assess its safety profile in nonclinical juvenile toxicity studies to support pediatric clinical development in epilepsy.

Method: Juvenile rats were treated orally with lacosamide up to 180 mg/kg/day for 6 weeks starting on postnatal day 7 followed by a 4-week recovery period and mating within a previously treated subgroup. In addition, juvenile dogs were treated orally with lacosamide up to 25 mg/kg/day for 6 weeks starting at the age of 8 weeks.

Results: In the juvenile animals, in principle the same effects as in chronic toxicity studies with adult animals were noted, i.e. there was no indication of age-specific toxicity. In rats, body weight reduction was dose-limiting and, as a secondary effect to this, a slightly delayed development of the high dose groups in general was observed. Importantly, no treatment-related adverse effects were noted on the developing rat brain neither on the histomorphological nor functional level.

Conclusion: Lacosamide showed a favourable profile in nonclinical juvenile toxicity studies.

T216
LONG-TERM TREATMENT OF PARTIAL EPILEPSY WITH ESLICARBAZEPINE ACETATE: RESULTS OF A 1-YEAR OPEN-LABEL EXTENSION STUDY

A. Guekht, C. Elger†, P. Halasz‡, J. Maia§, L. Almeida§, and P. Soares-da-Silva§*

**Russian State Medical University, Moscow, Russia; †University of Bonn, Bonn, Germany; ‡National Institute of Psychiatry and Neurology, Budapest, Hungary; and §BIAL – Portela & Co, SA, S Mamede Do Coronado, Portugal*

Purpose: To investigate the safety and maintenance of the therapeutic effect of eslicarbazepine acetate (ESL) as adjunctive therapy in adult patients with partial-onset seizures over a 1-year open-label period.

Method: Optional 1-year open-label treatment with ESL for those subjects who completed the double-blind part of Study BIA-2093-301. Starting dose was 800 mg once-daily, for 4 weeks. After that, dose could be titrated up or down at 400-mg intervals. Doses of concomitant AEDs were to be kept stable.

Results: Three hundred fourteen patients were enrolled, and 239 (76.1%) completed 1 year. The mean daily dose of ESL throughout the 1-year treatment was 877¡À189 mg (median=800 mg; range=400–1600 mg). Treatment-emergent adverse events (TEAEs) were reported by 51% patients. The most frequent TEAEs were headache (10%), dizziness (10%), diplopia (5%) and nasopharyngitis (5%). TEAEs were mostly (97%) of mild to moderate severity. Eleven (3.5%) patients discontinued due to TEAEs. There were no results of laboratory tests raising safety concerns. In relation to baseline of the double-blind part of the study, seizure frequency decreased by 32% during the first 4 weeks and by 38% in weeks 5–16 to 41% in weeks 41–52 (intent-to-treat population). The responder rate (¡Ý50% decrease in seizure frequency) was 41% during weeks 1–4; thereafter, ranged between 48% and 53%. Proportion of seizure-free patients per 12 week interval increased over time, from 8.7% (weeks 5 16) to 12.5% (weeks 41 52).

Conclusion: Adjunctive therapy with ESL proved to be safe and well tolerated, and resulted in a marked and sustained decrease in seizure frequency over a 1-year open-label treatment period. Supported by BIAL-Portela & Co, SA.

T217
EFFICACY AND SAFETY OF ESLICARBAZEPINE ACETATE AS ADD-ON TREATMENT IN ADULTS WITH REFRACTORY PARTIAL-ONSET SEIZURES: BIA-2093-303 STUDY

J. Lopes-Lima, A. Gil-Nagel†, J. Maia‡, L. Almeida‡, and P. Soares-da-Silva‡*

**Hospital Santo Antonio, Porto, Portugal; †Hospital Ruber Internacional, Madrid, Spain; and ‡BIAL – Portela & Co, SA, S Mamede Do Coronado, Portugal*

Purpose: To investigate the efficacy and safety of eslicarbazepine acetate (ESL) when used as add-on in adult patients with partial-onset seizures per 4 weeks despite treatment with 1–2 AEDs.

Method: During this multicenter, double-blind, parallel-group, placebo-controlled study, patients were randomized to placebo (n=87) or ESL 800 mg (n=85) or 1200 mg (n=80) once-daily after a 8-week baseline period. Patients were given half of the maintenance dose during 2 weeks before entering a 12-week maintenance period.

Results: The most frequently coadministered AEDs were carbamazepine (56% of patients), followed by valproic acid (31%) and levetiracetam (21%). Primary analysis was an ANCOVA of log-transformed seizure frequency in the intent-to-treat population. The least-square means of the difference to placebo increased in a dose-dependent manner (-1.6, and -1.9 with 800 mg and 1200 mg, respectively). The difference to placebo was significant ($p<0.05$) for both 800 mg and 1200 mg. Median relative reduction in seizure frequency was 42% (1200 mg), 38% (800 mg) and 17% (placebo). The responder rate was 38% (1200 mg), 35% (800 mg), and 23% (placebo). Discontinuation rates due to treatment-emergent adverse events (TEAEs) were 6.9% (placebo), 8.2% (800 mg) and 11.3% (1200 mg). TEAEs occurring in >10% in any group were dizziness, somnolence and headache. Most TEAEs were mild or moderate in severity.

Conclusion: Adjunctive therapy with ESL 800 mg and 1200 mg once-daily was well tolerated and effective in reducing partial-onset seizures in patients refractory to treatment with 1 or 2 AEDs.

Supported by BIAL- Portela & Co, SA.

T218
SIMULTANEOUS ANALYSIS OF 11 NEWER ANTIEPILEPTIC DRUGS BY RAPID RESOLUTION LC/ TRIPLE QUADRUPOLE MASS SPECTROMETRY

D. Dietmann, U. Juerges*, B. Steinhoff*, and J. Wendt†*

**Epilepsy Center Kork, Germany; and †Agilent Technologies, Waldbronn, Germany*

Purpose: The antiepileptic drugs lamotrigine, oxcarbazepine, felbamate, zonisamide, gabapentin, pregabalin, tiagabine, topiramate, levetiracetam, rufinamide and stiripentol are traditionally summarized under the term newer antiepileptic drugs. For the therapy of seizures therapeutical drug monitoring (TDM) is an important instrument for the physician. Rapid Resolution LC combined with Triple Quadrupole Mass Spectrometry allows a focussing of the TDM. The present work describes a new LC/MS/MS method to identify and quantify eleven newer antiepileptic drugs in a single analytical run.

Method: Two different sample preparation steps were evaluated, a simple precipitation step and a liquid-liquid extraction. All sample analysis were performed on a LC/MS/MS system consisting Rapid Resolution Liquid Chromatograph and a Triple Quadrupole Mass Spectrometer, operated with an electrospray ionization source in positive polarity. Different columns with 1.8um particle size were explored in combination with different solvents, flow rates and column parameters to optimize the speed of the analysis, while maintaining a good chromatographic resolution.

Results: The presented LC/MS/MS method, combining RR-LC and Triple Quadrupole Mass Spectrometry, allows the simultaneous determination of 11 newer antiepileptic drugs in human serum. The method is fast, selective, sensitive and robust. Sample preparation was done by a simple precipitation step to remove proteins. The total run time, using a Zorbax 100*2.1mm RRHT column with 1.8um particle size, was kept at eight minutes. The method proved to be accurate and precise (intra-day precision below 2%, inter-day precision below 3%).

Conclusion: Rapid Resolution LC combined with Triple Quadrupole Mass Spectrometry allows a focussing of the TDM. The present work describes a new LC/MS/MS method to quantify 11 newer antiepileptic drugs in a single analytical run in only eight minutes.

T219
EFFICACY OF TOPIRAMATE FOR THE PREVENTION OF MIGRAINE WITH MINIMAL ADVESE EVENTS

S. Ristic, and D. Ristic†*

**Epilepsy Unit, KC NIS, Serbia; and †Institute of Pulmonary Diseases, Nis, Serbia*

Purpose: Topiramate is approved for the treatment of epilepsy and prophylaxis of migraine headache in adults. The present analysis of pooled data from those 3 trials was performed to characterize the efficacy and adverse events of topiramate for migraine prevention in subjects who had used other migraine preventive medications.

Method: We analyzed patients with migraine, who had used migraine preventive medications (tricyclic antidepressants, beta- blockers or neurostabilisers other than topiramate) within approximately 8 months period. Patients with a history of glaucoma, kidney stone were excluded. We analyzed monthly migraine frequency from baseline period to endpoint. We compared different dosage of topiramate, so as the presence od adverse events. We started with 25mg/day od topiramate and this lasted for 7 days and we increased dosage of topiramate 25 mg/week. Maximum dosage was 200 mg/day.

Results: Of sum of 67 patients, 42(62,69%) female, aged between 21–59 years (mean age 39,2) were recruited. Subjects treated with topiramate (50, 100, or 200 mg/day). More subjects on topiramate 50 mg/day (39%), 100 mg/day (62%) and 200 mg/day (51%) exhibited 50% reductions in monthly migraine frequency. Most common adverse event was paresthesis, incidence was 12%, fatigue 3%, nausea 2%. Mean duration of paresthesia was 21 days. Cognitive sympthoms was registered in 1 patient. Anorexia, glaucoma, kidney stone were not registered.

Conclusion: In subjects who had previously taken other migraine preventives, treatment with topiramate100 mg/day and 200 mg/day significantly reduced mean monthly migraine frequency. Adverse events are rare and most frequent are paresthesia which disappears in 3 weeks.

T220
ERDHEIM-CHESTER DISEASE AND EPILEPSY: CASE REPORT

E. Vitelli, R. Spagliardi, V. Badioni, L. Cucurachi, and M. Riva
Azienda Ospedaliera Della Provincia Di Lodi, Italy

Purpose: Erdheim-Chester disease (ECD) is a rare non-Langerhans histiocytosis with systemic involvement (mainly bone, heart, lung, and kidney). Neurological manifestations are present in 45% of reported patients (Lachenal F et al J Neurol 2006;253:1267–1277) and seizures in 12%. NMR shows different patterns of involvement: infiltrative, meningeal or both. We hereby describe epileptic manifestations and treatment in a case of ECD.

Method: A 27 year-old man affected by histologically proved ECD (multiple bone lesions, diabetes insipidus) was observed for 3 focal seizures (head turning, automatisms of the right arm) followed by tonic–clonic generalization. Neurological examination was unremarkable except for mild cognitive impairment (MMSE 26/30). The EEG showed slow posterior theta-delta activity, without epileptiform discharges. NMR showed an infiltration of parietooccipital cortex bilaterally with spreading to brainstem and cerebellum, without enhancement. Levetiracetam (LEV) was titrated up to 2000 mg/day.

Results: LEV was preferred for its lack of interactions with drugs used for treatment of ECD (a polytherapy), for its simple dosing schedule and lack of adverse events. During the follow-up (24 months) only 2 seizures occurred, due to patient inadequate compliance.

Conclusion: Seizures are not surprising in this case of ECD if the diffuse cortical involvement is considered. LEV showed to be effective. We also underline that in the complex treatment of ECD the support of a neurologist is needed, particularly in paucisymptomatic cases, in which the neurological involvement may be subtle or may be the heralding feature.

T221
DOES LEVETIRACETAM EFFICACY CONTINUE TO BE STABLE? RESULTS OF A LONG-TERM OPEN LABEL STUDY ON THE EFFICACY OF LEVETIRACETAM AS ADD-ON THERAPY IN REFRACTORY PARTIAL EPILEPSY

G. Boero, M. Stuppiello†, N. Specchio‡, T. Francavilla§, M. La Dogana§, L. Specchio†, P. Lamberti§, and A. La Neve§*
**SS. Annunziata Hospital, Taranto, Italy; †Clinic of Nervous System Diseases, University of Foggia, Italy; ‡Division of Neurology, Ospedale Bambino Gesù, Rome, Italy; and §Epilepsy Center, University of Bari, Italy*

Purpose: To evaluate long-term efficacy of levetiracetam in maintaining seizure freedom in adults with refractory partial epilepsy.

Method: Patients refractory to > 2 previous antiepileptic drugs (AEDs), with >2 focal seizures over an 8-week baseline period, were treated with levetiracetam. Levetiracetam was titrated up to 1000mg/day (2 weeks). Patients with no seizures for at least 36 months were considered seizure-free. Efficacy evaluation started after titration: number of seizure-free patients (SFPs) and duration of seizure freedom period were considered.

Results: 119 patients were enrolled (81 F, mean age 39 years, range 11–75, 56% remote symptomatic, mean levetiracetam dose 2300mg/day) . Mean follow-up was 31 (0–72) months. 20 (16.8%) patients (9 on levetiracetam 1000 mg/day, 5 on 2000 mg/day, 6 on 3000 mg/day) were seizure free for a mean period of 56 (36–72) months. In SFPs levetiracetam was associated with 1 (10/20, 50%) or 2 (10/20, 48%) other AEDs. After seizure freedom was attained the therapy was not modified in 10 SFPs : in 1/10 patients seizures recurred spontaneously after 63 months. 6 SFPs (3 triple therapy, 3 double therapy) continued to be seizure-free after 1 AED was withdrawn; 2 SFPs (1 triple therapy, 1 double therapy) continued not to have seizures when one AED dose was reduced; seizures returned in 2 SFPs on double therapy during reduction of the associated AED.

Conclusion: This study shows good efficacy of levetiracetam in obtaining stable, long-term freedom from seizures, even after withdrawing one add-on AED.

T222
INTRAVENOUS LEVETIRACETAM AS TREATMENT FOR STATUS EPILEPTICUS – EXPERIENCE FROM TWO GERMAN CENTRES

S. Berning, F. Boesebeck†, and C. Kellinghaus†*
**Klinikum Osnabrück, Germany; and †Diakonie Hospital, Rotenburg, Germany*

Purpose: Status epilepticus (SE) is an important neurological emergency. Although there are established drugs of first choice for its treatment, potentially hazardous side effects of these agents are not uncommon. Levetiracetam (LEV) is a novel anticonvulsant with favourable pharmacokinetics and good tolerability that could be a good alternative for treatment of SE when the standard drugs fail or should be avoided.

Method: We retrospectively identified patients from two teaching hospitals in northern Germany who had been treated with LEV i.v. for status epilepticus. Their charts were reviewed regarding sociodemographic, SE- and AED-related variables, tolerability and outcome.

Results: Thirty-two patients (15f, 17m, median age: 70 years) were identified. LEV i.V. was administered because benzodiazepines or phenytoin could not be used due to comorbitity or respiratory insufficiency, or unsuccessful treatment with benzodiazepines (16 patients each). SE was convulsive in three, nonconvulsive in 22, and simple focal in seven patients. Eleven patients received LEV within the first six hours of SE.

Median bolus dose was 2000mg. LEV i.v. terminated the SE within six hours in 17 patients (11 within 30 minutes) and within more than six hours in seven patients without the application of additional anticonvulsants. LEV i.v. could not terminate SE in eight patients. We saw nausea and emesis in one patient and clinically insignificant elevation of liver enzymes in another patient. In 7 patients we observed sedation during and after LEV infusion, but all of these patients had received benzodiazepines immediately before LEV.

Conclusion: LEV i.v. seems to be a good alternative for treatment of SE in elderly and multimorbid patients.

T223

A COMPARATIVE STUDY ON EFFICACY AND TOLERABILITY OF TRADITIONAL AEDS VERSUS OXCARBAZEPINE IN BRAIN TUMORS-RELATED EPILEPSY

M. Maschio, L. Dinapoli, C. Carapella, A. Pompili, A. Pace, A. Mirri, A. Fabi, A. Vidiri, and B. Jandolo
National Institute For Cancer Regina Elena, Rome Italy

Purpose: We conducted a study to compare two groups of patients with epilepsy related to brain tumor: the first group in treatment with oxcarbazepine (OXC), the second in therapy with traditional AEDs. Aim of the study was to assess if there were any differences in terms of efficacy and tolerability.

Method: We performed a prospective study on 35 patients who assumed de novo OXC or switching from other AEDs for side effects or inefficacy. Seizure frequency was assessed based on entries in daily seizure diaries. We performed a retrospective chart review on 35 BT patients with traditional AEDs. Seizure frequency was assessed on number of seizures collected by using clinic notes. The appearance of side effects was recorded. Primary variable of efficacy was the mean of seizure per month and safety variables were the drop-out for side effects and the total incidence of side effects. In order to minimize selection bias and other source of bias, we applied the Propensity Score technique.

Results: Statistical analysis showed for both groups a significant reduction of seizure frequency between first visit and last follow up visit ($p<0.0001$) whereas the comparison between groups and interaction Group*Visit was not significant. Fisher exact test showed a significant difference between OXC group and Traditional AEDs group both for total incidence of side effects ($p=0.0063$) and for drop out due to side effects ($p=0.0090$).

Conclusion Results showed a similar efficacy of OXC and traditional AEDs over time but different profiles of tolerability. Traditional AEDs group had more side effects than OXC group.

T224

PREVENTION OF EPILEPTOGENESIS USING LEVETIRACETAM IN A RODENT MODEL OF CORTICAL DYSPLASIA.

R. O'Dwyer, A. Alexopoulos*, S. Yates†, S. Nagel*, C. Tilelli*, G. Hiremath*, and I. Najm**
**Neurological Institute, Epilepsy Center, Cleveland Clinic, Cleveland, OH, USA; and †UCB, Inc., Medical Affairs*

Purpose: In addition to its seizure-suppressing properties levetiracetam (LEV) has been shown to possess potential antiepileptogenic effects in various animal models. Using a well-characterized model of cortical dysplasia (CD), we explored the role of postnatal administration of LEV prior to a second hit that leads to the expression of seizures in these animals.

Method: Sixteen male Sprague Dawley rats were irradiated with 145cGY in utero on day E17. After birth irradiated animals were divided into two groups of eight (LEV+, LEV-). During PND42-48, the first group was given 54mg/kg s.c. LEV q8, the other received 54mg/kg s.c. LO60 (inactive LEV enantiomer) q8. On PND55 they were implanted with epidural electrodes over the frontal and parietal regions bilaterally. On PND60 all rats were given a convulsive dose (50mg/kg s.c.) of pentylenetetrazol (PTZ; second hit) and their behavior and EEG was monitored for a subsequent six hours.

Results: Only three LEV+ rats as opposed to 5 of 8 LEV- rats developed generalized tonic–clonic seizures (Racine Stage 5). Latency to the first absence-like episode (based on Video-EEG and behavioral observation) was longer in the LEV+ group (516s 'b 403s vs. 268s 'b 97s; $p= 0.11$). Latency to the first myoclonic jerk was also longer in the LEV+ group (566s 'b 225s vs. 400s 'b 167s; $p=0.15$).

Conclusion: Postnatal LEV appears to impede of the expression of acute seizures induced by a second hit in CD rats. These findings suggest a disease modifying effect of LEV in this animal model. Further experiments with larger numbers are needed to confirm these results.

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T225

PHARMACOKINETIC INTERACTION BETWEEN ESLICARBAZEPINE ACETATE AND TOPIRAMATE IN HEALTHY SUBJECTS

T. Nunes, E. Sicard†, L. Almeida*, J. Huguet†, J. Brunet†, M. Lefebvre†, and P. Soares-da-Silva**
**BIAL – Portela & Co, SA, S Mamede Do Coronado, Portugal; and †Algorithme Pharma Inc, Montreal, Québec, Canada*

Purpose: To evaluate (A) the effect of eslicarbazepine acetate (ESL) on the topiramate (TPM) pharmacokinetics, and (B) effect of TPM on the ESL pharmacokinetics in healthy subjects.

Method: Multiple-dose, open-label, one-sequence, two parallel-group design study (n=16/group). Each group received a sequentially ESL or TPM alone followed by a combination of the two drugs. One group received ESL 600 mg once-daily (QD) for 2 days and 1200 mg QD for 6 days, followed by coadministration of ESL 1200 mg QD and TPM 100 mg QD for 2 days, ESL 1200 mg QD and TPM 100 mg twice-daily (BID) for 2 days, and then ESL 1200 mg QD and TPM 200 mg QD for 15 days. The other group received TPM 100 mg QD for 2 days, 100 mg BID for 2 days, and 200 mg QD for 4 days followed by coadministration of ESL 600 mg QD and TPM 200 mg QD for 2 days, and then ESL 1200 mg QD and TPM 200 mg QD for 17 days. End/start of treatment geometric mean ratios (GMR,%) and 90% confidence intervals (90%CI) were calculated for Cmax and AUC0-24 of eslicarbazepine (major metabolite) and TPM at Day 8 and Day 27.

Results: (A) Following ESL 1200 mg, TPM Cmax and AUC0-24 GMR (90%CI) were 82% (77%; 85%) and 82% (80%; 84%), respectively. (B) Following TPM 200 mg, eslicarbazepine Cmax and AUC0-24 GMR (90%CI) were 87% (81%; 93%) for Cmax and 93% (89%; 96%), respectively.

Conclusion: (A) ESL caused a small decrease (18%) on TPM systemic exposure. (B) No effect of TPM on ESL pharmacokinetics was observed.

Supported by BIAL – Portela & Co, SA.

T226

BIOEQUIVALENCE OF FINAL TABLET FORMULATION AND RESEARCH TABLET FORMULATION OF ESLICARBAZEPINE ACETATE IN HEALTHY VOLUNTEERS

R. Lima, T. Vasconcelos*, R. Cerdeira*, M. Lefebvre†, E. Sicard†, T. Nunes*, L. Almeida*, and P. Soares-da-Silva**
**BIAL – Portela & Co, SA, S Mamede Do Coronado, Portugal; and †Algorithme Pharma Inc, Montreal, Quebec, Canada*

Purpose: To investigate the bioequivalence of the final tablet formulation of eslicarbazepine acetate (ESL) and the tablet formulation used in pivotal clinical studies.

Method: Single centre (Algorithme Pharma, Quebec, Canada) consisting of three single-dose, randomized, two-way crossover sub-studies in healthy subjects. In each substudy (n=20), the bioavailability of BIA 2-005 (active metabolite) following a given ESL tablet strength (400 mg, 600 mg or 800 mg) of the final formulation (Test) was compared with the corresponding tablet strength of the research formulation (Reference), under fasting conditions. The statistical method for testing bioequivalence was based upon the 90% confidence interval (90%CI) for the Test/Reference geometric mean ratio (GMR) for Cmax, AUC0-t and AUC0-a. Bioequivalence was to be assumed when the 90%CI fell within the recommended acceptance interval 80.00%; 125.00%.

Results: The Test/Reference GMR and 90%CI for BIA 2-005 were as follows: 400 mg tablets C 105.37% (99.57%; 111.52%), 102.83 (99.19%; 106.61%) and 102.83% (99.13%; 106.66%) for Cmax, AUC0-t and AUC0-a, respectively; 600 mg tablets¨C 102.65% (97.27%; 108.33%), 102.40% (99.00%; 105.93%) and 102.38% (98.97%; 105.90%) for Cmax, AUC0-t and AUC0-p, respectively; 800 mg tablets¨C 104.16% (95.44%; 113.67%), 100.34% (97.85%; 102.90%) and 99.88% (97.65%; 102.16%) for Cmax, AUC0-t and AUC0-a, respectively.

Conclusion: The 90%CI of all pharmacokinetic parameters of interest (Cmax, AUC0-t, and AUC0-p) fell within the acceptance range of 80.00%; 125.00%. Therefore, bioequivalence of the final tablet formulation and the tablet formulation used in the pivotal clinical trials of ESL has been demonstrated.

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T227

DOSAGE FORM PROPORTIONALITY AND FOOD-EFFECT OF THE FINAL TABLET FORMULATION OF ESLICARBAZEPINE ACETATE IN HEALTHY VOLUNTEERS

C. Fontes-Ribeiro, T. Macedo*, T. Nunes†, C. Neta*, T. Vasconcelos†, R. Cerdeira†, R. Lima†, J. Rocha†, A. Falcatildeo‡, L. Almeida†, and P. Soares-da-Silva†*
**CEB – Bioavailability Studies Centre, AIBILI, Coimbra, Portugal; †BIAL – Portela & Co, SA, S. Mamede Do Coronado, Portugal; and ‡4Health Ltd, Cantanhede, Portugal*

Purpose: A) To investigate the effect of food on eslicarbazepine acetate (ESL) pharmacokinetics. B) To investigate the dosage form proportionality of the final tablet formulation.

Method: Single centre (CEB, Coimbra, Portugal), randomized, 3-way crossover study in 18 healthy subjects. Subjects received a single oral 800 mg dose of ESL following a standard meal in one period, and following 10 hours of fasting in two periods. The statistical method was based upon the 90% confidence interval (90%CI) for the Test/Reference geometric means ratio (GMR) for Cmax, AUC0-t and AUC0-a. Bioequivalence was assumed when the 90%CI fell within the 80.00%; 125.00% acceptance interval.

Results: Following oral administration of a 800 mg tablet in fed (Test) and fasting (Reference) conditions, the Test/Reference GMR (%) and 90%CI for BIA 2-005 (active metabolite) were 100.96% (94.08%; 108.35%), 96.79% (94.34%; 99.32%) and 96.75% (94.27%; 99.29%) for Cmax, AUC0-t and AUC0-a, respectively. Following a single 800 mg dose in the form of 1x800 mg tablet (Reference) and in the form of 2x400 mg tablets (Test), the Test/Reference GMR and 90%CI for BIA 2-005 were 100.78% (93.91%; 108.16%), 100.37% (97.82%; 102.99%) and 100.48% (97.91%; 103.13%) for Cmax, AUC0-t and AUC0-a, respectively.

Conclusion: A) The presence of food did not change the ESL pharmacokinetics. B) The bioequivalence criteria between the 400 mg and 800 mg tablets were met. Since the 400 mg, 600 mg and 800 mg tablets are homothetic, it can be assumed that the 600 mg tablet is bioequivalent to the 400 mg and 800 mg tablets. Supported by BIAL- Portela & C SA.

T228

A ONE YEAR FOLLOW-UP, OPEN-LABEL AND OBSERVATIONAL STUDY OF THE EFFICACY AND TOLERABILITY OF ZONISAMIDE

A. Marinas-Alejo, B. Giráldez*, A. Molins†, J. Salas-Puig‡, J. Sánchez§, A. Gil-Nagel¶, V. Villanueva**, and J. Serratosa**
**Fundación Jiménez Díaz. Madrid, Spain; †Hospital Josep Trueta. Gerona, Spain.; ‡Hospital Central De Asturias. Oviedo, Spain.; §Hospital U. Virgen De Las Nieves. Granada, Spain; ¶Hospital Ruber Internacional. Madrid, Spain; and **Hospital La Fe. Valencia, Spain*

Purpose: To analyze the efficacy and tolerability of zonisamide (ZNS) in partial seizures at 12 months in daily clinical practice conditions.

Method: Patients with partial seizures started on ZNS as add-on therapy between 2006 and 2007 were included. Patients were evaluated at baseline and at months 3, 6 and 12. The following data were collected: age, gender, age at onset of epilepsy, seizure and epilepsy types, etiology, monthly seizure frequency, adverse events and number of previous antiepileptic drugs (AEDs). Response was analyzed in 12 month completers and defined as a >50% reduction in monthly seizure frequency in the last 6 months, compared with the one-year pre-ZNS treatment.

Results: Seventy-three patients were enrolled in the study. After one year, 36/73 patients (49.3%) continued on ZNS. Drop-outs were related to side effects or lack of efficacy. Mean seizure frequency at baseline was 15/month and mean number of AEDs used in the past was 4.11. The mean number of concomitant AEDs was 2.03. Mean ZNS dose at month 12 was 351.6 mg/d (range 200–500). The responder rate was 58.3% (21/36). Seizure freedom was achieved in 7/36 (19.4%). Adverse events were experienced in 44/73 (60.2%) and resulted in withdrawal in 26 (35.6%). The most common adverse events were somnolence, weight loss and headache.

Conclusion: In this long term study, ZNS showed efficacy in 58.3% of patients in daily clinical practice conditions. Tolerability was good in this drug-resistant population.

T229

STATUS EPILEPTICUS ASSOCIATED WITH INTERFERON BETA-1A-TREATMENT IN A PATIENT WITH SYMPTOMATIC FOCAL EPILEPSY DUE TO MULTIPLE SCLEROSIS

K. Goetz-Trabert, A. Carius*, S. Dedner*, and A. Schulze-Bonhage**
**Epilepsy Centre Freiburg, Germany*

Purpose: A 38-year-old patient suffering from symptomatic focal epilepsy due to multiple sclerosis received treatment with Interferon Beta-1a (30 ug i.m. weekly) and developed recurrent status epilepticus.

Method: Case report.

Results: The patient suffered from relapsing-remitting MS from age 19. Starting from age 26, the patient developed symptomatic focal epilepsy with simple partial, complex partial and secondarily generalized seizures, the first manifestation was status epilepticus. The patient was seizure free for approximately ten years under valproate monotherapy. In close time correlation to the initiation of therapy with interferon Beta-1a, the patient suffered from status epilepticus, and the treatment was changed to a combination of valproate and levetiracetam. Under this therapy, status epilepticus occurred again repeatedly during the following two years, and

levetiracetam was increased while valproate being kept stable at therapeutic dosage. MRI showed general atrophy with typical supra- and infratentorial lesions. There were bitemporal subcortical lesions, no further temporal pathology and only slight progression of multiple sclerosis over that year. Therapy with interferon Beta-1a was stopped and subsequently changed to natalizumab.

Conclusion: Therapy with interferon Beta-1a is a widely used treatment option of multiple sclerosis and usually tolerated well. In patients with symptomatic epilepsy due to multiple sclerosis, treatment should occur keeping in mind that epilepsy may worsen and the serious complication of status epilepticus might occur.

T230
SAFETY AND TOLERABILITY OF LACOSAMIDE: A SUMMARY OF ADVERSE EVENTS IN EPILEPSY CLINICAL TRIALS

V. Biton, N. Fountain†, F. Rosenow‡, A. Gil-Nagel§, T. Sullivan¶, D. Hebert¶, and P. Doty¶*
**Clinical Trials, Inc.; †University of Virginia, USA; ‡Philipps-University, Marburg, Germany; §Hospital Ruber Internacional, Madrid, Spain; and ¶Schwarz Biosciences (A Member of The UCB Group)*

Purpose: To analyze safety and tolerability of lacosamide, a new drug candidate under investigation as adjunctive therapy for partial-onset seizures.

Method: Subjects receiving at least 1 dose of placebo or lacosamide in three fixed-dose, randomized, double-blind, placebo-controlled Phase II/III clinical trials (SP667, SP754, SP755) were pooled. Adverse events (AEs), laboratory parameters, ECGs, vital signs, and body weight were evaluated.

Results: In these trials, 944 subjects were randomized to lacosamide (200mg/day [n=270], 400mg/day [n=471], or 600mg/day [n=203]) and 364 subjects were randomized to placebo. Most subjects (78%) were exposed to lacosamide for at least 85 days; 85% of subjects randomized to lacosamide were receiving ≥C3 concomitant AEDs, most commonly carbamazepine, lamotrigine, levetiracetam, valproic acid, topiramate, oxcarbazepine, and phenytoin. The overall percentage discontinuing treatment was 13%, 18%, 23%, and 38% for the placebo, 200, 400, and 600mg/day lacosamide groups, respectively. The most common reasons for discontinuation were AEs (14%) and withdrawal of consent (4%). Frequently reported treatment emergent AEs (occurring in 10% of the pooled lacosamide group) versus placebo were dizziness (31% vs 8%), headache (13% vs 9%), nausea (11% vs 4%), and diplopia (11% vs 2%). Dizziness, nausea and diplopia appeared dose-related, with highest incidence in the 600mg/day group. Across all lacosamide groups, no clinically relevant concerns were observed on laboratory parameters, ECGs, vital signs, or body weight measurements. A small, dose-related increase in PR interval was observed.

Conclusion: Lacosamide was generally well tolerated when combined with up to three concomitant AEDs. A dose relationship was seen for frequently reported nervous system and GI adverse events.

T231
EFFICACY AND SAFETY OF LACOSAMIDE AS AN ADJUNCTIVE TREATMENT FOR PARTIAL-ONSET SEIZURES

S. Chung, M. Sperling†, V. Biton‡, G. Krauss§, M. Beaman¶, D. Hebert¶, and S. Study Group*
**Barrow Neurological Institute, AZ, USA; †Thomas Jefferson University, PA, USA; ‡Clinical Trials, Inc.; §Johns Hopkins Hospital, Maryland, USA; and ¶Schwarz Biosciences, Inc., (A Member of The UCB Group)*

Purpose: To investigate the efficacy and safety of lacosamide as adjunctive treatment in subjects with partial-onset seizures taking 1–3 concomitant antiepileptic drugs (AEDs).

Method: Subjects (N=405) reporting 8 seizures with a <21-day seizure-free period during an 8-week baseline were randomized (1:2:1) to placebo, lacosamide 400 or 600mg/day (bid), respectively. Concomitant AEDs remained stable throughout the trial. A 6-week titration to the randomized dose in 100mg/week increments preceded a 12-week maintenance phase. Efficacy was evaluated by seizure frequency data. The safety evaluation included analyses of adverse event (AE), vital sign, clinical laboratory, body weight and ECG data.

Results: Median percent reduction in seizure frequency per 28 days was 20.8%, 37.3%, and 37.8% for placebo, lacosamide 400 and 600mg/day, respectively. Both lacosamide doses significantly reduced seizure frequency compared to placebo (400mg/day: P=008; 600mg/day: P=.006). The 50% responder rates were 18.3%, 38.3%, and 41.2% for placebo, lacosamide 400 and 600mg/day, respectively. Both lacosamide doses were statistically significant over placebo for the responder rate analysis (400mg/day: P.001; 600mg/day: P.001). Among completers, nine were seizure-free: 0, 4 (2.5%) and 5 (8.1%) in the placebo and treatment groups, respectively. Most common AEs (10% in any lacosamide group) included dizziness, nausea, diplopia, blurred vision, vomiting, headache, tremor, abnormal coordination, somnolence, and nystagmus. Lacosamide had no clinically relevant influence on vital sign, laboratory, body weight and ECG variables.

Conclusion: In this trial, oral lacosamide (400 and 600mg/day) significantly reduced seizure frequency in patients with partial-onset seizures and was generally well tolerated with dose-related side effects.

T232
LACOSAMIDE HAS LOW POTENTIAL FOR DRUG-DRUG INTERACTION

D. Thomas, U. Scharfenecker*, B. Nickel*, P. Doty†, W. Cawello*, and R. Horstmann**
**Schwarz Biosciences GmbH, (A Member of The UCB Group), Monheim, Germany; and †Schwarz Biosciences Inc. (A Member of The UCB Group), Raleigh, NC, USA*

Purpose: To investigate the pharmacokinetic drug-drug-interaction (DDI) potential of lacosamide, an investigational drug currently under development for the treatment of epilepsy and diabetic neuropathic pain.

Method: Data from preclinical studies as well as from nine Phase 1 trials (N=184 subjects), a Phase 2 trial (N=91 patients) and three Phase 3 trials of subjects with partial onset seizures with or without secondary generalisation (N=1,311) were evaluated.

Results: In vitro lacosamide is not substantially metabolized and shows no or low potential to inhibit or induce CYP isoforms. Additionally, since lacosamide has low binding to plasma proteins (<15%), drug displacement interactions are unlikely. In DDI trials with healthy subjects, lacosamide did not affect the pharmacokinetic profile of carbamazepine (CYP450 inducer) or valproic acid (CYP450 inhibitor) and was similarly unaffected by co-administration of these drugs. In another Phase 1 trial of extensive and poor CYP2C19 metabolizers, the activity of CYP2C19 had no clinically relevant effect on lacosamide plasma concentrations. Further, the rate or extent of absorption of lacosamide was unaffected by the coadministration of food. DDI trials with metformin, digoxin, omeprazole and the oral contraceptive Microgynon showed no relevant influence of these drugs on lacosamide and vice versa. Additionally, in Phase 3 clinical trials, no influence of lacosamide on plasma concentrations of common antiepileptic drugs and no clinically relevant changes in lacosamide plasma concentrations were observed.

Conclusion: Based on preclinical, clinical pharmacology and clinical trial results showing the lack of drug-drug interactions, lacosamide appears to have a low potential for such interactions in clinical use.

T233
LEVETIRACETAM IN SEIZURE EMERGENCY SITUATIONS

E. Rosati, G. Muscas*, C. Di Bonaventura†, and A. Giallonardo†*
**Careggi Hospital, Florence, Italy; and †University 'La Sapienza', Rome, Italy*

Purpose: To analyze the efficacy and safety of levetiracetam (LEV) in patients with seizure emergency situations including status epilepticus (SE).

Method: We screened, from a retrospective 2 year database of two adult tertiary referral hospitals, patients with SE treated with LEV. The diagnosis of the condition which will lead to the administration of LEV or other AEDs was done by an expert neurologist on the basis of all clinical, laboratory and instrumental parameters.

Results: The sample included 18 patients (8 male, median age 70 years, range 43–90 years) with convulsive and nonconvulsive SE. Eleven cases had acute aetiology and 7 remote symptomatic epilepsy. Patients received an intravenous (i.v.) benzodiazepine as first-line treatment and LEV (6 administered i.v. and 12 through a nasogastric tube) was the second-line treatment in 5, third-line in 7 and four-line in 6. In 8 critically ill patients with refractory SE serum levels documented adequate absorption. In 3/4 patients with early or established SE, seizure activity ceased and didn't recur after LEV administration. Eight/14 patients with refractory SE, showed symptoms and EEG improvement within the first 24 hours after LEV administration; of the remaing 6 patients, 3 died and the other improved (up to 96 hours). No major adverse effects were registered, although less prominent changes may have been masked by the already severely compromised condition of these patients.

Conclusion: LEV should be considered for critically ill patients with SE. The drug seems to be effective and safe according to the data for this small cohort.

T234
CLINICAL EFFECT OF A SWITCH FROM AN ORIGINAL TO A GENERIC AGENT IN DRUG-RESISTANT EPILEPSY—PROSPECTIVE STUDY

P. Czapinski, and E. Czapinska
Epilepsy And Migraine Treatment Centre, Krakow, Poland

Purpose: Approximately 1/3 of physicians are anxious to employ generic drugs in epilepsy treatment, 2/3 fear deteriorated seizure control following a switch, recurrent seizures or poorer tolerance of a new drug.

Method: In a group of 646 patients with drug-resistant epilepsy with partial seizures aged 18–66 years, who were treated with 1–3 new generation antiepileptic agents, a switch was made from an original to a generic drug. The group included 68 patients with two original agents switched to generic drugs. The investigations were carried out in patients in gabapentin (GBP) n=182, lamotrigine (LTG) n=284 or topiramate (TPM) n=160.

Results: A switch of either of the above original agents to generic drugs did not result in increasing seizure frequency (mean seizure frequency per month before and after a switch was 8.2 vs 8.0 in GBP group, 6.7 vs 6.9 in LTG group and 9.9 vs 9.6 in TPM group). The percentage of patients that needed to be switched back to the original medication was 0–2.1%. In the LTG group, even switching the drug several times in consequence of pharmacy substitution did not affect seizure frequency.

Conclusion: It appears that the use of generic drugs in patients with drug-resistant epilepsy is fully justified.

T235
LACOSAMIDE: AN INTERIM EVALUATION OF LONG-TERM SAFETY AND EFFICACY AS ORAL ADJUNCTIVE THERAPY IN SUBJECTS WITH PARTIAL-ONSET SEIZURES

W. Rosenfeld, N. Fountain†, G. Kaubrys‡, L. Heinzen§, and C. McShea§*
**The Comprehensive Epilepsy Care Center For Children And Adults, St. Louis, MO, USA; †University of Virginia School of Medicine, Charlottesville, VA, USA; ‡Vilnius University Hospital, Vilnius, Lithuania; and §Schwarz Biosciences, Inc. (A Member of The UCB Group), Research Triangle Park, NC, USA*

Purpose: Lacosamide is an antiepileptic drug under investigation as adjunctive treatment for partial-onset seizures. This interim report from an open-label follow-on trial evaluates long-term safety and effectiveness of lacosamide in subjects with partial-onset seizures.

Method: Subjects enrolled in this open-label extension following participation in previous, double-blind or open-label trials. Dosage adjustment of lacosamide (100–800mg/day) and/or concomitant AEDs (if applicable) was allowed to optimize tolerability and seizure reduction. Adverse events (AEs), vital signs, body weight, clinical laboratory data, ECG, and continuous and categorical analyses of seizure frequency based on subject diaries were evaluated.

Results: of the 370 enrolled subjects, 76.8%, 60.5%, and 55.7% had >12, >24, or >30 months of lacosamide exposure at the time of this interim analysis. Across all subjects, the median lacosamide modal dose was 400mg/day; 30.8% of subjects had a modal dose of 600–800mg/day. Common AEs (10%) were dizziness, headache, fatigue, nasopharyngitis, diplopia, upper respiratory tract infection, nausea, coordination abnormal, contusion, vision blurred, vomiting, skin laceration, and sinusitis. Discontinuations due to AEs were 11.1%; dizziness (1.6%) was the only event leading to discontinuation in >1% of subjects. Long-term lacosamide treatment was not associated with changes in hematology, clinical chemistry, vital signs or body weight. A small increase in median PR interval (5–9ms) was observed. The median percent reduction in 28 day seizure frequency during open-label treatment from Baseline was 45.9%; the V50% responder rate was 46.6%.

Conclusion: Long-term (¡Ü5.5 years), open-label lacosamide as adjunctive treatment for partial-onset seizures was generally well tolerated and reduced seizure frequency.

T236
A REVIEW OF THE ASSOCIATIONS BETWEEN SECOND GENERATION ANTIEPILEPTIC DRUGS (AEDS) ON SLEEP AND DAYTIME FATIGUE IN ADULT PATIENTS WITH EPILEPSY

M. Mychaskiw, and D. Hoffman†*
**Pfizer Inc, New York, NY, USA; and †Pfizer Inc, New London, CT, USA*

Purpose: There is a complex and reciprocal interaction between epilepsy and its treatment on sleep and daytime fatigue. The current review synthesizes published data on associations between sleep, daytime tiredness/fatigue and eight second generation antiepileptic drugs (AEDs; gabapentin, lamotrigine, levetiracetam, oxcarbezepine, pregabalin, tiagabine, topiramate, zonisamide) in adult patients with epilepsy.

Method: Literature search was performed in electronic databases (MEDLINE [1990–2008], EMBASE [1990–2007], Cochrane Central Register of Controlled Trials [2007]). Reference lists of published articles were searched. Controlled studies published in the English language were reviewed.

Results: Twelve studies met criteria for review. Second generation oral AEDs varied in terms of their impact on both objective and subjective aspects of sleep and daytime fatigue. Patients using either lamotrigine or topiramate did not differ from controls on any outcome assessed. Patients using levetiracetam did not differ from controls on objective sleep outcomes, but findings from an objective measure of daytime sleepiness showed significant increases in napping episodes and duration. Compared to controls, patients on levetiracetam reported significant improvements on subjective assessments of sleep quality and significant worsening on feeling alert in the morning and on wakening. Compared to controls, patients using pregabalin demonstrated significant improvements on number of awakenings and subjective reports of previous night's sleep, sleep disturbance and sleep quantity, with no differences in perceived daytime fatigue. Gabapentin improved sleep by increasing slow wave sleep.

Conclusion: The differential impact of second generation AEDs on aspects of sleep and daytime fatigue may be important considerations when selecting among available treatments for epilepsy.

T237
LEVETIRACETAM IN DRUG RESISTANT PATIENTS WITH JUVENILE ABSENCE EPILEPSY

V. Chiesa, A. Vignoli, E. Zambrelli, F. La Briola, R. Canger, and M. Canevini
Regionale Epilepsy Center, Ospedale San Paolo, Brazil

Purpose: Juvenile absence epilepsy (JAE) is an age-related idiopathic generalized epilepsy characterized by the recurrence of typical absences, frequently associated with generalized tonic–clonic seizures. The response to therapy is good, but in different studies 24–40% of patients result not completely controlled by classical drugs (VPA, LTG, ESM) (Wolf P et al. In: J. Roger et al, Epileptic Syndromes in infancy, childhood and adolescence. John Libbey, 2002; 331–334.). There is at present no study specifically investigating newer antiepileptic drugs in JAE. Levetiracetam is known to be effective in juvenile myoclonic epilepsy (Genton P et al. Epil Disord 2000; 2:209–212), and recently it resulted to be effective in eyelids myoclonia with absences (Striano P et al. Epilepsia 2008; 49:425–430). The aim of our report is to evaluate the effectiveness of levetiracetam in drug resistant patients with JMA.

Method: We studied retrospectively all patients with JAE followed at present in our Epilepsy Centre (n = 49), looking for drug resistant patients that have been treated at some point with levetiracetam.

Results: In our Epilepsy Center 49 patients with JAE are actively followed up (25 females, 14 males; mean age 40,3 years). 13 patients (10 females, 3 males; mean age 37.4 years) were not seizure free with classical drugs. In 6 drug resistant patients we started levetiracetam (mean dosage of 2250 mg/die), and 4 of them became seizure free (mean follow up of 16 months).

Conclusion: Even if we experienced the use of levetiracetam only in few patients with JAE, our data suggest that it could be a good therapeutic option.

T238
EURAP GERMANY: UPDATE ON SUPPLEMENTATION OF FOLIC ACID AND VITAMIN K DURING PREGNANCY AND BREAST-FEEDING IN EPILEPSY PATIENTS

V. Gaus, I. Coban†, R. Kretz*, B. Wandschneider*, W. Henrich*, and B. Schmitz**
**Charité Universitätsmedizin Berlin, Germany; and †Epilepsy Centre, Bethel, Bielefeld, Germany*

Purpose: Periconceptional lack of folic acid is associated with a higher rate of foetal malformations, especially neural tube defects. Some AED have been shown to alter the folate metabolism and to decrease folate blood levels. Preconceptional supplementation of folic acid is therefore recommended for all women planning a pregnancy. Women treated with AED are advised to take higher doses (4–10mg/d). Enzyme-inducing AED can aggravate degradation of vitamin K and promote vitamin-K-deficiency in neonates which can lead to foetal haemorrhage due to a lack of vitamin-K-dependant coagulation factors.

Method: EURAP is an international prospective study to investigate pregnancies with AED-exposition. The primary objective is to assess the risk of major foetal malformations but further pregnancy-related data are also collected. In Germany additional information about vitamin-K-supplementation and breastfeeding is obtained.

Results: Until March 2008 in 435 of the completed prospective pregnancies information about folic acid supplementation is available: In 49,9% the application of folate started preconceptional, 74,2% of these women received doses between 4 and 10mg/d. In 397 cases vitamin-K-related data were obtained: 13,3% of the women were given vitamin K prenatally and 54,9% of the children received vitamin K postpartal (80,5% p.o.). 40,9% (159 of 388 documented cases) of the EURAP-women breastfeed.

Conclusion: With only half of the patients receiving folic acid preconceptional and only ¾ of these in an appropriate dose the german therapy standards need to be improved in this matter. Compared to the German general population, the low amount of women who breast-feed is remarkable (86% vs. 41%).

T239
ADVERSE EFFECTS OF NEWER AND OLDER ANTIEPILEPTIC DRUGS IN PATIENTS WITH EPILEPSY: A POPULATION SURVEILLANCE STUDY

P. Striano,†, J. Cramer‡, L. Hlinkova§, A. Bergmann¶, C. Baukens**, P. Edrich**, and S. Buyle***
**Epilepsy Centre, Federico II University, Naples, Italy; †Unit of Muscular And Neurodegenerative Diseases, Istituto 'G. Gaslini', Genoa, Italy; ‡Yale University And Epilepsy Therapy Project, Orange, CT, USA; §Neurologicka Ambulance, Prague, Czech Republic; ¶Neurologie, Neuburg/Donau, Germany; and **Global Medical Affairs CNS, UCB Pharma SA, Brussels, Belgium*

Purpose: To explore the adverse effects (AEs) of newer and older antiepileptic drugs (AEDs) in patients with epilepsy.

Method: This observational, cross-sectional, noninterventional study investigated AEs in epilepsy patients (age >=4y), stable on 1–2 AEDs for >=3m, using standardized physician-completed questionnaires.

Results: 1,019 patients (47.6% male), mean age 31.5y (4–85y) were included. 56.9% and 43.1% of patients took 1 or 2 AEDs. 71.3% took older AEDs (or combination older+newer) and 28.7% newer AEDs exclusively. Most frequently used older AEDs: valproate (47.7%), carbamazepine (23.7%); newer AEDs: lamotrigine (21.9%), levetiracetam (17.9%), oxcarbazepine (11.2%). Overall 68.3% patients reported >=1 AE (61.3% on newer AEDs; 71.1% on older AEDs). 66.0% patients on monotherapy reported >=1 AE (61.6% on newer AEDs; 68.4% on older AEDs). Patients on newer AEDs were significantly less likely to report >=1 AEs (OR 0.64, 95%CI 0.46–0.89, p=0.0079). Changes in treatment/dose occurred at the study visit for 22.8% (17.5% on newer AEDs; 24.9% on older AEDs) with most frequent reasons (newer vs. older): lack of efficacy (6.2% vs. 7.8%); AEs (4.1% vs. 8.4%); freedom from seizures (3.8% vs. 4.0%). Levetiracetam- (n=182) or lamotrigine- (n=223) treated patients were significantly less likely to report >=1 AEs (levetiracetam OR 0.33 [95%CI 0.19–0.56, p<0.0001]; lamotrigine OR 0.51 [95%CI 0.31–0.84, p=0.0082]) or modify treatment (levetiracetam OR 0.33 [95%CI 0.19–0.57, p<0.0001]; lamotrigine OR 0.52 [95%CI 0.32–0.85, p=0.0088]).

Conclusion: Patients on newer AEDs were less likely to report AEs. Patients treated with levetiracetam or lamotrigine were less likely to report AEs and change treatment.

Study sponsored by UCB.

T240
PHARMACOKINETICS, SAFETY AND TOLERABILITY OF BRIVARACETAM IN HEALTHY ELDERLY SUBJECTS

M. Sargentini-Maier, M. Homery†, and A. Stockis**
**UCB Pharma SA, Braine-L'Alleud, Belgium; and †Biotrial SA, Rennes, France*

Purpose: The efficacy and safety of brivaracetam are currently investigated in confirmatory trials in patients with epilepsy, in the dose range between 5 and 150 mg/day. The purpose of the study was to assess the pharmacokinetics, safety and tolerability of brivaracetam in healthy elderly subjects.

Method: Sixteen healthy male and female subjects (ten aged 65–75 and six aged >75 years) were evaluated after 200 mg single dose and 10-day twice-daily oral administration of brivaracetam. Pharmacokinetic parameters were calculated from plasma and urine concentration versus time profiles. Safety and tolerability were assessed by recording of adverse events, laboratory tests and neurological examinations.

Results: Absorption of brivaracetam was rapid, with median time to peak plasma concentration occurring at 1.5 hours. Plasma concentrations decayed mono-exponentially, with a median half-life of 7.7 hours (range 6.5–9.8) and 8.6 hours (range 7.8–11.4) in the 65–75 and >75 years groups, respectively. Steady-state plasma clearance of brivaracetam in elderly males was slightly lower (0.74 mL/min/kg) than in young healthy males (0.83 mL/min/kg). Brivaracetam was generally well tolerated. Adverse events were of mild intensity, transient and comparable to those observed in a younger population. No clinically relevant abnormalities were observed in laboratory parameters, vital signs or neurological examinations.

Conclusion: In healthy elderly subjects, the pharmacokinetics and tolerability of brivaracetam were comparable to those observed in a younger population, indicating that no dose adjustment of brivaracetam in elderly patients would be required. Study sponsored by UCB.

T241
PHARMACOKINETICS OF BRIVARACETAM IN SUBJECTS WITH HEPATIC IMPAIRMENT AND IN MATCHED HEALTHY CONTROLS

Y. Horsmans, M. Sargentini-Maier†, and A. Stockis†*
**Saint Luc University Hospital, Universite Catholique De Louvain (UCL), Brussels, Belgium and †UCB Pharma SA, Braine-L'Alleud, Belgium*

Purpose: Brivaracetam is partially metabolized by hepatic-CYP-dependent pathways. The objective was to characterize the effect of increasing hepatic impairment on its disposition relative to matched healthy controls.

Method: 26 subjects (age 37–71 years, 7 female, 19 male) stratified according to Child-Pugh classification for mild (A; n=6), moderate (B; n=7) and severe (C; n=7) hepatic impairment and matched healthy controls (n=6) received a single oral dose of 100 mg brivaracetam. Plasma and urine concentrations of brivaracetam and metabolites were measured over 96h.

Results: The geometric mean plasma half-life of brivaracetam was 9.8h, 14.2h, 16.4h and 17.4h in healthy controls and in subjects in classes A, B and C. The area under the plasma concentration-time curve (AUC) was 29.7 (healthy controls), 44.6 (class A), 46.7 (class B), and 47.1 ug.h/mL (class C). The AUCs of brivaracetam and of the acid metabolite in liver-impaired subjects were 1.5–1.6 and 1.6–1.9-fold higher than in healthy controls. The AUCs of the hydroxy-and hydroxy-acid metabolites were reduced to 60–20% and 50% of healthy controls. All adverse events were mild to moderate, and their incidence was similar in the four groups.

Conclusion: The relative importance of brivaracetam biotransformation pathways is altered in hepatic impairment, with a decrease in the CYP-dependent hydroxylation pathways and a concomitant increase of the formation of the acid metabolite (pharmacologically inactive). Dose adjustment is not mandatory but the starting dose may be considered on a case-by-case basis, according to individual response and safety/tolerability.

Study sponsored by UCB.

T242
STEADY-STATE PHARMACOKINETICS OF RETIGABINE AS ADJUNCTIVE THERAPY IN PATIENTS WITH EPILEPSY

G. Loewen, H. Mansbach*, P. Shin*, A. Leyco*, B. Abou-Khalil†, R. Armstrong‡, R. Aung-Din§, R. Leroy¶, and W. Rosenfeld***
**Valeant Pharmaceuticals International, USA; †Vanderbilt University Medical Center, Nashville, TN, USA; ‡Asheville Neurology Specialists, Asheville, NC, USA; §Ovelace Scientific Resources, Inc., Sarasota, FL, USA; ¶Comprehensive Epilepsy Care Center For Children & Adults, St. Louis, MO, USA; and **The Comprehensive Epilepsy Care Center For Children & Adults, USA*

Purpose: To determine steady-state pharmacokinetics (PK) of retigabine (RTG) when administered Q8H as adjunctive therapy in patients with refractory partial-onset seizures.

Method: Patients who had enrolled into a long-term, open-label extension of a multicenter, double-blind Phase 3 trial in which patients were randomized to retigabine (RTG) or placebo added to 1–3 AEDs were eligible to enter the PK study. Patients had to be on a stable RTG dose that had been adjusted according to clinical need. After an overnight fast in patients on stabilized dosages, blood samples were drawn before the first daily dose, and at 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, and 8 hours postdose.

Results: Plasma concentrations were analyzed in 15 Caucasian patients (7 males; 8 females; mean age, 39 yrs). Stabilized RTG dosages (mg/day): 600, n=2; 900, n=4; 1050, n=4; 1200, n=5. Mean (+SD) Cmax (μg/mL): 600 RTG, 0.94(0.18); 900 RTG, 1.01(0.37); 1050 RTG, 1.43(0.33); 1200 RTG, 1.85(1.00). Mean (+SD) trough plasma concentrations (μg/mL): 600 RTG, 0.51(0.02); 900 RTG, 0.34(0.16); 1050 RTG, 0.74(0.28); 1200 RTG, 0.89(0.16). Mean (+SD) average plasma concentrations (μg/mL) over 8-hr dosing interval: 600 RTG, 0.68(0.01); 900 RTG, 0.66(0.26); 1050 RTG, 1.07(0.23); 1200 RTG, 1.34(0.64). Mean Tmax according to stabilized dosage: 1.0, 1.0, 1.4, 2.3 hrs, respectively.

Conclusion: Pharmacokinetic parameters of RTG, the first specific KCNQ channel opener, increase with daily dosage over a range of 600 (200Q8H) to 1200 (400Q8H) mg.

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Monday 22 – Wednesday 24 September 2008
Traditional Poster Session
Epilepsy Syndromes

T243
HEMICONVULSION-HEMIPLEGIA-EPILEPSY SYNDROME: FOCAL SEIZURES WITH ABDOMINAL PAIN AND SEIZURE OUTCOME AFTER ANTERIOR TEMPORAL LOBECTOMY (ATL)

G. Baumgarten, M. Kurthen, G. Krämer, and T. Grunwald
Swiss Epilepsy Centre Zurich, Zurich, Switzerland

Purpose: The rare hemiconvulsion-hemiplegia-epilepsy syndrome (HHE) is supposed to be caused by prolonged hemiconvulsive febrile seizures in childhood resulting in a hypoxic cerebral edema. Patients suffer from hemiparesis and pharmacoresistant focal epilepsy. Up to now, the most common epilepsy-surgical approach to treatment has been functional hemispherectomy.

Method: A 1.5 year old girl developed a right-sided hemiconvulsive status epilepticus due to sustained fever. She recovered with an ipsilateral hemiparesis and drug-resistant focal seizures. On admission in 2006, the 20 year old left-handed woman's main complaints were frequent and severe abdominal cramps sometimes evolving into automotor seizures. Several gastroenterological workups had not found any pathological results. MRI showed leftsided hemiatrophy of the brain and hippocampal sclerosis. During video-EEG-monitoring we recorded several focal seizures with abdominal pain as main clinical symtom and left temporal onset and course of the ictal EEG. Functional MRI demonstrated right-sided language dominance and unilateral right temporal activation during memory tasks. Since the patient did not want to take the risk of a postoperative hemianopsia, left-sided ATL was performed. Since then, the patient has remained seizure-free for more than one year.

Conclusion: In accordance with earlier studies (Eschle D et al. Mayo Clin Proc 2002; 77 (12): 1358–60), our case demonstrates that abdominal pain can be caused by focal seizures originating within the mesial temporal lobe. Moreover it shows that ATL is a promising epilepsy surgical approach in selected HHE-patients (Kim DW et al. Neurology 2008; e-Pub ahead print).

T244
A SERIES OF 34 PATIENTS WITH RASMUSSEN'S ENCEPHALITIS: CLINICAL COURSE, EEG- AND MRI FINDINGS

M. Tokarzewski, F. Woermann*, M. Hoppe*, I. Tuxhorn†, and B. Polmann-Eden‡*
**Bethel Epilepsy Centre, Bielefeld, Germany; †Epilepsy Center-Neurologic Institute, Cleveland Clinic Foundation, Cleveland, OH, USA; and ‡Dalhousie University, Halifax, Canada*

Purpose: Rasmussen encephalitis (RE) is a rare epilepsy syndrome manifesting primarily in childhood characterized by unilateral, progressive hemispheric inflammation of unknown etiology. Refractory focal epilepsy and epilepsia partialis continua, progressive hemiparesis, hemianopsia and cognitive decline are the cardinal features. Our retrospective study analyses the longitudinal course of the electroclinical and imaging features of 34 patients.

Method: 34 patients (range 1.8 – 14.7 years at first seizure) presenting between 1988 and 2006 in the Bethel Epilepsy Centre were studied and included clinical parameter: age onset, seizure types, status epilepticus (SE), Todd's paresis, EEG patterns and MRI findings.

Results: Three distinctive phases could be identified in 90% patients which were categorized as: prodromal=PP, acute =AP and residual=RP. Focal and generalized SE presentation most often occurred in the AP of RE and was particularly correlated with bad prognosis when found as an initial symptom. 76% of RE patients had focal slowing on EEG already in the PP, mainly in the temporocentral region. Epileptiform activity was seen in 72% of the PP and in 100% of the AP. Signal increase on MRI was progressive over time (22% PP, 44% AP, 93% RP); local atrophy was present in already 11% of the PP subgroup and 100% when RP was reached.

Conclusion: Despite the heterogeneity of the clinical course, there was a striking intercorrelation between clinical, functional (EEG) and morphological (MRI) data reflecting continuous progression of the disease and allowing subcategorization in at least 3 subgroups.

T245
STATUS IN SYMPTOMATIC EPILEPSY. FREQUENCY AND TYPES

J. Marquez Sanchez, and F. Marquez Daniel†*
**Private Practice, Spain; and †Hospital Sant Jaume Olot / Hospital Joisep Trueta Girona, Spain*

Purpose: To determinate the frequency and types of status in symptomatic epilepsy.

Method: We did a retrospective study in a group of 1609 patients between 1 month old and 94 years old, visited between 1974 and 2007. All patients had been diagnosed of epilepsy by clinical criteria and complimentary test, such as EEG, MRI, CT, blood tests. Data base programs used were Open Acces IV initially and Microsoft Acces posteriorly.

Results: From the total of 1609 patients, 764 (47,5%) were catalogued of symptomatic epilepsy corresponding to 17,8% to cerebral tumors, 14,4% to anoxia-encephalopathy, 12,3% to cranioencephalic trauma, 9,4% to vascular malformations, 8,63% to alcoholism, 7,2% to stroke, 5,7% to AIDS, 5,2% to infections (meingitis-meningoencephalitis), 19,3% to other causes. From a total of 94 patients with status, 64 (8,3%) belonged to the group of symptomatic epilepsy and 30 to the idiopatic group. The most frequent cause was cerebral anoxia (25% ot the total of status) followed by cerebral tumors (20,3%). The rest of causes had frequencies between 7 and 11%.

Conclusion: Epileptic status is 2,3 more frequent in symptomatic epilepsy than in idiopatic epilepsy. The main cause of symptomatic epilepsy is cerebral anoxia followed by tumors. The rest of causes have a much lower frequency.

T246
INSUFFICIENT EFFECT OF IMMUNOMODULATORY THERAPY ON SEIZURE ACTIVITY IN ADULT-ONSET RASMUSSEN'S ENCEPHALITIS (A-RE)

*M. Tormašiová, J. Janèo, E. Feketeová, E. Klímová, and D. Kozáková**
Pavol Jozef Safarik University, Slovak Republic

Purpose: Immune system is proposed to play a key role in the unclear pathogenesis of RE, therefore IVIG is recommended as the first-line immunotherapy in patients with A-RE.

Case report: A 35 year old male with normal history of psycho – motor development, whose disease onset occurred at the age of 20 with sporadic partial simplex seizures, followed 8 years later by secondary generalized epileptic seizure, then frequent secondary generalized partial complex seizures and several status epilepticus with postictal left hemiparesis. The first signs of epilepsia partialis continua on left upper extremity appeared 14 years after onset. Gradually cognitive deficit has developed. At present, the patient experiences pharmacoresistant, mostly insular seizures from frontal operculum almost every day. Repeated MRI studies showed progression of hemiatrophy in right FTP cortex, hippocampus and caudate nucleus. EEG recordings revealed slow-wave abnormity over frontal quadrants and right FT epileptiform activity, later in the course of the disease bilateral FCT epileptiform discharges occurred. Interictal SPECT and FDG-PET proved severe hypoperfusion and hypometabolism involving FTP lobes. Routine blood and standard immunological serum and CSF tests were normal. Fifteen years after onset, IVIG was administered in therapeutic dose of 0.4 g/kg/day 5 days in a month, repeated 8 times. As the immunomodulatory therapy showed ineffective, corticotherapy was introduced, initiating methylprednisolon 400mg/m2/day without improvement.

Conclusion: No beneficial effect on seizure frequency was achieved despite application of recommended therapy. We suppose that late timing of immunotherapy is crucial for treatment failing.

T247
CHROMOSOMAL ABNORMALITIES IN EPILEPSY: WHAT EVIDENCE IS THERE THAT ASSESSMENT BEYOND THE EPILEPSY ALONE IS IMPORTANT?

J. Budden, and S. Sisodiya
UCL Institute of Neurology, UK

Purpose: To examine the literature on the complex needs of people with additional needs to epilepsy due to a chromosomal disorder. To identify associated features and evidence of interventions to improve health.

Method: A literature review was performed using PubMed. Additional sources of evidence included contact with patient charities and support groups. (Unique and the Wolf Hirschhorns Support Trust). Reference lists of retrieved articles were examined for relevant citations.

Results: Evidence (mainly from case studies) of 33 patients included in 5 studies of Miller Dieker Syndrome and 38 patients included in 5 studies of Wolf Hirschhorns syndrome showed epilepsy to be the most common feature. Seizures occurred in 88% and 90% respectively. There was a considerable range of manifestations. Common features related to growth, nervous system, craniofacial abnormalities, cardiovascular, and urogenital complications. Some features may have a significant effect on mortality. Respiratory tract infections were the leading cause of mortality. Recent reports suggest the emergence of cancer should be taken into consideration during long-term follow-up.

Conclusion: Chromosomal abnormalities are increasingly recognized in genetic studies. Clinically, few chromosomal syndromes associated with epilepsy are widely recognized. Literature highlighted bias in publications towards identifying genes and detection of these conditions. There was a significant lack of positive interventions. Evidence suggests whilst epilepsy may dominate the clinical picture attention should be drawn to other possible features. The lack of literature on the natural history highlights the need for evaluations at initial diagnosis to establish extent of disease, symptomatic management of complications and long term ongoing surveillance.

T248
MULTIFOCAL CORTICAL DYSPLASIA: A REPORT OF SIX CASES

S. Fauser, H. Huppertz†, B. Steinhoff‡, K. Strobl‡, A. Schulze-Bonhage*, and J. Zentner§*
**Epilepsy Center, University of Freiburg, Germany; †Swiss Epilepsy Center, Zürich, Switzerland; ‡Epilepsy Center Kork, Kehl-Kork, Germany; and §Department of Neurosurgery, University of Freiburg, Germany*

Purpose: Focal cortical dysplasia (FCD) is generally considered as a circumscribed area of cortical dyslamination. In histological investigations, however, dyslamination sometimes appears disseminated rather than confined to a single patch. Also EEG and volumetric MRI investigations pointed to a more widespread brain involvement. Here we present six patients with MRI evidence of multifocal FCD.

Method: All six patients were referred to the Epilepsy Center of the University of Freiburg, Germany, between 2002 and 2007.

Age at epilepsy onset ranged from 0 to 18 years (mean 5 years, median 0.5 years), age at invasive recordings/surgery ranged from 3 to 41 years (mean 21.8 years, median 22.5 years). Five patients underwent epilepsy surgery. Histological findings in FCD were classified according to Palmini. Additionally, genetic investigations were performed in order to assess possible mutations in the genes for tuberous sclerosis complex (TSC).

Results: In five of six patients, the FCDs were located in the same hemisphere, one case presented with bilateral FCDs. Seizures arouse from both FCDs in 4 patients, in one patient seizures started exclusively from the hippocampus, in another patient the second lesion only showed interictal activity. In patients with removal of both FCDs (n=4) the histological subtype was identical in both lesions and was classified as Palmini type 2. Four of 5 operated patients became seizure-free. None of the patients had mutations in the TSC genes.

Conclusion: FCD can be multifocal showing different degrees of epileptogenicity. Removal of both lesions leads to a good postoperative outcome. Multifocal FCD seems not to be related to tuberous sclerosis.

T249
ANTIBODIES TO GLUTAMIC ACID DECARBOXYLASE IN PATIENTS WITH ETIOLOGICALLY UNCLEAR EPILEPSIES

M. Malter, C. Elger, and C. Bien
University of Bonn, Germany

Purpose: Antibodies (abs) to glutamic acid decarboxylase (GAD) have been detected in patients with different otherwise unexplained CNS disorders including epilepsies. Here, we studied a cohort of patients with etiologically unclear epilepsies for the presence of GAD abs in serum.

Patients and Method: From a database of 139 patients admitted for etiologically unclear epilepsy and suspected immunological origin (2002–2007), patients with the typical GAD ab staining pattern on indirect immunohistochemistry on rat brain and a positive result on a radioimmunoprecipitation assay were evaluated.

Results: We identified eight patients with elevated GAD abs titers. These patients could be divided into two groups: one group contained five patients with recent (<5 years) limbic encephalitis (LE)-like presentation (one patient with a definite diagnosis based on histological analysis; four with otherwise unexplained temporomedial MRI signal increase); all were young females (19–47 years of age at disease onset); all received a steroid therapy under which all patients improved on neuropsychological testing; seizures, however, persisted in all cases; no further atrophy of the temporomesial structures was observed on follow-up MRIs. The remaining three patients had divergent clinical appearance and normal brain MRIs. Two of them had type-I-diabetes. None of these patients received an immunotherapy.

Discussion: GAD abs may define another subgroup of LE besides paraneoplastic LE and VGKC ab-associated LE. Characteristics of this subgroup are an onset of disease at young age, female gender, temporomesial MRI signal increase, and cognitive (but not epilepsy-wise) improvement under steroid therapy.

T250
ALEXIA AS THE SOLE MANIFESTATION OF PARTIAL SEIZURE INDUCED BY READING TEXT IN THE MOTHER BUT NOT THE FOREIGN LANGUAGE, IN A PATIENT WITH READING EPILEPSY: A CLINICAL, VIDEO-EEG, MRI, AND FMRI STUDY

S. Giannakodimos, I. Kapsalakis*, D. Vergenelakis†, P. Toulas†, and S. Gotsis†*
**Epilepsy Clinic, Neurology Department, General Hospital of Athens, Greece; and †Encephalos-Euromedica Center Athens, Greece*

Reading epilepsy (RE) is a form of epilepsy, where epileptic seizures are induced by reading. Rarely, reading-induced seizures have been reported with ictal alexia as the prominent clinical symptom. A case of RE with alexia as the sole manifestation of reflex seizures to reading

text in the mother but not the foreign language is reported. A 28-year old right-handed computer-programmer, presented following his second-ever GTCS. On questioning, multiple, stereotyped, frequent (>2/month), and brief (of ~ 20 sec duration) episodes were reported to occur during the previous 5 years. During the episodes the patient experienced a sudden difficulty in word recognition, resulting in stopping reading, with no other ictal symptoms. Both GTCS were preceded by the described episodes. Symptoms occurred only when the patient was reading text in his mother language (Greek) but not in foreign language (English) despite that he was daily reading texts in English. English language was learned after the age of 8 years. A video-EEG with long periods of reading both English and Greek texts was performed. Partial seizures with ictal alexia and a secondary GTCS were recorded only during reading Greek text. Ictal EEG showed discharges of rhythmic theta at 5Hz over the left temporoparietal area, lasting 5–20 secs. Alexia was the sole ictal symptom. MRI-brain was normal. fMRI showed different activation areas during reading texts in English and Greek, a finding which may explain the ictal symptoms. The clinical, video-EEG and fMRI findings in this patient may suggest that alexia as the sole manifestation of partial seizures in RE may result from ictal dysfunction of the comprehension of written language responsible area of the dominant hemisphere.

Monday 22 – Wednesday 24 September 2008
Traditional Poster Session
Genetics

T251
ASSOCIATION ANALYSIS AND MUTATION SCREENING OF CANDIDATE GENES FOR PHOTOSENSITIVITY IN THE CHROMOSOMAL REGION 13Q31

S. Von Spiczak, T. Sander†, H. Muhle*, S. Kara*, I. Helbig*, J. Hampe‡, S. Schreiber‡, and U. Stephani**
**Clinic of Neuropediatrics, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany; †Cologne Center for Genomics, University of Cologne, Cologne, Germany; and ‡Institute for Clinical Molecular Biology, Christian-Albrechts University, Kiel, Germany*

Purpose: Photosensitivity (photoparoxysmal response, PPR) is a common highly heritable EEG trait frequently associated with idiopathic generalized epilepsy (IGE). As IGE syndromes are clinically and genetically heterogeneous disorders, we used PPR as an endophenotype to unravel the complex genetic background of these syndromes.

Method: Based on a genome-wide linkage study, which showed a susceptibility locus for photosensitivity on chromosome 13q31 (Tauer et al. Ann Neurol 2005;57:866–873), we performed linkage disequilibrium mapping of this candidate region (84 to 98 Mb) by investigating 155 single nucleotide polymorphisms (SNPs) localized approximately every 90 kb in 293 German photo-sensitive subjects (175 ''PPR only'' and 118 ''PPR and IGE'') and 700 population controls.

Results: Associations at the type-I error level of $p < 0.05$ with PPR were found for: 1) ten SNPs located in intron 2 of the GPC6 gene (glypican 6, involved in cell growth and division); 2) three SNPs located in intron 1 of FARP1 (a protein linking the cytoskeleton to the cell membrane); and 3) one SNP in intron 5 and intron 12 of RANBP5 (mediating nucleocytoplasmic transport).

Conclusion In contrast to studies where candidate genes are chosen based on functional aspects and their presumed impact on epileptogenesis, we were able to identify three positional candidate genes – GPC6, FARP1 and RANBP5 – for photosensitivity without applying a priori hypotheses. The importance of these candidate genes is currently investigated by sequence analyses.

T252
WHOLE GENOME LINKAGE ANALYSIS IN A FAMILY WITH TALKING-INDUCED JAW JERKS AND PHOTOSENSITIVITY.

D. Kasteleijn- Nolst Trenité,†, A. Bader†, G. de Haan‡, H. Schippers§, D. Lindhout†, W. Perquin¶, P. van Domburg**, and B. Koeleman†*
**University La Sapienza Rome Italy; †University Medical Center Utrecht, Utrecht, The Netherlands; ‡Stichting Epilepsie Instellingen, Heemstede, The Netherlands; §Mesos Medisch Centrum Oudenrijn, Utrecht, The Netherlands; ¶Medisch Cenrum Haaglanden, Den Haag, The Netherlands and **Laurentiusziekenhuis, Roermond, The Netherlands*

Purpose: Mapping a susceptibility gene by linkage analysis in a three-generational family (27 normal intelligent subjects; age 14- 87 years) with a dominant clinical picture consisting of speaking-evoked jaw jerks starting at the age of around 50, limb jerks, complaints related to visual stimuli since puberty and a photoparoxysmal reaction(PPR).

Method: Eighteen family members (10 F,8 M) have been investigated with standardized intermittent photic stimulation with frequencies ranging from 2–60 Hz (Grass PS33)in three eye conditions. All four subjects with speaking evoked jaw jerks had also jerks in the limbs provoked by light and a PPR still in their fifties. Another four subjects had jerks esp. provoked by flickering lights and a PPR and one a ''subclinical'' PPR. DNA samples were available from 21 family members, including the clinically affected oldest family member (mother of the proband, a teacher in her fifties). The family was genotyped using the Illumina linkage panel chip and whole genome linkage analysis was performed.

Results: Suggestive linkage was found on chromosome 19 with a LOD score of 2.8. The LOD-minus-1 confidence interval gave a region containing around 12 genes. None of these genes are ion- channels.

Conclusion: Although jaw jerks have been connected exclusively with reading epilepsy, in our family these seemed to be connected with speaking and an age above 50. Interestingly, they all started with photosensitivity in broad sense in adolescence and had jerks in the limbs as well. We discuss some interesting candidate genes that are located in the linked region. Marie Curie Grant on Visual Sensitivity MEXCT-CT-2005-024224 FP6 EU program.

T253
ASSOCIATION ANALYSES OF METABOTROPIC GLUTAMATE RECEPTOR GENE (GRM4) POLYMORPHISMS WITH IDIOPATHIC GENERALIZED EPILEPSIES (IGES) AND PHOTOPAROXYSMAL RESPONSE

H. Muhle, V. Gaus†, S. von Spiczak*, S. Kara*, H. Lerche‡, Y. Weber‡, A. Lie-Kleefuss§, C. Elger§, and T. Sander†,¶*
**University Hospital Kiel, Germany; †Charité University Medicine, Berlin, Germany; ‡University of Ulm, Germany; §University of Bonn, Germany; and ¶University Cologne, Germany*

Purpose: The gene encoding the group III metabotropic glutamate receptor GRM4 is located on the chromosal segment 6p21.3 where tentative susceptibility genes for juvenile myoclonic epilepsy (JME) and photoparoxysmal response (PPR) have been mapped. PPR occurs frequently associated with idiopathic generalized epilepsies (IGE). The present candidate gene association study tested whether variation of the GRM4 gene confers susceptibility to idiopathic generalized epilepsies (IGE) or photosensitivity.

Method: The case-control cohorts included 564 IGE unrelated patients, 313 patients exhibiting PPR and 733 population controls of German descent. Association analysis was carried out for 17 single nucleotide polymorphisms (SNPs) located in the genomic GRM4 sequence for all IGE patients as well as for two IGE syndromes (juvenile myoclonic epilepsy (215 JME patients), childhood absence epilepsy (175 CAE patients)) and the PPR group (313 PPR probands). Those patients were included in the genome wide association analysis (EPICURE project).

Results: Allelic associations were detected between IGE and seven GRM4 SNPs (p: 0.037 – 0.0036), as well as in JME and five SNPs (p: 0.042 – 0.0106) and CAE and two SNPs (p: 0.0466 – 0.0021). No significant association was found for PPR.

Conclusion: Our association study suggests that genetic variation of GRM4 confers susceptibility to IGE but not to PPR.

T254
POLG MUTATIONS CAUSE SEVERE EARLY ONSET EPILEPSY WITH LIVER FAILURE

P. Isohanni,†, T. Lönnqvist*, T. Linnankivi*, J. Uusimaa‡,§, A. Harju†, A. Paetau¶, H. Kalimo¶, L. Valanne**, A. Suomalainen†, and H. Pihko**

**Hospital For Children and Adolescents, Helsinki University Central Hospital, Helsinki, Finland; †Biomedicum-Helsinki, University of Helsinki, Helsinki, Finland; ‡University of Oulu, Oulu, Finland; §Clinical Research Center, Oulu Univerity Hospital, Oulu, Finland; ¶University of Helsinki, Helsinki, Finland; and **Helsinki Medical Imaging Center, University of Helsinki, Helsinki, Finland*

Purpose: Mutations in mitochondrial polymerase-gamma (POLG) can present from infancy to adulthood with variable clinical presentations like Alpers-Huttenlocher syndrome, recessive ataxia-neuropathy syndrome (MIRAS) and PEO (progressive external ophtalmoplegia). We describe five Finnish patients of infantile/childhood-onset encephalopathy with compound heterozygous missense mutations in POLG1 gene.

Method: Patients were evaluated clinically. Neuroradiological and neurophysiological investigations were done. Muscle biopsy was performed with respiratory chain enzyme analysis and immunohistochemical studies. Neuropathological examination was performed on two patients. POLG1 gene was sequenced.

Results: We found 5 children with 5 different mutations in POLG1. All patients had either W748S or A467T mutation, the other mutation varied. The disease onset was encephalitis-like with vomiting, decreased consciousness and recurring seizures progressing to epilepsia partialis continua and status epilepticus, myoclonias, hemiparesis, ataxia, tremor and visual disturbance. Age at onset was 9 months – 6 years. Elevated liver transaminases were detected, often connected with the start of an-tiepileptic medication, but the administration of sodium valproate caused irreversible liver failure. Patients died 5 months-11 years after disease onset. They had no typical mitochondrial pathology in muscle biopsy or respiratory chain enzyme analysis. EEG findings consisted of focal slow wave or spike-slow wave discharges shifting from one hemisphere to the other. MRI findings included transient lesions and atrophy; laminar cortical necrosis and hippocampal atrophy were seen in neuropathological examination.

Conclusion: POLG mutations are an important cause of early-onset encephalopathy with severe epilepsy, and sodium valproate is toxic to these patients and can lead to fatal liver failure.

T255
MUTATIONAL ANALYSIS FOR REPETITIVE FEBRILE SEIZURES AND SPORADIC FEBRILE SEIZURES PLUS IN JAPANESE

G. Fukuma, A. Ishii*, J. Wang†, H. Kurahash‡, S. Miyake§, S. Kaneko¶, and S. Hirose**

**School of Medicine, Fukuoka University, Fukuoka, Japan; †Qilu Hospital, Shandong University, Jinan, China; ‡Nagoya University Graduate School of Medicine, Nagoya, Japan; §Kagawa Prefectural Central Hospital, Takamatsu, Japan; and ¶School of Medicine, Hirosaki University, Hirosaki, Japan*

The prevalence of febrile seizures (FS) in Japanese is significantly high compared to that in the rest of the world suggestive of a unique trait for FS of Japanese. FS may be repetitive whereas frequent FS followed by FS beyond 6 years of age and/or afebrile seizures is differently defined as FS+. FS+ is also a cardinal manifestation of autosomal dominant epilepsy referred to as generalized epilepsy with FS+ (GEFS+). As causes of GEFS+, mutations of the genes encoding Na+ channel subunits have been identified. The aim of this study is to see if mutations of such genes underlie repetitive FS and sporadic FS+ in Japanese. We recruited 30 individuals with FS+ consisting 19 males and 11 females ranging from 1 to 23 years old (mean 8.63) at the study and 53 individuals with FS consisting 36 males and 17 females from 1 to 29 years old (mean 5.75). Genetic abnormalities within exons and their flanking introns of the genes encoding major subunits of the Na+ channels (SCN1A, SCN2A, SCN1B and SCN2B) were sought using a direct sequencing method. In these cohorts, only one heterozygous missense mutation, D1740H in SCN1A was found in a girl with FS+. Her epilepsy phenotype was not narrowly-defined FS+ but similar to that of borderline severe myoclonic epilepsy in infancy as psychomotor retardation had become evident after 6 years of age. These finding suggest that mutation of Na+ channel does not contribute, if any, to the pathogeneses of repetitive FS and narrowly-defined FS+ in Japanese.

T256
A GAIN-OF-FUNCTION MUTATION IN SCN2A IS ASSOCIATED WITH INFANTILE-ONSET EPILEPSY AND EPISODIC ATAXIA

A. Anttonen, Y. Liao†, E. Liukkonen‡, E. Ahonen*, H. Lerche†, and A. Lehesjoki**

**Folkhälsan Institute of Genetics,, University of Helsinki, Helsinki, Finland; †University of Ulm, Ulm, Germany; and ‡Epilepsy Unit, Hospital for Children and Adolescents, Helsinki University Central Hospital, Helsinki, Finland*

Purpose: Previously, mutations in SCN2A encoding the brain sodium channel Nav1.2 have been associated with benign neonatal-infantile seizures, a relatively mild epilepsy syndrome presenting within the first year of life and having a favorable outcome. We screened SCN2A for mutations in a group of patients with intractable epilepsy and no SCN1A mutations.

Method: All coding exons of SCN2A were amplified from genomic DNA of 28 patients and sequenced. The electrophysiological properties of the identified mutation were studied using the patch clamp technique and expressing the mutant human isoform of the Nav1.2 channel together with the auxiliary beta1 and beta2 subunits in the mammalian cell line tsA201.

Results: We identified a novel de novo missense mutation, c.788C>T (p.Ala263Val), in SCN2A. The patient presented with infantile-onset partial motor and tonic–clonic seizures and episodes of ataxia after 18 months of age. Electrophysiological analysis of the mutant channel showed a threefold-enhanced noninactivating, persistent sodium current and a slower time constant of fast inactivation. The voltage dependence of both activation and inactivation was shifted towards more depolarized

potentials and the slope factor of the steady-state fast inactivation curve was increased leading to an increased window current.

Conclusion: SCN2A mutations may associate with both infantile seizures and episodic ataxia. The gain-of-function properties of the mutant channel could explain the neuronal hyperexcitability of pyramidal and cerebellar neurons resulting in seizures and ataxia. A differential spatial and temporal expression of this channel might explain the distinct age dependence of the neurological symptoms.

T257

BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES FOLLOWING BENIGN NEONATAL SEIZURES RESULTING FROM A MUTATION OF KCNQ2

A. Ishii, T. Miyajima†, G. Fukuma*, H. Kurahashi*,‡, J. Wang*,§, S. Yasumoto*, S. Kaneko¶, and S. Hirose**
**School of Medicine, Fukuoka University, Fukuoka; †Tokyo Medical University, Tokyo, Japan; ‡Nagoya University Graduate School of Medicine, Nagoya, Japan; §Qilu Hospital, Shandong University, Jinan, China; and ¶School of Medicine, Hirosaki University, Hirosaki, Japan*

Molecular pathogenesis of benign childhood epilepsy with centrotemporal (Rolandic) spikes (BECCT) remains unclear whereas mutations of the gene encoding components of KCNQ K+ channels, KCNQ2 and KCNQ3, have been identified as causes of benign familial neonatal convulsions. Association of both epilepsy phenotypes have been reported while only a few cases of such association were documented in relation to the mutations of KCNQ2. We here report a girl with benign neonatal convulsions followed by BECCT, for whom a mutation of KCNQ2 was identified. She was born to nonconsanguineous and seizure-free parents and had a completely normal perinatal history. From 2 days of age, she developed tonic seizures with laterality lasting a few to 20 seconds and the seizures became frequent but disappeared spontaneously at 14 days of age. In the follow-up course, consecutive EEG recordings showed centrotemporal spikes since 2 years of age, and a sylvian seizure occurred at 5 years and 8 months of age during sleep. Since carbamazepine therapy was instituted, no seizures had been observed although the centrotemporal spikes remained. Her psychomotor development was normal. A heterozygous deletional mutation (c.910-2delTTC or TTT, F304del) of KCNQ2 was identified in the patient but not in the parents and thus considered to be a de novo mutation. Electrophysiological study revealed null function of the mutant KCNQ K+ channels. This case of BECCT in a patient who had a mutation of KCNQ2 resulting in benign neonatal convulsions may give us a clue to the understanding of the molecular pathogenesis of BECCT.

T258

VARIATION OF JME FAMILY PHENOTYPE ANTICIPATED BY PREVIOUS EEG CHARACTERIZATION: CLINICAL AND GENETIC EXPLORATION

A. Martins Da Silva,†,‡, P. Lacerda§, L. Guedes§, J. Lopes*, B. Leal†,‡, P. Pinho e Costa†,‡,§, and B. Martins da Silva†,‡,§*
**S Neurofisiologia-Hospital Santo Antonio – Centro Hospitalar Porto, Portugal; †UMIB/ICBAS – Universidade Porto, Portugal; ‡ICBAS – Universidade Do Porto, Portugal; and §INSA-Dr. Ricardo Jorge, Porto, Portugal*

Purpose: To study the relationship between the clinical picture and EEG patterns, after seizures occurrence in previously unaffected members of a JME plus Photosensitivity family. To screen the EFHC1 gene (myoclonin) for mutations in the present family.

Method: Fifteen individuals from three generations of a family including two brothers with JME (one with Photosensitivity), three members with only photosensitivity, and another with febrile convulsions were studied four years ago. Assessment of new seizure cases was complemented by photosensitivity study protocol (Neurophys. Clin. 1999; 29:318–24). All exons of the EFHC1 gene were submitted to high resolution melting mutation analysis. Confirmatory sequencing was performed.

Results: New seizures occurred recently (proband mother and niece). Now reevaluated, their EEG findings maintain similar features, with more expressive and frequent abnormalities. Mother had four (spontaneous?) CP evolving to generalized seizures. Niece had two generalized seizures occurring when watching TV. Further genetic studies, including mutation screening of the myoclonin (EFHC1) gene were carried out. No association of clinical or EEG features with EFHC1 mutations was apparent.

Conclusion: EEG changes on photic stimulation anticipate seizures occurrence in three generations of the same family. Seizures had different expression in different members (females are photosensitive and the male has only JME features). Apparently the female from the first generation was the carrier of the genetic trait subjacent to seizure and photic expression. Our results do not support the involvement of the EFHC1 gene in the etiopathogenesis of JME in this family. This finding was not unexpected given the peculiar phenotypes observed.

Monday 22 – Wednesday 24 September 2008
Traditional Poster Session
Neuroimaging

T259

EEG-MRI STUDY IN PATIENTS WITH PARTIAL EPILEPSY

I. Fedotova
Kharkov State Medical University, Ukraine

Purpose: To investigate Blood Oxygen Level Dependent (BOLD) responses to interictal epileptic discharges (IEDs) during EEG-correlated functional MRI (EEG-fMRI) in patients with partial epilepsy.

Method: We studied 15 patients who had a diagnosis of partial epilepsy and active spiking on routine scalp EEG recording. Sessions of continuous EEG-fMRI were recorded, and spikes (identified after online artifact removal) were used as events in the fMRI analysis. Regions of BOLD signal change in response to interictal epileptic discharge were assessed and epileptogenic zone localization was electroclinically identified.

Results: 15 patients with partial epilepsy were recruited (10 males, 5 females, mean age 21.6, mean onset age range 0.5–27). 4 who underwent EEG-fMRI were excluded from further analysis: one due to absence of epileptic discharges, the other due to excessive head motion. Eight sessions of EEG-fMRI scanning in 8 patients were obtained: 5 with activation and deactivation, one with activation only, and one with deactivation only. Focal activations corresponding to electroclinical localization occurred in 7 sessions, 5 of which were maximal.

Conclusion: Maximally activated areas detected by EEG-fMRI in patients with partial epilepsy appear to be concordant with epileptogenic areas as defined by electroclinical localization data. In most patients with focal epilepsy, positive BOLD responses seem to be mainly in epileptogenic zones and the corresponding contralateral areas. Responses to deactivation seem less associated with IEDs. So EEG-fMRI is a useful tool to study the pathophysiological mechanisms of epilepsy and may assist in presurgical evaluation of epilepsy.

T260
TARIQUIDAR-INDUCED P-GLYCOPROTEIN INHIBITION AT THE RAT BLOOD–BRAIN BARRIER STUDIED BY POSITRON EMISSION TOMOGRAPHY WITH (R)-[11C]VERAPAMIL

J. Bankstahl,†, C. Kuntner‡, A. Abrahim‡,§, R. Karch§, O. Langer‡,§, and W. Löscher*,†*
**University For Veterinary Medicine Hannover, Germany; †Center for Systems Neuroscience, Hannover, Germany; ‡Austrian Research Centers GmbH – ARC, Seibersdorf, Austria; and §Medical University of Vienna, Austria*

Purpose: The multidrug efflux transporter P-glycoprotein (Pgp) is believed to play an important role in resistance to antiepileptic drugs. Modulation of Pgp at the blood–brain barrier (BBB) by the highly selective inhibitor tariquidar may be a promising strategy to overcome drug resistance by enhancing the brain penetration of antiepileptic drugs.

Method: We used small-animal positron emission tomography (PET) and the new Pgp substrate tracer (R)-[11C]verapamil to study modulation of cerebral Pgp activity by tariquidar in naïve rats. To enable a comparison with human PET data, we performed kinetic modeling to estimate the rate constants of radiotracer transport across the rat BBB. Wistar Unilever rats underwent (R)-[11C]verapamil PET scans 2 hours after i.v. administration of tariquidar (15 mg/kg).

Results: Following tariquidar administration, the distribution volume (DV) of (R)-[11C]verapamil was 12-fold higher as compared to baseline (3.68±0.81 versus 0.30±0.08; P=0.0007). The increase in DV could mainly be attributed to an increased influx rate constant K1 of (R)-[11C]verapamil into the brain, which was about 8-fold higher after tariquidar. A preliminary dose-response assessment provided an estimated half-maximum effect dose (ED50) of 6.5 mg/kg (95% confidence interval, 4.9–8.2).

Conclusion: Our data demonstrate that tariquidar is a potent inhibitor of Pgp at the BBB that enhances intracerebral uptake of Pgp substrates. The next step will be to establish a dosing protocol for tariquidar to inhibit BBB Pgp in humans. The study was supported by the European 7th framework program collaborative project European research initiative to develop imaging probes for early in vivo diagnosis and evaluation of response to therapeutic substances (EURIPIDES).

T261
TRANSIENT LESIONS IN THE SPLENIUM OF THE CORPUS CALLOSUM IN EPILEPTIC PATIENTS

T. Procházka, H. Malíková*, I. Mareèková*, Z. Vojtìch*, J. Vymazal*, and M. Kalina**
**Na Homolce Hospital, Prague, Czech Republic*

Purpose: Transient focal lesions in the splenium of the corpus callosum (SCC) have been previously described in patients with several different conditions. The objective of this study was to describe these lesions in patients with epilepsy.

Method: We retrospectively reviewed magnetic resonance images (MRI) of 115 adult epileptic patients who had undergone EEG monitoring at the Epilepsy Center Na Homolce.

Results: of 115 epileptic patients, 2 (1,7%) had SCC lesions. One patient had juvenile myoclonic epilepsy and MRI was performed 4 days after discontinuation of carbamazepine therapy. The other had intractable temporal lobe epilepsy, MRI was obtained 7 days after resumption of original treatment, lamotrigine was reduced to two-thirds of the admission dose. In both cases brain MRI revealed ovoid lesion in the SCC characterized by high signal on T2-weighted images and no enhancement after gadolinium infusion. One patient had MRI protocol supplemented by diffusion-weighted (DW) sequences and the lesion had restricted diffusion. Both patients were asymptomatic and a follow-up MRI showed complete resolution of the SCC lesions.

Conclusion: Different pathogenetic mechanisms might be at the origin of SCC lesions. However, in our cases, sudden antiepileptic drug (AED) withdrawal or AED fluctuation with a consequent impact on fluid balance appears to be the most likely cause. It is important to be aware of the benign and transient nature of the lesions in the population of patients with epilepsy.

T262
NEUROPSYCHOLOGICAL PERFORMANCE OF PATIENTS WITH POLG1 MUTATION AND EPILEPSY: EVIDENCE OF MORE PRONOUNCED RIGHT THAN LEFT HEMISPHERE DYSFUNCTION?

A. Gramstad,†, L. Bindoff*,‡, A. Lillebo*,‡, C. Tzoulis*,‡, and B. Engelsen*,‡*
**Haukeland University Hospital, Bergen, Norway; †University of Bergen, Bergen, Norway; and ‡Institute of Clinical Medicine, University of Bergen, Bergen, Norway*

Purpose: Mutations in polymerase ã (POLG) may give rise to different clinical symptoms including ataxia, epilepsy and cognitive dysfunction. We have recently described the general neurological and epileptological semiology of these patients. The latter could suggest more prominent dysfunction of the right than the left hemisphere in patients with POLG1 mutations with genotype 467/467, 467/748 and 748/748. We investigated if neuropsychological test results could support this hypothesis.

Method: Eight patients (6 women and 2 men, mean age at testing 22.3 years) with epilepsy and POLG1 mutations with genotype 467/467 and 748/748 were tested with an intelligence test (WAIS). Four of the patients were also given memory tests and a comprehensive neuropsychological test battery. Differences between verbal and nonverbal IQ and memory and neuropsychological left and right hemisphere dysfunction scales were tested for significance (paired samples t-test; SPSS).

Results: Full scale IQ was 77.4. Verbal IQ was 84,3, nonverbal IQ was 71.8. This difference was significant ($t = 5.23$, $p = .001$). In 4 patients, General Memory Index was 76.5 and General Neuropsychological Deficit Scale was 46.8. Verbal Memory Index was 84.0, Visual Memory Index was 68.8. Left Neuropsychological Deficit score was 9.0, Right Neuropsychological Deficit score was 6.3. These differences were not significant.

Conclusion: The patients had subnormal scores on cognitive tests. POLG1 mutation was associated with a higher verbal than nonverbal IQ and better verbal than nonverbal memory. This may indicate more pronounced right hemisphere dysfunction. However, a comprehensive battery gave no clear indication of lateralized dysfunction. Thus, further studies are needed to clarify this.

T263
AN OPTIMIZED VOXEL-BASED MORPHOMETRIC STUDY OF GRAY MATTER CHANGES IN PATIENTS WITH LEFT AND RIGHT MESIAL TEMPORAL LOBE EPILEPSY AND HIPPOCAMPAL SCLEROSIS (MTLE/HS)

M. Pail, M. Brázdil, R. Mareèek, and M. Mikl
St. Anne's University Hospital and Faculty of Medicine, Masaryk University, Czech Republic

Purpose: To determine whether the changes of the gray matter volume or concentration differ according to the affected side in MTLE/HS syndrome.

Method: Gray matter volume (GMV) and gray matter concentration (GMC) of the whole brain was assessed using voxel-based morphometry (VBM) with or without a modulation step. Twenty patients with left-sided MTLE/HS, 20 patients with right-sided MTLE/HS, and 40 sex- and age-matched healthy controls were included in the study. Statistical parametric maps were used to compare structural changes between patients and controls separately for the left and right-sided subgroups.

Results: Significant GMV reduction in the left MTLE/HS was observed in the ipsilateral hippocampus, parahippocampal gyrus, amygdala, and thalamus. Obviously more extensive GMV reduction was revealed in the patients with right-sided MTLE/HS. In the patients of this subgroup, the reduction of volume was detected in the ipsilateral hippocampus, parahippocampal gyrus, amygdala, and thalamus, but also in the ipsilateral insula and contralateral thalamus (mediodorsal nucleus and pulvinar). Significant GMC differences were detected in both subgroups of patients in the hippocampus and parahippocampal gyrus only, and in the right MTLE/HS also in the ipsilateral thalamus.

Conclusion: More extensive structural abnormalities were detected in the right MTLE/HS subgroup. It seems that the degree and location of a neural cell loss is dependent on the side of MTLE/HS, and that right MTLE/HS is not a 'mirror' of left MTLE/HS. We confirmed neither more widespread neuronal loss in patients with left MTLE nor identical pattern of GM decrease in the two subgroups of patients as described in previous studies. The study was supported by MŠMT ÈR Research Program no. MSM0021622404.

T264

THE CORRELATION OF BOLD CHANGE IN CONTINUOUS FMRI AND EEG RECORDING AT 3T MRI SCANNER IN PATIENTS WITH PARTIAL EPILEPSY

E. Lee, J. Kang*, M. Song†, H. Yoon‡, J. Chung‡, D. Im†, and H. Park†,§*

**University of Ulsan College of Medicine, Asan Medical Center; †fMRI Laboratory, Brain Science Research Center, Korea Advanced Institute of Science and Technology, Daejeon, South Korea; ‡Neuroscience Research Institute, Gacheon University Gil Medical Center, Korea; and §Korea Advanced Institute of Science And Technology, Daejeon, South Korea*

Purpose: Functional MRI with continuous EEG recording continuous EEG-fMRI) in epilepsy may be useful to localize the generators of interictal epileptiform discharges (IED) by correlating BOLD signal changes with the occurrence of epileptic spikes. This study was to analyze the spatial correlation between BOLD activations and interictal spikes in patients with partial epilepsy to find the usefulness of continuous EEG-fMRI.

Method: A total of twenty patients underwent EEG recording with a magnetically compatible recording system inside a 3 T MRI scan. Image data were analyzed using SPM2 with canonical hemodynamic response function to detect fMRI activations in each patient who had IED during continuous EEG-fMRI. We analyzed BOLD activations and correlated them with electro-clinical features.

Results: Among the twenty patients, eight were not analyzed because of the absence of spikes during recording (n=4) and poor-quality EEGs de to pulse artifacts (n=4). Ten of the remaining twelve patients with spikes showed BOLD activation areas. Among them, nine patients showed BOLD activation concordant with EEG and MRI abnormalities, whereas BOLD activation in one patient was not. Two patients who had BOLD activation were performed epileptic surgery, and BOLD activation areas were well correlated with epileptic foci.

Conclusion: In our study, BOLD activation areas in continuous fMRI-EEG were well correlated with EEG and MRI findings. Continuous fMRI-EEG study may be useful to localize the epileptic zone in presurgical evaluation of epileptic patients. This work was partly supported by the Korean Ministry of Science and Technology (grant no. M1-0107-07-0001).

T265

SIMULTANEOUS RECORDING OF INTERICTAL EEG AND FUNCTIONAL MAGNETIC RESONANCE IN THREE PATIENTS WITH PARTIAL REFRACTORY EPILEPSY. USEFULNESS OF THIS TECHNIQUE IN EPILEPSY SURGERY

I. Maestro, A. Donaire*, M. Carreño*, S. Fernandez*, N. Bargallo*, C. Falcon†, and J. Rumia**

**Hospital Clinic Barcelona, Spain; and †IDIBAPS-BBN, Barcelona, Spain*

Purpose: Simultaneous recording of electroencephalogram (EEG) and functional magnetic resonance (FMRI) in epileptic patients is a novel technique that can help to localize the irritative and epileptogenic zones during presurgical evaluation. We present three patients with focal refractory epilepsy who underwent interictal combined EEG-fMRI studies.

Method: Three patients with refractory focal epilepsy who underwent prolonged video-EEG monitoring in our epilepsy unit are reported. They all had MRI, SISCOM and PET. One of the patients was also studied with subdural electrodes. All patients underwent interictal simultaneous EEG-FMRI study. Sequential analysis of fMRI was performed applying the framework of general lineal model.

Results: The EEG recording of interictal epileptiform activity during fMRI showed, interictal spikes starting over the right frontocentral region in patient 1, interictal spikes over both fronto-central regions in patient 2, and generalized spikes and polyspikes and wave in patient 3. The simultaneous fMRI showed activation over the right frontocentral region in patient 1, over the left frontal cortex in patient 2 and over the right frontal region in patient 3, concordant with SISCOM, PET and invasive EEG recording.

Conclusion: Simultaneous recording of EEG and fMRI may be a useful tool during presurgical evaluation of refractory epileptic patients. Areas showing increase in BOLD signal during interictal discharges correlated with areas involved in seizure generation as shown by other tests of functional neuroimaging and invasive studies. Interictal EEG-fMRI may help to localize the irritative and epileptogenic zones.

T266

3T MR SPECTROSCOPY IN DRUG-RESISTANT TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL ABNORMALITIES

S. Battaglia, A. Marliani*, V. Clementi†, M. Maffei*, D. Zimatore‡, R. Agati*, G. Rubboli*, L. Volpi*, R. Michelucci*, P. Tinuper§, C. Tassinari§, M. Giulioni*, and G. Marucci¶*

**Bellaria Hospital, Bologna, Italy; †GE Healthcare Technologies, GE Healthcare, Bologna, Italy; ‡Radiology, Fellow, University of Bari, Italy; §Neurologic Clinical Institute of Bologna University, Italy; and ¶Section of Pathology University of Bologna, Bellaria Hospital, Italy*

Purpose: 3T MR systems allows more accurate anatomical investigations and more precise MRS studies. Proton magnetic resonance spectroscopy (1H-MRS) of hippocampal regions might provide lateralizing informations in the presurgical evaluation of patients with drug-resistant temporal lobe epilepsy (TLE).

Method: From December 2005 to March 2008 we performed 3T 1H-MRS (Signa Excite system, GE) on bilateral hippocampal regions in 17 patients (7 males – 10 females, aged from 27 to 50) suffering from intractable TLE associated with mesial temporal sclerosis (MTS). All patients underwent surgery; pathological examination of surgical specimens demonstrated MTS in all cases, with associated cortical dysplasia in some. 1H-MRS spectra were obtained by a PRESS sequence with TE 35 ms, TR 2000 ms. Data postprocessing was performed using LCModel. The tNAA/Cr, tNAA/Cho, tCho/Cr, mI/Cr, Glx/Cr ratio were calculated and compared with data collected from 12 healthy volunteers. Data from patients versus normal subjects, and data from the affected hippocampus versus the contralateral healthy, one were compared and statistically evaluated (Student's t-test).

Results: Our preliminary analysis shows: (1) a statistically significant ($p<0.01$) bilateral reduction of tNAA/Cr in hippocampal regions in patients as compared to normal subjects; (2) in all patients a statistically significant increase ($p<0.01$) of the mI/Cr ratio in the affected hippocampus as compared to the contralateral one.

Conclusion: Our study demonstrates concordance between increased hippocampal mI/Cr ratio and pathological hippocampus; an additional interesting finding was the bilateral reduction of hippocampal NAA/Cr ratio as compared to normals, suggesting metabolic abnormalities in both hippocampi.

T267

THE COMPARISON BETWEEN ICTAL SPECT AND INTERICTAL PET IN RELATION TO ICTAL SCALP EEG PATTERNS IN PATIENTS WITH UNILATERAL HIPPOCAMPAL SCLEROSIS

G. Lee, E. Lee*, K. Im*, J. Kim†, J. Kim*, J. Lee*, S. Lee*, and J. Kang**

**University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea; and †Korea University College of Medicine, Guro Hospital, Seoul, Korea*

Purpose: The interictal hypometabolism on PET may be correlated with ictal hyperperfusion on SPECT. The aim of this study was to compare hypometabolic area on PET with ictal hyperperfusion area on ictal SPECT according to initial ictal EEG patterns in the HS-MTLE to find the relationship between ictal and interictal changes.

Method: Twenty patients with surgically proven HS-MTLE were classified into 2 groups based on initial ictal discharge frequency on scalp EEG: those with a sustained regular 5- to 9-Hz with a restricted temporal or subtemporal distribution (group 1, N=8) vs those with an irregular 2- to 5-Hz with a widespread distribution (group 2, N=12). PET results of each group were compared with age- and sex matched controls to identify regions of significant hypometabolism by SPM2. Ictal SPECT images were spatially normalized to SPECT templates using SPM2. Significant decreases in glucose metabolism or significant increases in cerebral perfusion were estimated at a threshold of $p<0.001$, uncorrected for multiple comparisons.

Results: Interictal hypometabolism on PET and ictal hyperperusion on SPECT in group 2 were larger than those in group 1. The areas of ictal hyperperfusion on SPECTs were larger than those on PETs in both groups. The hyperperfusion areas on SPECT in both types included ipsilateral hippocampal area, basal ganglia, and thalamus, wider in group 2. No significant between-group difference was found in clinical characteristics.

Conclusion: This study showed that hypometabolic area on PET was well correlated with ictal hyperperfusion area according to initial ictal EEG patterns in the HS-MTLE.

T268

HEMODYNAMIC RESPONSE RELATED TO INITIATION VS. PROPAGATION OF INTERICTAL SPIKES CAN BE DISCRIMINATED USING EEG SOURCE IMAGING AND EEG-FMRI DATA

S. Vulliemoz, R. Thornton, R. Rodionov, M. Guye, and L. Spinelli

Institute of Neurology, University College of London, UK

Purpose: Increasingly used to localize epileptogenic activity, EEG-fMRI has high spatial resolution but low temporal resolution. Combination of EEG driven fMRI analysis with EEG source imaging (ESI) has been shown to help distinguishing between BOLD clusters associated with initiation vs propagation of interictal epileptic activity. ESI is generally applied on EEG recording acquired outside the scanner. ESI based on the EEG recorded simultaneously with fMRI data offers the advantage of analyzing the same events with ESI and fMRI, which is a prerequisite for advanced EEG analysis applied to EEG-fMRI.

Method: EEG driven fMRI data (3T MRI scanner, 32-channel EEG) analysis was performed on 5 patients with focal epilepsy as described previously (Lemieux, Magnetic Resonance Imaging, 2007). ESI was based on the distributed linear inverse solution algorithm LAURA using an individual realistic head model based on the SMAC approach (Michel, Clin. Neurophysiology, 2004).

Results: In all patients, ESI on EEG inside the scanner was of good quality. ESI at the first period of stable EEG topography was consistent with one BOLD cluster of activation, thus localizing the interictal spike initiation. ESI of later time frames showed propagation of the interictal spike corresponding to other BOLD clusters of activation.

Conclusion: Joint analysis ESI and EEG-fMRI results allow labeling of the BOLD activation related to spike initiation and propagation areas. The ESI-fMRI combination is ideal because the temporal resolution of the ESI allows identification of the primary focus while the fMRI allows precise anatomical localization of the epileptogenic zone.

T269

FEASIBILITY OF SIMULTANEOUS INTRACRANIAL EEG-FMRI: A PRELIMINARY INVESTIGATION OF RF INDUCED HEATING.

D. Carmichael,†, J. Thornton‡, R. Rodionov*,†, R. Thornton*,†, A. McEvoy§, P. Allen¶, and L. Lemieux*,†*

**UCL Intitute of Neurology, London, UK; †MRI Unit, National society for epilepsy, Chalfont St Peter, UK; ‡Lysholm, NHNN, London, UK; §Victor Horsley, NHNN, London, UK; and ¶NHNN, London, UK*

Purpose: Performing intracranial EEG and fMRI concurrently presents a unique opportunity to study both normal and epileptic neuronal dynamics at different spatial and temporal scales. However, MRI of patients with implanted electrodes poses health risks – primarily from RF induced heating.

Method: We performed experiments on a realistic test object and Ad-Tech electrodes simulating a clinical arrangement to determine tissue heating during MRI. Cables were attached and two extremes of electrical loading were tested; (1) external cable-terminations physically separated; (2) all cable-terminations electrically shorted in conductive gel. Head- and body-RF transmit coils were tested as was cable position within the bore with the same 6-minute fast spin-echo sequence. Temperature measurements were made from three electrode contacts and one ambient position continuously using an MR-compatible thermometer during imaging within a 3T Siemens Tim-Trio.

Results: For the head RF coil moderate heating was observed (+0.6°C) with the cables lying along the body and with the cable terminations shorted which was reduced (+0.3°C) when the cables were terminated in

an open circuit. With the body coil much larger temperatures were recorded (+6.9°C).

Conclusion: Regulatory guidelines state that brain temperature increases should not exceed 1°C. With the head RF coil temperature changes <1°C were observed. However, with the body coil temperature increases far exceeding the guidelines were obtained. This preliminary work suggests that icEEG-fMRI can be performed safely in terms of RF heating in certain specific circumstances, however, caution is required; conditions were found that caused dangerous levels of tissue heating. Electrical and stimulation safety require evaluation.

T270

RETROSPECTIVE CORRECTION FOR PHYSIOLOGICAL ARTIFACTS IMPROVES EPILEPSY CORRELATED FMRI

P. Van Houdt,†, P. Ossenblok*, J. de Munck†, F. Leijten‡, D. Venis§, and P. Boon**
**Epilepsy Centre Kempenhaeghe, Heeze, The Netherlands; †VU Medical Centre, Amsterdam, The Netherlands; ‡UMC Utrecht, Utrecht, The Netherlands; and §SEIN, Heemstede, The Netherlands*

Purpose: EEG correlated functional MRI (EEG-fMRI) has become applicable to the preoperative planning of epilepsy surgery, in which EEG is used to detect epileptiform activity and fMRI for spatial delineation. However, fMRI is highly sensitive to respiratory and cardiac artifacts, especially in case of abnormal function, thus complicating delineation of the epileptogenic area. The aim of this study was to model irregularities in these functions in order to improve epilepsy correlated fMRI.

Method: In a study of presurgical candidates with lesional epilepsy (n = 10) EEG together with respiratory and pulsation signals was measured during fMRI scanning. Artefact correction was applied to both EEG and fMRI. Respiration and pulse were analyzed on a beat-to-beat basis, yielding all the parameters of the signals. In addition to six heartbeat and respiratory confounders (Glover et al., Magn Reson Med, 2000, 44:162–167) irregular breathing and cardiac parameters were used as regressors in the general linear model (GLM).

Results: Results will be presented of the analyses of data of a patient with right temporal lobe epilepsy and an irregular breathing pattern during registration. Before correction fMRI showed a diffuse correlation pattern, especially at the edges of the image. Using the added regressors the effects of irregular functioning were strongly diminished resulting in a dominating BOLD response in the right temporal lobe. These findings were in concordance with MEG dipole localizations and the intraoperative electrocorticogram.

Conclusion: This study shows that correction for physiological artifacts, such as abnormal breathing, allows a more reliable identification of the epileptogenic area using EEG-fMRI.

T271

ATYPICAL LANGUAGE LATERALIZATION ASSOCIATED WITH RIGHT FRONTAL GREY MATTER INCREASES – A COMBINED FMRI AND VBM STUDY IN LEFT SIDED MTLE PATIENTS

M. Mertens, V. Magalova-Mertens*, A. Ebner*, J. Janszky†, and F. Woermann**
**Bethel Epilepsy Center, Mara Hospital, Bielefeld, Germany; and †University of Pecs, Pecs, Hungary*

Purpose: By combining language functional MRI (fMRI) and voxel-based morphometry (VBM), we addressed the question whether in patients with left-sided mesial temporal lobe epilepsy (mTLE) atypical language dominance is associated with extratemporal changes of grey matter volume (GMV).

Method: Only patients with unilateral hippocampal sclerosis and with unilateral EEG changes were included. Using language fMRI (Woermann et al, 2003), we identified 23 patients with an atypical language lateralization (i.e. an lateralization index of their individual fMRI activation $-0.2 < LI < 1$). These patients were compared with a group of 23 matched patient controls. Using T1-weighted 3D MR-images of all patients and optimized VBM, we compared GMV of patients with atypical language lateralization to GMV of patients with typical language lateralization.

Results: Using SPM5, small volume correction in a volume covering both frontal lobes, and a method to correct results for multiple comparisons, there were no areas of grey matter increase in patients with typical language. In patients with atypical language, there were increases of GMV in both frontal lobes. These were statistically significant in a cluster (max T = 4.66; 27347 voxels) covering the right sided subcallosal gyrus, mesial superior frontal gyrus, cingulated gyrus, and medial frontal gyrus.

Conclusion: Left-sided mTLE patients with atypical language lateralization showed an increase of GMV in both frontal lobes, implicating mainly right-sided (para-) limbic areas.

T272

TEST–RETEST RELIABILITY OF BOLD RESPONSES IN A COVERT VERBAL FLUENCY FUNCTIONAL MRI TASK

J. O'Muircheartaigh, C. Vollmar†, P. Thompson†, V. Kumari*, G. Barker‡, J. Duncan†, M. Koepp†, and M. Richardson**
**Institute of Psychiatry, King's College London, London, UK; †Institute of Neurology, University College London, Queen Square, London, UK; and ‡Centre For Neuroimaging Sciences, Department of Clinical Neuroscience, Institute of Psychiatry, King's College London, UK*

Purpose: Functional MRI language tasks are increasingly being looked at as an alternative to the invasive intracarotid amobarbital testing for assessment of language lateralization in patients with epilepsy. Quantitative assessment of the test–retest reliability of these tasks is crucial for them to be of any benefit as a clinical tool.

Method: Here, a simple covert verbal fluency task was performed by ten subjects on four occasions across two sites to assess BOLD test/retest reliability using a simple language task. Reliability was assessed using voxel-wise intraclass correlation coefficient analysis.

Results: Although intersubject reliability was moderate, intrasubject reliability was high. Patterns of language lateralization were found to be consistent within-subjects and across sites.

Conclusion: The low intrasubject variability of BOLD response reinforces the role of this cognitively simple task as a reliable measure of language-related eloquent cortex.

T273

MRI CHANGES IN STATUS EPILEPTICUS: A SYSTEMATIC REVIEW IN A TERTIARY CENTRE

T. Lema-Facal, M. Carreño, A. Donaire, S. Fernández, I. Maestro, and N. Bargalló
Hospital Clinic, Barcelona, Spain

Purpose: Our objective was to find out the percentage of patients who display MRI changes associated to status epilepticus (SE), and to correlate them with clinical and EEG data.

Method: We systematically reviewed 112 patients who were discharged with the diagnostic of SE during the years 2000–2007. Twenty four patients (mean age 51, range 20–88, 12 women, 12 men) who had MRI performed during the admission were included. Seven patients had generalized SE; eleven patients had complex partial SE; six patients had simple focal motor SE, evolving to generalized convulsive in 3. Mean time from onset of SE until image acquisition was 5 days (1–17). MRI included T1, T2, FLAIR, DWI and ADC sequences. EEG was performed in all patients. We evaluated the presence and location of signal changes and their correlation with clinical and EEG data.

Results: MRI changes suggestive of focal edema were found in 13 patients, six of them with previous history of epilepsy and 7 with status due to other etiologies. Most patients (9) in this group had complex partial SE. All patients, but three, had MRI changes involving cortical gray matter; additional changes were found in hippocampus, amygdalas and bilateral thalami. Correlation between the location of the MRI changes and the location of the discharges in the EEG (suspected epileptogenic zone) was found in 8 patients.

Conclusion: A significant percentage (54,16%) of all episodes of status epilepticus show signal changes in MRI. These changes may correlate with the anatomic location of the epileptogenic zone.

T274
AN FMRI ASSESSMENT OF LANGUAGE REORGANIZATION IN TEMPORAL LOBE EPILEPSY (TLE) WITH HIPPOCAMPAL SCLEROSIS (HS)

F. Villani, F. Ghielmetti*, S. Dylgjeri*, S. Angelo†, C. Marras*, M. Bruzzone*, C. Rosazza*, L. D'Incerti*, and R. Spreafico**

**Neurological Institute Carlo Besta, Milano, Italy; and †Politecnico University, Milan, Italy*

Purpose: The risk of language deficits after surgery for drug-refractory TLE may be influenced by a rearrangement of the language areas. fMRI is a noninvasive procedure for functional brain topography with high spatial resolution increasingly used in the epilepsy presurgical workup.

Method: i) To assess by fMRI the reorganization of the language network in a homogeneous cohort of TLE-HS patients; ii) to correlate this findings to the electroclinical data.

Method: Eighteen right-handed patients (6 males and 12 females) with refractory TLE-HS were submitted to presurgical assessment (complete history, long-term Video-EEG, MRI, FDG-PET, neuropsychological tests) at the Istituto Neurologico 'C. Besta'. Right TLE-HS (rTLE-HS) (n=9) and left TLE-HS (lTLE-HS) (n=9) were equally distributed. fMRI studies were performed on a 1.5 T scanner. Verbal fluency and reading comprehension tasks were always administered. Data were analyzed by SPM99: ROIs were located in the frontal and temporal areas and were rated separately after brain normalization. Laterality indices (LI) were calculated with the standard formula (L-R)/(L+R), the results ranging in the interval between 1 and -1 (1=left lateralization; -1=right; 0=bilateral).

Results: Analysis of the frontal lobe activations showed mean LI values of 0,75 for the rTLE-HS group and 0,4 for lTLE-HS. Mean LI values obtained from the temporal lobe activations were respectively 0,6 (rTLE-HS) and 0,55 (lTLE-HS). lTLE-HS patients showed a trend for bilateral activation both in the frontal and temporal lobes whereas in the rTLE-HS patients left lateralization was more preserved, particularly in the frontal lobe.

Conclusion: Language fMRI, investigating language reorganization due to plasticity in TLE, may be a useful tool for minimizing the risks of language deficit after epilepsy surgery.

T275
MAGNETIC RESONANCE SPECTROSCOPY IN NONCONVULSIVE STATUS EPILEPTICUS PATIENTS

Z. Aydin Özemýr, E. Terzibaþýolu, S. Sencer, and B. Baykan

Istanbul University, Turkey

Purpose: We aimed to study the metabolic differences in nonconvulsive status epileptic (NCSE) patients diagnosed with IGE by using MR Spectroscopy and correlating the results with age and sex matched normal subjects.

Method: Four patients with IGE who have recurrent NCSE attacks were investigated. MRS measurements of N-acetylaspartate (NAA), choline-containing compounds (Cho), creatine (Cr) were performed in the frontal, occipital cortex and thalamus bilaterally using a stimulated echo acquisition mode (STEAM) technique with a voxel size of 20x20x20 mm, the values of the patients with NCSE were compared with those of the normal controls by appropriate statistical tests.

Results: Right frontal and right thalamus NAA values were decreased and left occipital NAA concentration was increased without reaching statistical significance. MRS was carried out in one of these patients during ictal and interictal periods. Cholin level was decreased in all voxel areas particularly in the frontal lobes except left occipital lobe while she had NCSE in comparison to the interictal state.

Conclusion: This is a preliminary study in NCSE to investigate the pathophysiology by using MRS and we showed some neurochemical changes, in a small number of patients.

T276
fMRI IDENTIFIES DYSFUNCTIONAL CORTEX IN PATIENTS WITH NONLESIONAL FRONTAL LOBE EPILEPSY

C. Vollmar, J. O'Muircheartaigh†, M. Richardson†, M. Koepp*, M. Symms*, G. Barker†, V. Kumari†, P. Thompson*, and J. Duncan**

**University College London, London, UK; and †Kings College London, London, UK*

Purpose: Frontal lobe epilepsy patients are a heterogeneous group, presenting with a range of possible clinical manifestations. The absence of a structurally visible MRI lesion can challenge the presurgical evaluation, especially if other diagnostic methods also fail to clearly localize a seizure focus.

Method: In an ongoing study we investigated five patients with nonlesional frontal lobe epilepsy and 15 healthy controls. Subjects had to perform a set of frontal lobe fMRI tasks, including verbal fluency, verb generation, spatial and verbal working memory, saccadic eye movements and emotional processing. fMRI images were acquired on a 3T Scanner, using a whole brain acquisition of 50 slices, 2.5 mm slice thickness and a TR of 2.5 sec. fMRI analysis was carried out using SPM 5 and FSL 4 software.

Results: Two patients showed normal cortical activation in all tasks. Two patients showed a reduced left frontal activation in both language tasks and emotional processing, but normal activation in other tasks. In one patient the left frontal failed to activate in any of the cognitive tasks, whilst other areas activated normally. In this case seizure semiology was not lateralizing and EEG showed bilateral findings, more pronounced on the left side. fMRI was the first diagnostic method clearly lateralizing, and indicating dysfunction of the structurally normal left frontal lobe.

Conclusion: In patients with nonlesional focal epilepsy, fMRI with a comprehensive set of cognitive tasks can help to localize cortical dysfunction. This can therefore guide further presurgical evaluation, including the Implantation of invasive electrodes.

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T277
HOW FREQUENT ARE SEIZURES AND ICTAL PATTERNS IN RECORDINGS FROM ROUTINE ELECTROENCEPHALOGRAPHIC LABORATORY?

Z. Vojtech, T. Prochazka, I. Mareckova, and M. Kalina
Na Homolce Hospital, Prague, Czech Republic

Purpose: To establish the frequency of occurrence of seizures and ictal EEG patterns in routine EEG recordings.

Method: We reviewed reports of EEG recordings performed during a 10 years' period in a routine EEG laboratory. We retrieved those containing clinical seizures and/or ictal EEG patterns.

Results: During a period between January 1998 and December 2007, we evaluated 19,261 patients. We identified 47 recordings performed in 39 patients fulfilling inclusion criteria. These recordings contained 63 episodes (46 behavioral seizures and additional 17 ictal EEG patterns). 59 episodes were epileptic, 4 nonepileptic (3 PNES and 1 convulsive syncope). The diagnosis of epilepsy (22 remote symptomatic, 8 acute symptomatic, 1 genetic, 2 unknown) had been established in 36 patients and it preceded the evaluated recording by 12 years on average. All 3 psychogenic patients had been erroneously diagnosed as epileptic. 25 patients were video-EEG monitored, 13 before and 12 after ictal routine recordings.

Conclusion: Ictal recordings were rare in our material (0.24%) and occurred mostly in intractable epilepsy population and in patients suffering from acute symptomatic seizures. In intractable patients, these recordings added little new information and video-EEG was necessary before operation in most of them. Routine EEG was useful in conscious patients with acute symptomatic seizures. Ictal recordings might alert physicians to the possibility of nonepileptic events.

T278
QUALITY-OF-LIFE IMPROVEMENT DURING LONG-TERM TREATMENT WITH ESLICARBAZEPINE ACETATE

J. Cramer, J. Maia†, L. Almeida†, and P. Soares-da-Silva†*
**Yale University School of Medicine, USA; and †BIAL – Portela & Co, SA, S Mamede Do Coronado, Portugal*

Purpose: To assess the quality-of-life outcome during long-term adjunctive therapy with eslicarbazepine acetate (ESL) in patients with partial epilepsy.

Method: During an open-label extension of a phase III study (BIA-2093-301) with ESL, the Quality-of-Life in Epilepsy Inventory 31 (QOLIE 31) was applied at the end of the treatment period (1 year or early discontinuation) and the results were compared with those at baseline. Most patients were treated with ESL 800 mg once-daily (range: 400–1600 mg).

Results: In the intent-to-treat (ITT) population (n=255), significant improvements from baseline were found in overall quality-of-life ($p<0.0001$), seizure worry ($p<0.0001$), energy-fatigue ($p<0.05$), cognitive functioning ($p<0.05$), medication effects ($p<0.0001$), social function ($p<0.01$), and the overall score ($p<0.0001$. In the per-protocol (PP) population (n=224), significant improvements were found in all scores: overall quality-of-life ($p<0.0001$), seizure worry ($p<0.0001$), emotional well-being ($p<0.01$), energy-fatigue ($p<0.001$), cognitive functioning ($p<0.01$), medication effects ($p<0.0001$), in social function ($p<0.001$), and overall score ($p<0.0001$). In the ITT population, the mean relative improvement was 16% in overall quality-of-life, 51% in seizure worry, 7% in emotional well-being, 16% in energy-fatigue, 15% in cognitive functioning, 33% in medication effects, 36% in social function, and 12% in overall score. In the PP population, improvement was 19% in overall quality-of-life, 59% in seizure worry, 10% in emotional well-being, 20% in energy-fatigue, 18% in cognitive functioning, 34% in medication effects, 41% in social function, and 14% in overall score.

Conclusion: Quality-of-life, as assessed by QOLIE 31, showed statistically and clinically significant improvement from baseline during long-term open-label adjunctive therapy with ESL in partial epilepsy.

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T279
THE IMPACT OF PROLONGED AMBULATORY EEG ON DIAGNOSIS OF EVENTS IN AN EPILEPSY CLINIC

A. Mohamed, J. Boserio, M. Pereira, and A. O'Connell
Royal Prince Alfred Hospital, Sydney, Australia

Purpose: To assess the diagnostic usefulness of prolonged ambulatory EEG recording in an outpatient epilepsy clinic.

Method: We retrospectively reviewed all consecutive ambulatory EEGs (AEEG) performed for the diagnosis of reported events on outpatients referred from a single epilepsy clinic. Patient medical records and AEEGs were reviewed to determine the provisional diagnosis, previous EEG results and change in diagnosis as a result of the AEEG. From a total of 150 patients tested, 98 (53 female) were done for diagnosis of events. Patients were recorded for an average of 3.3 days (range of 1–4). The median number of days taken to record an epileptic event was 2 and a non-epileptic event 1 day.

Results: An event was recorded in 50/98 (50%) of patients. Epileptic seizures were recorded in 11/98. Events other than epilepsy were recorded in 39/98 and included pseudoseizures (n=13), syncope (n=9), orthostatic intolerance (n=3), parasomnias (n=3), bradyarrhtyhmia / sinus pause (n=2) and periodic limb movements (n=1). Two patients had both epileptic and pseudo-seizures recorded. In 17/98 patients who had previous nondiagnostic EEGs, AEEG recordings confirmed a diagnosis of epilepsy. Following the AEEG the diagnosis remained unchanged in 59/98, was revised from epilepsy to a diagnosis other than epilepsy in 20/98, from a diagnosis other than epilepsy to epilepsy in 6/98. The diagnosis remained unknown in 13/98.

Conclusion: Prolonged AEEG recording has a substantial impact on the diagnosis even when patients have been referred from a specialist clinic.

T280
CHANGES OF NEOCORTICAL AND HIPPOCAMPAL EPILEPTIFORM DISCHARGES DURING SLEEP-WAKING CYCLE

E. Saralidze, L. Khuchua†, and T. Ioseliani†*
**Shota Rustaveli State University, Batumi, Adjara, Georgia; and †Ivane Javakhishvili State University, Tbilisi, Georgia*

Purpose: The purpose of our work was investigation of the changes of hippocampal and neocortical epileptiform discharges at different stages of sleep-waking cycle (SWC).

Method: In vivo experiments were carried out on chronic Wistar rats. Under ketalar anesthesia stimulating (bipolar) and recording (unipolar) electrodes, made of insulated stainless metal wire of 150 ƒÝm in diameter, were implanted in the neocortex and dorsal hippocampus (DH) according to stereotaxic coordinates by Paxinos and Watson atlas. Bipolar electrodes were also implanted in cervical muscles and orbital cavity for the recording of muscular tone and eye movements. The epileptiform discharges (EDs) which were induced by high-frequency electrical stimulation (30Hz) of dorsal hippocampus were recorded with 8 channels electroencephalograph (Medicor 8 S; Hungary). After each set of experiments the animals were sacrificed, brains were removed and immersed in

10% solution of formalin. Locations of electrode tips were identified in frontal sections of the brain.

Results: It was found that EDs of hippocampal origin were more durable at the stage of slow sleep than in wakefulness. Consequently during slow sleep the hippocampal epileptogenic threshold was lowered. And consistently epileptiform discharges increases. According to the data obtained one of important factors increasing susceptibility of hippocampus to EDs, at the stage of slow sleep, should be the weaking of tonic inhibitory influence of the cortex upon hippocampus, result of which is decrease of epileptogenic threshold in the latter. Epileptogenic thresholds of neocortex were lower during wakefulness than in stages of slow sleep and epileptiform discharges increases during wakefulness, than in stages of slow sleep.

Conclusion: Neocortical epileptiform discharges increase in stage of wakefullness and decreases in stage of slow sleep. Hippocampal epileptiform discharges decreases in stage of wakefullness and increases in stage of slow sleep.

T281
POLYSOMNOGRAPHIC STUDY IN RING CHROMOSOME 20 SYNDROME

A. Vignoli, E. Zambrelli*, G. Didato*,†, M. Mastrangelo‡, L. Nobili†, V. Chiesa*, F. La Briola*, R. Canger*, M. Canevini*, and I. Fiocchi‡*
**Epilepsy Center, San Paolo Hospital, Milan, Italy; †C. Munari Epilepsy Surgery Center, Niguarda Hospital, Milan, Italy; and ‡Pediatric Neurology, V. Buzzi Hospital, ICP, Milan, Italy*

Purpose: Ring chromosome 20 [r(20)] syndrome is a well-defined chromosomal disorder characterized by epilepsy, mild to moderate mental retardation and lack of recognizable dysmorphic features. Since epilepsy is often the most important clinical manifestation of the syndrome, distinct and various electroclinical features have been described, probably depending on the age of the patients at the time of evaluation. So far, the wakefulness EEG patterns peculiar of this syndrome have been described, but the polysomnographic features of sleep have not yet been evaluated in these patients.

Method: We studied the peculiar pattern of sleep in 6 patients (2 males, 4 females) aged 2 – 49 years with r (20) syndrome who underwent one polysomnographic recording.

Results: We describe the evolution of sleep pattern as progressive deterioration ranging from a normal sleep (in early childhood, before seizure onset) to a destructuration of activity both in NREM and in REM sleep phases. Recognizable phasic elements were recorded at pediatric age, while variable degree of NREM sleep alteration (sleep spindles difficult to detect, reduced/absent slow wave sleep) with persistence during REM sleep of the same theta rhythm of wakefulness was observed in adulthood. EEG abnormalities detected during wakefulness persisted during sleep with some morphological changes with deepening of sleep.

Conclusion: Similarly to other genetically determined syndromes also patients with r (20) syndrome show important changes of sleep architecture that seem to be age-related. A potential role of cortical and thalamocortical dysfunction in determining sleep structure abnormalities is discussed.

T282
'THERE'S NO PLACE LIKE HOME' – A PROSPECTIVE CONTROL STUDY OF HOME VIDEO TELEMETRY VERSUS INPATIENT VIDEO TELEMETRY AT KINGS COLLEGE HOSPITAL

L. Drummond, and F. Brunnhuber
Kings College Hospital NHS Trust, UK

Introduction: Inpatient video telemetry is the gold standard and the requirements for seizure classification and presurgical evaluation. At least 50% of the patients referred for video telemetry are for seizure classification. However, there are limitations to the procedure. We pose the question, 'could video telemetry be provided outside the hospital'?.

Purpose: To assess the clinical and technical accuracy of seizure/event classification and feasibility of home video telemetry compared with inpatient video telemetry (gold standard) in a series of pediatric patients.

Method: Primary: A prospective control study in which each patient receives home video telemetry, the results of which are compared to their in-patient telemetry visit (each patient is his own control).

Results: Set-up of the system in the home, quality and complications of the recording in the home environment, the number of days to record, percentage of habitual seizures/events captured, technical problems, actual technician involvement, monitoring of quality assurance, financial constraints to the Trust, patient/carer satisfaction. Secondary: The video data only acquired at home is independently reported and compared to the classification and/or diagnostic outcome of the 'gold standard' video recorded as an inpatient.

Conclusion: The preliminary data of the first 10 patients will be discussed. Our preliminary findings indicate that home video telemetry was an inexpensive alternative to inpatient video telemetry and could become a clinical service.

Monday 22 – Wednesday 24 September 2008
Traditional Poster Session
Neuropsychology

T283
PROSPECTIVE MEMORY IN JUVENILE MYOCLONIC EPILEPSY PATIENTS AND THEIR HEALTHY UNAFFECTED SIBLINGS

B. Wandschneider, U. Kopp*, M. Kliegel†, and B. Schmitz**
**Charité Universitätsmedizin Berlin, Berlin, Germany; and †University of Zuerich, Zuerich, Switzerland*

Purpose: Patients with juvenile myoclonic epilepsy (JME) have deficits in prospective memory (PM), a process dependent on executive functions (EF). JME has a strong genetic predisposition; accordingly, cognitive deficits could be genetically determined rather than due to seizures or medication side effects. The present study aimed at investigating differences in PM between JME patients, their siblings and healthy controls (HCs).

Method: 28 JME patients, 14 siblings and 29 HCs were examined with a complex PM paradigm (Kliegel M et al. Memory and Cognition 2000;28(6):1041–1049.) including different phases of PM (i.e. intention formation, intention retention, intention initiation and intention execution).

Results: ANOVAs showed a significant group effect for intention formation (F=15.33; p<. 001) and intention execution (F=17.79; p<. 001). Post hoc analysis revealed a better performance for HCs in intention formation than both JME patients and their siblings but without significant difference between patients and siblings. For intention execution JME patients performed worse than siblings and HCs but there was no difference between siblings and HCs.

Conclusion: This is the first study demonstrating deficits in PM in healthy siblings of JME patients. Siblings were specifically impaired in intention formation. JME patients also showed deficits during intention execution. Different phases of PM are modulated by specific EF; therefore these results may indicate similar deficits in planning abilities during

intention formation for both siblings and JME patients. Accordingly, our results support the hypothesis of genetic factors underlying cognitive deficits in JME.

T284

CHANGES OF PRE- AND POSTOPERATIVE MEMORY PERFORMANCES AFTER APICAL TEMPORAL-LOBE RESECTION THAT SPARES THE HIPPOCAMPUS COMPARED TO MESIAL TEMPORAL-LOBE RESECTION INCLUDING THE HIPPOCAMPUS

S. Horstmann, H. Pannek*, F. Woermann*, R. Schulz*, H. Elsharkawy*, J. Aengenendt*, H. Steffen*, C. Gyimesi†, J. Janszky†, and A. Ebner**

**Epilepsy Center Bethel, Bielefeld, Germany; and †University of Pécs, Rét 2, 7623, Pécs, Hungary*

Purpose: Temporal lobe epilepsy patients often suffer from memory deficits that may potentiate after a temporal lobe resection (TLR). Based on the well documented involvement of the hippocampus in memory processing, we examine how TLR with (mesial) and without (apical) resection of the hippocampus affects the memory performance.

Method: The apical TLR is a comparatively new method of resection that here, for the first time, is examined on a major sample (N=113). Patients were examined with standardized verbal and visual learning and memory tests before and after the surgical intervention. We expected that patients after apical TLR perform better at memory tests compared with patients after mesial TLR.

Results: Results show a decrease in verbal learnig ability after apical TLR of the dominant hemisphere but an increase after apical TLR of the nondominant hemisphere. With regard to visual learning and memory performances, no differences between patients after left- or right-hemispheric apical TLR were evident. A comparison of the two resection methods shows that patients achieve overall better cognitive performances before and after apical TLR compared with patients before and after mesial TLR. In particular, verbal memory performances drop after mesial TLR while patients after apical TLR can keep their level. However patients after TLR of the dominant hemisphere show a drop of performance in verbal learning after apical and mesial TLR.

Conclusion: We conclude that the apical TLR as a surgical intervention that on the whole leads to less distinctive postoperative verbal learning and memory deficits.

T285

APPLICATION OF PROPOFOL IN WADA TEST. FURTHER EXPERIENCES

P. Soluch, O. Szymanska, A. Rysz, B. Majkowska-Zwolinska, P. Kulisiewicz, and M. Jaworski

Medical University of Warsaw, Poland

Purpose: Inaccessibility of amobarbital and methohexital sodium salt constrain us to look for new anesthetic available for Wada Test procedure. Positive experiences of Kyoto University Graduate School of Medicine group (Takayama M et al. Neurology 2004;63:510–515) encourage us to use Propofol.

Method: I. In 6 of first 9 trials prepared according to KUGSM intense psychomotor agitation and disorientation was observed, which precluded any objective assessment of evoked neurological deficits. We introduced modified version of the procedure altering the speed of application of the solution, which effectively reduced adverse events. II. We assessed the application of intracarotid modified Propofol procedure in Wada double tests in 35 patients with MTLE prepared for the surgical treatment. 1 ml propofol diluted in 9 ml of saline salt administrated through catheter by Seldinger method, with prolonged the speed of application of the first 2 ml of solution to 20 sec. Remaining 8 ml were applied in bolus. Contralateral flaccid paresis of extremities was efficacy parameter. In few cases additional dose of 3 ml of agent was administrated. Cognitive tests performed in course of loss of contralateral muscle power. Interval between both trials was amount 30 minutes.

Results: Speech arrest was observed in all examinated patients; in most of trials – facial asymmetry and visual field deficits; in few cases – slight motor disquiet, lacrimation or/and trembling. No patients have vascular pain or delayed secondary memory disturbances.

Conclusion: Results confirmed our previously experiences about usefulness of Propofol in Wada test.

T286

DEPRESSIVE SYMPTOMS IMPROVEMENT DURING LONG-TERM TREATMENT WITH ESLICARBAZEPINE ACETATE

D. Hodoba, A. Czlonkowska†, J. Cramer‡, J. Maia§, L. Almeida§, and P. Soares-da-Silva§*

**Clinical Psychiatric Hospital Vrapce, Zagreb, Croatia; †Institute of Psychiatry And Neurology, Warsaw, Poland; ‡Yale University School of Medicine, CT, USA; and §BIAL – Portela & Co, SA, S Mamede Do Coronado, Portugal*

Purpose: To assess the depressive symptoms change during long-term add-on treatment with eslicarbazepine acetate (ESL) in patients with partial epilepsy.

Method: During an open-label extension of a phase III study (BIA-2093-301) with ESL, in which most patients were treated with 800 mg once-daily (range: 400–1600 mg), the Montgomery Asberg Depression Rating Scale (MADRS) was applied at the end of the treatment period (i.e., 1 year or early discontinuation). The results were compared with those at baseline.

Results: In the intent-to-treat (ITT) population (n=264), significant improvements were found in the total score ($p<0.0001$), apparent sadness ($p=0.0001$), reported sadness ($p<0.01$), inner tension ($p<0.001$), concentration difficulties ($p<0.0001$), lassitude ($p<0.001$), inability to feel ($p<0.01$), and pessimistic thoughts ($p<0.05$). In the per-protocol (PP) population (n=232), significant improvements were found in the total score ($p<0.0001$), apparent sadness ($p<0.0001$), reported sadness ($p<0.01$), inner tension ($p<0.0001$), concentration difficulties ($p<0.0001$), lassitude ($p<0.001$), inability to feel ($p<0.01$), and pessimistic thoughts ($p<0.01$). In the ITT population and PP populations, the mean relative improvements were 34% and 38% in apparent sadness, respectively, 40% and 41% in reported sadness, 31% and 34% in inner tension, 48% and 53% in reduced sleep, 57% and 62% in reduced appetite, 30% and 33% in concentration difficulties, 38% and 39% in lassitude, 38% and 35% in inability to feel, 26% and 31% in pessimistic thoughts, and 56% and 60% in suicidal thoughts.

Conclusion: Depressive mood, as assessed by MADRS, showed statistically significant improvement from baseline during long-term open-label adjunctive therapy with ESL in patients with partial epilepsy.

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T287

COGNITIVE DYSFUNCTION BEYOND MEMORY IMPAIRMENT IN TEMPORAL LOBE EPILEPSY PATIENTS

J. Amlerova, P. Marusic*, H. Krijtova*, M. Tomasek*, and A. Javurkova*,†*

**Charles University, 2nd Medical Faculty, Motol Hospital, Prague, Czech Republic; and †Kralovske Vinohrady Hospital, Prague, Czech Republic*

Purpose: Memory functions connected to temporal lobes are routinely assessed pre- and postsurgically in temporal lobe epilepsy (TLE) patients. The aim was to expand battery of neuropsychological tests and evaluate for other functions that may be associated with temporal lobes; and to compare results of patients and controls.

Method: We included 22 left-speech dominant TLE patients, 11 left-sided (mean age 36,4 years, FSIQ 89) and 11 right-sided (mean age 40,6 years, FSIQ 104). Control group consisted of 10 subjects (mean age 36,5 years, FSIQ 109). Patients and controls were examined with standard neuropsychological battery expanded with Boston Naming Test (BNT), Face Recognition Test, Emotion Recognition Test and Faux-Pas Test. Scores were not correlated to intelligence level.

Results: There was no difference between patients and controls in face recognition, however, right-sided patients had more false-positive answers. Patients scored worse in emotion recognition than controls, the impairment was more pronounced in left-sided. Left-sided patients had lower scores in BNT, right-sided patients scored similarly to controls. Patients differed from controls in Faux-Pas Test, left-sided had worse outcome than right-sided.

Conclusion: Except from face recognition, patients scored worse than controls in all tests, right-sided were similar to controls in BNT. Tendency for more pronounced impairment in emotion recognition and Faux-Pas Test in left-sided patients compared to right-sided was observed. Intelligence level of left-sided TLE patients was lower than in right-sided and may possibly influence the difference in results, this need to be investigated in further studies.

T288
NONEPILEPTIC PSYCHOGENIC SEIZURES AND EPILEPTIC SEIZURES: A NEUROPSYCHOLOGICAL STUDY

R. Curral,‡, C. Silveira*,‡, D. Maia*,†, I. Dominguez*, A. Norton*, I. Pires*, G. Sousa*, F. Barbosa†, A. Pacheco Palha*,‡, and A. Roma Torres**

**Hospital São João Porto, Porto, Portugal; †Faculdade de Psicologia e Ciências da Educação da Universidade Do Porto, Porto, Portugal; and ‡Faculdade de Medicina da Universidade Do Porto, Porto, Portugal*

The authors present the preliminary results of a correlational study among the scales of Luria Nebraska Neuropsychological Battery (LNNB), the Mini Mental State Examination (MMSE) and clinical variables (disease onset and duration, type of crisis).

The aim of this study is assessing the existence of a relationship between neuropsychological variables and clinical variables. 12 female patients with both nonepileptic and epileptic seizures with a mean age of 39,6 years (±12,3), followed at Psychiatric and Neurophysiology Services, were recruited. It were used the following instruments: socio demographic and a clinical interview, the LNNB and the MMSE.

The results indicate that the emergence of nonepileptic seizures occurs on average 9 years after the onset of the epileptic disease; the duration of epilepsy is the clinical variable most correlated with the clinical scales of LNNB. The highest value (worst performance) was found on the scale that assesses the Intellectual Functions (30,73). From 11 clinical scales, 6 (motor, tactile, expressive speech, write, arithmetic and memory) are negatively correlated with the MMSE. These results are very similar with the results reported by Horton & Alana.

T289
DECISION MAKING IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

K. Labudda, K. Frigge*, S. Horstmann†, J. Aengenendt†, F. Woermann†, A. Ebner†, H. Markowitsch*, and M. Brand**

**University of Bielefeld, Bielefeld, Germany; and †Mara Hospital, Epilepsy Center Bethel, Bielefeld, Germany*

Purpose: Decision making – a very important function of every-day life – depends on affective processes and executive functions. Although it is well known that patients with temporal lobe epilepsy (TLE) can have impairments in both executive functioning and emotion processing, the ability to make decisions under ambiguity and risk has not been investigated in these patients, to date. We aimed to study whether TLE patients exhibit deficits in decision making situations primarily associated with emotional processes (decision making under ambiguity) and those situations additionally linked to executive functions (decision making under risk).

Method: We examined 20 TLE patients and 20 healthy individuals (CG) with a task assessing decision making under ambiguity (Iowa Gambling Task, IGT), a task measuring decision-making under risk (Game of Dice Task, GDT) and a neuropsychological test battery.

Results: GDT performance did not differ significantly between the patients and the CG ($p=.26$). On the IGT patients with TLE selected the disadvantageous alternatives more frequently compared to the CG ($p=.03$). Side of epileptogenic focus did neither impact GDT nor IGT performance ($p's>.62$). GDT and IGT performance was associated with executive subcomponents, e.g. interference susceptibility ($p's<.05$).

Conclusion: In summary, TLE-patients are selectively impaired in decision-making under ambiguity that commonly depends on processing previous feedback to learn the option's contingencies. Probably, this deficit is linked to alterations within the epileptogenic mesiotemporal region. By contrast, decision making under risk conditions that is based on explicit knowledge about consequences and their probabilities seems to be intact, most likely due to unimpaired executive functions of the TLE patients studied.

T290
ATTENTION IMPAIRMENT IN TEMPORAL LOBE EPILEPSY: NEUROPHYSIOLOGICAL APPROACH BY THE STUDY OF THE P300 WAVE

P. Bocquillon, V. Phalempin, N. Betrouni, K. Dujardin, E. Houdayer, J. Bourriez, P. Derambure, and W. Szurhaj

Lille University Medical Center, Lille, France

Purpose: Attention is often impaired in temporal lobe epilepsy (TLE). The P300 wave, an endogenous event-related potential, is a correlate of attention. It is usually recorded during an oddball paradigm, the subject being instructed to detect a rare target stimulus among frequent, standard ones. In order to better understand the alterations of attentional networks in TLE, we compared P300 characteristics in 10 TLE patients and 10 healthy controls.

Method: Every subject underwent a high density EEG recording (128 channels) during an auditory and a visual oddball-paradigm. The P3b latency and amplitude were compared between both groups. The P3b sources were localized on individual 3D MRI with the LORETA method and a statistical group comparison was performed with SPM.

Results: We showed a diminution of P3b amplitude in TLE subjects ($p<0.001$). Nevertheless our main results concern the evidence of a significant decreased P3b current density of P3b in TLE patients in right superior temporal gyrus, left inferior temporal gyrus and fusiform gyrus, right inferior frontal gyrus and right post–central gyrus. In visual condition, this source reduction was noted in right inferior, middle and superior temporal gyrus, in bilateral fusiform gyrus, in right dorsolateral frontal cortex, and in right post–central gyrus ($p<0.001$).

Conclusion: The reduction of temporal and frontal sources in TLE subjects may reflect a direct local cortical dysfunction secondary to the epileptic focus or a more complex interference between epileptic networks and normal attentional pathways.

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Pediatric Epileptology

T291
THE QUALITY OF LIFE IN CHILDREN WITH WEST SYNDROME IN HOSPITAL INFANTIL SUR IN SANTIAGO DE CUBA

G. Naranjo Pelayo, M. Casamajor Castillo†, Y. Popa Rosales*, and E. Soler Fuentes‡*

**Hospital Universitario Clínico Quirúrgico Juan Bruno Zayas, Santiago De Cuba, Cuba; †Hospital Universitario Pediátrico Infantil Sur, Santiago De Cuba, Cuba; and ‡Policlínico Municipal Julio Antonio Mella, Santiago De Cuba, Cuba*

The evaluation of the quality of life is a challenge to the modern medicine, especially for those who try to improve parameters in order to give to some people the hope they consider as lost. Evaluate the quality of life in children with West syndrome or infantile spasms and in their parents is the main objective of this research paper, trough the application of Test Cave, used exclusively in children with this disease. Our specific objectives are based on know the main problems after apply the Test and to modify the way of life of these children and their relatives. There were used each medical history and the general files of all these patients to do an exhaustive work finding all kind of data on it. There were serious problems in the social behavior and the adaptation of these patients to the environment, familiar and school also marked neurocognitive dysfunction. After analysis of those results we started a project of multidisciplinary work between neuropsychologists and neurophysiatrist to insert those kids and their parents in the community and to provide a better quality of life not only to them but to parents, teachers and the people that surrounds them and make sure they have a better life.

T292
EVALUATION THE FREQUENCY OF HYPOXIC-ISCHEMIC ENCEPHALOPATHY IN HOSPITALIZED NEONATES

F. Eghbalian, and A. Monsef

Hamadan University of Medical Sciences, Hamedan, Iran

Evaluation the frequency of hypoxic-ischemic encephalopathy in hospitalized neonates.

Purpose: A considerable number of pathophysiologic mechanisms can cause to damage the developing brain of the neonates. Neonatal seizures may have different causes with different history and clinical manifestations. Determining seizure causes is very important because it helps to treat and also determine the prognosis. Seizure due to hypoxic-ischemic encephalopathy usually occurs in 24–48 hours after a history of asphyxia and may cooperate with metabolic common cause of seizure in neonates. The aim of the present study was to evaluate the frequency of hypoxic-ischemic encephalopathy in hospitalized neonates.

Method: This cross-sectional study implemented for the tow year evaluation of 1295 neonates admitted at neonatal ward of Ekbatan hospital in Hamedan province of Iran for hypoxic-ischemic encephalopathy. Data such as CT scan findings, blood gas findings, Apgar score of 5th minute, decreased muscle tone and consciousness, seizure, age, sex, birth weights, serum calcium, glucose and sodium, were entered into the questionnaires and data were analyzed using SPSS 13.

Results: 34 patients (2.62%) out of 1295 evaluated neonates had seizure. From 34 neonates with neonatal seizure, 11 (32.4%) had hypoxic-ischemic encephalopathy. The mean age was 14.03+/−10.05 days (1–29 days). 25 (73.5%) neonates were boys and 9 neonates (26.5%) were girls.

Conclusion: According to the results of our study, The incidence rate of hypoxic-ischemic encephalopathy in hospitalized neonates was 32.4%.

T293
DRUG UTILIZATION PATTERN OF ANTIEPILEPTIC DRUGS IN CHILDREN 0–7 YEARS OF AGE: A PHARMACOEPIDEMIOLOGIC STUDY IN CROATIA

L. Cvitanovic-Sojat, I. Bielen†, and A. Sruk†*

**University Hospital Sestre Milosrdnice, Zageb, Croaria; and †General Hospital Sveti Duh, Zagreb, Croatia*

Purpose: The aim of this study was to investigate the antiepileptic drug (AEDs) pattern for the treatment of various forms of epileptic seizures in children. Information on AED utilization is an useful objective parameter in the evaluation of the standard of care of children with epilepsy.

Method: The analyzed patient data were collected by means of questionnaires completed by primary health care physicians (PHPs) from different regions in Croatia. The diagnosis of epilepsy in preschool-children (0–7 years) was previously confirmed by neuropediatricians. Only children with active epilepsy were included.

Results: A total of 37 PHPs provided the required data (33 pediatricians and 4 family physicians). They were in charge of 34 467 children in age of 0–7 years and in that population a total of 119 children (51.3% boys, 48.7% girls), mean age 4.84 ± 1.76 years, with previously verified active epilepsy were identified. Monotherapy was used in 88/116 (75.9%) and polytherapy in 28/116 (24.1%) of children, missing data 3/119 (2.5%). Valproate (55.2%) was the most frequently prescribed AED, followed by topiramate (19.0%), phenobarbiton (14.7%), lamotrigine (11.2%), carbamazepine (9.5%), metilphenobarbiton (8.6%), clonazepam (2.6%), primidon (1.7%), other AEDs (6.1%). The children with epilepsy and associated handicaps were more often treated with polytherapy. In those children, lamotrigine and topiramate is frequently use in mono or polytherapy.

Conclusion: AED monotherapy was much more frequently used, the most commonly used were valproate and topiramate. Polytheraphy was significantly more common in children with one or more handicaps.

T294
EFFICACY AND SAFETY OF INTRAVENOUS LEVETIRACETAM IN CHILDREN WITH ACUTE EPILEPTIC SEIZURES

J. García-Peñas, J. Lara-Herguedas, M. Rodrigo, A. Duat-Rodríguez, M. Ruiz-Falcó, and L. González Gutiérrez-Solana

Hospital Infantil Universitario Niño Jesús, Madrid, Spain

Purpose: To describe the efficacy and safety of intravenous levetiracetam (LEV) in children with acute epileptic seizures.

Method: We retrospectively analyzed data from 15 consecutive children aged 14 days to 18 years treated with intravenous LEV. Medical records of these patients were reviewed for demographic data, underlying neurologic disorders, the indications, dose, and duration of use of intravenous LEV, seizure control, and adverse events. There was no bolus administration, but in 9 patients we used an attack dose of 30 mg/kg (maximum dose of 1.500 mg). In all patients, the given dose was infused for 10–15 minutes. The frequency of administration was every 8–12 hours.

Results: Intravenous LEV was used for control of acute repetitive seizures in 10 patients and for refractory status epilepticus in 5 patients. The mean dose used was 50.6 mg/kg/day. All patients received previously treatment with intravenous diazepam and phenytoin, and the 5 patients with refractory SE also needed intravenous valproate and phenobarbital and continuous intravenous midazolam infusion. A symptomatic etiology was found in 12 patients (80%) including inherited metabolic disorders, malformations of cortical development and acute viral encephalitis. Nine patients (60%) showed a seizure frequency reduction of more than 50%

including 6 patients (40%) who became seizure-free. LEV was generally well tolerated although 7 patients (46%) reported side effects. Somnolence was the most commonly reported adverse event (40%).

Conclusion: Our results indicate that intravenous LEV may be an effective and safe alternative in the treatment of acute repetitive seizures and refractory status epilepticus in children.

T295
EVALUATION OF THE BIOCHEMICAL PARAMETERS OF BONE METABOLISM AND BONE MINERAL DENSITY IN AMBULATORY EPILEPTIC CHILDREN RECEIVING NEWER ANTIEPILEPTIC DRUGS

S. Chung
Kyung Hee University Hospital, Suwon, South Korea

Purpose: To assess the effects of newer antiepileptic drugs (nAEDs) on the biochemical parameters and bone mineral density (BMD) in epileptic children.

Method: Thirty-five epileptic children, aged 2 to 15 years, 14 treated with topiramate-alone (TPM), 10 lamotrigine-alone (LMT), and 11 oxcarbazepine-alone (OXC) for more than 1 year were included in the study. Thirty-five normal children were chosen by age and sex matched to each patient as control. Serum levels of calcium, phosphorus, alkaline phosphate, vitamin D3 (25-hydroxycholecalciferol; 25OHD, 1,25-dihydroxycholecalciferol; 1,25(OH)2 D) were evaluated. BMD was measured at lumbar spine (L1-L4) by the dual-energy x-ray absorptiometry.

Results: Vitamin D3 levels of OXC (25-OHD: 40.3 – 10.5 ng/ml, 25(OH)2D: 57.9 – 15.2 pg/ml) were significantly lower than the control (44.6 – 11.5, 66.2 – 10.5) ($P<0.05$), but not significant in TPM (42.8 – 10.3, 62.7 – 13.4), and LMT (42.6 – 11.3, 61.7 – 12.4) ($P>0.05$). There were no significant differences among each study group. The rest biochemical parameters were not significantly different between the control and the study groups. BMD were significantly reduced in OXC (L1-L4: 0.84 – 0.06) than in the control (0.73 – 0.11 g/cm2) ($P<0.05$), but not significant in TPM (0.82 – 0.08) and LMT (0.81 – 0.14). BMD of OXC was significant reduced than TPM or LMT.

Conclusion: BMD was significantly reduced in OXC than in the control and the other nAEDs, but not in vitamin D3. BMD was not related to vitamin D3, however, in patients treated with nAEDs, monitoring of bone metabolism is indicated.

T296
COGNITIVE IMPAIRMENT AND LACK OF RESPONSE TO ANTIEPILEPTIC DRUG TREATMENT ARE FREQUENT IN CHILDREN WITH FRONTAL LOBE EPILEPSY

H. Braakman, and W. Renier†*
**University Hospital Maastricht, Maastricht, The Netherlands; and †Canisius-Wilhelmina Hospital, Nijmegen, The Netherlands*

Purpose: To study the frequency and risk factors of cognitive impairment and refractoriness in children with frontal lobe epilepsy.

Method: We reviewed the medical files of children (age<18 years) diagnosed with frontal lobe epilepsy, in the out-patients' department for Children with Epilepsy and Paroxysmal Disorders in a university hospital in the Netherlands, between 1995 and 2005. We assessed the frequency and risk factors for cognitive impairment and refractoriness.

Results: We found 23 children with frontal lobe epilepsy, 11 boys and 12 girls. Twenty patients (87%) had cognitive impairment. Refractoriness (60% in the cognitive impaired group versus 0% in the cognitive unimpaired group) and low age at seizure onset (4.4 years in the cognitive impaired group versus 10.6 years in the cognitive unimpaired group) were frequent among children with cognitive impairment. Twelve children (52%) had refractory epilepsy. Absences with a frontal lobe focus were only observed in patients who eventually developed refractory epilepsy (n=9; 75%).

Conclusion: Cognitive impairment and refractoriness are frequent in children with frontal lobe epilepsy. Risk factors for cognitive impairment may include refractoriness and low age at seizure onset. Therefore, the cumulative effect of epileptic activity seems to have a negative influence on the developing brain, especially on cognitive functioning. Absences as seizure type may be a risk factor for refractoriness. The causal mechanisms remain unknown and warrant further study.

T297
PERVASIVE DEVELOPMENTAL DISORDERS (PDD), EPILEPSY AND EEG PAROXYSMAL ABNORMALITIES: HOW ARE THEY LINKED?

G. Barcia, A. Posar, E. Raimondi, M. Scaduto, M. Santucci, and A. Parmeggiani
University of Bologna, Bologna, Italy

Purpose: Pervasive developmental disorders (PDD) are heterogeneous clinical conditions with a prevalence of 64.9/10.000 (Fombonne E. et al., Pediatrics, 118(1): e139–50, 2006). Although epilepsy and EEG abnormalities have been described in PDD, the recurrence is extremely variable (Giovanardi Rossi P. et al., Brain and Development, 22: 102–106, 2000; Levisohn P.M., Epilepsia, 48 s9: 33–35, 2007).

Method: Our Italian sample includes 300 patients affected by PDD according to DSM-IV TR. The aim of the study is to evaluate occurrence and features of epilepsy and EEG paroxysmal abnormalities in different age and diagnostic subgroups.

Results: At the last observation, the mean age of patients is 10.4 years; 209 patients have autistic disorder; 72 PDD not otherwise specified, 12 Asperger disorder, 7 childhood disintegrative disorder. Familial antecedents for epilepsy are present in 23.7% of patients. Epilepsy and/or febrile seizures occur in 25.0% of cases and EEG paroxysmal abnormalities without epilepsy in 25.0%. Epileptic seizure onset has two peaks, one early and one during adolescence. On the other hand EEG abnormalities are more common during childhood. Partial and generalized epilepsies are both represented.

Conclusion: The higher prevalence of epilepsy and EEG paroxysmal abnormalities in PDD seems to be related to genetic factors rather than cerebral lesions. Probably an early brain dysfunction is responsible for PDD and epilepsy. How EEG paroxysmal abnormalities influence clinical picture is still debated. These findings emphasize the importance of EEG recordings during the evolution of PDD patients.

T298
NEUROPSYCHOLOGICAL ASPECTS OF BENIGN ROLANDIC EPILEPSY

H. Goldberg-Stern, O. Gonen, D. Inbar, K. Rabin, and M. Sadeh
Schneider Childrens Medical Center, Petach Tiqva, Israel

Purpose: Benign rolandic epilepsy, also known as benign childhood epilepsy with centrotemporal spikes (BCECTS), is the most common epileptic childhood disorder. It is known from previous studies that children with BCECTS have learning difficulties, mainly in the field of verbal functioning, compared with healthy controls, as expressed on neuropsychological tests. It is not clear whether the source of these difficulties lies in the electrical impairment, the seizures or is an adverse effect of treatment with antiepileptic drugs. The purpose of the study was to compare neuropsychological test scores of children with BCECTS with those of children with normal electroencephalograms (EEGs) in order to investigate the effect of the disorder on cognitive abilities without the confounding factors listed above.

Method: We compared the cognitive functions of 36 children with BCECTS prior to commencing treatment with antiepileptic drugs with 15 children who underwent EEG monitoring for various reasons and had normal results. We provided neuropsychological tests to both groups.

Results: Children with BCECTS had statistically significant lower scores in tests of verbal functioning. No relationship was found between the lateralization of the epileptic focus and the scores in neuropsychological tests. A higher number of seizures did not result in lower neuropsychological test scores.

Conclusion: Children with BCECTS have an impaired ability to process verbal information. It appears that this impairment derives from the pathological electrical discharges which are part of this syndrome and not from drug treatment, laterality of the epileptic focus or number of seizures.

T299
PREDICTORS OF INTRACTABLE EPILEPSY IN CHILDREN: A CASE CONTROL STUDY

G. Aithala, and L. Sztriha†*
**UiTM, Shah Alam, Malaysia and †University of Szeged, Szeged, Hungary*

Purpose: To determine the clinical, electroencephalographic and radiological factors associated with medically intractable seizures in children in the Al Ain Medical District in United Arab Emirates.

Method: A prospective, case-control study of children with epilepsy in the age range of 2 months and 13 years referred to pediatric neurology and neurodevelopmental clinics at Tawam and Al Ain University Hospitals from December 1997 to December 2002.

Results: There were 55 children with intractable epilepsy; their data was compared with 50 children who responded well to antiepileptic medications and were seizure-free for at least 2 years. Onset <1 year of age, a high seizure frequency at onset, positive history of neonatal seizures, developmental delay and status epilepticus, neurological deficits and abnormal brain imaging results were found to be significantly more common in the study group. Children in this group had symptomatic localization related epilepsy more commonly than in the control group.

Conclusion: Our study suggests that children who present with idiopathic localization-related and generalized epilepsy syndromes with few seizures at onset, with no neurological deficits tend to have a relatively good prognosis.

T300
SUBCLINICAL EPILEPTIFORM DISCHARGES AND SEIZURE OCCURRENCES IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER

W. Kim, and Y. Lim
Chungbuk University Hospital, Cheongju, South Korea

Purpose: Our objectives were to: (1) assess the relationship between seizure activity and EEG (Electroencephalography) abnormality of attention deficit hyperactivity disorder (ADHD) patients; (2) study the influences of methylphenidate to seizure activity of ADHD patients.

Method: EEGs were obtained from 164 children with ADHD from 1999 to 2006. We assessed the seizure activity and the severity of ADHD according to the results of the EEG. In cases of abnormal EEGs, we analyze the seizure activity and risk factors between a group taking and a group not taking methylphenidate.

Results: The average age of ADHD patients was 8.7 years old and there were 141 boys and 23 girls (6.13: 1). 135 (82.3%) children showed normal EEG findings and 29(17.7%) children showed abnormal findings. The relationship between the EEG findings and seizures showed a correlation (p-value<0.0001, Fisher's exact test). The severity of ADHD is not different between normal and abnormal EEGs (p-value 0.106). There was no statistical difference between the 14 patients (48.3%) taking methylphenidate with abnormal EEGs, and the 15 patients (51.7%) not taking methylphenidate with abnormal EEGs. Among 29 children with abnormal EEGs, 4 patients taking methylphenidate had seizures and 3 children not taking methylphenidate had seizures. There was no statistical relationship between seizure activity and treatment with methylphenidate (p-value 0.682).

T301
INTELLECTUAL DEVELOPMENT AND EEG OF CHILDREN BORN BY MOTHERS WITH EPILEPSY AND EXPOSED TO AED IN UTERO

A. Kozhokaru, V. Karlov†, and A. Serkina**
**Nevromed-Clinic, Moscow, Russia; and †Medical Dental University, Moscow, Russia*

Purpose: To assess the intellectual development of children born to mothers with epilepsy who were administered AED during pregnancy.

Method: VideoEEG monitoring. Weksler method. Forty-four children aged 6 months to 16 years (main group); 22 controls. Twenty chidren (main group) and 15 children (control group) aged 4 to 16 years were evaluated by Weksler method. Neurological status and psychomotor development assessment revealed psychomotor retardation in 11.3% of children aged 6 months to 3.5 years.

Results: In 6.8% of subjects in the main group vs. 4.5% in controls total IQ scores were significantly decreased; in 13.6% of the subjects in the main group nonverbal intelligence (DIQ) was decreased. In 9% of the children EEG changes were revealed and the diagnosis of epilepsy was established; 15.9% of the subjects had various EEG changes, but epilepsy was not revealed. Intellectual retardation was associated with EEG findings: 6.8% of the subjects had the diagnosis of epilepsy and a decrease in total IQ scores; in 13.6% of the subjects DIQ was decreased, there were EEG changes and no epilepsy. Among mothers with epilepsy during pregnancy 68% received monotherapy, 20% received polytherapy, and 12% were not administered any AEDs. High-dose mono- or polytherapy was associated with a decrease in total IQ scores in 13% and 4.5% of cases, respectively, or with a decrease in DIQ scores in 9% and 4.5% of cases, respectively.

Conclusion: Low total IQ scores were found in children diagnosis of epilepsy.

T302
ACOUSTIC EFFECTS OF LAMOTRIGINE IN PEDIATRIC PARTIAL EPILEPTIC PATIENTS

S. Kim, M. Yun, and Y. Choi
Chonbuk National University, Jeonbuk, South Korea

Purpose: The aim of this study was to investigate the acoustic effects of lamotrigine in pediatric epileptic patients.

Patients and Method: Newly diagnosed 27 partial epileptic patients (aged 5–15 years) were assessed through a Computerized Speech Lab (CSL) applied before the beginning of therapy with lamotrigine and 2 months after dosage had been stabilized (Target dosage: 7mg/kg/day). Language tests had been used Velopharyngeal incompetency and articulation screening test. We compared the data from patients and similar aged healthy volunteers.

Results: Mean VOT and TDs for all lenses and fortes increased and; for aspirates /ph, kh/ they increased and for /th/ and it decreased after lamotrigine antiepileptic therapy. However, none of these change show significance (P>0.05). The first formant (F1) of vowels /a, i, e, o/ and the second formant (F2) of /i, e, o/ increased; F1 of /u/ and F2 of /a, u/ decreased (P>0.05). Pitch range decreased from 206 ¡¾ 37.0 Hz before

the therapy to 203.9 ¡¾ 37.5 Hz after. The energy level measured by loudness also decreased from 47.7 ¡¾ 6.0 dB to 46.7 ¡¾ 4.6 dB after the lamotrigine antiepileptic therapy (P>0.05). Speaking rate of counting one to ten; duration of counting decreased from 8.8 – 2.5 to 8.2 – 1.8 after the therapy (P > 0.205). Precise articulation rates before and after the therapy were 93.1% and 92.7% respectively.

Conclusion: No significant negative acoustic effect of lamotrigine was found in this study. Lamotrigine is safe for acoustic function in pediatric epileptic patients.

T303
EARLY PREDICTORS OF INTRACTABLE EPILEPSY IN CHILDREN WITH CEREBRAL PALSY

A. Trabacca, G. De Agazio, L. Losito, L. Gennaro, and M. De Rinaldis

Scientific Institute I.R.C.C.S. E. Medea Association 'La Nostra Famiglia', Ostuni, Italy

Little is known about early prediction of intractable epilepsy in children with cerebral palsy. Such information could help guide the use of suitable therapies in these selected patients.

Purpose: to examine the importance of early predictors of outcome in epilepsy and to determine the real risk of intractable epilepsy in children with CP at the time of initial diagnosis.

Method: we have retrospectively valued the clinical and electroencephalogram (EEG) characteristics of epilepsy in patients with cerebral palsy for the 18 months after the onset of epilepsy and at last follow-up visit.

Results: 54 patients, mean age 11.9 (DS "b 3.53 years), of which 27 boys and 27 girls, were included in the study. 83,3% had spastic tetraplegia, 12,9% had spastic hemiplegia, 3,8% had spastic diplegia. Classification according to seizure type demonstrated that generalized seizures dominated in epileptic patient (68,5%). 48,1% of patients showed intractable epilepsy at 18¢X month after the onset and 33,5% at last follow-up visit. Early onset epilepsy, initial high seizure frequency and high seizure frequency at 12¢X and 18¢X month after the onset of epilepsy, EEG slowing and generalized seizures at the onset of epilepsy, acute status epilepticus were associated with an increased risk of intractable epilepsy (p < 0,05).

Conclusion: our data suggest that children at greater than average risk of developing intractable epilepsy can be identified early.

References: Berg AT, Shinnar S, Levy SR, et al. Early development of intractable epilepsy in children: a prospective study. Neurology 2001, 56: 1445–1452.

T304
HIPNAGOGIC MYOCLONIC EPILEPSY: A NEW EPILEPTIC SYNDROME?

F. Sanmartí, O. Sans Capdevila*, I. Alonso*, and A. Donaire†*

**Sant Joan De Deu University Hospital, Barcelona, Spain; and †Epilepsy Unit Hospital Clinic Barcelona Spain*

Purpose: Present a unique case-report of a new epileptic syndrome.

Method: A 13 years old female patient was referred with chief complaint of frequent nocturnal awakenings that were increasing in number and duration for a 3 months period. Family reported several episodes per night, lasting from few seconds up to 30 minutes of muscular jerks in limbs without loss of consciousness. Pathologic antecedent was behavioral problems, anxiety-phobic attacks and low scholar performance at 12 years of age. After 6 months on olanzapine all behavioral problems improved. No other personal or familial pathological findings were present. Possible diagnostic entities: Insomnia, Parasomnias, Nocturnal Epilepsy, or Pseudoseizures. Initial neurological examination, wake video-EEG and cerebral MRI were normal. After the first visit an external neurologist decided to start antiepileptic treatment with Topiramate and Clonazepam. There was disappearance of nocturnal awakenings for a period of 20 months. During that time the patient was followed up in our unit. Nine months after starting medication, a nocturnal video-PSG (NVPSG) was normal. Reappearance of symptoms occurred 20 months later. To understand the reason of relapse, all medication was stopped. A new NVPSG demonstrate four episodes of generalized epileptic myoclonic jerks that woke up the patient from slow wave sleep. Episodes lasted from 15 secs. to 13 minutes. Photic and photoconvulsive responses were also found.

Conclusion: Electroclinical findings and response to 500 mg/24h of valproate support the diagnosis of hipnagogic myoclonic epilepsy. To our knowledge and after review of the scientific literature we did not find reports on this new entity.

T305
POPULATION PHARMACOKINETIC ANALYSIS OF LEVETIRACETAM IN PEDIATRIC PATIENTS WITH EPILEPSY AGED 1 MONTH TO 16 YEARS

N. Toublanc, M. Lovern, M. Sargentini-Maier, and A. Stockis

UCB Pharma SA, Braine-L'Alleud, Belgium

Purpose: To characterize levetiracetam pharmacokinetics in children with epilepsy, including identification of clinically relevant covariates, and to propose dosing adaptation rules in children younger than 4 years.

Method: 197 children received single or multiple bid doses of levetiracetam as add-on therapy in 6 studies. Levetiracetam concentration-time data were analyzed using nonlinear mixed-effect modeling. Age, gender, race, body weight, body surface area, creatinine clearance, dose and concomitant antiepileptic drug (AED) were tested as possible covariates. Sensitivity analysis was performed to eliminate nonrelevant covariates.

Results: 112 males and 85 females provided a total of 1182 plasma concentrations. Levetiracetam concentrations were adequately described by a one-compartment model. Body weight and age were identified as factors affecting both apparent clearance (CL/F) and apparent volume of distribution (V/F). The age effect on CL/F was an asymptotic function to account for renal maturation in the first postnatal months. The effect of age on both parameters decreased as age increased, becoming negligible by approximately 4 years of age. Overall, intake of concomitant enzyme-inducing AEDs increased CL/F by 19%. Simulations indicated that only children aged 1 to 6 months would require a 30% decrease in dose (mg/kg) relative to 4-year-old children to obtain the same exposure.

Conclusion: The main factor explaining the interindividual variability in levetiracetam pharmacokinetics was body weight, followed by inducing AEDs and age. A nomogram was established to help with dose adjustment in children from 1 month to 4 years of age.

T306
PEDIATRIC UNIT OF VIDEO-ENCEPHALOGRAPHY – RESULTS FROM 4 YEARS IN OPERATION

A. Helena, C. Carlos*, R. Eduardo*, C. Enrique†, V. Teresa*, M. Eduardo*, D. Rosario*, and P. Alberto**

**Universtary Hospital Virgen De La Arrixaca, Murcia, Spain; and †Universtary Hospital Santa María Del Rosell, Murcia, Spain*

Purpose: The degree of difficulty in the diagnosis of children epilepsy determines that the video-electroencephalogram is an invaluable exploration for its diagnosis and monitoring. The aim of our study is to describe the main indications of the video-electroencephalogram, its usefulness for the diagnosis and the advantages on the conventional intercritical EEG in a reference neuropediatrics section.

Method: Checking of the clinical records of the patients on which a video-electroencephalogram has been used between October 2000 and October 2004. The diagnosis of epilepsy is established through the simultaneous clinical evaluation of two of our professionals. The data is saved in Access and the descriptive and inferential statistical analysis is made by the SPSS13.0 program.

Results: There were 212 video-electroencephalograms from 172 patients. Indications: 58 cases were to differentiate epilepsy and pseudocrisis, 89 to clarify the epileptic phenotype and 65 to keep and/or change the treatment. Diagnosis: 54 without epilepsy, 25 intertemporal epilepsy, 10 idiopathic generalized epilepsy, 19 symtomatic generalized epilepsy, 16 idiopathic partial epilepsy, 30 symtomatic partial epilepsy, 3 less distinctive idiopathic epilepsy, 4 myoclonic-astatic epilepsy, 1 atypical Aicardi epilepsy, 2 reflex epilepsy, 2 Lennox-Gastaut syndrome, 3 POCSL, 1 infantile spasm without electroencephalographic alteration, 1 West syndrome, 1 EGGF+. In our group, the positive predictive value from the clinic is 87%, from the EEG is 34.4% and from the video-EEG is 86.7, in the selected subgroups.

Conclusion: In our group, the correct clinical selection of the patients and the video-electroencephalographic record obtains a higher diagnostic accuracy in the infantile epilepsy than the conventional intercritical EEG.

T307

TOPAMAX MONOTHERAPY IN CASES OF CHILDREN'S AND ADOLESCENT'S FOCAL EPILEPSY

N. Freydkova, and V. Karlov†*
**Morozovskaya Children's Clinical Hospital, Moscow, Russia; and †Moscow State Medico-Stomatological University, Moscow, Russia*

Purpose: Evaluate the efficiency and safety of using topamax (TPM) for long time as monotherapy.

Method: An open randomized study of 71 patients (44-male, 27-female) aged 2 – 18, who received TPM since 6 months to 5 years, dose varied 2–10mg/kg/day. All patients were subjected to dynamic clinical monitoring, EEG and MRI. Rolandic epilepsy (RE) was diagnosed in 11 cases and in 60 – symptomatic/cryptogenic epilepsy (SCE) (17 and 43 respectively). The drug was administered as starting therapy to 33 patients and to 38 as 2 or 3 medicine.

Results: 11 patients (15,5%) discontinued the treatment due to drug inefficacy or negative effects: seizures aggravations (2 cases-2,8%) and adverse events (11 cases-15,5%). With RE the medicine was effective in 8 cases (72,7%), whereas with SCE a remission took place in 32 cases (53,3%). The attacks were arrested to a degree of 50% or higher in 7 patients (12,7%)/ In 8 cases transitory side effects were documented. Only in 1 situation we used TPM for 2 years and the drug was withdrawal because renal stones appeared.

Conclusion: TPM was efficacy in cases of focal epilepsy of different etiology (74,2%). For children, the dose program would be from 2 to 10 mg/kg/day. A long-term use of the drug does not trigger any serious side effects. TPM has a high level of efficiency and tolerability with children and adolescents.

T308

LEVETIRACETAM MONOTHERAPY IN IDIOPATHIC GENERALIZED EPILEPSY OF CHILDHOOD AND ADOLESCENCE

D. Pruna, S. Casellato†, T. Pisano*, D. Simula†, M. Scioni*, I. Chillotti*, and C. Cianchetti**
**University of Cagliari, Cagliari, Italy; and †University of Sassari, Sassari, Italy*

Purpose: This study evaluates efficacy and tolerability of LEV monotherapy in a cohort of newly diagnosed patients with idiopathic generalized epilepsy (IGE) or IGE resistant/intolerant to previous AEDs.

Method: We reviewed medical records of 25 patients with IGE (18 females and 7 males, age 5–22 years) treated with LEV. Thirteen were newly diagnosed patients and 12 resistant or intolerant to previous AEDs. Patients were subdivided according to syndromic classification: 14 juvenile myoclonic epilepsy (JME), 7 childhood absence epilepsy (CAE), 3 juvenile absence epilepsy (JAE) and 1 benign myoclonic epilepsy of infancy (BMEI). We reviewed clinical and EEG data, LEV doses, side effects and therapeutic response. Follow-up was 2 months-2 years.

Results: LEV monotherapy has been effective in 12/25 patients (48%) that are seizure-free (SF). In particular, 10/14 JME (71%) are SF; of these 5 were newly diagnosed patients. In the other 4 JME patients LEV was partially effective or ineffective. In the 7 patients with CAE, only one child is actually SF. In 6/7 of whom 4 resistant to previous AEDs, LEV was ineffective. In the small group with JAE, 1/3 (33%) is SF with LEV monotherapy. In the whole group of patients with absences, 2/10 (25%) are SF. LEV was also effective in the only patient with BMEI. LEV dose was 500–2000 mg per day (15–40 mg/kg/day). No side effect has been reported.

Conclusion: This study confirms efficacy and safety of LEV as first line treatment of JME while it seems to be less effective in patients with absences.

T309

FUNCTIONAL NETWORKS OF WORKING MEMORY IN CHILDREN WITH EPILEPSY AND COMBINED ADHD IN COMPARISON TO CHILDREN WITH DEVELOPMENTAL ADHD

N. Bechtel, M. Kobel*, P. Weber†, M. Burri†, M. Klarhöfer†, K. Scheffler†, K. Opwis*, and I. Penner**
**University of Basel, Basel, Switzerland; and †University Children's Hospital Basel, Basel, Switzerland*

Purpose: Children with epilepsy have a significant risk for attention deficit/hyperactivity disorder (ADHD) and in consequence often show deficits in working memory performance. However, it is not yet clear whether there are specific differences in the underlying mechanisms of working memory capacity between children with epilepsy and ADHD, and children with developmental ADHD.

Method: 7 boys with diagnosed epilepsy and ADHD, 13 boys with ADHD only and 12 healthy controls were investigated using fMRI. For fMRI three different N-back tasks with increasing difficulty were applied. Participants had to respond to visually projected numbers by button-press according to the instructions. Functional images were recorded on a 3T human head scanner.

Results: In the easiest 0-back task all boys performed on a high level. In the more demanding 2- and 3-back tasks healthy controls performed on a significantly higher level than boys with epilepsy and/or ADHD. Between the patient samples, no behavioral difference could be detected. On a functional level, all boys showed the expected frontal and parietal activations, which were more pronounced in the 2- and 3-back tasks. Only healthy controls showed additional activation in the cerebellum.

Conclusion: These preliminary data indicate that working memory capacity of children with combined epilepsy and ADHD is as deficient as in children with developmental ADHD. These behavioral results are also reflected by functional data indicating similar activation patterns in both patient groups. It can be assumed that the neural dysfunctions of working memory performance are comparable in children with epilepsy and/or ADHD.

T310
SEIZURE RESPONSE AND COGNITIVE FUNCTION IN CHILDREN AND ADOLESCENTS TREATED WITH TOPIRAMATE

U. Brandl, G. Kurlemann†, B. Neubauer‡, K. Rettig§, A. Schreiner¶, and B. Schauble¶*
**University of Jena, Jena, Germany; †University of Muenster, Muenster, Germany; ‡University of Giessen, Giessen, Germany; §GEM, Meerbusch, Germany; and ¶Medical & Scientific Affairs EMEA, Janssen-Cilag, Neuss, Germany*

Purpose: To explore seizure outcomes and cognitive function in children with epilepsy treated with topiramate.

Method: Open label, noninterventional multicenter trial (TOPMAT-EPP-401) in children age 6–16 with epilepsy and treatment with flexible dose TPM for 12 weeks. Kaufman-ABC, digit symbol test (HAWIK-3), verbal learning memory test (VLMT), tolerability were recorded. Seizure frequency was compared to a 12-week retrospective baseline.

Results: 54 patients (52% male; median age 11 years) with a mean duration of epilepsy of 32 months (SD±40 months) were followed. 22% discontinued due to AE(9%), insufficient efficacy (11%). Maximum dose TPM was 3.5mg/kg/day (age 6–12) and 2.49mg/kg/day (>12) at endpoint. 56% had >=50% seizure reduction and 35% became seizure free. K-ABC, VLMT and digit symbol test was tested at baseline and endpoint. Four groups were defined: AED naïve patients with continuous monotherapy (group 1: n=14), patients converting to monotherapy (group 3: n=18), patient remaining on add-on therapy (group 4: n=21). Pairwise comparisons between group 1, 3 and 4 showed no significant differences between groups, in the pre-post comparisons within groups on the Kaufman-ABC or VLMT. The digit symbol test did not reveal differences between groups at first and last visit. 33 AEs were at least possibly related to TPM (AE >=7: paresthesias 7%, fatigue 7%, speech and language disorder (7%)).

Conclusion: Findings suggest that topiramate is associated with a reduction in seizure frequency in children and adolescents with epilepsy. In addition, there was no significant change in cognitive function as measured by VLMT and digit symbol test at described doses.

T311
HYPERVENTILATION INDUCED HIGH AMPLITUDE RHYTHMIC SLOW ACTIVITY WITH ALTERED AWARENESS (HIHARS) IN CHILDREN: IS IT A TRULY NONEPILEPTIC PHENOMENON?

J. Ng, R. Kandler†, and S. Mordekar**
**Sheffield Children's Hospital, Sheffield, UK and †Royal Hallamshire Hospital, Sheffield, UK*

Purpose: HIHARS is increasingly identified in children and is thought to be nonepileptic. HIHARS has similar clinical features to absence epilepsy. It is important to establish whether it is a truly nonepileptic phenomenon. We investigate clinical outcome in children with HIHARS.

Method: Thirteen children (M: F 5:8 Age range: 5–9y Mean 6y) with HIHARS were identified from the clinical neurophysiology database. Case notes and video-EEG were reviewed retrospectively.

Results: All children had typical EEG/clinical features of HIHARS. Four had an additional inter-ictal epileptiform EEG abnormality. Nine presented with blank spells (BS) and the others with generalized tonic clonic seizures, daytime sleepiness, deteriorating school performance and nocturnal events. Three children had a previous diagnosis of epilepsy: childhood absence (CAE) in 2 and unclassified in 1. Following the EEG, anticonvulsant medication was not introduced in 10 and was continued/ commenced in 3 children. The children were followed for 4–72 (mean 18) months. BS spontaneously resolved in 5 of 9 children. BS resolved in 1 child after changing anticonvulsant medication. One child has continuing BS in association with CAE. One child developed BS a year after EEG. Two have continuing BS and remain under follow-up. None of the children went on to be diagnosed with a subsequent epilepsy.

Conclusion: Outcome of HIHARs appears to be heterogeneous and appears to be benign and nonepileptic in most children. The significance of HIHARS in children with epilepsy remains difficult to interpret. The importance of follow up in these children is emphasized.

T312
CLINICAL CHARACTERISTICS OF EPILEPSY IN RETT SYNDROME

K. Kim, B. Lim*, A. Cho*, K. Koh*, H. Hwang*, J. Chae*, Y. Hwang*, and H. Park†*
**Seoul National University Hospital, Seoul, South Korea; and †Eulji University Hospital, Daejeon, South Korea*

Purpose: Rett syndrome (RS) is an X-linked dominant neurodevelopmental disorder showing gradual developmental regression in spite of normal early development. Epileptic seizures occurred in about 2/3 of cases. This study was performed to investigate clinical characteristics of epilepsy in the patients with RS.

Method: Thirty-five patients with RS were retrospectively evaluated. Diagnosis of RS was made according to consensus diagnostic criteria in 2001. Among the 33 patients in whom MECP2 gene analysis was done, 14 showed mutations.

Results: Epileptic seizures were present in 30 patients (85.7%). The mean age of seizure onset was 40 months. Seizures developed during the stage I in 3 patients (10%), stage II in 9 (30%), and stage III in 18 (60%). Seizure types were partial in 12 patients, generalized in 6 and both in 6 patients. Eight patients showed only one seizure type, however, 20 patients had two different seizure types, and 2 patients had three seizure types. Sixteen patients (53%) achieved seizure freedom with antiepileptic drug treatment during clinical stage III and IV. EEG (available in 18 cases during stage II, 20 during stage II and 8 during stage IV) showed deterioration of background activity and decrease in frequency of epileptiform discharges according to the evolution of clinical stages.

Conclusion: Seizure types were variable and EEG features were not pathognomonic. However, EEG patterns and response to treatment changed as clinical stage progressed. Therefore, EEG findings may be helpful in evaluation of clinical features. And treatment plan should be decided considering the clinical courses.

T313
LEVETIRACETAM: EFFICACY AND TOLERABILITY IN EPILEPSY OF PEDIATRIC POPULATION

I. Pieri, R. Vittorini, and G. Capizzi
University Turin, Turin, Italy

Purpose: To evaluate efficacy and tolerability of levetiracetam (LEV) as adjunctive and in monotherapy in children with treatment resistant seizures.

Method: The population consisted of 42 (26 males, 16 females) patients between 3 and 18 years. Subjects had diagnosis of treatment resistant partial or generalized onset seizures (ILAE classification, 1989) and were receiving a dose regimen of one-two AEDs. Stable dose of 20–40 mg/kg/day in titration individually. Patients were followed at baseline¨C six months, for AEDs, frequency seizures, efficacy (assessed as responder rate 75% – 50% – <50% seizure frequency reduction) and tolerability.

Results: We included 42 patients (26 male, 16 female), mean age was 11.5 – 4.5 years; 28 (67%) had symptomatic partial epilepsy, 4 (9%) cryptogenetic partial epilepsy, 2 (5%) symptomatic generalized epilepsy,

5 (12%) cryptogenetic generalized epilepsy, 3 (7%) idiopathic generalized epilepsy. Sixteen of 42 patients (38%) showed a ≥75% reduction in seizure frequency. A ≥50% reduction was seen in ten of 42 patients (23%). Concomitant AEDs therapy at baseline was present in all patients; after six months 16 patients (38%) were in monotherapy with LEV. Mean age at introduction LEV is 10.2 ± 5.5 years. Adverse events occurring in 8 patients (19%): most commonly headache, somnolence, nervousness, emotional lability, infections. There was evidence that LEV, in our study, exacerbate seizure in EPS in two patients (therapy with LEV and carbamazepine). Interruption LEV was necessary in 6 patients (14%) for lethargy and seizures increase.

Conclusion: LEV demonstrate good efficacy and tolerability in multiple type seizures in pediatric population, in add-on and in monotherapy.

T314
LEVETIRACETAM IN CHILDHOOD ABSENCE EPILEPSY: LONG-TERM EFFICACY IN NEWLY DIAGNOSED PATIENTS

A. Verrotti, C. Cerminara†, A. Romigi†, S. Domizio*, A. Mohn*, E. Franzoni‡, C. Garone‡, G. Coppola§, E. Cesaroni¶, N. Zamponi¶, P. Parisi**, A. Spalice††, P. Iannetti††, F. Chiarelli*, and P. Curatolo†*
**University of Chieti, Chieti Scalo, Italy; †Tor Vergata University, Rome, Italy; ‡University of Bologna, Bologna, Italy; §University of Naples, Naples, Italy; ¶Salesi Hospital, Ancona, Italy; **University of Rome, Rome, Italy; and ††University of Rome 'La Sapienza', Rome, Italy*

Purpose: To assess the efficacy and tolerability of levetiracetam (LEV) monotherapy in children and adolescents with childhood absence epilepsy (CAE).

Method: Thirty-four subjects (18 male; 16 female) with CAE (mean age of onset ± SD: 13.2 ± 0.8 years) from seven centres in Italy were enrolled in this prospective study. The number of seizures was recorded prior to treatment (baseline). Seizures and any adverse events were recorded during treatment. LEV monotherapy was initiated at 250 mg/day and was gradually up-titrated to 1000–2000 mg/day. All patients were evaluated following 6 months' treatment and 18 patients were also re-evaluated after 12 months' treatment.

Results: At the 6-month evaluation, out of 34 patients studied, 17 (50%) were seizure free and 2 (5.8%) experienced a ≥50% reduction from baseline in absence seizures. Less than 50% reduction of absence seizures was observed in 15 patients (44.1%). At the 12-month evaluation, 13/18 (72.2%) patients were completely seizure free, 2/18 (11.1%) were seizure-free with some anomalies (e.g. sporadic polyspike) upon EEG. One (5.5%) patient who had not responded to LEV at the 6-month evaluation subsequently responded at the 12-month evaluation. LEV did not have an effect in 2/18 (11.1%) patients (also nonresponders at 6 months). LEV was generally well tolerated; only two patients reported an adverse event over the entire study: these were transient somnolence and irritability.

Conclusion: Our results suggest that LEV monotherapy is effective and well tolerated in children with CAE. Large-scale, prospective, long-term double-blind studies are needed to confirm these findings.

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T315
IMPROVEMENT OF BEHAVIORAL AND EMOTIONAL DISORDERS AFTER SURGERY IN CHILDREN WITH INTRACTABLE EPILEPSY

E. Nakagawa, A. Arai, K. Sugai, M. Sasaki, and T. Otsuki
National Center Hospital For Mental, Nervous And Muscular Disorders, NCNP, Tokyo, Japan

Purpose: We evaluated the effect of epilepsy surgery on behavioral and emotional disorders (BED) in children with intractable epilepsy.

Method: We assessed eight patients who underwent epilepsy surgery for intractable epilepsy (4 males and 4 females, aged 1 to 11 years). The subjects consisted of two patients with mesial temporal lobe epilepsy, four with frontal lobe epilepsy, one with parietal lobe epilepsy, and one with generalized epilepsy. Seven patients underwent lober or cortical resection and one patient had callosotomy. Presurgical evaluation included video EEG monitoring, MRI, PET, ictal SPECT, and MEG. Developmental scales and Achenbach's Child Behavior Checklist were evaluated.

Results: EEG showed epileptic discharges over the frontal and/or temporal areas. Ictal SPECT revealed hypoperfusion and interictal FDG-PET showed hypometabolism in the frontal area in 6 cases, in the caudate and thalamus in 6 cases, and in the mesial temporal area in 2 cases. Seizure outcome resulted in Engel's class‡T in 5 cases and class ‡U in 3 cases. Inattentive, hyperactive or impulsive behaviors and developmental age were also improved.

Conclusion: Epileptic seizure activities and propagation of paroxysmal discharges into the frontal and temporal areas, corpus striatum, and thalamus may influence (exacerbate) BED in pediatric severe epilepsy. For patients with intractable epilepsy of frontal or temporal origin and concomitant severe BED, surgical treatment can be an important treatment option for BED as well as epilepsy.

T316
LEVETIRACETAM MONOTHERAPY IN 12 INFANTS PRESENTING WITH NEONATAL SEIZURES

J. Dinger, D. Friebel, U. Reuner, H. Ikonomidou, and G. Ramantani
Klinik Und Poliklinik Für Kinder- Und Jugendmedizin, TU Dresden, Germany

Purpose: Neonatal seizures are common, especially in prematurity, and should be treated, since they may precipitate further neuronal injury. Phenobarbital (PB) represents the antiepileptic drug (AED) of choice, despite recently shown to increase neuronal apoptosis in animal models and cognitive impairment in subjects. Levetirazetam (LEV) is a newer AED with proven efficacy beyond four years and a favorable profile regarding apoptosis.

Method: In a prospective feasibility study, LEV was applied in neonatal seizures, after ruling out hypoglycemia, hypocalcaemia, hypomagnesaemia, pyridoxin dependent seizures and following PB treatment failure (no seizure control/severe adverse effects). In 9 premature infants (gestational age 23–30 weeks, birth weight 550–1370 g) and 3 term infants (37–41 weeks, 2960–3400 g) PB was discontinued and 10 mg/kg increments up to 30–50 mg/kg LEV were administered (intravenously, then orally) in 3 days. Based on clinical observation, EEG tracings (aEEG/routine EEGs), and LEV-titer monitoring, drug safety and anticonvulsant efficacy were assessed over 3–6 months.

Results: Infants were seizure free on day 4 of treatment with 15,3–55 mg/kg LEV, while EEGs were markedly improved in 11/12 patients on day 7. LEV plasma levels were 12,5–55 μg/ml under intravenous/oral administration (reference values 5–65,0 μg/ml). In 9 cases, LEV was discontinued after 3 months seizure-freedom. No severe adverse effects were observed.

Conclusion: These results illustrate the safety of LEV treatment in neonatal seizures, especially in prematurity, and illuminate LEV anticonvulsive efficacy in sustaining seizure freedom. Evaluation of LEV efficacy as primary therapy is called for, in order to establish a reasonable alternative to PB.

T317
LANGUAGE LATERALIZATION IN CHILDHOOD-ONSET FOCAL EPILEPSY: EVIDENCE FROM FMRI

G. Pahs, P. Rankin*, J. Cross†, G. Northam*, F. Vargha-Khadem*, and T. Baldeweg**
**Institute of Child Health, London, UK; and †Great Ormond Street Hospital, London, UK*

Purpose: We investigated language lateralization using functional MRI (fMRI) in children suffering from left-sided medically refractory, childhood-onset focal epilepsy and determined factors associated with atypical lateralization.

Method: Sixteen children (mean age 13.4yrs, range 8–17yrs, 38% female) suffering from drug-resistant epilepsy (range of seizure onset 1–12yrs) with a left hemisphere lesion on MRI underwent fMRI-scanning using a covert verb-generation task. Sixteen healthy volunteers, matched for age and gender, served as controls. Images were analyzed using SPM5 and lateralization indices (LI) were calculated within regions of interest (Broca¡s area, temporal lobe, cerebellum) using the LI-toolbox (Wilke et al., J Neurosci Methods, 2007;163:128–36). Factors contributing to atypical language distribution were investigated including: age at seizure-onset, seizure frequency, handedness, lesion location and lesion size.

Results: FMRI language lateralization in Brocas area was reduced in epilepsy patients (mean LI=0.15) compared to controls (LI=0.68, p<0.05) with 8 patients showing atypical language distribution, including 2 bilateral (LI<|0.2|) and 6 right-sided (LI¡Ü-0.2) cases. A reverse pattern of lateralization was found in the cerebellum (p<0.05). Among the variables investigated, presence of a multilobar lesion (|Ö2=4.27, p<0.05) and left-handedness (|Ö2=6.23, p<0.05) were associated with atypical language. Left-handedness (n=4) was only observed in patients with multilobar lesions. There was no relationship between language LI and verbal and nonverbal intelligence.

Conclusion: Atypical language distribution is a common reorganizational pattern in children suffering from lesional left-sided epilepsy. Even though individual reorganization patterns are difficult to predict, our findings suggest that the likelihood of atypical language representation increases with lesion size.

T318
INFRINGEMENT OF CREATINE METABOLISM IS ONE OF REASONS OF RESISTANT FORMS OF EPILEPSIES IN CHILDREN OF EARLY AGE

L. Kirillova, M. Vasilenko, Z. Rozkova, L. Tkachuk, L. Silaeva, and A. Shevchenko*
Obstetrics and Gynecology Academy of Medical Sciences of Ukraine, Kiev, Ukraine

Further is presented case of the boy V., two years old, who stayed in our pediatric psychoneurological clinic department. Perinatal anamnesis-without peculiarities. In the age of 5 month the parents noticed attacks of short-time loss of consciousness. Epilepsy attacks were in the form of simple and complex absences from 10 to 12 per day. Before admission to our clinic the boy underwent inpatient treatment at home place, he received Topamax (Topiramatum) 75 mg per day, Depakine (valproate) 3.5 ml (110 mg) per day, Vitamin Â6. The number of attacks did not decrease. The Topamax dose was increased to 100 mg (8 mg/kg) a day. The number of attacks decreased to 3 – 5 a day; later they became more frequent, up to 7 – 10 a day. Due to absence of effect the child was directed to treatment in our department. His status did not contain focal neurological symptomatology. According to logopedist conclusion the child demonstrated slight development delay. According to electroencephalography results epileptic activity was not revealed. Magnetic resonance tomography of the brain did not reveal structural changes. Magnetic resonance spectroscopy discovered decrease in brain guanidinoacetate N-methyltransferase and 20% decrease in brain creatine. The patient received creatine monohydrate as dietary supplement and Topamax 3 mg/kg of body mass. The number of complex absences decreased to 3–4 a day. There can be concluded that resistant form of metabolic epilepsy in this child was caused by brain decrease of guanidinoacetate N-methyltransferase, which led to 20% drop in brain creatine. The combination of anticonvulsant therapy and creatine monohydrate intake, as well as restricting of arginine in diet led to the decrease in the number of attacks, but did not allow total control of them.

T319
FIRST EXPERIENCES WITH RUFINAMIDE IN LENNOX-GASTAUT SYNDROME IN CHILDREN OF THE EPILEPSY CENTER KORK

A. Wiemer-Kruel, J. Fahrbach, S. Dönmez, F. Mann, and J. Ernst
Epilepsiezentrum Kork, Kehl-Kork, Germany

Purpose: Rufinamide (RUF) is a newly licensed AED for treatment of Lennox-Gastaut syndrome in children older than 4 years. It is available in Germany since June, 2007. Until now, 11 children have been treated with RUF in the Epilepsy Centre Kork. The results of the treatments are presented.

Method: 11 children, 6 boys and 5 girls, at the age of 5 to 17½ years, have been treated with RUF. The number of AEDs used before was high, up to 24, 2 patients additionally have a NVS. The dosage was slowly titrated up to 40 mg/kg/d.

Results: 2 children have been under therapy for a longer time (5 and 8 months). In 4 children the therapy with RUF was already stopped, mostly because of side effects, mainly fatigue, reduced strength and impulse. Vomiting was not seen, also no fever and no infections. 5 children are in progress of titration. Till now only 2 patients show a positive response to RUF in regard of seizures.

Conclusion: In contrast to the literature, the results of the treatment with RUF in children with Lennox-Gastaut syndrome in the Epilepsy Centre Kork are not so favorable: only 2 from 11 children (18%) had a reduction of seizure frequency, and the tolerance was also reduced (in the literature, 45 mg/kg/d are reported as well tolerated). Learning from our experiences, one should raise the dose slowly to avoid side effects, i.e. every 5–7 days in steps of 100 or 200 mg from 10 to 40 mg/kg/d.

T320
DNA GAIN IN CHROMOSOME 1 (46,XX,1P+ DE NOVO), IN AN EPILEPTIC CHILD

P. Vorgia, O. Grafakou†, and S. Voutoufianakis‡*
**University of Crete, Iraklion, Greece, Medical School; †Health Center of Spili, Rethimnon Crete, Greece; and ‡Venizelion Hospital, Iraklion Crete Greece*

DNA aberrations related with epilepsy concerning chromosome 1 are mostly deletions of the long arm (1q). A probable unique series of 7 children with partial epilepsy was recently reported with a DNA gain in the short arm of chromosome 1 by CGH array (1). We report a four year female with DNA gain in the short arm of chromosome 1 by standard caryotype. Child of unrelated parents, after in vitro fertilization. Besides of an IUGR, pregnancy and delivery were uneventful. Epileptic seizures since the neonatal period. She presents partial epilepsy with secondary generalisation. Beside epilepsy she also presents mental retardation, fine movement immaturity and low stature and minor facial dysmorphic features. Cerebral MRI shows bilateral ventricular dilatation and white matter thinning and a few areas of increased signal behind the occipital horns compatible with a probable leukoencephalopathy. Recent EEG findings reveal generalized bursts of spikes, amplified at the parasagital regions bilaterally. All other hematological and imaging investigations are normal. In conclusion, in selected epileptic patients, cytogenetics and DNA analysis can highly contribute to the diagnosis. An interesting question is the probably relation of IVF to this chromosomal aberration. CGH array would elucidate the exact DNA abnormality of our patient.

Reference

1. Hye Sung Kim et al. Altered DNA copy number in patients with different seizure disorder type: by array-CGH. Brain & Development 29 (2007) 639–643.

T321

SUCCESSFUL TREATMENT WITH 2,25:1 KETOGENIC DIET – A CASE OF CHILD WITH DRUG RESISTANT EPILEPSY

M. Bachañski, D. Domañska-Pakiea*, J. Chmielik*, D. Rokicki*, and J. Kasprzyk-Obara**

**The Children's Memorial Health Institute, Warsaw, Poland*

Purpose: In our center as all over the world we treat children with drug resistant epilepsy with 4:1 and 3:1 ketogenic ratios. However not for all children those ratios are suitable. We describe a case of 5 years old child with drug resistant epilepsy successfully treated with low ketogenic ratio.

Method: Child with drug resistant epilepsy initially treated with 3:1 ketogenic ratio, which was unsuccessful due to excessive vomiting. The diet was decreased to 1.5:1, than gradually increased to 2:1 and stopped at 2.25:1 ratio. Lab values (and beta-hydroxybutyrate levels), eeg are provided. Over 2 years observation period.

Results: More than 99% reduction of seizures. Good tolerability of the diet.

Conclusion: Our observation confirms that low ketogenic diet ratio also could be efficacious in some particular children. Lower ketogenic ratio could be associated with a fewer number of adverse events. Gradually increased ketogenic diet is better tolerated. The diet should be tailored to the particular patient.

T322

OUTCOME AFTER HEMISPHERECTOMY – CONSEQUENCES FOR THE PROCESS OF DECISION MAKING

A. Hamad,†, J. Aengenendt*, A. Elsharkawy*, H. Freitag‡, V. Hans*, H. Pannek*, A. Sakamoto†, I. Tuxhorn§, F. Woermann*, and T. Polster**

**Bethel Epilepsy Centre, Bielefeld, Germany; †Sao Paulo Federal University, Sao Paulo, Brazil; ‡Charite Campus Virchow-Klinikum, Berlin, Germany; and §Cleveland Clinic Foundation, Cleveland, USA*

Treatment decisions imply cost-benefit-analyses. These are particularly relevant in irreversible procedures as epilepsy surgery with hemispherectomy and its modifications being the most invasive ones. We studied the cost-benefit-ratio in children after functional hemispherectomy/hemispherotomy operated for catastrophic epilepsies, analysing objective data as seizure control and neuropsychological outcome as well as the subjective evaluation of the families. Ninety children, operated at the Bethel Epilepsy Centre between 1990 and 2006, were retrospectively analyzed. Follow up was from 1 year to 17 years (mean 6.4); mean age at surgery was 5.4 years (0.4–17.9); mean duration of epilepsy before surgery was 4.2 years (0.2–16.6). 49 operations (54%) were left-sided. Etiology in most cases was malformation of cortical development (51.1%) and included 27 patients with hemimegalencephaly. Acquired pathology was seen in 26.7% and progressive disease (Rasmussen's encephalitis or Sturge-Weber syndrome) in 22.2%. Seizure outcome was similar in all etiologic groups and stable over time: Engel class I or II was seen in 64.3% of 84 patients at 2 years and remained at 63.4% after 5 years (52 patients). Cognitive development improved in 27.6% and remained stable in 67.2% after 2 years. Parents considered seizures as the most relevant problem and many did not regret the decision for surgery even with outcome Engel III. Motor function was judged by the parents as equal (24.6%) or even improved in 36.8% and reduced in 38.6%. Surgical decisions should primarily be oriented towards seizure control with adequately individualized discussion of the possible effects of hemispheric surgery on development and motor function.

Monday 22 – Wednesday 24 September 2008
Traditional Poster Session
Psychiatric / Social Issues

T323

PREVALENCE OF DEPRESSION IN EPILEPSY IN A DEVELOPING COUNTRY

H. Hecimovic, and V. Demarin**

**Zagreb Epilepsy Center, Zagreb, Croatia*

Purpose: Epilepsy is a common neurological disorder with complex relations with social and vocational functioning. Depression is a frequent comorbid condition in patients with epilepsy. Self-reported assessments suggest strong association of quality of life in epilepsy patients with depression. Majority of studies examined epilepsy patients in developed countries, whereas developing countries have different social and vocational background. In this study we evaluated prevalence of depressive symptoms in epilepsy patients in Croatia.

Method: We examined 92 consecutive and consenting epilepsy patients in a tertiary epilepsy clinic. We assessed their clinical and demographic data: age, gender, seizure factors, education, employment and their marital status. All subjects had their mood function evaluation in a psychiatric interview and with the Beck Depression Inventory (BDI).

Results: Mean age of the patients was 31 ± 11 years. Majority were females (62.4%), employed (68.3%) and single (62.9%). Most had complex partial seizures (n = 76, 82.6%), and 8 (8.7%) had primary generalized epilepsy. For eight patients the type of epilepsy was not defined. The mean seizure frequency was 2.4 ± 5.3 and epilepsy duration 10.78 ± 8.7 years. Assessment with the BDI showed that 32.7% of patients had recent depressive symptoms: 5.2% had mild, 13% moderate and 14.5% had severe depressive symptoms.

Conclusion: This is the first larger study assessing mood dysfunction in epilepsy patients in Croatia. Our results suggest similar prevalence of depression in epilepsy in developing countries, indicating less significant role of social and vocational factors in the etiology of the disease. This work was supported by the Epilepsy Foundation grant to Hrvoje Hecimovic.

T324

HOW ADULTS MANAGE THEIR EPILEPSY AND HOW GENERAL PRACTICE CAN IDENTIFY THOSE PEOPLE AT RISK FROM POOR SELF-MANAGEMENT

W. Smithson

Escrick Research Practice, York, UK

Purpose: To explore factors that predict how adults with epilepsy manage their condition and to suggest ways to identify patients at risk of suboptimal self-management.

Method: A community based cross-sectional self-completed questionnaire study Setting: 27 general practices in Yorkshire and Humberside Participants: 438 adults with epilepsy excluding those with cognitive impairment recruited from 1333 case notes reviewed through general practice databases Main outcome measure: Factors associated with self-management behavior scores and adherence with antiepilepsy medication.

Results: General practice was the preferred source of information about epilepsy for 49% of the sample, 39% had experienced seizures in the last

12 months of which 18% still held a drivers license. Young adults, those in education or employment, people living with others and those who described ictal visual disturbance or had recent seizures were more likely to achieve low self-management scores. No significant demographic associations were found for medicines adherence but low self-management scores, recent seizures or ictal visual disturbance were associated with nonadherence.

Conclusion: General practice can use the annual epilepsy review to identify adults with epilepsy who are at risk from their condition due to either poor self management behavior or nonadherence with epilepsy medication. These behaviors may be addressed in general practice because of the established systems to manage long-term conditions.

T325
NEUROPSYCHOLOGICAL STATUS OF CHILDREN WITH NEW ONSET EPILEPSY

T. Ko, M. Yum*, and H. Yoo**
**Asan Medical Center, University of Ulsan, Seoul, Korea*

Purpose: Cognitive impairment has been reported in children with epilepsy. But whether the problem may be present at epilepsy onset or not and the IQ patterns associated with epilepsy types remains to be determined. This study is an effort to characterize neuropsychological status of children with recent-onset epilepsy without symptomatic etiology and the differences of IQ between the different types of epilepsy.

Method: We performed Korean Education Development Institute-Wechsler Intelligence Scale for Children (KEDI-WISC) in Children (age: 6–15 years) with newly diagnosed (<12months) epilepsy (N=41) who had normal clinical MRI and no other neurological disorder. The children were classified to benign childhood epilepsy with centrotemporal spikes (BCECTS, n=10), other localization-related epilepsy (LRE, n=14), and idiopathic generalized epilepsy (IGE, n=17). The differences of IQ between the three types of epilepsy were evaluated by Kruskall-Wallis test.

Results: The mean IQ of these three epilepsy groups were within normal limits, but significant difference was observed in the domain of nonverbal IQ, especially in arrangement, and coding ($p<0.05$). The mean nonverbal IQ of the BCECTS appeared higher than LRE and IGE groups (113.0 vs 97.2 and 92.6). Among the patients with AED (n=36), significant differences were also noticed in the full-scale IQ, nonverbal IQ, arrangement, design and coding ($p<0.05$).

Conclusion: There were some different patterns between the types of epilepsy in the earliest stage of epilepsy. Follow-up study with large number of patients should be required to provide more information of the effect of epilepsy itself or AED on the intelligence of the children.

T326
ATTITUDES TOWARD AND AWARENESS OF EMPLOYMENT OF PEOPLE WITH EPILEPSY IN EMPLOYEES OF THE ENTERPRISE AMONG A LOCAL CITY IN JAPAN

S. Yoshioka, and M. Fukuda
School of Health Science, Faculty of Medicine, Tottori University, Yonago, Japan

Purpose: The employment is an important problem for the public participation of people with epilepsy. However, there is far a restriction in the employment of them in Japan. This study investigates the attitudes towards employment of people with epilepsy in employees of the enterprise in a local city, Japan.

Method: A questionnaire on knowledge of epilepsy and attitudes and awareness regarding working of people with epilepsy was distributed and completed by 99 employees participated in the enterprise workshop of the human rights held in Tottori city in October 2007. Statistical analysis with chi-square was used to identify factors associated with negative attitudes.

Results: of our responders 46.5% had read/heard/seen something in the epilepsy, 39.4% knew someone with epilepsy and 37.4% witnessed a seizure. Fourteen percent knew the treatment for seizure attack. People with epilepsy were in the employ at 3.0% of the enterprise. Regarding marriage to 28.3% were rejected it and regarding playing with a patient with epilepsy 12.1% were objected it. While regarding his employment 10.1% were positive, 72.8% were skeptical while 2.0% were against it. Attitudes towards employment of people with epilepsy were significantly influenced by their attitudes towards marriage to and playing with a patient with epilepsy.

Conclusion: The rejection attitudes towards employment of people with epilepsy in employees are relatively low. However, information campaigns are necessary in order to promote the employment of people with epilepsy, the employees' understanding of epilepsy and tolerance with epilepsy.

T327
PSYCHOLOGICAL SEQUELAE OF SWITCHING FROM AN ORIGINAL TO A GENERIC AGENT IN DRUG-RESISTANT EPILEPSY – A PROSPECTIVE STUDY

E. Czapinska, and P. Czapinski
Epilepsy and Migraine Treatment Centre, Krakow, Poland

Purpose: Although 50% of epilepsy patients accept a decrease in the cost of their therapy, the majority of them are afraid of changing drugs, being mostly concerned with effectiveness and safety of generic drugs.

Method: The prospective studies included 441 patients aged 18–58 years of life with drug-resistant epilepsy with partial seizures treated by lamotrigine (n=224), topiramate (n=104) or gabapentin (n=113). In each patient, the assessment included the frequency and degree of troublesomeness of epileptic seizures, quality and frequency of adverse effects and quality of life (the QOLIE-31-P scale). The subjects were tested prior to changing the medication and three months after the switch.

Results: The investigations have demonstrated that there is no significant difference in the frequency and troublesomeness of epileptic seizures in particular groups treated with original or generic lamotrigine, original or generic topiramate and original or generic gabapentin. After the switch, there were no differences in the frequency and quality of adverse effects. A switch from an original to a generic drug does not affect the quality of life either.

Conclusion: It appears that the use of generic drugs in patients with drug-resistant epilepsy is fully justified.

T328
PILOT PROJECT: BUILDING BRIDGES BETWEEN YOUNG PEOPLE WITH EPILEPSY AND EMPLOYERS

M. Lux, M. Wendler†, H. Schmid†, B. Steinhoff*, and J. Ernst**
**Epilepsy Centre Kork, Kehl-Kork, Germany and †Vocational Training Centre Waiblingen, Waiblingen, Germany*

Pilot project: 'Building bridges between young people with epilepsy and employers'.

Purpose: Young people with epilepsy are often facing difficulties in receiving the adequate education and finding a job. They are often confronted with discrimination in education, employment and social acceptance. The pilot project's intention is to improve the situation of young people with epilepsy.

Method: To better understand the needs of young adults with epilepsy, a qualitative study was undertaken. In this project, standardized questionnaires were distributed between more than 1100 people who are involved

in the occupational integration (employers, teachers, physicians, etc.). The poster will present the outcome of the analysis of the questionnaires.

Results: Building up a choice of vocation assessment. The findings revealed that there is a lack of knowledge in public, employers and mainstream career advisors. Fears of employers were cut down by providing information about epilepsy and assistance. 110 young adults are involved in the project until now. 44 could be transferred into a vocational education. Increasing general awareness of epilepsy by attracting professionals and nonprofessionals.

Conclusion: Following goals have to be implemented with all the stake holders involved: Identify gaps in occupational integration (services) for young people with epilepsy; Discuss strategies for a better occupational integration; Individual considerations: job requirements vs. kind of seizure; Understand the impact of epilepsy on young adults; Identify the unique psychosocial needs of young adults with epilepsy; Learn about possibilities to decrease discrimination.

T329
NALTREXONE IN THE TREATMENT OF NONEPILEPTIC PSYCHOGENIC (DISSOCIATIVE) SEIZURES

H. Straub,†,‡, and K. Bohlmann*,†,‡*
**Epilepsiezentrum Berlin-Brandenburg, Bernau, Germany;*
†Epilepsieklinik Tabor Bernau, Bernau, Germany; and
‡Universität Potsdam, Potsdam, Germany

Purpose: There is some data suggesting that naltrexone could be effective in the treatment of dissociative phenomena in postraumatic stress disorder (PTSD) and borderline personality disorder (BPD). We want to report our clinical experiences with naltrexone in the treatment of dissociative seizures in these patients.

Method: We selected 18 consecutive patients with established diagnosis of PTSD or BPD following DSM lV-criteria and chronic (duration 2–20 years), high-frequent (daily) dissociative seizures (diagnosed by video-EEG-monitoring), who showed no response to all precedent therapeutic interventions (inpatient setting, psychotherapy and psychopharmacological treatment). After informed consent they received 50mg naltrexone/day over one week to reduce seizure-frequency. Cognitive/behavioral psychotherapy was continued simultaneously, co-medication remained unchanged. Seizure frequency was assessed four weeks before and continuously after the treatment (follow up 0,5 -4 years, out-patient-based). Responders (seizure reduction > 75%) continued with an intake of naltrexone (50mg/day).

Results: 12 of 18 patients responded to naltrexone (5 patients: seizure reduction > 75%, 7 patients: seizure-free). Success occured immediately in all responders and persisted over a follow-up -period of 0,5–4 years (mean 2,1 years). Significant side effects were not observed.

Conclusion: Our small pilot study shows a lasting effect of the opioid-antagonist naltrexone in the treatment of dissociative seizures in a psychotherapeutic setting. This suggests that endogenous opiods can play a key role in the development of dissociative seizures. Further investigations are necessary to assess the role of opioid-antagonists in the treatment of dissociative phenomena.

T330
ELECTROENCEPHALOGRAPHY (EEG) ALTERATION IN AUTISM SPECTUM DISORDER (ASD)

I. Dobrescu, F. Rad, V. Simion, L. Ilie, and I. Jipescu
'*Prof. Dr. Alexandru Obregia*' *Hospital, Bucharest, Romania*

Purpose: Our purpose is to appreciate the prevalence of EEG alteration in children with ASD, with or without another psychiatric disorder.

Method: We have examined 77 children diagnosed with ASD, inpatient in Child and Adolescent Psychiatry Department, Bucharest. The age was between 1.5 and 6 years old. The diagnosis was formulated using DMS-IV-TR criteria for ASD. The sample was dividing in 5 groups after we evaluate EEG: Group 1: normal EEG Group 2: convulsive discharge (with clinical correspondent) Group 3: bioelectric immaturity (slow theta/subtheta rhythm) Group 4: epileptiform activity Group 5: bioelectric immaturity and epileptiform activity The most frequent EEG alteration was in Parietal-Temporal bilateral, Temporal bilateral and Occipital bilateral.

Results: From our sample with children diagnosed with ASD with age between 1.5 and 6 years old: 1.29% have normal EEG, 7.79% have convulsive discharge with clinical correspondent, 46.75% have bioelectric immaturity, 10.38% have epileptiform activity and 33.766% have bioelectric immaturity and epileptiform activity.

Conclusion: Our preliminary results are in concordance with dates from available literature. Between ASD and Epilepsy there is a debate relation (them are comorbid in 6.5–10–15%). Some of the children with ASD have clinical history of convulsions; some of them have only EEG alteration, without clinic correspondent. The relation between the role of epilepsy and epileptiform activity on ASD's etiology generate a lot of discussion. They are frequent associated but there is no evidence for their causal relationship.

T331
SHOULD PATIENTS WITH PSYCHOGENIC NONEPILEPTIC SEIZURES BE ALLOWED TO DRIVE? RECOMMENDATIONS OF GERMAN EXPERTS

U. Specht, and R. Thorbecke
Bethel Epilepsy Center, Bielefeld, Germany

Purpose: To seek expert opinion on the ability to drive of patients with psychogenic nonepileptic seizures (PNES).

Method: Similar to a study of Benbadis et al in the USA (Epilepsia 41, 2000, 895–7), 41 experienced German epileptologists were contacted by e-mail and were asked what they recommend in patients with PNES with regard to driving privileges. The choices were (1) apply the same restrictions as in official regulations for patients with epilepsy; (2) apply no restrictions; and (3) follow an individualized approach. The results were compared with those found by Benbadis et al.

Results: Thirty-four of 41 addressed epileptologists (83%) responded. 32% applied the same restrictions as stipulated for patients with epileptic seizures (USA: 49%), 68% decided on an individual basis (USA: 19%) while no physician perceived PNES patients fit for driving without any restrictions (USA: 32%).

Conclusion: More than two-thirds of epilepsy experts in Germany suggest an individual assessment of driving ability in patients with PNES. This seems to reflect the great variability of PNES concerning semiology, frequency, risks of injuries, etiology and prognosis of the attacks. In contrast to one third of neurologists in the USA, no German physician perceived PNES patients being fit for driving in general. This may be related to the German driving regulations where persons with PNES are dealt with similarly to those with epileptic seizures, who are considered unable to drive as long as a 'substantial' recurrence risk exists.

Monday 22 – Wednesday 24 September 2008
Traditional Poster Session
Surgical Treatment / VNS

T332
OUTCOME AFTER HEMISPHERECTOMY IN ADULTS WITH REFRACTORY HEMIPLEGIC EPILEPTIC SYNDROMES

C. Cukiert,†, M. Argentoni-Baldochi*,†, C. Baise-Zung*,†, C. Forster*,†, V. Mello*, A. Cukiert*,†, J. Burattini*,†, and P. Mariani*,†*

**Hospital Brigadeiro, Sao Paulo, Brazil; and †Clinica De Epilepsia De Sao Paulo, Sao Paulo, Brazil*

Purpose: Hemispherectomy is an extremely effective surgical procedure usually performed in children with Rasmussen encephalitis, hemispheric cortical dysplasia, hemimegaloencephaly, congenital or acquired hemiplegic epileptic syndromes or Sturge-Weber. Hemispherectomy is certainly an underused surgical procedure and many kids with refractory hemiplegic epileptic syndromes grow and are left without adequate treatment until adulthood. We report on our results obtained after hemispherectomy performed in adult patients with refractory hemiplegic epileptic syndromes.

Method: Fourteen patients were studied. Age ranged from 17 to 34 years (mean = 23 years). All patients had refractory hemiplegic epileptic syndromes. Daily unilateral simple partial motor seizures were present and prevailed in every patient. Complex partial seizures and tonic-clonic seizures were also present in 11 patients. MRI showed a gross hemispheric congenital lesion prevailing over the middle cerebral artery territory in all patients. Interictal EEG showed spiking restricted to the damaged side in 8 patients, bilateral synchrony in 2 patients, discharges prevailing over the nondamaged hemisphere in 2 patient and exclusively healthy hemisphere spiking in 2 patients. All patients were submitted to functional hemispherectomy. Follow up time ranged from 1 to 11 years (mean = 50 months).

Results: All patients underwent uneventful procedures. Six patients had an aseptic meningitis syndrome (headache, neck stiffness and fever) that needed no antibiotic treatment. All patients were seizure free one year after surgery. Two patients, who had unilateral preoperative EEG findings, had 2 and 3 generalized tonic–clonic seizures during the first postoperative month, respectively. The antiepileptic drugs were successfully reduced in all patients, and 5 patients were taking no drugs at last follow-up.

Conclusion: Functional hemispherectomy is highly effective in this adult patient population. Although effective in all age strata, this procedure should not be delayed; all these adult patients might have been good surgical candidates earlier in life.

T333
OUTCOME AFTER MAXIMIZED CALLOSOTOMY IN PATIENTS WITH PRIMARY GENERALIZED EPILEPSY

M. Argentoni-Baldochi,†, A. Cukiert*,†, P. Mariani*,†, J. Burattini*,†, C. Cukiert*,†, C. Baise-Zung*,†, C. Forster*,†, and V. Mello**

**Hospital Brigadeiro, São Paulo, Brazil; and †Clinica de Epilepsia de São Paulo, São Paulo, Brazil*

Purpose: Primary generalized epilepsy is usually considered a benign form of epilepsy and is usually treated with low dose anticonvulsant dosages. Some patients with primary generalized epilepsy belong to the refractory side of the biological continuum represented by this disease. We present the outcome after callosotomy in patients with refractory primary generalized epilepsy.

Method: Eleven patients with primary generalized epilepsy were studied. Age ranged from 17 to 43 years (mean=27 years). Two patients were classified as having juvenile myoclonic epilepsy and 9 as having childhood absence epilepsy. All patients had daily absence seizures and tonic-clonic seizures (mean frequency = 1 seizure / week) despite adequate medical therapy which included high dose valproate, lamotrigine and phenobarbital. MRI was normal or showed mild diffuse atrophy in all patients. Interictal EEG showed diffuse bilateral and synchronous spike (n=7) or polyspike (n=4) and wave discharges (2.5 to 3.5 Hz). Preoperative general IQ ranged from 75 to 110 (mean = 87). All patients were submitted to 90% callosal section under general anesthesia. Follow-up time ranged from 9 months to 7 years (mean= 32 months).

Results: At least a 85% reduction in seizure frequency was obtained in all patients, and 1 patient became seizure free. Postoperative EEG showed bilateral synchrony rupture in all patients during wakefulness; in 9 patients bilateral synchrony was rebuilt during slow wave sleep. MRI documented uneventful surgical procedures. One-year postoperative neuropsychological testing was available for 7 patients. There was a mean increase of 11 points in general IQ, basically related to increased attention.

Conclusion: Our results suggest that although etiology might vary, primary and secondary generalized epilepsy might share some pathophysiologic mechanisms, which should include an important role for the corpus callosum and subcortical modulation of the epileptic activity.

T334
POSTCALLOSOTOMY ALIEN HAND SYNDROME

P. Mariani,†, A. Cukiert*,†, J. Burattini*,†, C. Cukiert*,†, M. Argentoni-Baldochi*,†, C. Baise-Zung*,†, C. Forster*,†, and V. Mello**

**Hospital Brigadeiro, São Paulo, Brazil; and †Clinica de Epilepsia de São Paulo, São Paulo, Brazil*

Purpose: Alien hand syndrome had been reported in patients with heterogeneous brain lesions. Although it has also been reported after callosal section, its occurrence is extremely rare after this procedure. We describe a patient who had a transient alien hand syndrome after maximized (90%) callosal section.

Case Report: This 43 year-old man presented with refractory simple absence and tonic–clonic seizures since the age of 7 years. His MRI was normal and his mean IQ=85. Interictal and ictal EEG showed diffuse bilateral and synchronous spike and wave discharges, prevailing over the frontal regions. He underwent an uneventful 90% callosal section. The extent of section was documented by postoperative MRI and his postoperative EEG showed complete disruption of the secondary bilateral synchronous and asynchronous spike and wave discharges. One month after surgery, the general IQ remained stable. There was a 90% improvement in seizure frequency and marked improvement in attention. Immediately after surgery, he was unable to perform any bimanual task. Actually, the left hand would always interrupt or disturb the movement intention of the right hand. He remained highly incapacitated due to this condition for one week, after which the symptoms started to vanished. The symptoms disappeared forty-five days postoperatively.

Conclusion: Although rare, this transient condition could be highly disruptive of the normal daily activities. It is rarely seen postoperatively in callosotomy patients. This was the first time we documented this syndrome in our 133 callosotomy patients series. It might represent a very severe transient intermanual conflict deficit.

T335
DEEP BRAIN STIMULATION FOR TREATMENT OF REFRACTORY EPILEPSY

J. Burattini,†, A. Cukiert*,†, P. Mariani*,†, C. Baldauf*,†, C. Baise-Zung*,†, M. Argentoni-Baldochi*,†, C. Forster*,†, and V. Mello**

**Hospital Brigadeiro, São Paulo, Brazil; and †Clinica de Epilepsia de São Paulo, São Paulo, Brazil*

Purpose: Deep brain stimulation (DBS) for treatment of refractory epilepsy has been actively investigated over the last decades as a treatment modality option in patients who had failed or are not candidates for conventional resective or disconnective surgery. We report the findings in 4 patients submitted to DBS.

Method: Three patients (Patients 1–3) with generalized epilepsy previously submitted to callosal section and one patient (Patient 4) with bilateral periventricular nodular heterotopia previously submitted to temporal lobe resection were studied. All patients had daily seizures. All patients were implanted bilaterally at the thalamus using a Kinetra device (Medtronics). Patients 1–3 were targeted at the centro-median nucleus and Patient 4 at the ventral-anterior nucleus. Present electrode settings are: Patient 1- 2V, 300 usec and 100 Hz (18 months of follow-up); Patient 2- 0.8V, 300usec and 130 Hz (6 months of follow-up); Patient 3- 1V, 300 usec and 130 Hz (6 months of follow-up) and Patient 4- 2.25V, 300 usec and 100 Hz (18 months of follow-up).

Results: Patient 1 has presently 1 seizure / month. Interestingly, he is much more alert and verbal output is much higher than before DBS; Patient 2 presently has 1 seizure / 10 days; Patient 3 has 1 seizure / week. Patient 4 remained seizure free for 2 months after DBS. Her present seizure frequency is 2 seizures / month. All patients presented increased attention with stimulation parameters lower then those required for seizure control.

Conclusion: All patients benefit from the procedure. We are targeting the centro-median nucleus for patients with generalized epilepsy and the ventral-anterior nucleus in patients with focal epilepsy. Additional follow-up is needed to adequately assess the clinical outcome after DBS. Improvement in the attention deficit is precocious and seems unrelated to seizure control.

T336
EPILEPSY SURGERY IN ATHENS

A. Siatouni, S. Gatzonis*, N. Georgakoulias†, T. Bouras*, C. Tsekou*, E. Sigounas*, I. Aggelopoulos‡, M. Papathanassiou§, E. Aggelakis*, P. Patrikelis*, K. Konstantinidis¶, I. Kaskarellis*, I. Fassaris*, E. Patsouris**, and D. Sakas**

**Evangelimos Hospital, Athens, Greece; †Athens General Hospital, Athens, Greece; ‡Athens Medical School, Aeginition Hospital, Athens, Rome; §'Attikon' Hospital, Athens, Greece; ¶Cormed Company; and **Athens University, Athens, Greece*

Purpose: The study presents the presurgial evaluation protocol and the results of the epilepsy surgery programme of Epilepsy Surgical Center of Athens Medical School in Evaggelismos Hospital.

Method: Presentation of the presurgical evaluation protocol, the surgical procedures and the long term results.

Material: We present 53 patients, aged 14–63, 28 men and 25 women who were treated surgically for drug-resisting epilepsy. Group A includes 29 patients, with mesial temporal lobe epilepsy (MTLE) who underwent standard surgical procedures (anteriomedial, selective hippocampectomy). Group B consists of patients with extra temporal epilepsies who underwent tailored procedures.

Results: In group A, after the surgical treatment, eighty percent of patients have remained seizure free, while in Group B, fifty percent of patients who proposed for surgical therapy have remained seizure free.

Conclusion: The recently established program ''Epilepsy Surgery in Athens'' runs successfully and meets outcome rates no fare from these international accepted.

T337
EPILEPSY SURGERY OF THE TEMPORAL LOBE – LONG-TERM SEIZURES OUTCOME

J. Pimentel, C. Bentes, A. G. Campos, and A. Ferreira

Hospital Santa Maria, Lisbon, Portugal

Purpose: To present a series of temporal lobe operated patients regarding their long-term seizures outcome.

Method: Follow-up of at least 6 months, according to the Engel classification of seizures outcome.

Type of resections: Isolate amygdalohyppocampectomies(IAH),amygdalohyppocampectomies plus focal resections (AH+FR), isolated focal resections (IFR).

Results: 101 patients, 48 males, with a median age of 35.0 ± 13.1 years. Median time of follow-up of 9.5 months. IAH, AH+FR and IFR performed, respectively, in 69 (36 anterior and 30 selective), 27 and 5 patients. 12 patients lost for or with follow-ups of less than 6 months. Considering the 3 groups (89), 93.3% and 87.7% patients were in class I at 3 and 72 months, respectively. For IAHs, 95.1% and 78.5% were in class I at 3 and 72 months, while for the AH+FRs one, 91.3% and 83.0% were in the same class for similar periods. Still for IAHs, 100% and 90.0% of the anterior AH patients were in class I at 3 and 72 months respectively, while 88.0% and 75% of the selective AH patients were in class I. For the IFR group, 75.0% and 0.0% of the patients were in class I at 3 and 72 months, respectively.

Conclusion: Our series showed a favorable long-term seizure outcome. The better outcome for patients of the anterior AH subgroup, when compared to the selective AH one, might be due to some nonstudied seizure outcome predictors. The IFR group ran worse but the sample was too small.

T338
VAGUS NERVE STIMULATION (VNS) IN CHILDREN: TEN YEARS EXPERIENCE

J. Alving, H. Nielsen*, and K. Olofsson†*

**Danish Epilepsy Center, Dianalund, Denmark; and †Roskilde Hospital, Roskilde, Denmark*

Purpose: To evaluate the short- and long-term efficacy of VNS in children with intractable epilepsy.

Method: Follow-up study of 25 children, all with difficult-to treat epilepsy, in the period 1996–2006 Seven excluded from surgery after preoperative work-up All mentally retarded, half of them severely Epilepsy syndromes: 17 localization-related, 8 generalized 6–10 AEDs tried before VNS; Four also had tried the ketogenic diet.

Results: Seizure response Seizure reduction by 50% or more: after 1 year: 6/25, after 2 years: 7/19, after 3 years: 7/15. One child died during follow-up Failures: in 2 children, VNS was switched off, and in another two, the stimulator as removed. Adverse reactions after 1 year (N = 25): voice alteration (7), increased seizure frequency (6), coughing (5), dyspnoea (3), pain at stimulation site (2), nonconvulsive status (2), insomnia (2) Positive effects after 1 year (N = 25): Better mood (15), Improved attention (14), Successful aborting seizures (magnet) (7), shortened postictal phase (6).

Conclusion: VNS is a safe, well-tolerated and effective treatment option for children with intractable epilepsy. The effect seems to be sustained over a prolonged period, and in accordance with previous findings in adults, to increase over time. The high frequency of positive effects on mood and attention is noteworthy.

T339
VAGUS NERVE STIMULATION: LONGITUDINAL LONG-TERM FOLLOW UP IN ALL PATIENTS IN CZECH REPUBLIC TREATED OVER FIVE YEARS

R. Kuba, M. Bro¢zdil*, M. Kalina†, T. Proch¢zka†, J. Hovorka‡, T. Nedal‡, J. Hada§, K. Broovi¢§, L. Faladovi¢¶, V. Sebroovi¢¶, V. Komi¢rek¶, P. Marusi¶, H. Olejkovi¢**, J. Zi¢rubövé§, and I. Rektor**

**St. Anne's Hospital, Brno, Czech Republic; †Epilepsy Center Na Homolce Hospital, Prague, Czech Republic; ‡Na Frantisku*

*Hospital, Prague, Czech Republic; §Centre For Epileptology and Epileptosurgery, Thomayer Teaching Hospital, Prague, Czech Republic; ¶Charles University, Motol Hospital, Prague, Czech Republic; and **Brno University Hospital and Faculty of Medicine, Masaryk University, Brno, Czech Republic*

Purpose: The purpose of this study was to analyze the outcome of patients treated by the use of VNS over 5 years.

Method: We performed retrospective, multicenter, open-label study to evaluate the efficacy of vagus nerve stimulation (VNS) in all patients in Czech Republic treated more than 5 years. 90 patients were included. All suffered from refractory epilepsy and in all of them resective surgery was excluded.

Results: The mean last follow-up was 6.6 ± 1.1 years, i.e. 79 ± 13 months. Till the last follow-up, 12.3% of patients dropped out. The median percentage number of seizures in the whole group gradually decreased from 41.2 seizures/month (s/m) in the prestimulation period to 12.4 s/m at last follow-up visit. The average percentage seizure reduction was 63.2%. The responder rate in our series is in concordance with the decrease of overall seizure frequency. 1 year after the onset of VNS there were 44.4% responders and this number increased up to 58.7% at 2 years follow-up. There were 64.4% responders 5 years after the onset of VNS and at the last follow-up visit. At the last follow-up, 21.1% patients had 90% seizure reduction, and 6.7% patients were completely seizure-free. The separate analysis of patients younger than 16 years showed worse efficacy of VNS in comparison to the whole group. Complications and/or chronic adverse effect occurred in 13.3%.

Conclusion: VNS is a very effective and safe method for treatment of refractory epilepsy. Long-term data showed that in patients treated by VNS gradual improvement occurred.

T340
PROSPECTIVE LONGITUDINAL 10-YEAR SEIZURE OUTCOME OF RESECTIVE EPILEPSY SURGERY IN SWEDEN

A. Edelvik, B. Rydenhag*, R. Flink†, and K. Malmgren**Sahlgrenska Academy At Gothenburg University, Göteborg, Sweden; and †Akademiska University Hospital, Uppsala, Sweden*

Purpose: The long-term seizure outcome of epilepsy surgery is not well characterized. Length of follow-up has been associated with poorer outcomes. Few studies report the proportion of patients with sustained seizure freedom. This study aims at furthering knowledge about long-term outcome of resective epilepsy surgery.

Method: The Swedish National Epilepsy Register encompasses data on all patients operated since 1990. Long-term prospective follow-up 5 and 10 years after surgery was initiated in 2005. Patients operated 1995-97 underwent a semistructured telephone interview 2005–07, addressing the present seizure situation and changes since the 2-year follow-up, social situation, medication and driving.

Results: of 188 resective procedures 1995–1997 133 (71%) were temporal lobe resections (TLR), 55 (29%) various extratemporal (XTLR). 144/188 patients (77%) had 10 year follow-up, while 11/188 had been reoperated, 12/188 were dead and 21/188 were lost to follow up. 104/133 (78%) TLR patients had 10 year follow-up: 66/104 (63%) were seizure-free (compared to 61% at 2 years), 30/104 (29%) had sustained complete seizure freedom since surgery (compared to 44% at 2 years). 40/55 (73%) XTLR patients had 10 year follow-up: 20/40 (50%) were seizure free (compared to 40% at 2 years) and 12/40 (30%) had sustained complete seizure freedom since surgery (compared to 36% at 2 years).

Conclusion: In this study of seizure outcome 10 years after resective epilepsy surgery the seizure free rates are similar to the 2-year follow-up and higher for TLR. The proportion of patients with sustained complete seizure freedom since surgery is lower than at the 2-year follow-up.

T341
VAGUS NERVE STIMULATION FOR PATIENTS WITH GENERALIZED SEIZURES – A VNS PATIENT OUTCOME REGISTRY STUDY

P. Boon, V. De Herdt*, I. Dewaele*, and I. Danielsson†*Ghent University Hospital, Ghent, Belgium; and †Cyberonics, Inc, Houston, Texas*

Purpose: The purpose of this study was to determine the effectiveness of vagus nerve stimulation (VNS) among patients reporting generalized seizures.

Method: Query of the VNS Patient Outcome Registry yielded a constant cohort of patients with generalized seizures and data regarding changes in seizure frequency and quality of life at 3 and 12 months after implantation with the vagus nerve stimulation (VNS) device. of the 524 patients, 5 reported having other types of seizures in addition to generalized.

Results: The mean age at implantation was 26.1 (SD15.8); age at onset of epilepsy was 6.3 years (SD8.9). of the 524 patients, 270 (51.5%) were males, 90 (17.9%) were institutionalized, and etiology was unknown for 367 (70%). Median reduction in seizure frequency was 46% and 56%; =>50%: 48% and 56%; =>75%: 28% and 37%; =>90%: 16% and 21% (3 and 12 months, respectively). Improvements (better or much better) in quality of life were alertness: 58% and 65%; postictal: 47% and 53%; clusters: 39% and 44%; verbal skills: 39% and 44%; mood: 39% and 50%; achievements 24% and 31%; memory: 26% and 36% (3 and 12 months, respectively).

Conclusion: After 12 months of VNS, more than half of these 524 patients with generalized seizures reported reductions =>50% in seizure frequency, and more than two-thirds reported improved alertness. Additional studies of VNS for generalized seizures are warranted.

T342
VAGUS NERVE STIMULATION IN PATIENTS WITH MEDICALLY INTRACTABLE PARTIAL EPILEPSY: 15 PATIENTS EXPERIENCE

F. Lpez Gonzslez, X. Rodriguez Osorio*, J. Pardo Ferndez*, A. Prieto Gonzalez*, M. Peleteiro Ferndez*, J. Ferndez Ferro*, and M. Noya Garcia**Hospital Clinico Universitario de Santiago de Compostela, Santiago de Compostela, Spain*

Purpose: Vagus Nerve Stimulation (VNS) is an alternative treatment for patients with drug-resistant epilepsy not amenable to surgery. We report results of the follow-up of 15 patients treated with VNS in our Epilepsy Unit.

Method: Descriptive retrospective analysis of adult patients with refractory epilepsy who are not candidates for surgery after a complete presurgical evaluation including magnetic resonance imaging and EEG-Telemetry showing ictal recordings, with VNS for at least a year of monitoring.

Results: The median age was 35 years old [27, 51] with a median duration of epilepsy of 6 years [4, 16]. Number of seizures per month ¡Ü5 appeared in 20% of patients, between 5–20 in 40% and 40% with >20 episodes. Mean of AEDs in use prior to implantation was 3.3 (3–4). Mean period of follow up was 20.2 months (12–36). Mean intensity of stimulation was 1.43 mA (0.5–3). ±50% reduction in seizures occurred in 40% of the patients (n=6) (one became seizure free and 4 diminished frequency 75%). Among poor responders (n=9), who are 71.4% of the patients with >20 episodes, there was reduction in frequency <40% (13.3%) in 2, improvement in duration in 4 (26.6%) and no response in 3 (20%). 33.3% (n=5) suffered secondary effects (dysphonia, dyspnea or cough), all disappeared after diminishing intensity of stimulation.

Conclusion: VNS is a safe and well tolerated therapeutic option in most of our patients. Efficacy results, with 50% reduction in total seizure frequency in 40% of our patients, agree with literature data (DeGiorgio et al. Epilepsia 2000;41:1195–1200).

T343
EPILEPSY SURGERY WITH GAMMA KNIFE: SINGLE CENTER'S RESULTS

A. Artiges, N. Massager, P. Van Bogaert, D. Devriendt, P. Tugendhaft, and B. Legros
ULB – Hôpital Erasme, Brussels, Belgium

Purpose: Epilepsy surgery is an effective treatment for refractory focal epilepsy (RFE). Surgery with Gamma knife is an alternative developing technique. We reviewed all patients with RFE treated with gamma knife in our institution.

Method: We retrospectively reviewed the charts of 11 patients with RFE treated with gamma knife in ULB-Hôpital Erasme. Patients were separated in 3 groups according to the nature of the supposed epileptogenic lesion. Group 1 corresponds to 7 patients with hippocampal sclerosis, group 2 to 3 patients with hypothalamic hamartoma and group 3 to 1 patient with cavernous haemangioma located in eloquent cortex. Mean follow up was 36.9, 36.3 and 43 months respectively for groups 1, 2 and 3. The mean irradiation dose was 22.4, 17.3 and 25 Gy respectively.

Results: At last follow up, in group 1, no patient is seizure-free. 2 patients had a dramatic decrease in seizure frequency, one being almost seizure free, 2 patients conserved only auras and there was no change for 3 patients. In group 2, 1 patient had a spectacular decrease in seizure frequency and there was no change for 2 patients. In group 3, the patient is seizure-free. In term of morbidity, in group1, 1 patient (14%) had a delayed temporal lobe oedema requiring a temporal lobectomy and in group 2, 1 patient developed a nystagmus, probably due to a brainstem irradiation-induced lesion.

Conclusion: Gamma knife represents an interesting noninvasive technique for epilepsy surgery, but its indications and effectiveness should be evaluated in well-designed multicenter prospective studies.

T344
DEEP BRAIN STIMULATION IN LESIONAL TEMPORAL LOBE EPILEPSY

C. Boëx, S. Vulliémoz*, R. Tyrand*, L. Spinelli*, G. Foletti†, A. Rossetti†, E. Pralong†, C. Pollo†, and M. Seeck**
**University Hospital of Geneva and Lausanne, Switzerland; and †University Hospital of Lausanne, Lausanne, Switzerland*

In patients with pharmacologically intractable epilepsy who are not eligible for surgery, deep brain stimulation is currently under evaluation as an alternative treatment. In the present study, we report the effects of high (HFS – 130 Hz) vs low (LFS – 1 Hz) frequency stimulation with symmetrical versus asymmetrical biphasic pulses of the principal epileptogenic focus, in 5 patients with unilateral hippocampal sclerosis. The periods before, during HFS and LFS, as well as after up to 2 hours (post-HFS, post-LFS) were analyzed. HFS with biphasic symmetrical pulses was associated with a reduction of the interictal discharges for 2 out of 5 patients. Comparison of HFS periods and post-HFS periods indicated that HFS with symmetrical pulses was followed by a reduction of interictal discharges in 4 out of 5 patients and interrupted subclinical seizures in 2 patients. HFS with asymmetrical pulses did not reduce interictal discharges neither during nor after HFS. LFS with symmetrical pulses was associated with an increase of interictal discharges in 1 out of 5 patients. Interictal discharges after LFS reduced in 1 out of 5 patients. Our findings indicate that HFS with symmetrical biphasic pulses may have a more beneficial effect on interictal discharge reduction compared to asymmetrical pulses, which may even last after the stimulation stopped. HFS with asymmetrical pulses is preprogrammed in some commercial stimulation devices, and its use may explain the suboptimal efficacy of DBS reported elsewhere in patients with hippocampal sclerosis.

T345
QUALITY OF LIFE AFTER EPILEPSY SURGERY IN CHILDREN AND ADOLESCENTS

S. Koskinen, P. Putkonen*, M. Granström†, and E. Gaily†*
**Helsinki University of Technology, Espoo, Helsinki; and †Helsinki University Central Hospital (HUCH), Helsinki, Finland*

Purpose: Previous studies suggest that health related quality of life (HRQOL) of adults is improved after epilepsy surgery, but similar data are scarce in children and adolescents. We measured HRQOL in patients most of whom were less than 16 years old at surgery.

Method: Questionnaires measuring postoperative HRQOL were sent to 118 patients operated in HUCH from 1991 through 2004. 15D was used for patients over 16 years, 16D for ages 12–15 years and 17D for ages 0–11 years and disease specific QOLIE-31 for all patients. Clinical data was obtained from hospital charts.

Results: Forty-eight patients responded (29 patients <16 years old). The mean age at surgery was 8 years (range 0.4–15.6y) in children and adolescents and 32.4 years in adults (range 17–59y). Twenty patients underwent extratemporal resections, 24 temporal resections and four callosotomy. After one year, 31 patients had Engel I outcome, seven Engel II, five Engel III and five Engel IV. The mean HRQOL follow-up after operation was 4.4 years (range 0.28 -12.06y). The mean overall HRQOL scores were 0.85 (16D-17D), 70.7 (QOLIE-31) and for adults; 0.89(15D) and 71(QOLIE-31). Seizure outcome correlated with QOLIE-31 scores ($p=0.000$, $r=0.578^{**}$) and with 16D-17D scores ($p=0.005$, $r=0.579^{***}$) in children and adolescents. Follow-up interval did not covary with HRQOL results ($p=0.557$ for QOLIE-31 and $p=0.980$ for 15D-17D).

Conclusion: Good seizure outcome is associated with better quality of life by the instruments used in this study in children and adolescents after epilepsy surgery. The length of time after operation did not affect HRQOL scores.

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T346
SURGICAL TREATMENT OF SYMPTOMATIC EPILEPSY CAUSED BY FOCAL CORTICAL DYSPLASIA AT CHILDREN

L. Marushchenko, Y. Orlov, and I. Protsenko
Institute of Neurosurgery, Kiev, Ukraine

Purpose: Children with malformations of cortical development often suffer from intractable focal epilepsy. At children with resistance epilepsy the congenital disorder of neuronal migration have diagnosed in 12–25% cases. Many malformations of cortical development are genetically determined. This report considers clinical findings and seizure outcome of children with focal cortical dysplasia undergoing resective epilepsy surgery.

Method: We retrospectively analyzed the results of surgical treatment of intractable epilepsy of 5 children (2 male, 3 female) with focal cortical dysplasia. The age of children was from 2 to 5 year. All cases of resection operations were used with application of intraoperative electrocorticography. Seizure outcome was classified to Engel's score.

Results: The congenital disorders of neuronal migration are major reasons of drug resistance epilepsy. The basic clinical manifestations of cortical dysplasia were epileptic paroxysm with an early debut, resistant to anticonvulsive therapy with transformation in the partial forms of

epilepsy. The psychomotor retardation was at all patients. The characteristic feature was delay of speech development (at localization the focal cortical dysplasia in a dominant hemisphere) and also contralateral pyramidal insufficiency. After, on average, 2 years since treatment, 3 children became seizure free (Engel I) and 2 children the frequency of seizures decreased (Engel III).

Conclusion: High-frequency of epileptic syndromes at focal cortical dysplasia, the high risk of origin of refractory epilepsies with development of incapacitating children requires early diagnostics and optimum treatment of this category of patients. A timely diagnostics and resection operation allows successfully treating this category of patients, warning their severe invalidity.

T347
PROGNOSIS AFTER AMIGDALOHIPPOCAMPECTOMY IN 43 PATIENTS WITH MESIAL TEMPORAL SCLEROSIS

X. Rodriguez Osorio, J. Pardo Fernandez, J. Lopez Gonzalez, A. Arcos Algaba, A. Prieto Gonzalez, M. Peleteiro Fernandez, and M. Noya Garcia
Hospital Clinico Universitario. Santiago de Compostela. Spain

Purpose: Surgery is the treatment of choice in drug-resistant temporal lobe epilepsy and it provides the best results in epilepsy surgery. We analyze diagnostic protocol and prognosis in 43 patients.

Method: Retrospective descriptive analysis of 43 operated patients with mesial temporal (MT) epilepsy between 1998 and 2007 with 1 year of follow-up. Presurgical evaluation included magnetic resonance imaging (MRI) with epilepsy protocol, EEG-Telemetry with ictal and interictal recordings, neuropsychological evaluation and, if necessary, PET/SPECT, intracarotid sodium amobarbital procedure (ISAP) or foramen ovale electrodes. Partial resection of the anterior temporal lobe with amigdalohippocampectomy (Spencer technique) was performed. Prognosis was established with Engel scale.

Results: The median age was 33 years old [29.5, 37.5] with a median duration of epilepsy of 21 years [13.25, 29]. 90.7% (n=39) of patients presented with MT sclerosis in the MRI, resulting the most lateralizing test followed by ictal EEG-Telemetry (88.4%, n=38). ISAP showed a good contralateral hemisphere function in 72.2% of cases performed and 75% (n=3) of PET corresponded with the focus. Pathology confirmed MT sclerosis in 74.42%. Postsurgical complications (meningitis, epileptic status) appeared in 11.6%, none with definitive sequaela. Final outcome results were good in 90.7% of cases (84.61% Engel I and 15.39% Engel II) with a mean follow-up of 43.5 months (DS=9.65).

Conclusion: A correct following of the diagnostic protocol is helpful in identifying patients with MT epilepsy associated with structural changes in hippocampus (74.42%), and also contributes to provide these patients a good outcome after surgery (90.7%, Engel I and II).

T348
FUNCTIONAL HEMISPHEROTOMY IN ADULTS WITH INTRACTABLE EPILEPSY SYNDROMES – REPORT OF 4 CASES

B. Steinhoff, A. Staack*, S. Bilic*, A. Schulze-Bonhage†, and J. Zentner‡*
**Epilepsy Center Kork, Kehl-Kork, Germany; †Epilepsy Center, Albert-Ludwigs University of Freiburg, Freiburg, Germany; and ‡Department of Neurosurgery, Albert Ludwigs University, Freiburg, Germany*

Purpose: Functional hemispherotomy (FH) is mainly performed in children with catastrophic epilepsies and preexisting hemiparesis including the hand function. It is common sense that mainly patients at young ages with more or less complete loss of their hand function are suitable candidates for FH. However, we feel that FH should be considered also in some adults with devastating unilateral epilepsy syndromes.

Method: We report four cases of adults who underwent FH because of their intractable epilepsy syndromes. Three of the four patients had a reduced but not completely lost hand function. Careful outweighing of the risk-benefit ratio still led to the decision to perform FH in order to achieve postsurgical seizure freedom with the highest possible probability.

Results: All patients had a surgery outcome of Engel Class I, one of them suffered from postoperative psychogenic nonepileptic seizures which were treated successfully by consequent psychotherapy. No clinically relevant complications occurred.

Conclusion: We want to point out that FH is a possible surgical option in cases with catastrophic epilepsies of adulthood. Patients and relatives should strongly consider that the loss of a usually presurgically impaired hand function may be outweighed by the potential seizure outcome of FH. In all of our cases patients and relatives agreed that the surgical outcome led to a narked improvement of quality of life and that it had been the right decision to proceed with FH in spite of the natural negative impacts of the operation.

T349
BOSTON NAMING TEST IN PREDICTING SIDE OF SURGERY IN TEMPORAL LOBE EPILEPSY PATIENTS

P. Marusic, J. Amlerova*, J. Pikova*, and A. Javurkova*,†*
**Charles University, 2nd Medical School, Motol Hospital, Prague, Czech Republic; and †University Hospital Kralovske Vinohrady, Prague, Czech Republic*

Purpose: Results of neuropsychological testing may be helpful in predicting the side of surgery and possible postoperative functional decline. Memory functions are routinely assessed pre- and postsurgically in temporal lobe epilepsy (TLE) patients, confrontation naming tasks are used less routinely. The aim was to examine the utility of Boston Naming Test (BNT) in epilepsy lateralization and compare this test to delayed verbal memory score and FSIQ subtests.

Method: We included 40 left-speech dominant (based on Wada test) adult TLE patients; 22 left-sided (mean age 34,9 years, FSIQ 97) and 18 right-sided (mean age 37,5 years, FSIQ 102). Subjects with FSIQ <70, age >65 years, multifocal lesions or atypical language were excluded. Patients were examined with standard neuropsychological battery and BNT.

Results: All right TLE patients scored >50 in BNT, only six left TLE patients achieved such result ($p<0,001$), in FSIQ subtests 21 patients showed marked asymmetry in either direction, however only marked VIQ-PIQ difference pointed to the right side ($p<0,05$). The prediction of side of surgery was also less accurate with poor delayed verbal memory ($p<0,05$). All left-sided patients with BNT score >50 except one had major hippocampal involvement and poor delayed verbal memory score. Combination of low BNT score with normal delayed memory score pointed towards left extrahippocampal TLE.

Conclusion: In our study BNT showed to be more powerful predictor for side of surgery compared to delayed memory score and FSIQ subtests. Poor BNT score may be in some left TLE patients the only abnormal neuropsychological finding.

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E350
MEMORY AND EPILEPSY

S. Shaafi, M. Chenaghlou, and M. Nikanfar
Tabriz University of Medical Science, Iran

Purpose: Neuropsychological studies show memory defects in epileptics. These changes may be due to many factors such as etiology of epilepsy, age of seizures onset, duration of illness, frequency and severity of seizures. Also antiepileptic drugs and surgical treatments for epilepsy may be due to memory defects in patients with epilepsy. Repeated seizures and type of seizures are other factors that may cause structural and functional disturbances in epileptics. Although this fact is not mean that all patients with epilepsy have memory defects but shows that neuropsychological examination are more important in epileptics and must be performed in epilepsy clinics. The aim of this study is to evaluate the effect of variables such as etiology, age of onset and type of seizures, duration of illness, type AED, frequency of attacks with severity and incidence of memory defects in patients with epilepsy.

Method: 100 patients with known epilepsy (according to the international classification of epilepsy), 50 patients with tonic-clonic seizures and 25 patients with complex partial seizure and 25 patients with the other types of epilepsy were selected randomly. Then their demographic and historical data were filled in the questionnaire and Minimental status test was performed to evaluate their memory function. After gathering the information, statistical analysis was performed.

Results: From 100 patients 38% had severe memory defects.45% had moderate defects and 15% had not any defects in memory and 2% had mild defects. The most common effective variables were in order: the duration of illness, frequency of seizures, type of seizures, and age of onset.

Conclusion: Neuropsychological examination must be considered in epilepsy clinics as a routine exam. Cognitive function in epileptic patients is very important and must be pay attention for more detailed studies about the choice of drugs and intellectual performance and exercises in these patients.

E351
FREQUENCY OF NONCONVULSIVE STATUS EPILEPTICUS (NCSE) IN IMPAIRED LEVEL OF CONSCIOUSNESS

N. Jamil, M. Siddiqui*, A. Malik*, F. Shahab*, and K. Siddiqui†*
**Liaquat National Hospital, Karachi, Pakistan; and †King Fahad Medical City, Riyadh, Saudi Arabia*

Purpose: NCSE is an under reported, treatable cause of coma and has variety of clinical and EEG presentations.

Method: We retrospectively reviewed all EEG's in patients with impaired level of consciousness over four years from 2002–2006. Impaired level of consciousness was categorized into unconscious and semiconscious state's. All EEG's showing continuous epileptiform discharges were included. Findings of all these EEG's were divided into five sub-groups; generalized spikes and wave, generalized sharp and wave, focal spike and wave, focal sharp and wave and periodic lateralized epileptiform discharges (PLEDS).

Results: There were 785 EEG's recorded in patients with impaired level of consciousness. Out of which 56% (n=440) of patients were semiconscious and 44% (n=345) were unconscious. 1.5% (n=12) patients were identified with NCSE on EEG, 66.6% (n=8) were unconscious and 33.4% (n=4) were semiconscious. EEG findings in our patients with NCSE showed focal spike and wave seen in 4 (33%), generalized spike and wave 3 (25%), generalized sharp and wave 3 (25%), focal sharp and wave 1 (8.3%) and PLEDS in 1 (8.3%).

Conclusion: NCSE is a treatable entity which can be easily recognized by doing an EEG. Frequency of partial and generalized NCSE was almost same in our patients. Although in our cohort, numbers of patients with NCSE were small, as because awareness regarding this treatable cause for impaired level of consciousness was significantly low. We believe that there should be high index of suspicion of NCSE in intensive care and high dependency care settings and emergent EEG's should be performed, along with continuous EEG recording where available.

E352
FINDINGS ON MAGNETIC RESONANCE IMAGING IN CORRELATIONS WITH CLINICAL AND ELECTROENCEPHALOGRAPHIC PATTERNS IN TEMPORAL LOBE EPILEPSY

G. Melikyan
Erebouni University Clinic, Yerevan State Medical University, Yerevan, Armenia

Purpose: The objective of this study is to select the patients with TLE, analyze the EEG, MRI, and clinical data and to give criteria which can help to confirm the existence of pathogenic and organic centres of lesion.

Method: This study investigates the clinical course of 100 patients with temporal lobe epilepsy. We analyzed MRI, EEG and clinical data of 90 patients with mesial temporal lobe epilepsy: 45 patients with unilateral hippocampal sclerosis, 5 patients with bilateral hippocampal sclerosis, 20 patients with other temporal pathologies (uncinar gliosis, focal disgenesia, and mesiobasal vascular malformation), 20 patients with MRI-negative picture, and 10 patients with lateral temporal epilepsy. Ictal patterns were classified and correlated to signal abnormalities and volumetric measures of the temporal poles for HS- group.

Results: Psychomotor seizures were most frequent as an epileptic aura (46%), 26% had automatic seizures. Specific focal discharges were recorded in 59% of patients. Patients with anterior temporal sharp wave activity as the predominant interictal pattern tended to present asymmetry of temporal poles ($p < 0, 001$).

Conclusion: Psychomotor seizures were most frequent as an epileptic aura. Anterior temporal sharp-waves as an interictal pattern and RTA as an ictal pattern are the most frequent findings in patients with temporal lobe epilepsy due to unilateral HS. Temporal pole signal changes and volumetric reduction were commonly found in this group of patients, both abnormalities appearing always ipsilateral to the HS.

E353
LONG-TERM SURVIVAL OF STATUS EPILEPTICUS IN SERBIA: WHAT HAPPENS WITH PATIENTS A DECADE AFTER THE FIRST EPISODE?

A. Ristic, D. Sokic*, G. Trajkovic†, N. Vojvodic*, and S. Jankovic**
**Institute of Neurology Clinical Center of Serbia, Belgrade, Serbia; and †School of Medicine, University of Pristina, Kosovska Mitrovica, Serbia*

Purpose: To determine long-term survival in patients with status epilepticus (SE).

Method: We evaluated long-term survival in a cohort of patients treated for the first episode of SE between January 1, 1988 and December 31, 1997 at the Institute of Neurology CCS, Belgrade, Serbia. Patients were followed at yearly intervals until death or study termination. On the prevalence day (December 31, 2006), patients were categorized as alive or dead based on the last year's data. Etiology of SE was assigned as acute symptomatic (AS), progressive symptomatic (PS), remote symptomatic (RS), and idiopathic/cryptogenic (I/C).

Results: First episodes of SE occurred in 751 patients. A total of 120 patients (15.9%) died in 30-day period following SE. Of the 631 patients who survived, data for 207 patients (32.8%) were available on the prevalence date. In the later group, SE was caused by AS etiology in 65

(31.4%), PS in 29 (14%), RS in 38 (18.3%), and I/C in 75 patients (36.2%). There were 46 deaths (22.2%): 15 in AS, 20 in PS, 6 in RS, and 5 in I/C group. In 18 out of 36 patients death occurred during the first two years of follow up. The median duration of survival was significantly ($p<0.001$) shorter among patients with PS SE (2 years) in comparison to all other etiologies (10 years).

Conclusion: Approximately 1/5 of patients die within next 9 years after the first episode of SE. Patients with PS SE have significantly shorter survival in comparison with other SE etiologies.

E354
TEMPORAL LOBE EPILEPSY AND ACCELERATED FORGETTING

A. Yoshino, and Y. Tatsuzawa
National Defense Medical College, Tokorozawa, Japan

Purpose: Some patients with temporal lobe epilepsy (TLE) frequently complain of their forgetfulness a several weeks after their memorizing. These long-term memory difficulties are called accelerated forgetting. Some previous studies suggested that patients with TLE may have the accelerated forgetting. The present study estimated whether the left but not right mesial sclerosis (MS) accelerated the forgetting for verbal material.

Method: Eighteen patients with TLE who underwent 1.5 Tesla MRI of the brain participated in the study. Written informed consent was obtained from all participants after a detailed description of the study. Participants were assigned to 3 groups on the basis of existence and laterality of MS (left, 3; right, 6; no MS, 9). Participants were required to repeatedly learn a story from the WMS-R logical memory task to 80–100% correct. Long-term recall was subsequently tested 1 day, 1 week, and 4 weeks later. Recall rates were analyzed using repeated-measures ANOVA concerning 2 factors, subject group and time.

Results: There were no differences in age, education, length suffering from TLE, seizure frequency, number of antiepileptic drugs, MMSE score, and digit span among 3 groups. Concerning recall rates, an interaction between subject group and time was statistically significant; indicating that mean recall rate 4 weeks after the memorizing in the left MS group was lower than those in the right and no MS groups.

Conclusion: This result suggests that patients with left MS have accelerated forgetting for logical memory.

E355
NEUROPSYCHOLOGICAL OUTCOME OF TEMPORAL LOBE EPILEPSY SURGERY IN PATIENTS WITH POSTOPERATIVE SEIZURES AND UNSUCCESSFUL SURGICAL THERAPY

A. Abubakr, O. Onasanya*, and I. Wambacq†*
**Seton Hall University, New Jersey Neuroscience Institute, USA; and †Montclair University, Montclair, NJ, USA*

Purpose: Numerous studies have demonstrated significant improvement in cognition and memory following epilepsy surgery with good outcome (seizure-free). However, there is scanty information about any areas of cognition or memory that may improve in patients with suboptimal outcome. Therefore we assessed consecutive patients who had TL surgery and continued to have postoperative seizures.

Method: Medical records of patients with intractable TLE who underwent temporal lobectomy were reviewed. All patients had detailed phase I presurgical evaluation and subsequently had surgery. Detailed neuropsycholoy assessment was carried out in all patients preoperatively as well as 3 month and 12 month following surgery. Patients with Engel class 3 outcome were included in the study.

Results: Thirteen right-handed patients (age range 19–52 years) were included in the evaluation. Four had right and 9 had left temporal lobectomy. Various neuropsychological tests were assessed before and after surgery and the results were classified as improved, worsened or no changes. Regarding IQ result there were no differences in the number of patients with improved/unchanged and worsened scores (approximately 50% in each group). Similarly for verbal and visual-spatial memory there is no substantial difference between the number of patient's improved/unchanged and worsened. However, there is substantial number of patients improved on attention/executive function, language and psycho-emotional function.

Conclusion: Despite suboptimal epilepsy surgery outcome, this study demonstrates that attention and executive function, language, and psycho-emotional function improved substantially in this sample of patients. These results may be included to help counsel patients about some cognitive improvement in a setting of incomplete resolution of seizures following surgery, which may improve their quality of life.

E356
DAYTIME SLEEPINESS IN GEORGIAN POPULATION WITH EPILEPSY. A PILOT STUDY

L. Zhizhiashvili, L. Maisuradze†, G. Lomidze*, I. Toidze*, L. Abesadze*, and S. Kasradze**
**Epilepsy Prevention and Control Centre, Tbilisi, Georgia; and †Lab of Neurobiology of Sleep and Wakefulness Cycle, I. Beritashvili Institute of Physiology, Tbilisi, Georgia*

Purpose: Epilepsy is occurred in 0.57% of Georgian general population. As several reports indicate that sleep disorders and daytime sleepiness (DS) frequently coexist with epilepsy, the first questionnaire study was carried out to estimate the prevalence of DS among Georgian epilepsy patients.

Method: The unpaid volunteer subjects (n=175; mean age 33.33 years, SD=12.908, range 18–69 years) consisting of 91 healthy individuals (18 males, 73 females) and 84 patients with diagnoses of epilepsy (28 males, 56 females) completed Epworth Sleepiness Scale. The outpatients with epilepsy were divided into two groups: treated (T) with antiepileptic drugs (AEDs), 60 subjects (19 males, 41 females), and untreated (UT), 24 subjects (9 males and 15 females). Data analyses were performed by SPSS 13.0 for Windows.

Results: 8.7% of healthy individuals and 16.7% out of total epilepsy patients had DS. Percentage of AEDs-taking individuals with DS prevailed healthy subjects having this problem (18.3% vs. 8.7%; $p=0.084$). The overall prevalence of DS in epilepsy patients was higher in males than in females (28.6% vs. 10.7%; $p<0.05$). Although there were no significant differences in DS between the UT (12.5%) and T (18.3%) patients, DS was more prevalent among males than females in the UT group ($p=0.017$).

Conclusion: The findings of present study are in concordance with the literature about the accompanying epilepsy with DS, particularly during AEDs medication. Unlike the healthy individuals the gender differences in DS were noted in epilepsy patients, and among untreated patients, in particular. Further research is needed to investigate epilepsy with sleep problems.

E357
CLINICAL REVIEW OF ACUTE SEIZURE AMONG CHILDREN WHO VISITED THE EMERGENCY ROOM IN MASAN SAMSUNG HOSPITAL FROM 2004 TO 2006

J. Lee, S. Kim†, W. Lee*, and K. Cho**
**Sungkyunkwan University Masan Samsung Hospital, Korea; and †Hallym University Kangnam Sacred Heart Hospital, Korea*

Purpose: The purpose of this study was to evaluate acute childhood seizures, one of the most important causes of emergency room visits, to provide appropriate medical services.

Method: We reviewed the medical records of 433 (4.6%) pediatric patients with acute seizures that visited the emergency room at Masan Samsung hospital from 2004 to 2006.

Results: The male to female ratio was 1.4:1 and the mean age was 40.9, 34.9 months range. The order of geographical distribution was Masan, Changwon, Haman, and others. Fever was present in 40.6% of patients; December (14.8%) was the most frequent month for visits and generalized tonic–clonic seizures (62.7%) were the most common type of seizure. The average frequency and duration of the seizure was 1.5, 1.0 and 6.7, 13.2 minutes respectively. Febrile seizures were present in 69.7% of patients and afebrile seizures in 30.3%. The causes of the febrile seizures were acute pharyngotonsillitis (44.6%), acute bronchitis, gastroenteritis, pneumonia, urinary tract infection, and unknown origin, in order of frequency. The most common cause of an afebrile seizure was epilepsy (71.5%) followed by a benign convulsion with mild gastroenteritis (BCwMG), sequela of a perinatal brain injury or brain malformation, and acute CNS infection. Evaluation of the causes of an acute seizure according to age showed that febrile seizures, epilepsy, and the sequela of perinatal brain injuries were more common between 2 and 6 years of age and epilepsy, febrile seizures and acute CNS infection, in order of frequency, were common between 6 and 15 years of age. Many patients, 49.4%, were discharged without admission.

E358
REVERSIBLE EFFECTS OF ANTIEPILEPTIC DRUGS ON THYROID HORMONES IN MEN AND WOMEN WITH EPILEPSY – A PROSPECTIVE RANDOMIZED DOUBLE-BLIND WITHDRAWAL STUDY

M. Lossius,¶, T. Erik†,‡, P. Mowinckel§, and L. Gjerstad†,‡*
**National Centre for Epilepsy Norway; †Division of Clinical Neurosciences, Rikshospitalet Medical Centre, Norway; ‡Faculty of Medicine, University of Oslo, Norway; §Division Woman And Child, Ullevål University Hospital, Norway; and ¶Akershus University Hospital, Norway*

Purpose: Antiepileptic drugs (AEDs) may affect serum thyroid hormone concentrations in men and women. The aim of this study was to evaluate thyroid function in men and women with epilepsy on AED monotherapy before and after double blinded withdrawal of AED treatment, and see if possible effects were reversible.

Method: The study was prospective, randomized and double blinded. 168 patients were included and 160 randomized to withdrawal or not and 150 (80 females, 70 males) patients went through the intervention and was included in the study for 12 months. Complete serum samples from before and 4 months after completed withdrawal/no withdrawal were obtained from 130 patients (63 females, 67 males).

Results: Following AED-withdrawal we found significant increase in serum free thyroxine (FT4) in men (n= 20) (mean increase 1.91 pM, p=0.02) and women (n= 19) (mean increase 2.05 pM, p=0.001) treated with carbamazepine (CBZ), compared to the nonwithdrawal group. Serum free triiodothyronine (FT3) decreased significantly in valproate (VPA) treated women (n= 8) in the withdrawal group (mean decrease -0.54 pM, p=0.04) compared to the nonwithdrawal group. The other AEDs used could not be analyzed because of few cases.

Conclusion: CBZ reduced FT4 concentrations in men and women with epilepsy. Conversely, VPA was associated with increased serum FT3 levels in women. Our study also showed that these changes were reversible, even after years on treatment.

E359
HANDEDNESS, NEUROPSYCHOLOGY AND EPILEPSY

T. Bodner, G. Walser, E. Trinka, M. Delazer, and T. Benke
University Hospital Innsbruck, Germany

Purpose: Neuropsychological evaluation of patients before epilepsy surgery includes the assessment of handedness and the lateralization of language functions. The aim of the study is to compare the predictive value of a handedness inventory and a pegboard test for language lateralization.

Method: We retrospectively analyzed 154 consecutive patients (median age = 38.1; f:m 83:71) with temporal or frontal lobe epilepsy who were evaluated for epilepsy surgery in the comprehensive Innsbruck Epilepsy Surgery Program (INES). We used data from the Edinburgh Handedness Inventory (EHI), the Pegboard test and the WADA-test.

Results: Cerebral dominance for language was restricted to the left hemisphere (wada lateralization index from +60 to +100) in 106 out of 140 (76 percent) right handed (EHI from +60 to +100) patients, and in about 4 out of 14 (29 percent) of non-right handers. 54 out of 75 (72 percent) of right handed patients with a left-sided epileptic focus presented left-sided cerebral language dominance. Correlation analyses of the three different measures (EHI, Pegboard test, WADA-test) revealed a significant correlation between the EHI and the WADA lateralization index (Pearson 0.259, p-value=0.001).

Conclusion: Language lateralization correlates significantly with the EHI but not with the pegboard test. In order to precisely determine language dominance lateralization, handedness alone is an insufficient predictor and the WADA-test, which is still considered the gold standard for language lateralization, must also be applied.

E360
ELECTROENCEPHALOGRAPHIC CHANGES IN PATIENTS WITH RENAL FAILURE

D. Milikic, and L. Radulovic
Clinic of Neurology, Clinical Centre of Montenegro, Podgorica, Montenegro

Purpose: Renal failure, particularly when acute in onset or rapidly progressive, is commonly associated with encephalopathy. The electroencephalogram (EEG) remains for a long time normal. Abnormality in EEG appears with diffuse slowing and may show triphasic complex and sometimes paroxysmal activity that includes spikes or sharp waves. The aim of this study was to correlate the EEG abnormalities with laboratory findings, neurological impairment as well divided according to the duration of hemodyalisis, type EEG changes, the level of creatinine clearens, duration of dialysis and neurological abnormalities.

Method: EEG records in 24 patients undergoing hemodialysis for a period of 1–10 years were related to minimental state and biochemical parameters.

Results: EEG abnormalities were most common in patients who were under dialysis between 5–10 years (62.5%) and 3–5 years (50%). Increased creatinine clearence and EEG abnormalities were most common during the first years of dialysis, later they were less significant.

Conclusion: EEG may deteriorate during or after dialysis, sometimes before any clinical change has occurred, showing increased paroxysmal activity with spikes and sharp waves. In our patients, most EEG abnormalities were found in patients who were longer under hemodyalisis. They consisted of background slowing (in theta range), followed by a mixture of unspecific and epileptiform changes.

E361
THALAMIC TUMOR AND PHOTOSENSITIVE ABSENCES

V. Iváñez, J. Ojeda, M. Abenza, and M. Aguilar-Amat
Hospital Universitario La Paz, Madrid, Spain

Purpose: We describe a patient with an otherwise clinically typical juvenile absence epilepsy with photosensitive seizures associated with a

unilateral thalamic tumor. Structural lesions are very unusual in apparently idiopathic generalized epilepsies (IGE); we have not found any other case of photosensitive absences associated with thalamic lesions.

Method: Woman, 18 years old, who suffered an episode of generalized tonic-clonic seizure when she was 15. At that time, she reported she had been having episodes of absences several times in a month. She provoked them by watching TV or with flicker stimuli. An EEG showed a photoparoxysmal response elicited by 10 Hz intermittent photic stimulation. MRI and spectroscopy showed a right thalamic lesion suggestive of a low grade astrocytoma. Lamotrigine was started at 50 mg tid. Seizures did not disappear until she stopped provoking them.

Discussion: Thalamic lesions have been associated with generalized epilepsies in few cases. None of them were clinically compatible with IGE or presented photosensitive seizures. The well-known thalamic-cortical connections in the pathogenesis of absences support the idea that this is not an independent association. The presence of photosensitive absences also suggests that thalamus may play a role in the patogenesis of photosensibility.

Conclusion: Although very scarce, a thalamic tumor may cause a clinically typical IGE (Juvenile Absence Epilepsy in this case) and photosensitive absences. This observation questions the recommendation that MRI studies are not mandatory in IGE.

E362
EXPRESSION OF LAMININ ß1 AND INTEGRIN A2 IN BRAIN TISSUE OF PATIENTS WITH INTRACTABLE EPILEPSY

Y. Wu, X. Wang†, J. Li†, X. Mo*, Y. Zeng†, T. Lin†, Z. Xi†, F. Xiao†, and J. Zheng**
**Guangxi Medical University, Guangxi, China; and †Chongqing Medical University, Chongqing, China*

Purpose: To investigate the expression of laminin β1 and integrin α2 in the anterior temporal neocortex tissue of patients with intractable epilepsy and explored the role of these molecules in the pathogenesis of this disease.

Method: Immunohistochemistry and immunofluorescence were used to test the expression of laminin β1 and integrin α2 in samples (from the brain bank of our department, n=32) of surgically removed anterior temporal neocortex tissues from intractable epilepsy patients, and the results were compared with those of controls (n=10).

Results: We found that laminin β1 and integrin α2 protein expression was significantly increased in the anterior temporal neocortex as compared with controls (immunohistochemistry optical density: laminin β1 = 0.36±0.01 vs. 0.10±0.03 for control; integrin α2 = 0.42±0.02 vs. 0.04±0.01 for control; P <0.05). Immunofluorescence staining indicated that laminin β1 and integrin α2 accumulated in the plasma membrane and cytoplasm, with strong fluorescence intensity in the anterior temporal neocortex tissue of patients with intractable epilepsy.

Conclusion: Our work demonstrates that laminin β1 and integrin α2 expression is elevated in anterior temporal neocortex tissue from patients with intractable epilepsy.

E363
LEVETIRACETAM MONOTHERAPHY FOR LATE POSTSTROKE SEIZURES IN ELDERLY

G. Kutlu, Y. Gomceli, Y. Unal, and L. Inan
Ministry of Health Ankara Research and Training Hospital, Ankara, Turkey

Purpose: Stroke is the most common cause of seizures in elderly. Antiepileptic drugs are used to treat most patients with late poststroke seizures. The aim of this study was to evaluate efficiency and tolerability of levetiracetam (LEV) in patients at the age of 60 or older with late-onset poststroke seizures.

Method: This prospective study evaluated patients of 60 years of age or older, who had at least two late-onset poststroke seizures and were given LEV monotherapy. Demographic data, features of seizure and stroke were recorded. Outpatient visits were made after 2, 4, 6, 9 and 12 months and every three months thereafter, and the effectiveness and tolerability of LEV were investigated.

Results: Thirty-four patients with a mean age of 69.76±6.41 were included in this study. Average seizure frequency before treatment was 3.61±3.02 /month. Mean follow up time was 17.68±3.24. 82.4% of the patients were seizure free at a daily dose of 1000–2000 mg, seven patients (20.6%) had side effects, but LEV was discontinued in one patient because of severe somnolence. The treatment of two patients were switched to the another antiepileptic drug because of uncontrolled seizures despite a dose increase up to 3000 mg/day.

Conclusion: LEV monotherapy can be effective and well tolerated in late-onset poststroke patients for elderly.

E364
PREDICTING FACTORS OF OUTCOME AFTER POST-STROKE STATUS EPILEPTICUS

J. Kim, E. Sengee, and J. Lee
Chungnam National University Hospital, Taejon, Korea

Purpose: Status epilepticus (SE) is a major neurological emergency associated with significant mortality. As the elderly population is rapidly increasing in Korea, SE associated with cerebrovascular disease (CVD) has increasing importance in clinical practice.

Method: The aim of this study was to find the prognostic factors predicting the outcome of poststroke SE. We performed this retrospective study for patients who admitted our hospital between Jan, 2000 to May 2007. Included patients had seizure lasting more than 30 minutes or recurrent seizures without regaining of consciousness. All the patients had previous or newly developed CVD verified with neuroimaging studies. Every patient underwent EEG during or just after the SE. Nonconvulsive SE or subtle SE was included only in the case of identifiable electrical SE activities in the EEG. We analyzed age, sex, stroke risk factors, types of SE, types of stroke, onset of SE after the stroke, interval between SE onset and initial treatment, and the duration of SE as a prognostic factors of SE.

Results: 38 patients were enrolled in this study. Mean age was 71.1,8.4, and men were 21 (women 17). Ischemic CVD were 26 (cortical 20, subcortical 6) and hemorrhagic CVD were 12 (ICH 10, SAH 2). The overall mortality rate in poststroke SE was 23.7% (9 patients). Three patients expired due to SE, and 6 patients expired due to medical complications. Gender, SE type, stroke risk factors, stroke type, cortical involvement, and previous SE history did not significantly affect the outcome of poststroke SE. Older age and delayed time to initial treatment tend to show poor prognosis. Early-onset SE (<30 days after stroke), longer duration of SE (> 2 hours) were significant poor prognostic factors of poststroke SE (p<0.05).

Conclusion: We conclude that higher mortality rate in poststroke SE is associated with early onset of poststroke SE and longer duration of SE.

E365
EXTENT OF SUBDURAL ELETRODE RESECTION AND SURGICAL OUTCOME OF EPILEPSY: INTRACRANIAL EEG ANALYSIS

H. Kim, S. Lee*, D. Kim†, K. Chu*, and C. Chung**
**Seoul National University Hospital, Korea; and †Kon Kuk University Hospital, Korea*

Purpose: The objective of this study is to identify how the extent of resection guided by subdural electrodes affects surgical outcome.

Method: Intracranial EEGs were analyzed in the consecutive 179 patients who underwent resective epileptic surgery between 1996 and 2003. We reviewed MRI, intracranial EEG patterns and extent of resection. We analyzed the relationship between the surgical outcome and the various factors: the presence of lesion, the rhythm, focality, and spreading pattern of ictal discharges, the inclusion of ictal onset zone, pathlogical delta slowing, or frequent interictal spikes in the resection. We also divided the patients into three groups according to the inclusion of early spreading electrodes in the resection.

Results: The average follow-up period was 7.1 years and 39.7% of patients were seizure free (Engel class I). The seizure-free outcome was significantly associated with wide electrode resection, resection including total ictal onset zone, presence of MRI lesion, slow propagation and focal or regional ictal onset. The surgical outcome was linearly correlated with extent of electrode resection: 23%, 47.6% and 53% in each group. However, subgroup analysis revealed no relationship between surgical outcome and resection extent in temporal lobe epilepsy. On stratified analysis by resection extent, focality of onset was significant only in group I. All patients with rapid propagation belonged to group I and propagation time did not affect surgical outcome in this group. The patterns and specific location of ictal discharges did not influence surgical outcome.

Conclusion: The extent of subdural electrode resection can be specific predictive factor for surgical outcome, especially in extratemporal lobe epilepsy. Further prospective studies are needed to validate this Results.

E366
THE CLINICAL AND GENETIC FACTORS PREDICTING THE RESPONSIBILITY TO LAMOTRIGINE

S. Kim, S. Kim†, S. No‡, O. Kwon§, S. Lee¶, and J. Shin¶*
**Inje University Busan Paik Hospital, Busan, Korea; †Dona A University, Korea; ‡Bong Sang Hospital, Korea; §Kyung Sang University, Korea; and ¶Pharmacogenetic Research Center, Inje University, Korea*

Purpose: Pharmacoresistance to antiepileptics (AED) is multifactorial and may include both of genetic and clinical factors. To keep be a homogeneous condition, we performed this study on the epilepsy patients taking a single AED, lamotrigine (LTG), regardless of monotherapy or polytherapy, to search the clinical and genetic factors associated with the LTG-resistance (LR).

Method: Single nucleotides polymorphisms (SNPs) of 73 with LR and 180 with LTG-controlled (LC) patients were genotyped by PCR and direct sequencing. The candidate SNPs for this study were as follows: 1 SNP from uridine diphosphate-glucuronosyltransferase (UGT1A4 142T>C), 2 SNPs from ATP-binding cassette B1 (ABCB1 2677G>A>T, 3435C>T), 18 tagging SNPs from sodium channel type 1A (SCN1A). LR was defined as the occurrence of any unprovoked seizure for at least 1 year up to the last follow-up with at least 3 AEDs at maximally tolerated doses. The clinical and genetic factors were analyzed by multiple logistic regressions.

Results: The clinical factors were significantly associated with the LR; age of onset 27 years {adjusted OR 3.0, (95% CI 1.19–4.61, p<0.0001)}, seizure frequency before treatment 9 {adjusted OR 4.9, (95% CI 3.00–8.13, p<0.0001)}, symptomatic/cryptogenic etiology {adjusted OR 5.7, (95% CI 1.92–17.11, p=0.001)}. Neither the ABCB1 nor the SCN1A genotypes were associated with the LR. However, besides the clinical factors, the haplotype of ABCB1 (T-C allele at 2677G>A>T and 3435C>T) was significantly associated with the LR {adjusted OR 2.7, (95% CI 1.12–6.66, p=0.027)}.

Interpretation: The genetic as well as clinical factors can predict the LR.

E367
COGNITIVE IMPAIRMENT IN PATIENTS WITH DIFFERENT FORMS OF EPILEPSY

M. Tereshchuk, L. Volkova, and E. Vahrusheva
1st Regional Clinical Hospital, Ekaterinburg, Russia

Purpose: The aim of our work was investigation of following psychological functions in patients with epilepsy: the level of some cognitive functions, especially memory; speech in patients with different forms of epilepsy; the comparing of cognitive impairment ranges in patients with different forms of epilepsy; the detection of the most significant factors for cognitive functions decrease.

Method: We followed 54 patients (39 women and 15 men) that suffered (during more then 5 years) idiopathic generalized epilepsy (30 patients) and cryptogenic focal epilepsy (24 patients). In all patients we investigated neurological status, EEG, neuropsychological status (8 spatial tests to estimate different cognitive functions), MRI in patients with focal epilepsy to exclude some conditions with potential significance for development of cognitive impairment.

Results: All patients had lower cognitive status than average population, but some parameters were not statistically significant due to the limitedness of groups. The results of our study showed evidence of some functional cognitive disorders in clinical structure of epilepsy.

Conclusion: We revealed signs of mild cognitive impairment like bradifrenia, impairment of memory due to dysfunction modal specific and unspecific structures of memory in patients with 5 years history of idiopathic generalized and cryptogenic focal forms. There weren't any clearly recognized statistically significant distinctions of memory impairment in patients with different forms of epilepsy. Impairment of memory was detected predominantly in unspecific structures (anatomically the media structure of brain limbic system), dysfunction of modal specific structures were secondary. One of significant factors of cognitive impairment in epilepsy is polytherapy (use more than one antiepileptic drug).

E368
THE FLEP SCALE IN DIAGNOSING NOCTURNAL FRONTAL LOBE EPILEPSY, NREM AND REM PARASOMNIAS

R. Manni, M. Terzaghi, and A. Repetto
IRCCS Institute of Neurology C. Mondino, Pavia, Italy

Purpose: To test the usefulness, in a clinical setting, of the FLEP scale which was set and proposed as a tool for distinguishing Nocturnal frontal lobe epilepsy from parasomnias (1).

Method: The FLEP scale was applied to seventy-one subjects (60 male; 11 female; aged 54+21) referred to an outpatients' sleep and epilepsy unit for diagnostic assessment of nocturnal motor-behavioral episodes, which turned to be arousal parasomnias (11 subjects), NFLE (14 subjects) or idiopathic RBD (46 subjects), based on the findings of in-lab full night video polysomnography with extended EEG montages.

Results: The sensitivity of the scale as a diagnostic test for NFLE was 71.4%, the specificity 100%, the positive predictive value 100%, and the negative predictive value 91.1%. The FLEP scale gave an incorrect diagnosis in 4/71 (5.6%) of the cases, namely NFLE patients with episodes of nocturnal wandering, and uncertain diagnostic indications in 22/71 subjects (30.9%).

Conclusion: The FLEP scale shows high positive and negative predictive values in diagnosing NFLE versus arousal parasomnias and RBD. However, the scale is associated with a real risk of misdiagnosis in some patients and gives uncertain indications in about one-third of cases, mainly RBD. Our investigation highlights the inadequacy of some of the items in the scale. The item investigating wandering, as presently formulated, may be unable to distinguish nocturnal wandering from sleepwalking. The items about recall and clustering of the events throughout the

night may increase the likelihood of mistaking RBD for seizures. Further testing of the reliability of the FLEP scale items appears to be needed.

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E369
COMMUNITY PERCEPTION OF EPILEPSY IN KADUNA RURAL AREA, NORTHERN NIGERIA

J. Ogboi, G. Oju†, K. Sabitu*, and S. Idris**
**Ahmadu Bello University, Nigeria; and †Frederal Psychiatry Hospital, Barnawa, Kaduna, Nigeria*

Purpose: Among neuropsychiatry disorders, epilepsy carries a high burden of social morbidity with stigmatization and many cultural misconceptions in various communities of Nigeria. The aim of this study is to determine the community's perception of epilepsy with a view to obtaining base line information on epilepsy from the community that will be used to subsequently plan interventions, enhance the community's knowledge, attitudes and practices for the prevention and control of epilepsy using antiepileptic drugs (AEDs).

Method: A cross-sectional descriptive study using both qualitative and quantitative methods was used. Using a multistaged sampling technique, 400 respondents were sampled with equal allocation between care givers of epilepsy and household heads and data was collected using pretested close-ended questionnaires and qualitative data from eight focus group discussions (FGDs) was also obtained.

Results: The finding of the study indicated a poor knowledge of the cause, method of transmission and complications of epilepsy with a high perception of seriousness, curability, preventability, stigmatization and symptoms of the disease. Seeking treatment and self-treatment with over the counter (OTC) drugs and herbs from traditional healers were found to be very high however; there was low utilization of public health facilities. The health seeking behavior and knowledge of epilepsy management among patent medicine vendors and health care workers is very poor in the community.

Conclusion: This study reveals that perception and belief systems of the community on stigmatization against people with epilepsy and their families is high without the adequate knowledge of the cause of the disease. There is need to provide opportunities for meaningful involvement of epileptic patients and communities with proper case treatment and management. Also, policy should be introduced to train community health officers and extension workers and patent medicine vendors on the management of epilepsy with activities of traditional healers being assessed and integrated on protective measures against seizures.

E370
ETIOLOGICAL FACTORS AND PATTERN OF LATE ONSET EPILEPSY IN NIGERIA

L. Owolabi, R. Akinyemi†, M. Owolabi‡, and A. Ogunniyi‡*
**Aminu Kano Teaching Hospital, Kano, Nigeria; †Federal Medical Centre, Abeokuta, Nigeria; and ‡University College Hospital Ibadan, Nigeria*

Purpose: Late-onset epilepsy is an area that has not been fully explored in the developing countries; a detailed knowledge of various etiologies, pattern and associated conditions of the disease will influence its management positively.

Objective: Generally to determine the pattern of presentation of late onset epilepsy in Nigeria and specifically to identify the etiologic factors, classify and describe the pattern of their seizure.

Method: A total of 120 patients presenting with epilepsy after 25 years of age were recruited from the general and medical outpatient Clinic of UCH over a two and a half year period a structured proforma was completed per eligible subject. EEG & CT Brain were done in all cases.

Results: The commonest seizure type was partial seizure diagnosed in eighty nine subjects; forty-one subjects (34.2%) were simple partial, twenty six (21.7%) were complex partial and twenty-two (18.3%) were secondarily generalized. On examination, 43.3% had abnormal neurological findings. 56.2% of those with partial seizures had abnormal neurological findings as compared 6.5% patients with primarily generalized seizures, $p<0.05$. CT was normal in 36.7% subjects and abnormal in sixty eight (56.7%) subjects. The commonest abnormalities were cerebral infarcts and tumors.

Conclusion: Partial seizure appeared to be the commonest seizure type in late onset epilepsy of this; simple partial seizure appeared to be the most common then secondarily generalized. The commonest CT abnormalities appeared to be cerebral infarct and cerebral tumor closely followed by cerebral atrophy.

E371
ICTAL SEMIOLOGY IN MESIAL TEMPORAL LOBE EPILEPSY: IS IT DIFFERENT IN PATIENTS WITH BITEMPORAL ICTAL ACTIVITY?

R. Andre, C. Rito, A. Geraldo, and F. Sales
Unidade De Monitorizacao De Epilepsia E Sono, Serviço De Neurologia, Hospitais Universidade Coimbra, Coimbra, Portugal

Purpose: Ictal semiology remains a valid tool localizing the epileptogenic area. The presence of bitemporal ictal activity in Mesial Temporal Lobe Epilepsy (MTLE) has an uncertain significance. We aimed to characterize the semiology of patients with MTLE, particularly if there were differences in those with bitemporal activity in ictal EEG.

Method: We selected consecutive patients registered with MTLE in our Epilepsy Database from January/2005 to December/2006, and analyzed demographics, ictal semiology and auxiliary methods (EEG, MRI).

Results: 54 patients were obtained. Hippocampal sclerosis was right-sided in 28 (52%) and left-sided on 26 patients. Unitemporal activity existed in 29 (54%) and bitemporal in 25 patients. In the unitemporal group, 24 (83%) had automotor, 2 dialeptic and 3 simple motor seizures. In the bitemporal group, 24 (96%) had automotor and 1 simple motor seizures. Aura existed in 12 (48%) with bitemporal and in 17 (59%) with unitemporal activity. Nonresponsiveness presented in 17 (68%) with bitemporal and in 20 (69%) with unitemporal activity. Oro-mandibular automatisms existed in 14 patients each. Contralateral dystonia existed in 11 (44%) with bitemporal and in 19 (65%) with unitemporal activity. Bilateral dystonia appeared in 3 patients with bitemporal and in 2 with unitemporal activity. Unilateral automatisms existed in 19 patients each. Bilateral automatisms existed in 16 (64%) with bitemporal and in 14 (48%) with unitemporal activity. Positive motor components existed in 7 with bitemporal (28%) and 5 (17%) with unitemporal activity.

Conclusion: There were no statistically significant differences between the 2 groups. Larger studies are necessary.

E372
EFFICACY OF NEWS AEDS IN THE TREATMENT OF EPILEPSY CRYPTOGENIC IN THE ELDERLY (ECE)

B. Gennaro, T. Maddalena†, A. Pasquale*, V. Giacomo‡, and A. Sergio§*
**Aslna1, Napoli, Italy; †Clinica Santa Maria Del Pozzo Somma Vesuviana, Napoli, Italy; ‡ASLNA5, Italy and §Neurologo Territoriale ASLNA1, Italy*

Purpose: Is it possible, in the ECE, to make use of the news AEDs, in monotherapy and at low doses, in order to achieve the optimal control of the seizures in total absence or with the slightest risk of side effects?

Method: In all, are recruited 81 patients (36M,45F), all of aged over sixty (mean age 66.7 years). The seizure forms are been mainly focal (33 cases). All patients were with newly diagnosed epilepsy between 2004, 2005 e 2006 and their neurological examination and neuroimaging results were normal and had received monotherapy and at low doses. Antihypertensives, anti-arthrosises, hypoglycaemics and insulin were the drugs used for others diseases. The patients were followed-up for 18 months. All patients had TC and MRI of the skull. Every 3 months, patients' EEG reading were obtained and the Minimum Mental State Examination (MMSE), Short Form of Health Survey (SF-12) and the Caregiver Neuropsychiatric Inventory (NPI) was completed.

Results: The new drugs used are LEV, TPM, OXC, LTG, PGB e GBP. All the patients were seizure free during the whole follow up and the adverse events (AEs) were transient and mild in intensity, without interference with patients' daily activities. All AEs disappeared within four weeks.

Conclusion: ECE responded very well at all AEDS used in this study, in monotherapy and at low doses, without evidence of problem of pharmacological interaction and of serious AEs. This facilitates the task of neurologist as regards the choice of drug to use in this epileptic form.

E373
ANALYSIS OF SEIZURE METAPHORS DIFFERENTIATES BETWEEN EPILEPTIC AND NONEPILEPTIC SEIZURES

M. Reuber, and L. Plug†*
**University of Sheffield, UK; and †University of Leeds, UK*

Purpose: To increase understanding of the subjective symptomatology of seizure experiences by studying seizure metaphor use by patients with (psychogenic) nonepileptic seizures (NES) and epilepsy.

Method: 21 unselected patients taking part in this study were admitted for 48 hours of video-EEG observation because of uncertainty about the diagnosis. Eight were proven to have epilepsy, 13 NES. During their admission, patients were interviewed about their seizures by a neurologist. A linguist blinded to the medical diagnosis identified and categorized all seizure metaphors in verbatim transcripts. Between-group comparisons and logistic regression analysis were carried out.

Results: Of 382 metaphors identified, 80.8% conceptualized seizures as an agent/force, event/situation or space/place. Most patients used metaphors from all categories, but the profile of metaphor choice differed significantly between the epilepsy and NES groups (p=0.009 to p=0.039). Patients with epilepsy preferred metaphors depicting the seizure as an agent/force or event/situation. NES patients more often used metaphors of space/place. Logistic regression analyses predicted the diagnosis of NES or epilepsy correctly in 85.7% of cases (based on different metaphor types in the each category) or 81.0% (based on all metaphor tokens).

Conclusion: Patients with epilepsy and NES have different preferences in the metaphoric conceptualization of their seizures. Epileptic seizures are experienced as a more external, self-directed entity than NES which are a state or place patients go through. The differentiating value of metaphoric conceptualizations suggests that metaphor preference could form the basis of future diagnostic questionnaires or other diagnostic tools.

E374
LOCALIZATION OF WAR CRANIOCEREBRAL INJURY AS RISK FACTOR FOR POSTTRAUMATIC EPILEPSY

A. Kapidzic, and O. Sinanovic†*
**University Clinical Centre, Tuzla, Bosnia; and †Faculty of Medicine, University of Tuzla, Bosnia*

Purpose: The aim of the study is to illustrate deployment of certain zones of craniocerebral trauma and determine their importance for posttraumatic epilepsy.

Method: Prospective-retrospective study encompassed 50 veterans of war, with craniocerebral trauma and posttraumatic epilepsy. Control group consisted of 50 veterans of war, without epileptic seizures. Every examinee was identified with craniocerebral trauma zone through a CT scan of brain.

Results: Average veterans' age in examinees' group was 29,92 ± 8,91; in control group was 29,98 ± 9,97 ($p>0.05$). Parallel existence of injuries at several areas were registered at 22 (44%) opposite 8 (16%) patients of control group ($p< 0.05$). This increases the possibility of posttraumatic epilepsy appearance in 3, 5 times. Trauma of frontal area was experienced at 7 (14%) patients, opposite 15 (30%) patients ($p> 0.05$). Trauma of temporal area was present at equal number of patients in both groups, 6 in each (12%); injury of parietal area was present in 14 (28%) patients opposite 11 (22%) ($p> 0.05$). Occipital area was injured at one patient with posttraumatic epilepsy (2%) and 10 (20%) veterans in control group ($p< 0.05$).

Conclusion: Trauma of several areas at the same time increases the possibility of posttraumatic epilepsy. Trauma of certain brain areas does not represent the risk factor for posttraumatic epilepsy; trauma of occipital area was significantly more represented in group of patients without posttraumatic epilepsy. Key words: brain injury, posttraumatic epilepsy.

E375
DO SURFACE DC-SHIFTS DURING EEG-FEEDBACK AFFECT HIPPOCAMPAL PATHOLOGICAL ACTIVITY IN MESIO-TEMPORAL LOBE EPILEPSY?

N. Fritz, J. Fell, W. Burr, N. Axmacher, C. Elger, and C. Helmstaedter
University Clinic Bonn, Germany

Purpose: Despite considerable research on EEG-feedback of slow cortical potentials (SCPs) for seizure control in epilepsy, the underlying mechanisms and the direct effects on intracerebral pathological activity within the focal area remain unclear.

Method: Intrahippocampal EEG recordings from four patients with temporal lobe epilepsy and implanted electrodes were analyzed with regard to spike activity and power in 10 frequency bands (0.5–148 Hz) during SCP feedback from surface electrodes. Trials with positive, negative and indifferent SCPs were contrasted.

Results: Three of the four patients showed changes in spike activity during SCPs, but these were inconsistent between patients, and they result in increased and decreased activity in both positive and negative SCP(s. Spectral analysis revealed that in all patients' positive surface shifts showed a bi-hemispheric higher power in the high-frequency activity (HFA) above 40 Hz. Two patients showed a higher power also in negative shifts, both in HFA and one in most other frequency bands. The higher power in frequency bands was not associated with the focal side, and turned out to be intraindividually consistent.

Conclusion: Inconsistent change in spiking activity and the lack of decrease of power in pathology associated frequency bands during positive SCPs shows that SCP training does not decrease pathological activity within the epileptic focus. However, since both measures are not directly related to seizure occurrence this does not necessarily contradict eventual therapeutic effects. The authors thank NeuroConn GmbH (Ilmenau, Germany) for providing the DC-EEG-feedback system.

E376
EPILEPTIC PSEUDODEMENTIA: ASSSOCIATION BETWEEN EPILEPTIFORM ACTIVITY AND ALZHEIMER'S DISEASE

M. Ito, and N. Echizenya
Tenshi Hospital, Japan

Purpose: The potential link between epilepsy and Alzheimer's disease (AD) has recently been paid attention. We report four cases of epilepsy-

derived progressive memory disturbances which clinically resembled early-stage AD.

Method: The patients consisted of 3 males and 1 female, aged 56–79 years old. Both the patients and their families had been aware of memory disturbances for approximately one year. Recent memories showed the greatest disturbance, whereas remote memories and orientations were relatively intact. MMSE scores were 19–26/30. Mental dullness and a decline in daily activities were also observed. No overt seizures were observed in any of the patients. No apraxia, agnosia or aphasia was seen in any of the patients. MRI only revealed slight cerebral atrophy. SPECT showed areas of hypoperfusion in the left frontal, temporal, or parieto-temporal lobe in all patients. EEG revealed spikes in the left temporal region in three patients, and the left central regions in the other patient.

Results: The memory impairment was considered to be of epileptic origin on the basis of the EEG findings, and carbamazepine was prescribed. Performance of activites and memory improved rapidly in all patients with treatment. The MMSE score increased up to 8 points.

Conclusion: The persistent cognitive disturbances and the reduced activity levels observed in our patients could not be fully explained by epileptic seizures only. Subclinical continuous discharges involving the hippocampal-mesial temporal lobe may be responsible for interictal cognitive dysfunction. We speculate therefore that epileptic activities play a role in some patients with AD-like symptoms.

E377
THE EFFECT OF ANTIEPILEPTIC DRUGS ON BALANCE IN OLD PEOPLE

G. Lee, C. Lee, and J. Kim
College of Medicine, Dankook University, Korea

Purpose: The purpose of this study was to quantitatively assess the magnitude of subclinical balance dysfunction in older people taking antiepileptic drugs.

Method: Sixty-three patients who were at least 50 years old, without complaint of dizziness or imbalance, and on a stable dose of carbamazepine, lamotrigine or levetiracetam for at least 30 days were enrolled. Their scores on the measures of balance were compared with newly diagnosed untreated age and sex matched epilepsy patients (N=21). All the subjects underwent balance measurements that included an activities-specific balance confidence scale, standardized quantitative caloric and rotational chair vestibular testing and posturography. The spectral frequency analysis of body sway while standing upright was investigated. Sensory organization tests and motor control tests were done by posturography.

Results: The sway distance and the sway area of Center of pressure significantly increased in the patients treated with carbamazepine. Spectral frequency analysis showed a significant increase in spectral power at low and middle frequencies on the antero-posterior (Y) plane and at low frequencies on the lateral (X) plane. Computerized dynamic posturography showed no significant differences on sensory organization test results among the groups, but on motor control test, there were significant increase of latencies and slowed adaptations in the carbamazepine group.

Conclusion: These findings suggest that newer drugs such as lamotrigine or levetiracetam may induce less disequilibrium than does carbamazepine in older people on monotherapy for epilepsy. The disturbance is likely related to slowed central postural reflexes.

E378
SERUM PROLACTIN FOLLOWING FOCAL SEIZURES CLASSIFIED BY VIDEO EEG MONITORING

A. Rysz
Medical University of Warsaw, Russia

Purpose: To confirm value the serum prolactin (PRL) test in diagnosis and differentiation of focal epileptic seizures.

Method: During presurgical assessment of refractory partial epilepsy interictal serum PRL levels at baseline and 10–20 min after the video EEG documented seizures were prospectively studied, and compared with psychogenic nonepileptic seizures (PNES). Video-EEG monitoring revealed 53 seizures: 36 temporal, 14 nontemporal partial and 3 PNES.

Results: Serum PRL increased after all of 36 temporal seizures. PRL elevations: four times or more of baseline were seen following 13 (36%), two or three times after 18 (50%), and slight elevation after 5 (14%) temporal seizures.

Nontratemporal seizures were associated with marked elevation: four times or more of PRL following 4 (28%), two or three times following 6 (44%), and slight elevation following 2 (14%), and PRL was decreased after 2 (14%) of 14 seizures. Two patients with PNES had after seizures insignificant lower and one unaffected PRL serum level.

Conclusion: Subsequent to focal seizures serum PRL elevation were observed in all cases, except two nontemporal seizures.

PRL level were significantly elevated following almost all temporal seizures. Past PNES serum PRL were lower or unchanged as compared to baseline.

E379
ANOMALIES OF INFRATENTORIAL BRAIN STRUCTURES IN PATIENTS WITH MALFORMATIONS OF CORTICAL DEVELOPMENT AND EPILEPSY

G. Kuchukhidze, U. Iris, D. Judith, W. Gerald, H. Edda, K. Florian, G. Thaddaeus, F. Stefan, and T. Eugen
Medical University of Innsbruck, Austria

Purpose: Malformations cortical development (MCD) represent a heterogeneous group of cerebral abnormalities determined by disrupted stages of neuronal development. There is a paucity of reports on anomalies of infratentorial brain structures (AIS) and their relation with MCD is unclear. This study aimed to identify the spectrum and frequency of AIS in patients with MCD and epilepsy.

Method: We identified 228 patients (120w/108m) aged 1–75 years (mean 31.2 years) with MCD and epilepsy at the Seizure Unit, Department of Neurology, Innsbruck Medical University. All patients were clinically examined, underwent EEG and MRI. AIS were categorized according to nomenclature by Patel and Barkovich (Patel and Barkovich. Am J Neuroradiology 2002;23:1074–1087).

Results: AIS was identified in 41/228 (18%) patients with MCD and epilepsy; 24 had diffuse abnormality, 15 – focal and two – both. AIS was confined mainly to cerebellum (34/41; 83%); 24/34 (71%) had hypoplasia, 8/34 (23%) -dysplasia of cerebellum and 2/34 (6%) -both. The spectrum of cerebellar AIS included Dandy-Walker malformation (DWM, n=21), rhombencephalosynapsis (n=3), heterotopia (n=1), ponto-cerebellar hypoplasia (n=2), polymicrogyria with schizencephaly (n=3), diffuse cerebellar dysplasia (n=1), focal cerebellar hypoplasia (n=1) and DWM with polymicrogyria (n=2). Brainstem hemiatrophy (n=7) was invariably associated with ipsilateral perisylvian polymicrogyria. AIS were observed mainly in patients with cerebral polymicrogyria (15/47; 32%) and periventricular nodular heterotopia (11/31; 35%). The majority of patients with focal cortical dysplasia, hemimegalencephaly or ganglioglioma did not have AIS.

Conclusion: AIS were observed in 18% of patients with MCD and epilepsy; mainly in those with MCD of migrational or organisational origin.

E380
ANTIBIOTICS-INDUCED CONFUSIONAL STATES: NONCONVULSIVE STATUS EPILEPTICUS OR TRIPHASIC ENCEPHALOPATHY?

A. Primavera, S. Anfosso†, A. Leonardi*, and D. Audenino‡*
**University of Genova, Italy; †Division of Neurology-ASL1, Imperia, Italy; and ‡Division of Neurology, ASL 11, Vercell, Italy*

Purpose: Antibiotics may induce a confusional state (ACS), especially in elderly patients with chronic renal failure (CRF). We aimed to emphasise the role of EEG in evaluation of patients with antibiotics-induced delirium.

Method: We reviewed the files of 32 consecutive hospitalized patients (mean age of 65.5, SD 19.75) who performed EEG for an ACS, while being treated with antibiotics. All patients with ACS performed laboratory tests, a neuroimaging study and serial EEG evaluations. We reviewed the clinical and EEG features (slow wave activity, side-to-side asymmetry, presence of epileptiform discharges, triphasic wave).

Results: EEG showed focal or diffuse abnormalities in all patients and was suggestive of 'de novo' nonconvulsive status epilepticus (NCSE) in 8 patients presented with progressive disorientation (without sure clinical motor seizures, but with mild myoclonus in 3 cases) after starting antibiotics treatment. Cephalosporins were implicated in 7 cases with CRF and Clarithromyicin in a patient in treatment with low doses of amitripyline. The EEG showed in 2 cases recurrent electrical seizures and in 6 cases continuous generalized, atypical spike and wave and sharp- and slow-wave complexes, with triphasic aspect. Intravenous benzodiazepines were administrated in 6 patients with suppression of the epileptiform activity. Antibiotics were withdrawn and all patients improved, usually in the first week.

Conclusion: Despite the wide use of these antibiotics, there are only few reported cases, because this condition is probably underestimated, particularly in departments of internal medicine. We emphasize the utility of emergent EEG in patients with an ACS while receiving treatment with antibiotics, particularly when there is evidence of impaired renal function.

E381
PECULIARITIES OF THE PRECLINICAL EPILEPTOGENESIS IN ORGANIC ENCEPHALOPATHY

S. Khorshev, E. Korsakova, V. Slezin, and V. Mashukova
V.M. Bekhterev Psychoneurological Research Institute, Saint-Petersburg, Russia

Purpose: Currently there can be observed a considerable growth of the number of patients with the debut of epilepsy in whose clinical picture encephalopathy called by us 'organic' (OE) is diagnosed. The objective of the present investigation consisted in studying the peculiarities of the course of preclinical epileptogenesis (PE) depending on the presence of OE.

Method: 207 patients with PE including 181 with OE and 30 practically healthy volunteers were examined. The PE objectification was performed using the methods of fractal and cross-correlation analysis of EEG. Determined were fractal dimensionality of the alpha rhythm power fluctuations (D) in the O1 lead as well as alpha rhythm cross-correlation coefficient (R) between the F3 and O1 leads.

Results: In the instance of PE high negative R values characteristic of the norm weakened, whereas D increased ($p<0.05$). The number of observations with low R values equalled 76.8% in patients without OE and 98% in those with. The D heightening compared with its normal values in PE was found in 81.1% of examinees without OE and in 85.4% of those with OE. The transition to the clinical phase of epilepsy in the instance of PE was observed in 12.7% of patients with OE and in 11.5% of those without OE.

Conclusion: Thus the presence of OE represents a considerable dysadaptation factor contributing to a more aggressive course of preclinical epileptogenesis and is more often accompanied with the derangement of compensatory adaptation mechanisms of the cerebral homeostasis.

E382
MORTALITY OF EPILEPSY IN AN ADULT COHORT WITH A NEWLY DIAGNOSED EPILEPTIC SEIZURES: 13 YEARS OF FOLLOW-UP IN AN ESTONIAN POPULATION

A. Rakitin, M. Liik*, A. Õun*,†, and S. Haldre**
**University of Tartu, Estonia; †Kuopio University Hospital, Finland*

Background: One of the most important aspects of prognosis in epilepsy is the risk of premature death.

Purpose: To evaluate the mortality risk in adult epilepsy patients who were identified earlier in a population-based incidence study carried out in Tartu, a city of about 100000 inhabitants in Estonia.

Method: 81 persons aged 20 years and older (55 men, 26 women) were identified as epilepsy incidence cohort in 1994–1996. In 2008 the cohort was linked to the Estonian Death Register to obtain information on date of death until December 31, 2007. The standardized mortality ratio (SMR) was calculated.

Results: The cohort was observed for 790 person-years. At the end of follow-up 39 persons (29 males and 10 females) had died, compared with expected 11.1 and 4.0 deaths, respectively. The total cohort SMR was significantly increased (SMR 2.7; 95% CI, 1.9–3.7). The increased mortality risk was found during first year after diagnosis (SMR 3.6; 95% CI 1.2–8.3) and at years 7 (SMR 5.6; 95% CI 2.0–12.1) and eleven (SMR 4.6; 95% CI 1.3–11.8). With respect to seizure type the risk of death was significantly increased in patients with complex partial seizures (SMR 5.6; 95% CI 2.4–11.0) compared to the secondary generalized (SMR 2.7; 95% CI 1.7–4.3) and simple partial seizures (SMR 1.47; 95% CI 0.3–4.3).

Conclusion: Adult patients with newly diagnosed epilepsy had more than doubled mortality risk. This risk is more pronounced during first and after seventh year after diagnosis. Complex partial seizures significantly increase risk of death compared to other seizure types.

E383
LATERALIZING VALUE AND SURGICAL OUTCOME OF FORAMEN OVALE ELECTRODE IN MESIAL TEMPORAL LOBE EPILEPSY

S. Jang, Y. Cho, B. Lee, S. Park, J. Chang, and K. Heo
Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Purpose: Foramen ovale electrode (FOE) has been introduced to the patients with mesial temporal lobe epilepsy (MTLE) for lateralization of ictal onset. To assess its clinical utility, we analyzed lateralization pattern of epileptiform discharges and surgical outcome between scalp electrode and FOE.

Method: Patients with MTLE, not lateralized in phase I investigation due to independent ictal onsets or ambiguous onset, or contralateral onset, received FOE insertion. Three-contact FOE were implanted bilaterally through foramen ovale using fluoroscope under local anesthesia. Patients whom FOE failed to demonstrate clear ictal onset were further evaluated with depth or strip electrodes. All patients were followed for at least one year and surgical outcome was assessed with Engel classification.

Results: Between 2000 and 2006, 49 patients (28 women) were included. Interictal epileptiform discharges were more commonly identified (scalp 83.5/hr, 133.5, FOE 1268/h r, 1076.8, $p<0.001$) and lateralized (scalp 28.6%, FOE 68.6%, $P<0.001$) on FOE recording. FOE recording could reveal more ictal events (scalp 4.66, FOE 9.8, mean events per patient, $p<0.001$), especially subclinical one (29.6%). Ictal FOE recording could lateralize 81.6% of the patients. Five patients (8.2%) needed

further invasive intracranial recording. Of 45 patients received surgery, 76% were Engel class I. The lateralized group on ictal FOE showed higher seizure free rate, compared to not-lateralized group (83.3% and 55.6%, 0.093), although lack of its statistical significance.

Conclusion: FOE is a sensitive and reliable method for lateralization in MTLE patients, and a good surgical prognostic factor, when consistently lateralized.

E384
FATALITY OF GENERALIZED CONVULSIVE STATUS EPILEPTICUS AND POSSIBLE IMPACT ON DEATH IN ADULTS IN SOUTHWEST CHINA

J. Li
HUAXI Hospital of Sichuan University, Chengdu, China

Purpose: To evaluate the fatality of GCSE patients and impact factors in South-west China.

Method: A prospective study of GCSE from Jan 1996 to Dec 2007 was performed to determine the case fatality, etiology, experimental data and management. We used chi-square criterion, nonparametric test to identify impact factors between the dead and the alive; logistic regression models was also used to analyze predictors of death. The fatality and impact factors of death were compared to other data in different regions.

Results: A total of 203 cases in Southwest China were studied. The case fatality was 15.8%. Female patients occupied 59.4% (P=0.03). The case fatality in every year has no obvious change. GCSE mean duration was 26.59, 30.05 (hour) in dead patients and 15.30, 19.10 in alive group (P=0.048). The major etiologic factors were CNS infection (28%), toxic and hypoxia (21.9%) and brain trauma (15.6%). Predictors included artificial ventilation (OR 39.984, 95%CI 6.157~259.67 P<0.000); complication (OR 16.936 95%CI 5.281~54.309 P<0.000); SE duration (OR 1.748~95%CI 1.098~2.782 P=0.019).

Conclusion: The case fatality in GCSE adult in Southwest China was still high. The impact factors on death mainly included aetiologic factors as CNS infection, Toxic & hypoxia and Brain trauma, artificial ventilation, complication and SE duration. These impact factors were different as other international regions and call attention to the right management in the early windows. For samples in this study were limited, further studies are needed to evaluate more samples in other regions in China mainland.

E385
INCIDENCE OF EPILEPTIC SEIZURES ASSOCIATED WITH SPONTANEOUS INTRACEREBRAL HEMORRHAGE

A. Ilic
Health Center Studenica, Serbia

Purpose: Spontaneous (nontraumatic) intracerebral hemorrhage (ICH) makes up approximately 10% of all strokes. Only a small percentage of patients with spontaneous ICH develop seizures. Our aim was to determine the frequency and predisposing factors for occurrence of symptomatic epilepsy due to spontaneous intracerebral hemorrhage.

Method: This is a retrospective and prospective study, based on hospital population during a 7 years period (2000–2007). All patients were given a clinical examination, laboratory tests, EEG and neuroimage (brain CT and MRI).

Results: In our study 96 patients (mean incidence 8,9%) developed epileptic posthemorrhagic seizures, 52 male and 44 female. Patients were grouped as having early-onset (occurring at initial ICH and within two weeks of hemorrhage) and late-onset (occurring more than two weeks after ICH). 22 patients (22,9%) had early seizures and 74 patients (77,1%) late seizures. The mean age of males and female was 68 years. 95% of ICH occurs in the supratentorial compartment. EEG changes with slow rhytms and phatological waves were found in 78 patients (81,2%).

Conclusion: Incidence of epileptic posthemorrhagic seizures in our study is 8,9%. Supratentorial compartment is associated with a higher risk of seizures and epilepsy. EEG changes are predictors of seizures. Late seizures developed more often than early seizures.

E386
TACROLIMUS-INDUCED SEIZURES AFTER LIVER TRANSPLANT: A CASE REPORT

M. Baldini, M. Cosottini, P. Maritato, D. Perini, E. Bartolini, S. Gori, and A. Iudice
Clinic of Neurology, Pisa, Italy

Purpose: Seizures are among the commonest neurological complications in liver transplanted patients. Fits may occur during the first few weeks after transplantation, but also later. Generalized seizures are the most frequently encountered. Their etiology is usually multifactorial, thus requiring a comprehensive diagnostic-therapeutic approach.

Method: Female, 22 y.o., liver transplanted for HBV-hepatitis, and treated with immunosuppressive drugs (lamivudine and tacrolimus). Eight months later she had two generalized T-C seizures at night and the following morning apart. EEG showed slow diffused delta waves, predominant on the anterior regions.

Results: Brain MRI revealed a frontal lobe hyperintense area involving cortical-subcortical region, likely jatrogenic in nature. Tacrolimus was substituted with micophenolate, and oxacarbazepine started up to 600 mg/day. One week later, MRI findings showed a little reduction, clearer 2 months afterward. Other 3 generalized T-C seizures occurred 6–8 months from onset, but after oxcarbazepine increase to 1200 mg/day the patient is now seizure-free for 5 months. One year after the first seizure, MRI shows a complete recovery of lesion, but EEG delta waves, mainly on anterior regions, are still present.

Conclusion: This case report exhibits a posterior reversible encephalopathy syndrome (PRES), a clinical-neuroradiological transient condition that includes seizures, 'atypical' in its location (i.e. frontal), associated with tacrolimus. MRI features typically show oedema involving the white matter of cerebral regions, especially parietal-occipital, but also frontal and temporal lobes. Early recognition is of paramount importance both for removal of precipitating factors and treatment of seizures.

E387
ISOLATED SPEECH ARREST ASSOCIATED WITH BILATERAL SECONDARY SYNCHRONY ON THE EEG AS ELECTROCLINICAL EPILEPTIC FEATURE RELATED TO THE INVOLVEMENT OF THE SUPPLEMENTARY MOTOR CORTEX: A CASE INVESTIGATED WITH THE EEG FMRI

P. Borelli, M. Avesani, T. Zanoni, P. Manganotti, R. Cerini, E. Formaggio, S. Storti, G. Moretto, and A. Fiaschi
University of Verona, Italy

Purpose: Speech arrest is a rather uncommon seizure type usually related to the involvement of the supplementary motor area (SMA) on both emispheres. That is sometimes difficult to distinguish from the other more prominent clinical features. The bilateral secondary synchrony is an EEG pattern characterized by generalized spike and wave discharges resembling the idiopathic generalized epilepsies pattern. That is typically the result of epileptic foci on the mesial surface of the frontal cortex.

Method: We describe the case of a 36 yrs old woman with drug resistant seizures since the age of 5 taking the form of sudden speech arrest episodes sometimes followed by clonic jerks over the right half of the face and arm. Those may last some minutes and the patient is able to read and

write ictally. Conventional and 3T MRI were both normal. Interictal EEG showed theta activity on left frontal electrodes followed by generalized spike and wave discharges. EEG-fMRI showed a clear cut prominent activation of the left SMA. The case was eventually considered for surgery.

Conclusion: Speech arrest is not a very common epileptic feature sometimes difficult to recognize specially if associated to clear-cut motor phenomena such as bilateral tonic posturing, facial grimacing, violent vocalization, which are motor phenomena usually associated with SMA-seizures. Secondary bilateral synchrony is the typical EEG picture of mesial frontal epileptic foci. That does not provide on other hand clear localizing data. In conclusion the speech arrest even if isolated may be the result of SMA seizures. Given the often poor contribute of the scalp EEG in localizing both the area and the side of onset, the EEG f-MRI may provide reliable data about those especially in the context of surgical work-up.

E388
SWALLOWING REFLEX EPILEPSY: COULD ORAL THERAPY REPRESENT A PROBLEM?

P. Maritato, E. Bartolini, M. Baldini, D. Perini, S. Jensen, C. Frittelli, E. Bonanni, and A. Iudice
Clinic of Neurology, Pisa, Italy

Purpose: Reflex epilepsy is characterized by seizures triggered by a specific stimulus or external events. In some patients there is only pure reflex epilepsy, but in others spontaneous seizures may also be associated. Eating is considered a rare cause of reflex epilepsy.

Method: We present a 22-year-old boy with an history of perinatal asphyxia resulted in psychomotor retardation and epileptic encephalopathy. Since 12 years of age he suffered of generalized tonic–clonic seizures and absences, satisfactorily controlled by valproate and topiramate. In the last two years the absences were mainly provoked by swallowing; the EEG activity showed diffuse spike and slow waves. On July 2007 he had a convulsive status epilepticus after an ab ingestis pneumonia likely caused by a seizure, and was admitted to an intensive care unit.

Results: During hospitalization he continued to have tonic–clonic generalized seizures induced by swallowing, and it was difficult to switch from parenteral to oral antiepileptic therapy. A percutaneous endoscopic gastrostomy (PEG) was then performed, and the patient could resume enteral antiepileptic therapy with a seizure control.

Conclusion: Reflex eating epilepsy is rare but shows a good response to antiepileptic drugs (AEDs). This case reports a medical complication, ab ingestis pneumonia, frequently related to swallowing seizures. In this situation PEG (temporary or sustained) could represent a valid alternative route of administration of AEDs, useful also to warrant an appropriate dietary regimen.

E389
NEUROPSYCHOLOGICAL PERFORMANCE IN GREEK-CYPRIOT ADULTS WITH CHRONIC EPILEPSY: A PRELIMINARY STUDY

F. Constantinidou, S. Papacostas†, D. Themistocleous*, and M. Nicou**
**University of Cyprus, Cyprus; and †Cyprus Institute of Neurology and Genetics, Cyprus*

Purpose: The primary objective was to investigate verbal learning, working memory, and executive functioning abilities in Greek-Cypriots with epilepsy. This study is part of the first systematic research program exploring neuropsychological performance and quality of life issues in Greek-Cypriots with epilepsy.

Method: 30 Greek-Cypriot adults with chronic epilepsy (ages 18–55) were matched to 25 neurologically normal adults on age, gender, and education levels. All participants with epilepsy were recruited from the Cyprus Institute of Neurology and Genetics.

Method: A battery of neuropsychological tests and 2 quality of life assessments were implemented. Participants were screened for global cognitive decline and clinical depression.

Results: Mixed model MANOVA (a = 0.05) results indicated that the performance of participants with epilepsy was significantly lower than that of normal cohorts on repeated verbal learning tasks (RAVLT). Pairwise (a = .05) comparisons demonstrated that performance was lower on both verbal and nonverbal working memory measures, a = .05 (digit span forward/backwards, visual span forward/backwards, Rey Complex Figure Test, and paragraph recall immediate/delayed). In addition, performance was significantly lower (a = 0.05) on executive functioning and mental fluency tasks (COWAT, Symbol Digits Modalities Test, Trails A & B). Performance on executive tests correlated significantly (a=0.05) with memory performance.

Conclusion: Results indicate that chronic epilepsy hampers verbal learning and memory performance despite of the focus of the epileptic activity. Furthermore, the reduction in executive functioning which interferes with the use of active memory strategies contributes to the memory impairment observed in the present study.

E390
ETIOLOGY AND OUTCOME OF STATUS EPIEPTICUS IN PATIENTS ADMITTED TO A PEDIATRIC INTENSIVE CARE UNIT

F. Khodapanahandeh
Iran University of Medical Sciences, Tehran, Iran

Purpose: Status epilepticus (SE) is the most common neurological emergency in childhood. We conducted this study to determine etiology, factors influencing occurrence of SE and morality of patients.

Method: In a cross sectional retrospective stud files of 134 children (aged 1month to 12 years) were reviewed; Age, etiology of SE, factors predisposing to occurrence of SE (eg, previous neurological abnormality), course of the disease and mortality of patients were determined. Descriptive (mean±SD) and comprehensive statistics (÷2 analysis) were used. P <0.05 were considered significant.

Results: The mean age of patients was 4.8±4.5. Status epilepticus was most common in younger children with 45% of cases occurring in those younger than 2 years. 115 (85%) out of 134 patient admitted with their first episode of SE. While 19 (15%) presented with recurrence. The most common etiologic group was acute symptomatic (27.7%), whereas, progressive encephalopathy with only 10 patients (7.7%) formed the least common group. 40.3% (54/134) of patients were neurologically abnormal before the episode of SE (P <0.01) and the older the child the more susceptible to have SE in an abnormal neurological background. (P <0.001). 25 children died; 12 of them (50%) belonged to acute symptomatic group, 10 (38.4%) remote symptomatic, 2 (7.6%) idiopathic and only 1 patient (3.8%) died of febrile status epilepticus.

Conclusion: Children under 2 years included more patients than other age groups. The most common etiology was Symptomatic groups (acute and remote). Previous neurological abnormality was a significant factor in occurrence of SE. Acute symptomatic group was the most common etiology in death patients.

E391
NEW ONSET PSYCHOGENIC NONEPILEPTIC SEIZURES: CHARACTERISTICS OF A SERIES OF PATIENTS DIAGNOSED AT PRESENTATION TO A FIRST SEIZURE CLINIC

R. Duncan
Southern General Hospital, Glasgow, UK

Purpose: Most published populations of patients with PNES have an average delay to diagnosis of approximately 7 years.

We wished to determine whether a patient population studied at onset of PNES was different from populations studied long after onset.

Method: All patients presenting to a first seizure clinic serving a population of 330,000 who had a diagnosis of PNES in 2006 and 2007 (n=47) were studied by means of semi-structured interview. Past medical history was obtained from case records.

Results: Our calculated incidence was 6.96/100,000/year. 40/46 patients (85%) were women. Mean age at onset was 30.4 + 18.7 years, and age at presentation was 34.2 + 16.5 years. In 31 patients the time from onset to diagnosis was <1year. Only 12 patients were off work sick, and 3 unemployed. 22 patients admitted to no psychiatric symptoms, and 27 had no previous contact with mental health services. Sexual abuse was admitted by only 7 patients with a single sexual assault in a further 3 (total = 21.7%). 6 patients defaulted follow up. 26 patients were free of spells at 3 months post diagnosis.

Conclusion: Our incidence is much higher than previous estimates, at approximately one seventh that of epilepsy. This and our relatively good short-term outcomes raise the possibility that in a hitherto undescribed subset of patients PNES resolve.

E392
NEUROPHYSIOLOGICAL AND CLINICO-RADIOLOGICAL PECULIARITIES IN THE MOLDAVIAN PATIENTS WITH NEUROCYSTICERCOSIS

G. Nadejda, and G. Stanislav
Emergency Care Hospital, Chisinau, Moldova

Purpose: Neurocysticercosis is a parasitic disease, in which the seizures are more frequent clinical manifestation. Our objectives were to compare seizure origin by clinical, electroencefalografic (EEG) and computed tomography (CT) data.

Method: We examined 43 patients with CT findings suggestive for NCC (30 – with seizures and 13 patients – seizure-free) in a view to classify their seizures and to evaluate the concordance of ictal semiology and localization of seizures based on EEG and CT recordings.

Results: The most frequent type of seizure, according to ILAE classification, were partial simple seizures with (nine patients – 30%) or without secondary generalization (eight patients – 26.5%). Motor partial seizures were in eight patients (42%). CT data showed that more affected cerebral region was frontoparietal localization – in 57 instances and less was affected the occipital one – in 10 cases. Also, a very vulnerable area was the temporal lobe, especially deep structures – in 28 cases. This preferential localization may be due to an intensified vascularization of these regions. EEG recordings were normal in 1 patient (3.3%) from the NCC group with seizures, and in 6 patients (46.2%) from seizure-free group ($p<0.01$). Lateralizing EEG abnormalities was demonstrated in the first group in 12 patients (40%), and in the second group – in 3 patients (32.1%). Concordance of ictal semiology, EEG and CT data was found in 19 patients with seizures (63.3%). Absence of congruence was in 4 patients (13.3%). Clinical and EEG discordance was noted in 6 patients (20%) and clinical and CT data were discordant in 5 patients (16.6%). This discordance can be explained by seizure propagation from silent areas to cortex.

Conclusion: NCC is a real cause of seizures. More frequent ictal semiology is congruent with EEG and CT recordings in patients with NCC.

E393
EFFICACY AND TOLERABILITY OF LEVETIRACETAM IN PATIENTS WITH EPILEPSY FROM THE COMMON MEDICAL PRACTICE

Z. Zahariev, and E. Viteva
Medical University, Plovdiv, Bulgaria

Purpose: We evaluated long-term efficacy and tolerability of Levetiracetam (LEV) in patients with refractory/or no, partial/generalized epilepsy.

Method: Open-label, prospective clinical study, included 65 patients (41 females), mean age 32.68, 14.09y, followed from 6m to 1y.

Results: 38 undergone assessment up to now, 71,43% partial epilepsy, 28,57% generalized, 20% idiopathic, 55% symptomatic and 25% cryptogenic. The mean seizure frequency before starting LEV was 4.1, 6,4/w for partial seizures and 3,7,9,4 for generalized ones. LEV was given as adjunctive therapy mainly in combination with Valproate (VPA, 16,15%) and VPA+OCBZ (13,85%). As per LEV dosage, 4 groups were made out: 1000 mg/d, 1500 mg/d, 2000 mg/d and 3000 mg/d, mean LEV dosage 1646, 359mg/d. There was a minimal difference of the total effectiveness of the dosages 1500 and 2000 mg/d. Seizure frequency reduction 50% was 53,33% vs. 52,63%. 18,42% without change in the frequency of clinical manifestations, while in 15,79% there was worsening. The clinical effect was most marked in the 6th month for partial seizures. The mean month frequency at the end of the first year showed more than double frequency reduction (59%) for the generalized seizures. Seizure reduction was most rapid and highest for partial seizures and a gradual frequency reduction for generalized seizures. At the study end 2/4 patients with myoclonic seizures were with seizure frequency reduction higher than 50%.

Conclusion: Adjunctive LEV was highly effective in patients with partial and generalized epilepsies independent of their etiology. LEV shows long-term, consistent efficacy and tolerability with mild and transitory side effects.

E394
SOME PECULIARITIES OF PREGNANCIES IN WOMEN, SUFFERING FROM EPILEPSY IN VITEBSK REGION (BELARUS) DURING LAST 5 YEARS

H. Navumava, A. Prusakova, and A. Prusakou
Vitebsk Regional Center for Medical Diagnostics, Vitebsk, Belarus

Purpose: The aim of the investigation was evaluation of pregnancies peculiarities in women, suffering from epilepsy in Vitebsk region during last 5 years.

Method: We performed a population-based case ascertainment of all available sources of medical care since April 2002 till December 2007. Women of fertile age (15–41 years), suffering from epilepsy, were analyzed. Only cases with active epilepsy were included. All patients were examined by neurologist or psychiatrist. Pregnancies, their outcomes and children, who were born by suffering from epilepsy women were analyzed too.

Results: Incidence rate of epilepsy in 2002 was 16.3 and in 2007 – 17.5 per 100,000. The prevalence rate of epilepsy in 2002 was 137 and in 2007 – 135 per 100,000. In 2002 there were only 4 pregnant women, suffering from epilepsy with mean age of 23 years. There were 19 patients in 2003 (mean age 25 years). In 2004 appeared 48 women (mean age 26 years). And in 2005 there were 35 women (mean age 26 years). In 2006 and 2007 – 11 (24) and 16 (26) respectively. 70% of the women appeared to be primiparas. Idiopathic generalized epilepsy prevailed in our patients. No one woman took folic acid right from the moment of withdrawal of contraception. Caesarean section was performed in 20% of all cases. Two women have had nondeveloping pregnancies in terms of 12 and 18 weeks of gestation.

Conclusion: Congenital heart malformations have developed in 3 fetuses. All major heart malformations were diagnosed by fetal echocardiography in term of 18–20 weeks of gestation. 86% of all patients received monotherapy.

E395

PAROXYSMAL MOTOR EVENTS DURING SLEEP. SLEEP DISORDERS MIMICKING EPILEPSY OR SEIZURES MISDIAGNOSED AS PARASOMNIAS?

R. Silvestri, I. Arico, R. Condurso, G. Gervasi, G. Mento, and C. Casella

Sleep Medicine Center, Messina, Italy

Purpose: To validate the use of one night video-polysomnography (PSG) to establish the differential diagnosis of patients with nocturnal paroxysmal events.

Method: 18 pts (12 M, mean age 28, range 8–74) were referred over the last 6 months to our sleep centre due to nocturnal episodes of motor agitation. All underwent a full diagnostic interview by a neurologist with sleep/epilepsy expertise, neurological exam, neuroimaging and 1 night video-PSG with full EEG montage.

Results: Reported episodes by interview were consistent with disorders of arousal in 11/18 patients; seizure-like activity, partial or generalized, was reported by the remaining 7. Nocturnal interictal EEG was positive in 14 with frontal IEDs in 9 (bilateral in 6), temporal in 5. On PSG the alleged episodes were recorded in only 7/18 patients. Frequent comorbid disorders were OSAS (5), migraine (5), ADHD (3), cerebral lesions (3), PLMS (2). Sleep latency in the lab was overall quite good (20') and as well as delta latency (25'), whereas REM intervened consistently late (mean RL 147.5') with a mean Arousal Index of 17. Final diagnosis was consistent with centrotemporal benign epilepsy in 3 cases, temporal lobe epilepsy in 4, frontal lobe epilepsy in 3, generalized epilepsy in 2, DO in 4, complicated migraine and OSAS in 2. All patients but 1 was treated, mostly with levetiracetam (9) or with topiramate (6) with over 75% reduction in seizure frequency.

Conclusion: Video-PSG allowed us to formulate a highly probable diagnosis in all our patients and to address an efficient therapy.

E396

HANDEDNESS IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY AND HIPPOCAMPAL SCLEROSIS (MTLE/HS)

K. Borkovcova, M. Brazdil†, and R. Marecek‡*

**Brno Epilepsy Center, St. Anne's University Hospital And Faculty of Medicine, Czech Republic; †Masaryk University, Brno; Czech Republic; and ‡Brno University Hospital, Czech Republic*

Purpose: The relationship between mesial temporal lobe epilepsy with hippocampal sclerosis and hand dominance has not been yet studied. Based on empirical data and recent literature on the significant reorganization of speech and memory in left-sided MTLE/HS patients, a hypothesis of a significant impact of left-sided MTLE/HS on the organization of motor cortex and handedness was tested.

Method: To investigate hand dominance in subgroups of right- and left-sided MTLE/HS patients, 73 subjects with a definite diagnosis of unilateral MTLE/HS were included in the analysis (31 right and 42 left MTLE/HS; 41 females, 32 males). Hand dominance was assessed in each subject using a standard Edinburgh Handedness Inventory.

Results: In the subgroup of left-sided MTLE/HS, 33.3% of the patients were left-handed. In the subgroup of right-sided MTLE/HS, 12% of the patients were left-handed. Subsequent statistical analysis confirmed a significantly higher rate of left-handedness in subjects with left-sided epilepsy (Fisher P = 0.0399; chi-quadrat = 0.0453). In addition, within the subgroup of left-sided MTLE/HS patients, the age of seizure onset was significantly lower in the group of left-handers than in the group of right-handers (t-test P = 0.032, Mann-Whitney U test P = 0.017).

Conclusion: The higher rate of left-handedness in subjects suffering from left-sided temporal lobe epilepsy as well as the earlier age of seizure onset in the left-handers obviously support our hypothesis of a clinically important impact of the disease on the organization of the motor cortex. Theoretically, the spread of epileptic activity from the epileptic focus to the frontal lobe in the early childhood might produce a 'pathological left-hander'.

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E397

INVESTIGATION OF THE INFLUENCE OF ESLICARBAZEPINE ACETATE ON THE PLASMA CONCENTRATIONS OF CONCOMITANT ANTIEPILEPTIC DRUGS IN PATIENTS WITH PARTIAL EPILEPSY

M. Bialer, A. Falcão†, J. Maia‡, L. Almeida‡, and P. Soares-da-Silva‡*

**School of Pharmacy, Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel; †4Health Ltd, Cantanhede, Portugal; and ‡BIAL – Portela & Co, SA, S Mamede Do Coronado, Portugal*

Purpose: Eslicarbazepine acetate (ESL) will be used as adjunctive therapy in partial epilepsy. Here we report an exploratory analysis of the effect of ESL on the plasma concentrations of concomitant AEDs.

Method: Blood samples for monitoring of trough plasma concentrations (i.e., predose or Cminss) of concomitant AEDs were collected at the start of treatment with ESL and at end of 12-week maintenance period in phase III studies. End/start Cminss ratios and their 95% confidence intervals (CI) of mostly used concomitant AEDs were calculated.

Results: Mean Cminss ratios and their 95%CI (in parenthesis) were as follows: carbamazepine: 1.05 (1.00;1.10), 0.98 (0.92;1.03), 1.04 (0.89;1.20) and 0.87 (0.81;0.93) following placebo (n=124), ESL 400 mg (n=96), 800 mg (n=110) and 1200 mg (n=84), respectively; lamotrigine: 0.95 (0.85;1.06), 0.96 (0.84;1.08), 0.87 (0.73;1.01) and 0.75 (0.66;0.85) following placebo (n=41), ESL 400 mg (n=36), 800 mg (n=39) and 1200 mg (n=34), respectively; valproate: 0.99 (0.88;1.11), 0.91 (0.78;1.04), 1.16 (0.97;1.35) and 1.04 (0.78;1.30) following placebo (n=43), ESL 400 mg (n=23), 800 mg (n=44) and 1200 mg (n=36), respectively; levetiracetam: 1.02 (0.69;1.34), 1.05 (0.79;1.31), 0.94 (0.70;1.17) and 1.04 (0.68;1.40) following placebo (n=20), ESL 400 mg (n=21), 800 mg (n=19) and 1200 mg (n=22), respectively; topiramate: 1.03 (0.92;1.15), 1.04 (0.88;1.20), 0.95 (0.85;1.05) and 0.84 (0.76;0.92) following placebo (n=24), ESL 400 mg (n=18), 800 mg (n=26) and 1200 mg (n=24), respectively.

Conclusion: No significant changes in the trough plasma concentrations (Cminss) of concomitant AEDs occurred with ESL 400 mg and 800 mg, the later being expected to be the ESL maintenance dose for most patients. Small decreases in lamotrigine and topiramate Cminss were found with 1200 mg of ESL. Overall, the results show a low drug-drug interaction potential between ESL and other AEDs that may be administered concomitantly during polytherapy.

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E398

SEXUAL DERANGEMENTS AT PATIENTS WITH EPILEPSY

G. Ismayilova

'*Diagnoz*' *Medical Center, Baku, Azerbaijan*

Purpose: The purpose of the given work is to show typical features of sexual derangements at the patients, suffering the temporal form of epilepsy in the Azerbaijan population. The author has noted derangements of a sexual inclination (in the form of impotence) at 30–60% of men with inclination, and decreases in sexual reactions at women are poorly studied.

Method: Inspection of 48 patients in age category from 2 to 40 years which temporal form of epilepsy was shown presence of sexual derangements. Attracts attention that fact, that was not marked decrease in a sexual inclination at no one of women with temporal epilepsy, and on the contrary was present raised libido.

Results: Statistical researches carried out by us among women with epilepsy have shown that 99% of them to get married and early marriages in the age from 14 up to 18 are prevailing.

Conclusion: In marriage at patients is marked a high birth rate. At the same time patients express dissatisfaction at the sexual life. Also was marked at patients infringements of a cycle and polycystic ovary. It was most difficult with social adaptation of such patients. Characteristic of electroencephalography (EEG) at women patients with temporal epilepsy with hypersexuality: in background EEG observe decrease biopotential's voltage of brain up to 30–40 microBT. Also at patients were marked peak- and poly-peak waves in cinciput-temporal areas in a subdominant hemisphere.

E399
SEXUAL DYSFUNCTION IN WOMEN WITH EPILEPSY

V. Zelená, and R. Kuba
Masaryk University, St Anne's Hospital, Brno, Czech Republic

Purpose: The purpose was to analyze sexual function in a group of women with epilepsy, to search for possible correlations with psychological comorbidities and for differences between generalized, temporal and extratemporal epilepsy.

Method: Our study group consisted of 65 women of whom 27 suffered from temporal lobe epilepsy (TLE), 21 from extratemporal epilepsy (ETE) and 17 from primary generalized epilepsy (PGE). The average age was 31.7 years. To evaluate the quality of sexual function and parameters of psychological health we used battery of questionnaires – Female Sexual Function Index (FSFI) and Beck Depression and Anxiety Inventories (BDI, BAI).

Results: In TLE group 7 women had abnormally low FSFI score. In ELE group 2 women and in PGE group 1 woman were below the borderline. We didn't find significant difference in total FSFI scores of the three subgroups. We proved negative correlation between total FSFI score and BDI ($p<0,001$) and BAI ($p=0,048$) scores. Worse BDI score correlated with all dysfunction subtypes, worse BAI score correlated with dyspareunia only. Among women who were below the cutoff score there were significantly less seizure-free patients than among the group with normal FSFI score ($p=0,031$). No correlation between sexual function and seizure frequency was found.

Conclusion: In our group of women with both focal and generalized epilepsy sexual dysfunction (defined as low total FSFI score) was stated in 15.4%. In TLE group 25,9% of women were found dysfunctional, while in ELE and PGE group only 9,5% and 5,88% respectively. From the watched factors depression and anxiety are most obviously associated with sexual dysfunction and seizure freeness with better sexual function.

E400
STIFF PERSON SYNDROME IN ASSOCIATION WITH NONPARANEOPLASTIC LIMBIC ENCEPHALITIS

K. Franke, R. Schulz, M. Hoppe, E. Korn-Merker, U. Specht, and A. Ebner
Bethel Epilepsy Center, Mara Hospital, Maraweg 21, Bielefeld, Germany

Purpose: Stiff person syndrome (SPS) is a rare neurological condition characterized by muscle stiffness, rigidity and painful spasms that occurs as a paraneoplastic, autoimmune or idiopathic variant. The autoimmune variant is known to occur in conjunction with other autoimmune disorders especially diabetes mellitus type I and autoimmune thyroiditis.

Method: We describe the cases of two young women (21 and 25 years old) with refractory epilepsy due to limbic encephalitis (LE). Both patients initially presented with cognitive/psychiatric symptoms, memory loss and refractory temporal lobe seizures. MR imaging showed typical abnormalities in the medial temporal lobes for LE. Within the course of a few years (3–5 years) both of them developed additional motor symptoms with stiffness, increased muscle tonus and gait disturbance in the sense of a SPS, markedly alleviated by benzodiazepines.

Results: In both patients autoimmune status showed increased levels of antibodies against glutamic acid decarboxylase (GAD) but no classical onconeural antibodies. Screening for tumors did not reveal underlying malignancies. Interestingly both patients suffer from other autoimmune diseases: one of them developed diabetes mellitus type I, the other Hashimoto thyroiditis.

Conclusion: A SPS can occur in conjunction with LE. These cases support the assumption of common autoimmune pathogenetic mechanisms and a relevance of GAD antibodies. Autoimmune LE patients should be screened for possibly associated other autoimmune disturbances e.g. diabetes, thyroid disease and stiff person syndrome. Clinicians should be aware of accompanying immune-mediated diseases. To our knowledge this is the first report on SPS in conjunction with nonparaneoplastic LE.

E401
POLYMORPHISM IN THE *SCN1A* GENE AND RESPONSE TO ANTIEPILEPTIC TREATMENT

C. Angelopoulou, S. Veletza*, K. Vadikolias*, I. Heliopoulos*, C. Stathi†, and C. Piperidou**
**Democritus University of Thrace, University General Hospital, Alexandroupolis, Greece; and †General Hospital of Komotini, Greece*

Purpose: To examine the correlation between the SCN1A gene polymorphism IVS5-91 G>A and response to sodium channel blockers medicines: carbamazepine, phenytoin, sodium valproate, topiramate, oxcarbazepine, lamotrigine used as antiepileptic drugs (AEDs).

Method: The sample consists of 76 patients (33 men, 43 women) with confirmed diagnosis of epilepsy. Patients were being followed up as outpatients in epileptic Clinic of University Hospital of Alexandroupolis at 2-month intervals for 10 years. Syndromic classification was determined according to the International League Against Epilepsy (1989). Patients were divided in two groups according to drug response: patients who respond to AEDs and those with refractory epilepsy. Patients who respond to AEDs were further divided in two subgroups: patients who responded to monotherapy and those who responded to polytherapy. SCN1A IVS5-91 G>A polymorphism was genotyped using Taqman assay. Pearson x2criteria has been used for the statistical analyses.

Results: Prevalence of the A/G genotype in patients responding to monotherapy (A/G: 93,18%, G/G: 6,8%) in relation to the polytherapy group (A/G:72,2%,G/G:27,7%) was statistically significant ($p=0,025$). No statistically significant difference was detected between the patients responsive to AEDs and patients with refractory epilepsy.

Conclusion: Within patients responding to monotherapy the presence of allele A of SCN1A gene seems to correlate positively with response to AEDs.

E402
PERIICTAL HEADACHE IN PATIENTS WITH EPILEPSY FREQUENCY, CHARACTERISTICS AND PREDICTIVE FEATURES

M. Holtkamp, L. Ghaeni, J. Matzen, and B. Wawrzyniak
Charité – Universitätsmedizin Berlin, Germany

Purpose: Headache temporally linked to epileptic seizures is well known. The aim of this study was to assess frequency and characteristics of periictal headache (PIH) and to detect predictive features.

Method: All outpatients (? 18 years) with epileptic seizures seen in a tertiary epilepsy centre (11/2006–12/2007) underwent a semistructured interview. Occurrence and characteristics of preictal, ictal and postictal headache were assessed. Clinical variables in patients and seizure types with and without PIH were compared.

Results: A total of 201 patients (n=132 one seizure type, n=66 two, n=3 three) were assessed. PIH occurred in 72 patients (seizure type-related, n=80), and was preictal in n=18 (n=21), postictal in n=61 (n=67), pre- and postictal in n=8 (n=11) and purely ictal in n=1 (n=1). Characteristics of migraine (seizure type-related) were present in n=21 and of tension-type headache in n=48. Mean headache intensity (visual analogue scale) was 6.7 preictally and 5.9 postictally, 39% of patients used analgetics. Variables associated with PIH were female sex (58%, no headache 41%; p=0.019), long duration of epilepsy (? 19 vs. ? 14 years; p<0.0001), antiepileptic polytherapy (50 vs. 33%; p=0.02), and generalized tonic–clonic seizures (75 vs. 42%; p<0.0001). Seizure types associated with lack of PIH were absence seizures (9%, headache 1%; p=0.022) and simple partial seizures (18 vs. 4%; p=0.002).

Conclusion: PIH is frequent and under treated; predictors are female sex, long duration of epilepsy, antiepileptic polytherapy, and generalized tonic-clonic seizures. Physicians should ask patients for PIH, particularly those at risk, adequate analgetic treatment may relieve patients from this additional burden of epilepsy.

E403
ANALYSIS OF SEIZURE TYPE AND ANTIEPILEPTIC DRUG THERAPY IN MEN WITH EPILEPSY AND SEXUAL DYSFUNCTIONS

S. Vujisic,†, Z. Milovic*, and M. Kolinovic**
**Clinical Center of Montenegro, Montenegro; and †Medical Faculty University of Montenegro, Montenegro*

Purpose: The aim of this study was to analyze the type of seizure, antiepileptic therapy and disease duration as well as the possible impact of these factors on the occurrence of sexual dysfunctions in men with epilepsy.

Method: A group of 21 male outpatients with epilepsy, treated at the Dispensary for epilepsy, Clinical Centre of Montenegro, Podgorica, who reported the existence of sexual dysfunctions was investigated. All patients completed a detailed questionnaire. The neurological examination, EEG, CT and MRI were performed. The seizures were classified according to ILAE criteria. The problems in sexual functioning were divided into 4 categories: impotence, shortened erection time, decreased libido and infertility.

Results: The majority of patients in the examined group were in 5th and 6th decade of life (90.48%). Decreased libido was the most common problem (23.81%). The presence of more than one sexual dysfunction was reported by 52.38% of patients. Three (14.28%) patients were infertile. Complex partial seizure, with or without secondary generalisation was the most frequent seizure type (85.71%). In most patients (66.67%), sexual dysfunctions were associated with longer epilepsy duration (20 years and over). Carbamazepine was the most commonly used antiepileptic drug (80.95%). Only 5 patients were treated with monotherapy. The most commonly used drug combination was valproate and carbamazepine (14.28%).

Conclusion: Sexual dysfunctions in the observed group of men with epilepsy were most commonly associated with complex partial seizures. Carbamazepine and valproate were most frequently used drugs. Sexual dysfunctions were more common in patients with longer duration of epilepsy.

E404
USING THE INTERNET TO RECRUIT PATIENTS FOR EPILEPSY DRUG TRIALS

P. Bergin, R. Frith*, L. Sadleir†, N. McGrath‡, A. Ranta§, E. Walker*, R. Sheehan¶, and T. Ip¶*
**Auckland City Hospital, New Zealand; †Wellington Hospital, New Zealand; ‡Northland Base Hospital, New Zealand; §Palmerston North Hospital, New Zealand; and ¶University of Auckland, New Zealand*

Purpose: To develop a novel Internet-based approach to performing epilepsy drug trials, with patients recruited directly from routine neurology clinics.

Method: We created an Internet-based questionnaire and associated database, and invited neurologists and pediatric neurologists throughout New Zealand to register patients with epilepsy whenever they were uncertain of the optimal management. We produced an algorithm to select patients who had failed to respond to the first antiepileptic drug. We performed a pilot study in which these patients were randomized to receive one of several different drugs. Patients were registered from routine clinics and randomized immediately via the Internet. Follow-up data on all patients is being collected whenever they are seen again. Neurologists did not receive any financial recompense for participating.

Results: The pilot study recruited patients from mid June to December 2007, and 137 patients were registered, of whom 113 were considered suitable for drug trials. Thirty five patients who had used a single antiepileptic drug were enrolled and 14 were successfully randomized on line to receive a different drug. Patients were registered by 16 different neurologists from 8 different cities.

Conclusion: Patients can be recruited for randomized controlled trials via the Internet at low cost. Neurologists would register suitable patients whenever they were uncertain regarding the optimal management. Algorithms would be written to select patients with particular characteristics (eg seizure syndromes, specific aetiologies) who fulfilled entry criteria for specific studies. Patients would be recruited and randomized directly from routine clinics.

E405
EFFECTS OF SLOW ANTIEPILEPTIC DRUG WITHDRAWAL ON OCCURRENCE OF SEIZURE CLUSTERS AND STATUS EPILEPTICUS DURING PRESURGICAL VIDEO-EEG MONITORING

B. Aktekin, and G. Unal
Akdeniz University, Turkey

Purpose: We prospectively investigated the effects of slow Antiepileptic Drug (AED) withdrawal on seizure clusters and status epilepticus in patients with focal epilepsy who underwent video-EEG monitoring for presurgical evaluation.

Method: Between 2004 and 2007, 44 consecutive patients with drug resistant focal epilepsy who underwent video-EEG monitoring for presurgical evaluation in our department were recruited. AEDs being slowly decresaed in seven days prior to the admission and totally discontinued during the monitoring period. Seizure clustering was defined as three or more seizure within 24 hour and status epilepticus was defined as seizure was lasted more than three minutes. The monitoring was continued until three identical electroclinical seizures were recorded.

Results: In all, 44 patients had 89 partial seizures (mean 3,7 per patient), including 8 secondarily generalized. Eight patients experienced seizure clusters and six had generalized seizures that had been absent for years. However, none evolved to status epilepticus.

Conclusion: Slow AED withdrawal effectively provoked seizures in epilepsy patients undergoing presurgical video-EEG monitoring. However, nearly 20% of patients had seizure clusters but none SE was experienced in our series.

E406
PROSPECTIVE MULTICENTER SCREENING OF MIGRAINE CRITERIA IN BELGIAN PATIENTS WITH EPILEPSY

A. Van Dycke, E. Carrette*, K. Vonck*, V. De Herdt*, I. Dewaele*, H. Verhelst†, M. Van Zandijcke*,‡, L. Lagae§, G. Buyse§, L. Dom¶, L. De Meirleir**, A. Jansen**, E. Schmedding**, H. Hauman††, B. Ceulemans‡‡, K. Paemeleire*, and P. Boon**

**Reference Center for Refractory Epilepsy, Ghent University Hospital, Gent, Belgium; †Ghent University Hospital, Gent, Belgium; ‡General Hospital Sint-Jan Brugge, Brugge, Belgium; §University Hospital Gasthuisberg, Leuven, Belgium; ¶'Koningin Paola' Childrens Hospital, Antwerpen, Belgium; **Free University Hospital Brussel, Brussel, Belgium; ††Epilepsy Center CEPOS, Duffel, Belgium; and ‡‡Revalidation Center Pulderbos, Zandhoven, Belgium*

Purpose: Migraine and epilepsy are both prevalent chronic neurological disorders. The prevalence of migraine is 12% in the general adult population and 8,6% in children. However, there seems to be a higher prevalence of migraine in epilepsy patients. In this multicenter pilot study, we wanted to investigate what percentage of epilepsy patients also had a history of migraine.

Method: During 4 consecutive weeks every epilepsy patient (>6 years old) seen at the consultation in 8 different neurology departments in Belgium, was interrogated about the occurrence of migraine using a specially designed questionnaire (based on the ICHD-II migraine criteria).

Results: The questionnaire was completed in 397 patients. 231/397 patients were older than 17y (118M/113F), 166/397 were younger than 18y (89M/77F). The mean age of epilepsy onset was 16,5y (range 0–76y). 34/231 (9M/25F) adult patients were diagnosed with migraine. In children this was the case in 18/166 patients (8M/10F). This diagnosis was newly made when completing the questionnaire in 7 adults and 7 children. The mean age of migraine onset was 18,4y (range 6–45). 7/52 patients had migraine with aura. 12/52 patients (23%) had at least 1 first-degree relative with epilepsy and 23/52 (44%) had at least 1 first-degree relative with migraine.

Conclusion: In this Belgian multicenter study, 15% of adult epilepsy patients and 11% of the children were diagnosed with migraine. These results suggest a higher prevalence of migraine in epilepsy patients compared to a normal population.

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E407
SEVERE MYOCLONIC EPILEPSY IN MONOZYGOTIC TWINS: LONG TERM FOLLOW-UP

Y. Woo, Y. Kim*, J. Kim*, and K. Park†*

**Chonnam University Hospital, Korea; and †Mirae Children's Hospital, Korea*

Purpose: To report a pair of monozygotic male twins with SMEI who had familial history of seizures.

Method: By the review of the medical records.

Results: Twin 1st had an initial seizure at 3 months as prolonged generalized tonic–clonic seizures (GTC) with febrile illness. Two months later a new seizure was developed as complex partial seizure (CPS) without febrile episode. At 9 months, atonic seizures and myoclonic fits were started and since 11 months, alternating hemiconvulsion, GTC, myoclonic seizures, CPS, tonic and atonic drop attacks were presented frequently. Developmental milestones were delayed. On the routine EEGs, normal at early phase of illness, focal sharp or slow and generalized spike and wave discharges were recorded occasionally. Brain MRI and Tc99m HMPAO SPECT showed normal findings. On a video-EEG monitoring, myoclonic fits were frequently recorded during the sleep and wakefulness with generalized polyspikes or spikes and waves. GTC and CPS were also recorded with generalized fast activity followed by generalized spike and wave pattern, sometimes focal 5Hz recruiting activity coming from right or left temporoparietal area. His epileptic events were very intractable to various antiepileptic drugs. At 5 years of age, he died from status epilepticus associated with febrile illness. Twin 2nd showed similar clinical features and courses; an initial nonfebrile seizure at 4 months, repeated bouts of several types of seizures and hemiclonic status epilepticus at times, with interictal and ictal EEG abnormalities, no response to medications, and mental retardation with clumsy movement at 15 years of age by now.

Conclusion: We report an experience of a pair of monozygotic twins with SMEI who had concordant clinical features. These findings suggest the possibility that a genetic factor can be a determinant in the etiology of this peculiar syndrome.

E408
EVALUATING THE EFFICACY OF POLYTHERAPY ANTIEPILEPTIC DRUG COMBINATIONS IN PATIENTS WITH EPILEPSY

S. Dergalust, V. Nguyen*, J. Chen*,†, J. Stern*,†, J. Sayers*, and R. Sankar†*

**VA Greater Los Angeles Heatlhcare Center, USA; and †David Geffen School of Medicine At UCLA, USA*

Purpose: There are more than fifteen different antiepileptic drugs (AEDs) available for the treatment epilepsy. However, few studies have comprehensively described the response to and efficacy of all AED combinations within the same population. Our objective is to characterize common drug response phenotypes and compare and evaluate the efficacy and adverse effect profiles of all different poly-AED therapies used in the management of seizure disorders in the veteran population.

Method: Retrospective chart reviews will be conducted on all patients diagnosed with a seizure disorder and prescribed an AED at VA Greater Los Angeles from January 2001 to June 2006.

Results: Seizure response to multiple AED combinations at different dosages will be recorded and compared. AED failure, reason for failure, and time to escalation of therapy will be evaluated. Occurrence and incidence of adverse events at different dosages and with different combinations will be recorded and compared. Results will be combined with data collected from previous studies evaluating the efficacy of dual therapy combinations of AEDs in patients with epilepsy from the same VA population.

Conclusion: Cumulative findings from these studies will be presented. Implications for future pharmacogenetic studies of antiepileptic drug response will be discussed.

E409
'ICTAL-POSTICTAL FEVER' IN TEMPORAL LOBE SEIZURES

C. Tassinari, S. Silipo, R. Michelucci, G. Cantalupo, F. Pinardi, L. Volpi, P. Riguzzi, and G. Rubboli

Bellaria Hospital, Bologna, Italy

Background: Increment of the body temperature, reported in the literature as 'ictal-postictal fever (I-PIF)', has been described as a rare symptom of epileptic seizures. The relationships between the epileptic seizure and the appearance, the duration and intensity of this phenomenon have been

poorly investigated. We studied variations of body temperature in relation to temporal lobe seizures.

Method: We monitored auxillary temperature (AT) in 4 patients affected by drug-resistant temporal lobe epilepsy (TLE) during long-term video-EEG monitoring for presurgical evaluation (3 patients) or by personal measurements (1 patient). In the interictal period, AT was measured every 4–5 hours; in the ictal-postictal period up to every 15 minutes for at least three hours.

Results: We obtained data from 3–9 seizures per patient. I-PIF was observed from 50 to 100% of the analyzed seizures. I-PIF appeared with a latency ranging from few minutes to 1 hour following the ictal event, independently from the eventual occurrence of secondary generalization. In three patients, I-PIF lasted from 48 to 96 hours, with AT ranging from 37,7°C to 38,9°C; in the fourth subject lasted only 2 hours appearing as a mild increment of the AT (37,2°C).

Conclusion: In our patients I-PIF appeared in the postictal period, displaying in some subjects a long-lasting course (up to 96 hours). This phenomenon might be underestimated (particularly when AT increment is mild). Pathophysiological mechanisms of I-PIF in TLE may admit the ictal involvement of cerebral structures participating in autonomic control (such as hypothalamus and insula) strictly connected to the temporal lobes.

E410
EPILEPTIC SEIZURE AS THE FIRST SYMPTOM IN AORTIC DISSECTION

M. Ercegovac, L. Beslac Bumbasirevic, and D. Jovanovic
Institute of Neurology, Clinical Center of Serbia, Serbia

Purpose: A dissection of the thoracic aorta represents a rare but life-threatening emergency situation, and can involve either the ascending or descending aorta. Neurological symptoms occur in 8–33% of all patients. Only two-thirds of patients with neurological symptoms reported chest pain. Epileptic seizures rarely (3%) occur as the only or first symptom of aortic dissection.

Case report: A 54-year-old man, was hospitalized with first generalized tonic–clonic epileptic seizure during night sleep, with persisting light right hand weakness. He had no chest or back pain. After hospital admission, he became self functional. EEG showed interictal generalized sharp-slow wave max 2–3 sec, and left anterior accentuation. MRI showed massive ischemic stroke in the left hemisphere, MR angiography shove left ACC dissection and sub occlusion of right vertebral artery. On the fourth day he had cardiorespiratory arrest, and fatal outcome. Postmortal pathological findings detected primary aortal dissection with upstream spreading (type A), ACC dissection and consequential massive ischemic stroke (with epileptic seizure as the first symptom), and secondary dissection with downstream spreading and completely thoracic and abdominal aortal dissection (type I), which cause the fatal outcome.

Conclusion: Type A aortic dissection with neurological symptoms can occur with any significant chest or back pain, and symptomatic epileptic seizure is rarely mentioned as the present, especially first symptom, which can mislead correct diagnosis. Type A form especially type I of aortic dissection with presence of neurological deficit predicted an increased mortality especially in the group of patients treated with conservative therapy.

E411
POST TRAUMATIC EPILEPSY: A FOLLOW-UP OF 20 YEARS

J. Lopes, A. Santos*, and A. Martins da Silva*,†*
**Hospital De Santo António, Portugal; and †ICBAS – Universidade Do Porto, Porto, Portugal*

Purpose: To assess clinical, EEG and CT-Scan epilepsy evaluation of a population of head trauma patients prospectively randomized and followed up in a 20 years interval.

Method: A cohort of 152 patients with head trauma after civilian accidents and with acute seizures; or localized closed brain trauma: contusion, haematoma or with PHI, without previous medical history, was randomized. At admission severity GC Scale and functionality KS at one year were also used to parameterize clinical status. Clinical, EEG, CT scan were re evaluated at 6 and 12 months; 5, 10 and now 20 years after trauma.

Results: From initial group of 152 patients, 147 were included and followed up at the beginning. Sixty-nine patients reassessed at 5 years and 46 at 10 years after trauma. 15 Patients remain with Epilepsy at 10 and now 20 years after trauma. From those 8 patients remain with active epilepsy (seizures on the last 5 years and under AED – four out of them in monotherapy). All but one had focal cerebral contusion as imaging lesion and all but two remain with neurological deficits. All patients with epilepsy had EEG abnormalities.

Conclusion: PTE is a frequent consequence of closed cerebral head injury namely in patients with neurological deficits associated. Also in a high percentage the epilepsy remain active 15 to 20 years after trauma. Persistence of EEG abnormalities in a ten years evolution is associated to later active epilepsy.

E412
SALIVA MELATONIN CONCENTRATIONS IN DIFFERENT TIME AFTER TONIC–CLONIC AND COMPLEX PARTIAL EPILEPTIC SEIZURE

E. Motta, A. Golba*, Z. Kazibutowska*, Z. Ostrowska†, M. Dêbski*, A. Lasek-Bal*, E. Œwiêtochowska†, and G. WoŸnik†*
**Silesian Medical University, Katowice, Poland; and †Silesian Medical University, Katowice, Poland*

Purpose: Experimental and some clinical studies revealed both anticonvulsant and proconvulsant properties of melatonin (MEL). There are only few studies concerned with melatonin concentration after epileptic seizure. The aim of the study was to asses the influence of tonic–clonic and complex partial epileptic seizure upon melatonin concentration and to estimate how fast the concentration of MEL returned to normal values.

Method: The study included 30 patients (15 women) with drug resistant epilepsy aged 22– 55 years (37.17 ± 10.25 mean). Patients and controls (twenty healthy volunteers) had saliva collected at 4 -hour intervals during 24 hours period. Examinations were performed in autumn under the same meteorological condition. Patients had also saliva collected 15 minutes and 2 hours after seizure.

Results: Mean saliva melatonin concentration 15 minutes and 2 hours after both tonic–clonic and complex partial seizures did not differ significantly from mean MEL cicardian profile both in patients and controls. There was no significant difference between mean MEL values 15 minutes and 2 hours after day seizures and mean saliva melatonin concentration in epilepsy persons and controls. In patients with highest MEL concentration a 2 a.m. there was significant increase of its saliva values 15 minutes after night tonic–clonic seizure comparing with mean cicardian profile both in patients and controls.

Conclusion: Both tonic–clonic and partial complex seizure did not increase significantly saliva melatonin concentration in patients with epilepsy. Significant increase of melatonin serum level 15 minutes after night tonic–clonic seizures may probably suggest the proconvulsant role of melatonin.

E413
OCCIPITAL EPILEPSY – DIAGNOSTIC TRAPS

M. Macovei, and A. Ilinca
National Institute of Neurology and Neurovascular Disease, Bucharest

Purpose: The etiology of occipital epilepsy could be a challenge for any clinician.

Method: The authors studied 9 cases (4 females, 5 males) with mean age of 40 years, admitted in our service with a first episode of occipital epilepsy (crises of lost of consciousness with simple or complex visual aura).

Results: Three cases with acustic neurinoma (without clear symptoms of ponto-cerebellar angle), with pseudo-TIAs in the PCA territory. The increased level of albuminorachia+ the intracranial increased pressure induced vasospasm. The symptoms remitted after neurosurgical intervention with the ablation of the tumor; arteriovenous malformation with basilar migrenous crises, associated with occipital infarct (MRI confirmation). Splenium of corpus callosus syndrome, at the level of the splenic artery, with dyslexia without agraphia (fetal aspect of the basilar trunk-MRA), two cases of occipital lobe cavernoma with demyelination secondary to the repeated microbleedings, having as first clinical manifestation the occipital epilepsy, three cases with benign repeated intracranial hypertension (cephalgia, nausea, emesis, vertigo, diplopia) with simple and complex aura and psychomotor crises. The EEG aspect showed focal occipital discharges. Optic fundus signs showed papilar edema. Cerebral CT: small ventricles, secondary to cerebral edema; unilateral occipital calcifications (2 cases) and occipital bilateral+ basal nuclei calcifications (1 case). The cases were endocrinologically investigated and the diagnosis confirmed.

Conclusion: The authors insist on the diagnostic algorithm in the case of occipital epilepsy, anamnestic data, clinical not so evident symptoms and paraclinical investigations. The physiopathological mechanisms and the etiological corresponding therapy are discussed.

E414
ACCURACY OF ANAMNESTIC CHARACTERISTICS FOR THE DIAGNOSIS OF NOCTURNAL FRONTAL LOBE EPILEPSY (NFLE)

I. Naldi, F. Bisulli, F. Pittau, L. Vignatelli, L. Licchetta, F. Provini, J. Fares, P. Montagna, and P. Tinuper
University of Bologna, Italy

Purpose: To measure the diagnostic accuracy of clinical history in distinguishing NFLE from nonepileptic paroxysmal sleep disorders.

Method: Patients with following disorders were eligible: 1) NFLE; 2) parasomnias; 3) other sleep disorders confounding for NFLE. Clinical and laboratory features from the database of the Sleep Centre of our Department were retrospectively reviewed. Subjects were classified as having NFLE or NOT-NFLE by experts. Two major anamnestic characteristics (defining the semeiology of the epileptic event) and 15 additional features were listed on a form and telephonically administered to 101 subjects by a trained doctor blinded to the final diagnosis. The diagnostic accuracy (by means of sensitivity, specificity, diagnostic odds ratio – DOR) were calculated for each characteristic.

Results: 43 subjects were classified as NFLE, 58 as NOT-NFLE. Sensitivity was moderate (range 2.6–64.1%) and specificity high (range 91.1–99.1%) for all clinical associations. The presence of at least one of the two major characteristics had a DOR of 18.2 (5.9–56.3 IC95%). The highest diagnostic accuracy was obtained combining at least one major characteristic with one of the following: 1. vocalization (DOR 87.9, 41.5–186.3), 2. preceding aura (45.6, 21.3–97.6), 3. less than 2 minutes' duration (43.2, 9.1–203.9), 4. history of tonic–clonic seizures during sleep (30.5, 14.1–66.1), 5. stereotypy of motor phenomena (20.8, 6.2–69.4); 6. recurrence of seizures every night for one month (20.6, 5.5–77.4).

Conclusion: This preliminary study yielded criteria for the anamnestic diagnosis of NFLE. The diagnostic accuracy of these criteria had moderate sensitivity and high specificity. Further prospective validation is needed.

E415
SLEEP DISTURBANCES IN INTELLECTUAL DISABILITY AND SEVERE EPILEPSY: A RETROSPECTIVE STUDY USING VIDEO, EEG AND ACCELEROMETRY

N. Vandenbussche, I. Tan, T. Rentmeester, and J. Arends
Centre for Epilepsy and Sleep and Wake Disorders, Kempenhaeghe, The Netherlands

Purpose: The relation between epilepsy and sleep has been extensively studied. However, sleep research based on EEG or polysomnography in patients with intellectual disability (ID) is limited.

Method: 66 patients with ID and severe epilepsy underwent extensive examination with EEG, video, accelerometry and ECG. Data were retrospectively analyzed and categorized for severity of sleep disturbances, using a scale that involved EEG-pattern and seizure activity.

Results: 55 patients could be analyzed, in 29 (53%) sleep was moderately or severely disturbed. Sleep disturbance severity was determined by seizure activity, awakenings, and interictal spikes on EEG without recognizable increase of delta activity during sleep, a pattern comparable to CSWS (continuous spikes and waves during slow wave sleep). Sleep disturbance severity was not related to severity of ID or epilepsy syndrome.

Conclusion: Sleep disturbances occur in about half of the patients with ID and severe epilepsy. The severity of epilepsy seems to play a major role: seizure activity, increased sleep fragmentation and a CSWS-like pattern. Severity of ID and the epilepsy syndrome seem less important factors. To detect the role of epilepsy nocturnal video and EEG recording is necessary. Sleep study may be beneficial because it may result in changes in drug therapy or adjustments in daytime program.

E416
EFFICACY AND TOLERABILITY OF LEVETIRACETAM IN EPILEPSY (LONG-TERM PROSPECTIVE CLINICAL EVALUATION)

A. Ortenzi, A. Paggi, and N. Foschi
Epilepsy Center, Neurology Clinic, Azienda Ospedali Riuniti, Italy

Purpose: To evaluate efficacy and tolerability of LEV as add-on (group A) or as substitutive monotherapy (group B) in adolescent and adult epileptic patients.

Method: Prospective, open-label, not controlled trial. LEV was added to previous AEDs or converted from other AED because of inefficacy and/or poor tolerability. LEV was titrated in ÏC2 weeks to a maximum dose of 3000 mg/day. 81 patients included (mean follow-up: 401.38 days): 46 in group A (mean nã of AEDs=2.35), 35 in group B. Efficacy was evaluated only in patients whose therapy was changed because of previous AEDs failure and with 30 days of LEV exposure (n= 38 group A; n= 18 group B). Tolerability was evaluated through patient diaries (n= 81).

Results: Therapy was changed: Group A: 37 for inefficacy, 6 for poor tolerability, 3 for both. Group B: 18 for inefficacy, 16 for poor tolerability, 1 for both. Efficacy: Group A: 13/38 (34.2%) were seizure free and 10/38 (26.3%) reached >50% seizure reduction. Group B: 12/18 (66,6%) were seizure free (31.6%) and 1/18 (5.6%) with >50% seizure reduction. Tolerability: Group A: 13/46 (28.3%) reported AEs (9 discontinued). Group B: 12/35 (34.3%) reported AEs (8 discontinued). On the whole, 23/81 (28,4%) discontinued LEV treatment because of inefficacy and/or poor tolerability: 14 in politherapy and 9 in monotherapy. The retention rate (12 months) was 67.9%, (67.4% in group A; 68.6% in group B).

Conclusion: These data confirm a good efficacy and tolerability of LEV in epileptic patients both as add-on politherapy as monotherapy.

E417
LEARNING AND MEMORY IMPAIRMENT IN CHRONIC TEMPORAL LOBE EPILEPSY

L. Barkas, W. Gray, and E. Redhead
Southampton University, UK

Purpose: Temporal Lobe Epilepsy (TLE) often causes untreatable, progressive memory impairment, the mechanisms of which are unknown. This research focuses on the characterisation of the types of memory affected by TLE, and the underlying pathological cause. Adult neurogenesis has been positively associated with performance in spatial memory tasks in animals, and animal models of TLE and hippocampi resected from patients with intractable TLE show reduced neurogenesis.

Method: Memory skills in rats with kainate-induced TLE and humans with selective left or right Amygdalohippocampectomies were investigated using a Morris water maze and a virtual Morris water maze. Rats were given kainate 5 months before testing to create a condition comparable to chronic epilepsy.

Results: Behavioral: Humans and animals with TLE retain the ability to complete simple spatial tasks and associative learning tasks, but perform significantly worse in complex spatial memory tasks. Rats with TLE were also significantly impaired in the long term retention of complex spatial memories. Histological analysis of animal tissue: Principle cell loss on thionin staining showed no abnormalities in the kainate group. No difference was found in subgranular cell production, as marked by Bromodeoxyuridine (BrdU), however there was a significant reduction in neurogenesis five months post Kainate, with an associated decrease in the number of neurons in the dentate and hilus and diminished retention of complex long-term spatial memories.

Conclusion: Animals and humans with TLE have similar patterns of spatial memory impairment. Reduced neurogenesis may affect spatial memory retention.

E418
STATUS EPILEPTICUS: A 2-YEAR ANALYSIS OF CLINICAL PRESENTATION, CAUSE AND OUTCOME IN A HOSPITALIZED POPULATION

G. Pauletto, S. Vergine*, L. Cecotti†, R. Budai*, L. Lazzarino De Lorenzo†, G. Gigli*, and P. Bergonzi**
**DPMSC, Azienda Ospedaliero-Universitaria 'S. Maria Della Misericordia', Udine, Italy; and †Ospedale Di Gorizia, ASS 2 'Isontina', Gorizia, Italy*

Purpose: To analyze clinical presentations, EEG features and outcome of patients referring to our neurological emergency practice for status epilepticus (SE).

Method: We retrospectively reviewed the clinical data and the EEGs of patients who underwent emergency neurological evaluation over a 2-year period (2006–2007) for: suspected enduring seizures, acute confusional state or altered mental state. We selected all cases with a confirmed diagnosis of SE and EEG monitoring.

Results: 58 patients have been selected (28 males and 30 females), mean age 66.7 years. Nonconvulsive status epilepticus (NCSE) was found in the majority of cases (74.14%), while 25.86% of patients presented a convulsive status epilepticus (CSE). Preexisting epilepsy was found in 27% of cases. The most common cause of SE was stroke (36.3% ischemic and 10.34% haemorrhagic). 55.44% of patients were admitted in neurological ward; the remaining where already hospitalized (Intensive Care Unit 13.79%; Medical Department 25.86%; Cardiosurgery 6.86%). Intravenous BDZs were given to 74.14%, but they controlled SE only in 3.44% of cases, all with previous history of epilepsy. The majority of patients were treated with iv Valproate with a successful control of SE; a percentage of 25.86% was treated immediately with iv Valproate according to medical judgment and 18.96% needed major sedation and was accepted in ICU. Case fatality was 31.03%.

Conclusion: NCSE was predominant in hospitalized patients and difficult to treat with first-line drugs. The data are consistent with previous studies held in Italy, except for the emerging importance of VPA in the treatment of SE.

E419
SEX HORMONE ALTERATIONS IN WOMEN WITH PARTIAL EPILEPSY ON ANTIEPILEPTIC DRUGS: RELATIONSHIPS WITH SEIZURE FREQUENCY AND TREATMENT

C. Galimberti, G. Tamagno†, P. Ameri†, G. Ravera†, S. Colnaghi*,‡, F. Magri‡, and G. Murialdo†*
**IRCCS 'C. Mondino Institute of Neurology' Foundation, Pavia, Italy; †University of Genoa, Italy; and ‡University of Pavia, Italy*

Purpose: Sex hormones may modify neuron excitability. In epilepsy women, sex steroid levels may be influenced by seizures themselves as well as by antiepileptic drugs (AEDs). We evaluated the relationships between sex hormone levels and seizure frequency, in women with partial epilepsy (PE) on various AED regimens.

Method: Oestradiol (E2), Progesterone (Pg), Sex Hormone Binding Globulin (SHBG) levels and calculated free E2 (fE2) were determined during the follicular (F) and the mid-luteal (L) phases in 72 PE women, aged 16–47, and in 30 healthy age-matched controls. Hormonal data were correlated with clinical parameters including AED regimen, and a four-point seizure frequency score (SFS): 1=absent (n=26), 2=one per month or less (n=14), 3=four per month or less (n=27), 4=more than one per week until multiple per day (n=5).

Results: E2, fE2 and Pg levels in both ovarian phases and F-fE2/Pg ratios were lower, while SHBG levels were higher in patients than in controls. No significant changes in hormone levels and ratios were observed between patients divided according to their SFS. However, differences versus controls in F-E2, F-Pg and L-Pg, L-fE2, F-E2/Pg and F-fE2/Pg, were due to significant changes in SFS group 3 and/or 4 ($P<0.05$). Noticeably, 44.4–80.0% of women respectively in SFS group 3 and 4 (versus 23.1–35.7% in group 1 and 2) were on AED polytherapies.

Conclusion: Women with more than two seizures per month have significantly different sex hormone levels when compared with healthy subjects; this effect could be possibly explained by the use of AED polytherapies.

E420
EPILEPSY AND MULTIPLE SCLEROSIS

N. Pizova
Yaroslavl State Medical Academy, Russia

Purpose: Search the relationship between multiple sclerosis and epilepsy.

Method: We present four cases of multiple sclerosis which presented as epileptic crises. In a series of 97 multiple sclerosis patients, 4 subjects presented seizures, with an overall prevalence of 4.2%. We report the clinical, electroencephalographical and neuroimaging findings of four patients wiht multiple sclerosis who had epileptic seizures and those in whom there was no evidence of other potentially epileptogenic pathology.

Results: These seizures were partial sensory and/or motor with secondary generalization in free and absence in one. Epilepsy had begun followed MS onset. Epileptic seizures happened in acute phases of multiple sclerosis. The electroencephalogram showed paroxysmal discharges (focal or diffuse) in 2 patients and the EEG was normal in 2 patients with MS. Magnetic resonance imaging revealed an enhancing the cortical or

subcortical areas. Antiepileptic medication (finlepsin) was always effective in patients with partial seizures with or without secondary generalisation.

Conclusion: MS is a risk factor for developing epilepsy. The mechanism of the seizures is including areas of inflammation, edema, and/or demyelination in the cerebral white matter.

E421
QUALITY OF LIFE IN TREATMENT OF ELDERLY PATIENTS WITH EPILEPSY: LAMOTRIGINE AND TOPIRAMATE VERSUS CONVENTIONAL AEDS—CARBAMAZEPINE AND VALPROIC ACID

D. Petrovska-Cvetkovska, D. Nikodijevic, and I. Dzonov
Clinical Centre, Skpopje, Macedonia

Purpose: To evaluate the use of HRQL-QOLIE 89 in comparing new and conventional AEDs in elderly patients with epilepsy.

Method: We conducted a three years, prospective, open labelled study, which included 127 elderly patients with epilepsy. 33 patients received topiramate (100–300 mg/day), 31 were treated with lamotrigine (100–300 mg/day), 29 patients received carbamazepine (400–1200 mg/day) and 34 were treated with valproic acid (900–1500 mg/day). QOLIE 89 was used as a measure of therapeutic efficacy to compare new and conventional AEDs. Seizure reduction rate was also assessed in the four groups of patients.

Results: The improvement of HRQL score in lamotrigine group was 86%, where the reduction of seizures >50% was achieved in 62% of patients and in topiramate group showed improvement of 64% with reduction of seizures >50% in 58% of patients ($p<0.05$). The carbamazepine (CBZ) and valproic (VPA) group showed lower improvement of QOLIE 89 (CBZ-46% and VPA-52%), but seizure reduction >50% was registered in 64% of patients treated with CBZ and in 59% of patients treated with VPA.

Conclusion: Improvement of QOLIE 89 score was significantly higher in lamotrigine group, than 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 function.

E422
MISDIAGNOSIS OF AUTONOMIC SEIZURES IN ADULTS

J. Gomez-Alonso, D. Muñoz, M. Aguado, P. Bellas, S. Piñeiro, and C. Hervés
Hospital Xeral, Spain

Purpose: Autonomic manifestations are common in epileptic seizures, as well as in other prevalent medical disorders. When autonomic symptoms are the only component of simple partial seizures, their epileptic nature of the episodes may be unrecognized. We assessed the potential occurrence of such diagnostic errors.

Method: We collected patients with misdiagnosed autonomic seizures in adult patients seen at the Neurology Service of our district hospital. We analyzed their clinical features, their initial diagnoses, and the clues for the right diagnosis.

Results: We found six patients with misdiagnosed autonomic seizures. Their mean age at diagnosis was 59.8 years (range: 43–79). The mean delay in diagnosis was 51/2 years (from 2 months to 17 years). The initial diagnoses were: syncope in 4 patients (with seizures characterized by pallor and sweating, associated with a combination of dizziness and belching, or abdominal discomfort, diarrhoea, and change in consciousness), unspecified urogenital disorder (in a case of sexual seizures), and dyspnea secondary to mitral valve prolapse (in a case of seizures characterized by subjective shortness of breath, hyperventilation, pallor, sweating and borborygmus). The latter patient had cardiac surgery without improvement in his symptomatology. The most helpful steps for the eventual diagnosis were: a detailed history taking (5 cases), a positive trial with antiepileptic drugs (3 cases) and, rarely, the practice of new tests.

Conclusion: In adults, seizures presenting with isolated autonomic manifestations can represent a diagnostic challenge, and can go undiagnosed for years. Awareness of the existence of such seizures could avoid the mismanagement of these patients.

E423
CONGENITAL NEUROGENIC CENTRAL HYPOVENTILATION SYNDROME PRESENTING AS REFRACTORY EPILEPSY IN ADULTHOOD: CASE REPORT

T. de Haes, T. Rodrigues Velasco*, D. Paquito Vianna*, H. Haueisen Sander*, L. K da Silva*, M.M. Bianchin†, R. França Fernandes*, and A. Sakamoto**
**Ribeirão Preto School of Medicine-University of São Paulo, Ribeirão Preto, Brazil; and †Federal University of Rio Grande Do Sul, Porto Alegre, Brazil*

Purpose: Congenital Neurogenic Central Hypoventilation Syndrome (CNCHS) is a rare condition characterized by dysfunction of autonomic respiratory control, more dramatic during sleep, associated to a mutation in the gene PHOX2B, with variable outcome including death in more severe cases.

Method: We report the history of a 22-year-old female with refractory complex partial seizures since age 6, admitted to the Video-EEG (VEEG) Monitoring Unit of our Epilepsy Surgery Center for presurgical evaluation, in January, 2008. VEEG showed interictal sharp waves over the right temporoparietal region and seizures originated in both temporal lobes, confirmed by invasive study with bifrontotemporal strips. After a generalized tonic–clonic seizure, the patient had a prolonged apnea requiring intubation and continued having apneas with oxigen dessaturation, mainly during slow wave sleep, after extubation. A past history of neonatal central apnea leading to mechanical ventilation along the first weeks of life came up at this point. She was then submitted to a polissomnography, which showed 195 episodes of central apnea (27/hour), maximal dessaturation of 63%, with no obstructive sleep apnea.

Results: She was diagnosed as CNCHS and treated with BiPAP during sleep. Treatment with Benzodiazepines was interrupted and Carbamazepine dose reduced. She has no longer had epileptic seizures and has shown significant improvement in attention, humor and scholar skills. The association between respiratory sleep disorders (RSD) and worsening of epileptic seizures has been previously described.

Conclusion: We report the association of CNCHS, leading to initial diagnosis of refractory epilepsy, which became easily controlled after adequate treatment for the RSD.

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E424
SWITCHING GENERIC AEDS—TIME FOR A NEW APPROACH

M. Glynn
Brainwave, The Irish Epilepsy Assoc, Ireland

The purpose of this study was to determine whether any consensus existed amongst physicians, investigators and fiscal policy makers in the area of substitution and switching of branded and generic AEDs. Results indicate that little agreement exists on the medical, ethical and economic benefits of the practice. Current switching practice is based on very limited scientific data and no conclusive evidence exists that public health authorities gain substantially either due to concerns over high additional costs as the results of break through seizures. In addition, the track

records of many generic suppliers in supplying their product consistently, has been very poor. To ensure that patients with epilepsy do not continue to have exposure to risks from substitution or switching, particularly switching from one generic AED to another, this analysis concludes that a new system of regulation of the consistent supply of generic AEDs be implemented at national level that will protect patients and physicians while ensuring that health authorities pay the least amount necessary in supplying essential epilepsy drugs.

E425
AGE AND PLACE OF RESIDENCE PLAY NO ROLE IN SEIZURE CONTROL—A STUDY OF PATIENTS TREATED IN AN EPILEPSY CENTER.

J. Szaflarski, C. Lindsell*, A. Rackley*, S. Yates†, and M. Szaflarski**

**University of Cincinnati, Cincinnati, OH, USA; and †UCB Inc., Smyrna, Georgia, USA*

Purpose: Seizure control may be influenced by etiology, diagnosis, treatment, and treatment delivery settings among others. In this study we examine whether age and nursing home residence (NH) impact seizure control.

Method: 100 NH and 100 non-NH patients, matched for age, gender, and epilepsy duration, underwent retrospective chart review. Age was grouped as <55 vs. ≥ 55 years old. *t*-tests or chi-square tests were used to compare age groups and NH/non-NH patients. Generalized linear models compared the change in seizure frequency after transitioning care to an epilepsy provider between young and old and NH and non-NH patients. Patients treated in the epilepsy center for <1 year were excluded to prevent bias (N=22).

Results: 41/178 (23%) of patients were ≥ 55 years old. NH patients had earlier onset and longer duration of epilepsy ($p \leq 0.013$) and had higher incidence of neurological comorbidities (e.g., cerebral palsy; p=0.001). There were no age-related differences between institutionalized and non-institutionalized patients in epilepsy control (i.e., number of patients who were seizure-free), seizure frequency in the last year (p=0.339) or type of AED use (all $p \geq 0.05$). The change in seizure frequency was not impacted by age or NH status; there was no interaction between age and NH status ($p>0.1$).

Conclusion: These findings indicate that there was no discernable effect of age on medication prescription practices, nor was there an effect of age on the change in seizure frequency when being treated by an epilepsy specialist, regardless of whether or not the patients were institutionalized for their condition.

E426
NONCONVULSIVE STATUS EPILEPTICUS IN CRITICALLY ILL PATIENTS

G. De Maria, G. Perone†, B. Guarneri*, and L. Antonini**

**Clinical Neurophysiology, Spedali Civili, Brescia, Italy; and †Anestesiology and Intensive Care, University of Brescia, Italy*

Purpose: To determine the occurrence of nonconvulsive status epilepticus (NCSE) in critically ill patients on Intensive Care Unit (ICU), and to evaluate the etiology, the history of epilepsy, the clinical presentation, the severity score, the EEG findings, the therapy and the hospital outcome.

Method: We retrospectively identified 23 adult patients with NCSE, ranging age from 18 to 88 years, of 1730 patients admitted to the ICU from January 2003 to December 2006.

Results: Ttwenty-three patients (1.3%) were found to have NCSE. Intracranial haemorrhage was the most frequent etiology of NCSE in our population (21.7%), followed by hypoxic events (17.4%). The largest group of patients (73.9%) had no previous diagnosis of epilepsy. The majority of the patients (69.6%) had isolated seizures or convulsive status epilepticus prior to the onset of NCSE. EEG demonstrated focal or lateralized epileptiform discharges in 15 patients (65.2%), generalized or bilateral epileptiform discharges in 8 patients (34.8%). Fourteen (60.9%) of the patients were comatose, while 9 (39.1%) of the patients were obtunded/confused. All patients were treated with intravenous anticonvulsants, mostly MDZ and PHT. Three patients (13%) died of their underlying illness, and 20 (87%) patients survived to discharge.

Conclusion: NCSE is probably an under diagnosed condition: prompt recognition and treatment may be necessary to improve its neurological outcome.

E427
PUBLIC KNOWLEDGE AND ATTITUDE TOWARD THE PATIENTS WITH EPILEPSY

R. Mameniskiene, G. Kristopaityte†, S. Jaksyte†, J. Guk†, and R. Balcytyte†*

**Vilnius University Hospital Santariskiu Clinics, Neurology Center, Lithuania; and †Vilnius University, Faculty of Medicine, Lithuania*

Purpose: To evaluate the knowledge of different public groups about symptoms of seizures and the first aid during them, the attitude towards epileptics integration into the society.

Method: Four different groups (medical students before neurology course (MS1, n=100) and after (MS2, n=95), teachers (TCH, n=63) and salespersons (SP, n=65) were given a questionnaire regarding symptoms, first aid and their reaction during seizures and attitude towards epileptics integration into the society. Their knowledge was compared.

Results: Over 90% respondents have heard about epilepsy. 35% MS1, 46.3% MS2, 46% TCH, 64% SP saw the seizure. Convulsions, as a symptom of epilepsy, mentioned 94% MS1, 100% MS2, 95.2% TCH, 81.5% SP, unconsciousness – 63% MS1, 97.9% MS2, 57.1% TCH, 69.2% SP, tongue biting – 71% MS1, 89.5% MS2, 76.2% TCH, 78.5% SP. Fear (as a reaction towards seizure) was noted by 40% MS1, 26.3% MS2, 55.6% TCH, 50,8% SP. As the first aid 54% TCH, 60% SP would put a solid thing into the mouth. 66% MS1, 62.1% MS2, 61.9% TCH, 69.2% SP would forbid driving. Only 1/3 of all respondents if having epilepsy wouldn't hide it. 95% SM1, 100% SM2, 78.5% TCH and 90.2% SP know, that epilepsy can be successfully treated.

Conclusion: 1. Public knowledge about epilepsy is different. 2. Students' knowledge after neurology course is satisfactory. Salespersons' knowledge about the first aid is much worse although they have a bigger chance to face the seizure. 3. Epileptic patients suffer from stigmatization. 4. It is essential to increase the knowledge about epilepsy in the community.

E428
IDIOPATHIC GENERALIZED EPILEPSIES IN THE ELDERLY: THE VIEWPOINT OF A GERIATRICIAN

V. Nguyen Michel,†, Z. Ourabah*, C. Sebban*, and C. Adam†*

**AP-HP, Chu Charles Foix, Unité D'Explorations Fonctionnelles, Ivry Sur. Seine, France; and †AP-HP, Service de Neurologie 1, Hopital De La Salpêtrière, France*

Purpose: Long term follow-up studies indicate a weak remission rate in idiopathic generalized epilepsies (IGE) (Martinez-Juarez et al., 2006), suggesting they may persist to an advanced age. However there are few estimates of IGE frequency in the elderly.

Method: EEGs of 700 patients aged over 70 years, recorded between January 2006 and March 2007, were reviewed for anomalies consistent with IGE. We then examined the clinical history of patients with these anomalies.

Results: A persistent IGE was identified in four female patients (mean age, 79 years); in two cases it was a juvenile myoclonic epilepsy and in two a grand mal epilepsy. Seizures in three patients had begun in childhood or adolescence and in one at 40 years. Before hospitalization, few or no seizures were reported and IGE had not been diagnosed. IGE was revealed in each patient by a relatively severe event: an absence status epilepticus (ASE), sub continuous myoclonic seizures or repeated convulsive generalized seizures (CGS). These events were not situation-related. The discovery of diagnosis allowed stopping a worsening of seizures that was due to inappropriate therapy. The antiepiletic treatment was also modified in a second patient, while the two others responded well to Valproate.

Conclusion: IGE can exacerbate in the elderly, as different types of seizures including ASE, subintrant myoclonia or repeated CGS. Our data suggests persistent IGE are quite frequent in an aged population and may be underestimated. Correctly diagnosed, adjustment of treatment may offer substantial clinical improvements in IGE of the elderly.

E429
VIDEO ANALYSIS OF DIFFERENT SEMIOLOGIES IN PATIENTS WITH PSYCHOGENIC NONEPILEPTIC SEIZURES

L. Popovic, N. Vojvodic, D. Sokic, A. Ristic, and S. Jankovic
Institute of Neurology, Clinical Centre of Serbia, Serbia

Purpose: To establish the frequency of different semiological features in our patients with psychogenic nonepileptic seizures (PNES).

Method: We performed a retrospective study of 63 patients (10 men and 53 women) with PNES during the period of three years. The diagnosis of PNES was established in all patients by comprehensive analysis of all relevant data. At least one episode of PNES was recorded during video EEG monitoring in all patients, spontaneously (11 patients) or after the placebo induction (52 patients). The recorded PNES were reviewed with the family members or eyewitnesses and confirmed as the typical event.

Results: After analyzing the video recordings we could classify the clinical features of PNES into one of the following four categories: (1) Thirty patients (48%) had PNES with excessive out-of-phase motor activity ('hypermotor' PNES); (2) Thirteen patients (21%) had PNES with subtle trembling and minor motor activity ('hypomotor' PNES); (3) Nine patients (14%) had PNES consisting of unresponsive behavior in the absence of motor manifestations or falling to the floor ('atonic or drop-attack' PNES); (4) Eleven patients (17%) had PNES with shaking of one part of the body only ('focal' PNES).

Conclusion: The majority of our patients with PNES (52%) do not have the most characteristic semiology that involves hypermotor activity of limbs, head, and trunk during their typical events. This could make the differential diagnosis of PNES more difficult.

E430
RELIABILITY OF ICTAL SCALP EEG FINDING FOR LATERALIZATION OF EPILEPTOGENIC FOCUS IN TEMPORAL LOBE EPILEPSY

N. Vojvodic, D. Sokic, S. Jankovic, L. Popovic, and A. Ristic
Institute of Neurology Clinical Centre of Serbia, Serbia

Purpose: To determine the concordance of ictal scalp EEG findings with medial temporal structural lesions showed by MRI, and evaluate its reliability for lateralization of epileptogenic focus.

Method: Retrospectively, we analyzed 30 ictal EEG recordings of 22 patients with clinical features of temporal lobe epilepsy. The analysis of ictal EEG finding was segmented: (1) ictal beginning; (2) ictal duration; (3) ictal ending and (4) interictal EEG data. NMR of brain was previously conducted in all patients and showed unilateral nonprogressive abnormalities of medial temporal structures. We compared concordance of ictal EEG lateralization with MRI findings.

Results: The best concordance of ictal EEG lateralization with MRI data was at the ictal beginning (66.7% of seizures). The concordance of ictal duration was only 3.33%, and 23.33% of ictal ending. Regarding the interictal data, degree of concordance was 56.67%.

Conclusion: Our results showed the beginning of ictal activity as the most significant finding for lateralization of epileptogenic focus regarding the scalp EEG recordings in patients with temporal lobe epilepsy.

E431
PREDICTIVE RISKS OF SEIZURE-RELATED INJURY IN EPILEPTICS

S. Tiamkao, K. Sawanyawisuth, S. Arunpongpaisal, W. Phuttharak, N. Auevitchayapat, S. Vannaprasaht, S. Tiamkao, K. Phunikhom, A. Chaiyakum, and J. Saengsuwan
**Srinagarind Epilepsy Research Group, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand*

Purpose: The clinical risks factor for seizure-related injuries (SRI) were analyzed and used to develop predictive model.

Method: We performed a cross-sectional study at epilepsy clinic in the U.K. and Northeast Thailand. The eligible criterion was one who had at least one seizure attack during the past 12 months. We used the questionnaire to evaluate risk factors for SRI. The outcome was the occurrence of SRI. Backward elimination method was used to identify the significant predictive factors and model for having SRI.

Results: There were 76 of 100 and 247 of 300 consecutive cases enrolled in U.K. and Thailand site, respectively. Of those, 31 (40.79%) and 91 (36.84%) had SRI in respective site. The five significant predictive factors by the multivariate logistic analysis were numbers of antiepileptic drug (adjusted odds ratio [OR] 1.429, 95% confidence interval [CI] 1.017–2.006), male gender (OR 1.754, 95% CI 1.040–2.960), generalized tonic–clonic seizure or GTC (OR 2.342, 95% CI 1.364–4.019), daytime seizure attack (OR 4.000, 1.620–9.876), and history of falling during seizure attack (OR 4.320, 2.184–8.546). We developed the predictive model for having SRI by those five significant variables and the average number of seizure attacks. The predictive model had a good fit and fair discrimination property.

Conclusion: The significant predictive factors for SRI in epileptics were male gender, number of antiepileptic drug uses, GTC, having seizure attack during daytime, and history of falling during seizure. The predictive model was built and believed to solve the overprotection and economic issue in epileptics.

E432
CUED LEARNING TRIALS FOR CHILDREN WITH EPILEPSY IN STORY RETELLING: GAINS AT GROUP LEVEL, BUT NOT ALL INDIVIDUALS THRIVE

L. Van Iterson,†*
**SEIN, Netherlands; and †De Waterlelie, Netherlands*

Purpose: Semantic memory is essential for schoolwork. Inconclusive studies suggest that even children with uncomplicated epilepsy experience problems with initial acquisition and delayed recall of a story. Given the paucity of story-tests for Dutch children, we developed a story for age 6–10 years wherein initial free recall was followed by a maximum of four learning trials with ten questions (=cued recall); and free and cued recall after a 25-minute delay. We studied learning curves in children with epilepsy, on group and individual level.

Method: Study group: N=68 children (age 6–10 years); 34 with epilepsy and 34 age/sex-matched controls. Epilepsy: mean age at onset 4.8 years, duration 4.1 years; n=17 partial (10 left), n=11 generalized seizures, n=6 uncertain; AEDs: 0=21%, 1=41%, >1=38%; FSIQ>75. GLM-3 (repeated measures) for free and cued recall over various learning trials and after a delay. GLM-1 and chi-square focussing on individuals with weaknesses (z Ü-2).

Results: Free recall: Both groups showed significant gains (+25%) between initial and delayed recall. Children with epilepsy needed more learning trials and scored lower than controls in delayed free and cued recall. No significant group*trial interaction was seen. For delayed free and cued recall, 26% of the children with epilepsy and 0 controls had z Ü-2.

Conclusion: (1) Both groups profit from repeated cued trials; gains and curve shapes were similar. (2) Despite more learning trials, in epilepsy 26% show deficient delayed recall. Deficiencies appear associated with neuropsychological measures (initial learning, FSIQ, working memory) and less with epilepsy variables (seizure type, epilepsy onset or duration, number of AEDs).

E433
DISCONNECTING SURGERY IN TEMPORAL LOBE EPILEPSY: ARE INTERICTAL EPILEPTIFORM ACTIVITIES IN POSTOPERATIVE EEGS OF PROGNOSIS SIGNIFICANCE?

S. Hamelin, L. Minotti, L. Vercueil, A. Benabid, S. Chabardes, and P. Kahane
Grenoble University Hospital, France

Purpose: Disconnection has been proposed as an alternative surgical technique to treat mesial temporal lobe epilepsy (TLE) with normal MRI or isolated hippocampal sclerosis. In temporal lobectomy, persistence of interictal epileptiform discharges (IED) has been associated with poor clinical outcome. In contrast, the remaining epileptic cortex after disconnection is still able to generate IED. The study aimed at evaluating the prognostic value of postoperative EEG after TLE disconnection.

Method: This retrospective EEG analysis included 54 consecutive TLE patients treated by temporal lobe disconnection at Grenoble University Hospital between 1999 and 2005. Seizure outcome was evaluated according to the modified Engel's classification. Postoperative EEG was performed at 3 month and 2 years after disconnection. The EEGs was blindly classified in 3 groups: (1) No IED, (2) Abnormalities recorded over anterior temporal scalp electrodes, supposed to reflect the activity within the disconnected cortex ('focal' group) (3) Abnormalities recorded outside these limits ('extended' group).

Results: The mean duration of postoperative follow up was 46 months (range 14–80). At 2 years, 68% of the patients were in class Ia. At 3 months IED was observed in 71% of patients Ia, in 84% of the others (NS). 'Extended' IED was observed in 21% of patients classed Ia and in 60% of the others (p=0.021) (results at 2 years: 15 vs. 50% (p=0.049)).

Conclusion: After temporal lobe disconnection, analysis of the topography of IED appears to be useful for predicting seizure outcome, while the presence or absence of IED does not help.

E434
HEADACHE ASSOCIATED WITH EPILEPTIC SEIZURES

A. Doneva, and E. Cvetkovska†*
**Clinical Hospital 'Dr T. Panovski' – Bitola, Republic Of Macedonia; and †Clinic of Neurology, Skopje, Republic of Macedonia*

Purpose: Seizure related headache is frequent, long-lasting and severe symptom of epileptic seizures, causing major impairment of daily living. It is often reported, but ignored symptom of epileptic seizure. We analyzed frequency and characteristics of seizure-associated headache in patients with epilepsy.

Method: Over the period of twelve months, 141 patients with epilepsy we evaluated for seizure associate headaches, (78 female, 63 male patients), with different duration of the disease.

Results: Out of 141 patients 56 (39.7%) reported seizure related headaches, with different pain intensity . Interictal headaches we reported by eighty-eight patients (62.4%), mainly with migraine and tension type headache characteristics. Headaches related to seizure were: preictal in 10.7% (six patients), interictal 4 (7.1%), mostly postictal 43 (76.8), and combination in 3 (5.4%). According to type; migraine type reported more then a half -48.2% (twenty-seven patients), and tension type 19 (33.9%), unclassified in ten 17.9. Patient with TLE, reported ipsilateral and contralateral headaches.

Conclusion: We conclude that headache is very common in patients with epilepsy. Unilateral headache may represent a lateralising sign in focal epilepsy. Seizures often trigger postictal headaches with migraine features, which often are associated with migraine.

E435
LONG TERM FOLLOW UP OF FAMILIAL MESIAL TEMPORAL LOBE EPILEPSY

M. Morita, L. Conz*, C. Maurer-Morelli*, E. Kobayashi†, C. Yasuda*, L. Betting*, F. Pereira*, I. Lopes-Cendes*, and F. Cendes**
**State University of Campinas, Campinas, Brazil; and †McGill University, Montreal, Canada*

Purpose: Familial mesial temporal lobe epilepsy (FMTLE) is a well characterized syndrome. However, there has been no report of long term follow up of FMTLE. Our purpose was to analyze seizure outcome in individuals with FMTLE.

Method: We followed prospectively 64 individuals with FMTLE from 28 families. Patients who fulfilled clinical criteria for MTLE according to the ILAE were divided into three groups. (1) Remission: seizure-free for at least two years; (2) Benign: less than six complex partial seizure (CPS)/year and no more than two secondary generalized tonic–clonic seizures /year; and (3) Refractory: more than six CPS/year despite adequate antiepileptic drugs (AEDs).

Results: Mean follow up was 93.4±15.8 months (ranging from 45 to 121.9 months). At baseline they were divided in benign (n=29), remission (n=28) and refractory (n=7). At last follow up visit 12 (41.4%) patients with benign FMTLE remained classified as benign, 6 (20.7%) became refractory, 11 (37.9%) were in remission. In the subgroup of FMTLE in remission 21 (75%) remained without seizures; 6 (21.4%) were classified as benign FMTLE, and one died (3.6%) from cause unrelated to epilepsy. All refractory patients remained refractory.

Conclusion: Prospective follow up of more than 7 years in patients with FMTLE revealed that it is unlikely to achieve seizure control with AEDs for those with refractory seizures. By contrast, patients with benign FMTLE for more than one year are likely to remit or remain under good seizure control. The majority of patients who had achieved seizure remission remained seizure-free and none became refractory.

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E436
QUALITY OF LIFE IN PATIENTS WITH REFRACTORY EPILEPSY TREATED WITH LAMOTRIGINE

D. Nikodijevic, D. Petrovska-Cvetkovska, I. Dzonov, E. Cvetkovska, I. Kuzmanovski, and B. Maksimovska
Clinic of Neurology, Clinical Centre, Skopje, Macedonia

Purpose: To evaluate efficacy and tolerability of Lamotrigine in our patients with refractory epilepsy, with different seizures types, recording also adverse effects.

Method: The study was prospective, randomized in duration of 1 year, including 90 patients with epilepsy. The patients with diagnosis of refractory epilepsy were treated with lamotrigine in dose 100–300 mg/day and they were divided in groups by seizures types on patients with PSS, PCS, SGS and GTCS. The efficacy of treatment was registered by evaluating the reduction of seizure frequency, but also improvement of quality of life using QOLIE 89 questionnaire and other neuropsychological and cognitive tests. We evaluated and recorded adverse effects by using AEDs.

Results: The patients were on age from 14–65 years. From seizures types most representing was patients with SGS 42.2% and from etiological factors (by CT and MRI) most of the patients was with hyppocampal sclerosis, tumors and trauma. Analysis of reduction of seizures frequency show significant reduction >50% in 62 patients, >75% in 21 patients and without effects in 17 patients, without significant differences by seizures types ($p<0.05$). The improvement of QOLIE 89 score in lamotrigine treated patients was 89% also without significant differences by seizures types ($p<0.05$).

Conclusion: Our results suggest that lamotrigine is highly effective in treatment of patients with refractory epilepsy, probably due to reduction of seizure frequency, but also because of improvement of social, mood and cognitive function.

E437
SURGICAL TREATMENT OF EPILEPSY CAUSED BY INSULAR LESIONS: EXPERIENCE WITH 49 PATIENTS

C. Wuertenberger, A. Schulze-Bonhage†, and J. Zentner**
**University of Freiburg, Germany; and †University of Freiburg Epilepsy Centre, Germany*

Purpose: Intrinsic lesions of the insula frequently become symptomatic with epileptic seizures, which may be refractory to medical therapy. Clinical reports about surgical treatment of insular epileptogenic lesions are sparse, possibly due to the fact that eloquent areas are located in close vicinity to the insular cortex. In this study we summarize our experience with the surgical treatment of these lesions.

Method: Forty-nine patients were included in this study. Clinical and histopathological features, as well as operative morbidity and seizure outcome were analyzed. Seizure outcome was related to the histopathology and extent of the lesions.

Results: Complete resection (100%) was achieved in 10 patients, nearly complete (> 80%) in 34 and incomplete resection (50%–80%) in 5. Thirty-seven patients had a neoplastic lesion and 12 had nonneoplastic lesions (10 focal cortical dysplasias, 2 cavernomas). There was no operative mortality and only 3 patients (all with neoplastic lesions) suffered permanent deficits, accounting for an overall operative morbidity of 6%. During a mean follow-up of 29 months, 30 (61%) patients remained completely seizure free, 4 (8%) had ≤ 2 seizures per year, 9 (18%) showed seizure reduction of ≥ 75% and 6 (13%) had <75% reduction.

Conclusion: Neoplastic and nonneoplastic lesions of the insula causing epileptic seizures can be treated microsurgically with a high rate of seizure control and relatively low morbidity. Subtotal resection of neoplastic insular lesions (>80%) provides maximal safety for the patient, sufficient reduction in tumor volume and satisfying seizure outcome.

E438
EPILEPSY AND INTELLECTUAL DISABILITY – A JOINT APPROACH

H. Somerville,†, A. Bleasel*, and J. Capizzi**
**Westmead Hospital, Sydney, Australia; and †Children's Hospital Westmead, Sydney, Australia*

Epilepsy is common in people with intellectual disability (ID), especially in those with cerebral palsy (CP). Seizure control is often difficult and many medical issues and their treatment contribute. Common comorbid conditions requiring drug therapy in people with ID include dysphagia, poor nutrition, gastrooesophageal reflux, chronic lung disease, necessitating enteral feeding, osteoporosis and mental health disorders. Many patients are also taking medications for movement disorders. A joint epilepsy/ID clinic was established at a large Sydney hospital to provide coordinated management of epilepsy and a range of medical issues impacting on seizure control. Staffing comprises a neurologist, disability physician and clinical nurse consultant (CNC). Many patients are transitioning from pediatric to adult services and all have complex medical problems. A comprehensive review of pediatric records is undertaken, with a focus on seizure history, previous investigations and prior antiepileptic therapy. A detailed summary of other medical problems is provided by the disability physician and discussion follows on the impact of comorbid conditions, medications and nutrition. All patients have complex psychosocial needs and require prolonged consultation. The neurologist is able to concentrate on epilepsy management while the disability physician and CNC deal with the myriad of medical and psychosocial issues and coordinate management. This approach results in increased throughput of patients receiving specialist epilepsy consultation, compared to a standard 'stand-alone' epilepsy clinic. The CNC has an important educational and monitoring role with families and carers, improving seizure records and acute seizure management, reducing hospital admissions.

E439
COGNITIVE FUNCTIONS BEFORE AND AFTER SURGERY IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

R. Aldungarova, G. Nyamdordorzhiyn, and O. Arinova
Kazakh National Medicine University, Kazakhstan

Purpose: To evaluate the cognitive functions in patients with refractory temporal lobe epilepsy before and after anterior temporal lobectomy (TLE) with amygdalohippocampectomy.

Method: From the general number of the operated patients with refractory temporal lobe epilepsy (n-63) we selected 36 persons (9 female and 27 male), mean age 23 years) with different cognitive deficits who became seizure free after TLE (right-22, left-14). All patients were evaluated with a neuropsychological protocol that included the assessment of intelligence, memory, (Wechsler Memory scale), initiation, perseveration, attention, mood, word fluency and executive function. Quality of life was assessed using QOLIE-31-scale up to 5 years. We compared row values for each test before and after six months of surgery.

Results: Comparative analysis of cognitive functions before surgery showed that all patients performed more poorly neuropsychological tests and exhibition higher scores of anxiety and depression. We found memory dysfunction, especially significant more verbal learning impairment. Average verbal IQ identical to both right and left link sided damage was 74,7 (pf0,49). After surgery 26 patients showed improvement of cognitive abilities ($p=0,05$) and 10 patients came to total reduction of cognitive disadvantage ($p=0,03$). QOL also showed improvement which was positively correlated to seizure outcome. We did not reveal any significant differences for cognitive dysfunctions in the postoperative period.

Conclusion: Good outcome in surgery intervention (about 60% of patients with refractory TLE are seizure free, total reduction or significant improvement of cognitive functions and their quality of life) allow us to solve the questions of psychosocial rehabilitation that is the main content of the global concept Comprehensive Care for People with Epilepsy.

E440
SEIZURES AND MULTIPLE SCLEROSIS

J. Kruja, and S. Mijo
UHC Mother Theresa, Albania

Purpose: To evaluate the association between seizures and Multiple Sclerosis (MS).

Method: We retrospectively controlled the data of all patients with definite MS registered at the Service of Neurology, UHC Mother Theresa – Tirana, looking for the history of seizures or epilepsy. The diagnosis of MS is made according to McDonald revised criteria. The diagnosis of epilepsy was based on the criteria proposed by the ILAE, 1993 and seizures were classified according to the classification of ILAE, 1981. All patients with seizures or epilepsy were submitted to standard EEG recording and MRI imaging.

Results: In a series of 412 patients with definite MS (254 – 61.7% females; 173 – 38.3% males), we identified 11 (2.67%) patients with seizures or epilepsy (3 – 27.3% females; 8 – 72.7% males). The mean age at the onset of MS was 25.8 years old. Only two patients had a history of seizures before clinical MS onset. In six patients the seizures are related to a new relapse. 7 patients had secondary generalized seizures and 3 patients had simple partial seizures and 1 had complex partial seizure. The EEG was normal in 5 patients, focal changes are seen in 2 and generalized slowing was seen in 4 patients. The MRI revealed supratentorial lesions in all patients, mainly periventricular. In two patients there is evidence of sub cortical plaques.

Conclusion: Seizures are slightly more frequent in the MS patients, especially in males. Probably the seizure is a clinical manifestation of a relapse. The seizures course in all our patients is benign.

E441
HEADACHE PRECEDING EPILEPSY ONSET: EPILEPTOGENIC HEADACHE?

P. Benna, F. Bert, R. Colonna, and E. Montalenti
Università Di Torino, Italy

Purpose: Headache is often a postictal symptom; more rarely it is ictal or anticipates the seizure by minutes (preictal) to hours (prodromal symptom). We proposed to verify if headache can precede by a long time the epilepsy onset, association not recognized by the current International Headache Society classification (ICHD-II) (Cephalalgia 2004; 24 (s1): 23–136).

Method: A detailed anamnestic record was performed about subjective symptomatology in the month preceding the epileptic onset in 50 de novo patients.

Results: Three of 50 patients reported, in the month preceding the seizures onset, a headache not previously experienced. The pain was described as pressing, bilateral, mainly frontal, of growing intensity from mild to moderate; lasting several hours in day-time every day. The 3 patients presented different types of epileptic syndrome, respectively: partial posttraumatic epilepsy (duration of headache: 30 days), partial epilepsy symptomatic of cavernous angioma (15 days), idiopathic generalized epilepsy (3 days). The headache was responsive (till to disappearance) to antiepileptic drugs (oxcarbazepine, carbamazepine, valproate).

Conclusion: A headache preceding epileptic onset is not uncommon, probably underscored if the clinical history is not specifically addressed. Problematic is the physiopathologic interpretation of the phenomenon; we can suppose that a neuronal hyperexcitability give rise to the headache, on the one hand, and contribute to the activation of epileptogenic process, on the other hand.

E442
THE EFFECTS OF CHRONIC VAGUS NERVE STIMULATION THERAPY ON DEPRESSION PARAMETERS IN PATIENTS WITH PHARMACORESISTANT EPILEPSY

T. Urbanic Purkart, K. Zaar, E. Ott, and M. Feichtinger
University Hospital of Neurology, Graz, Austria

Purpose: Vagus nerve stimulation (VNS) has shown to be effective in cumulative seizure-control but also in improving depressive symptoms. However, to our knowledge there is no data on which aspects of depressive mood are particularly positively affected. Beck depression inventory (BDI) is a multiple-choice self-report inventory. It can assess both the cognitive component and the somatic component of depression. This components again are subdivided into items (cognitive subscale =8 items, somatic subscale= 13 items).

Method: 10 patients with pharmacoresitant epilepsy, age 14 to 56 Years, with VNS devices being implanted from November 2003 till January 2008 have been included in our pilot study. The neuropsychological testing and the Beck depression inventory (BDI) assessment have been performed pre- and post -VNS device implantation.

Results: The BDI sum-scores improved significantely after VNS implantation. (pre:15.6 vs. post:10.8) (t9=2.59, p<.05), with marked reduction in sadness (60% vs.30%), irritability (70% vs. 50%), loss of interest (70% vs. 30%) and indecisiveness (70% vs. 50%). The median monthly seizure frequency however was not reduced (Z9=-.52; ns), thus no correlation between changes in seizure frequency and depression scores was found (r=-.19;ns).

Conclusion: Our study suggests that VNS in patients with pharmacoresistant epilepsy improves predominantly somatic rather than cognitive components of depression and that such effects are independent from improvements in seizure control. However further investigation with bigger cohorts as well as correlations with neuroimaging (MRI, PET) results are needed.

E443
INTRACRANIAL ENCEPHALOMENINGOCELE AS A RARE CAUSE OF EPILEPSY

A. Pasnicu, E. Pasqualini, B. Carsin-Nicol, J. Ferré, S. Saikali, D. Ménard, and A. Biraben
CHU Ponchaillou, Rennes, France

Purpose: We describe four cases of epilepsies related to an intracranial encephalomeningocele.

Method: We retrospectively selected the patients with epilepsy and intracranial encephalomeningocele in our patient data base since year 2000. We excluded the patients with any other magnetic resonance imaging cerebral lesion, particularly cortical dysplasia, and dysembrioplastic neuroepitelial tumor. For each patient we reviewed all the clinical, electroencephalographic (EEG), and any other medical data in order to correlate the malformation with the epilepsy.

Results: As a tertiary centre for epilepsy, we admit about 150 new patients each year for presurgical evaluation. We found four patients with focal epilepsy and intracranial encephalomeningocele. Three patients have a temporal sphenoid encephalomeningocele; in these patients the onset of the epilepsy was during early life. One patient has an intra-diploic occipital encephalomeningocele; his epilepsy started at the age of 40. The clinical data, EEG data, video-EEG (one patient), magnetic encephalography (one patient), and surgical result (one patient) demonstrate that the encephalomeningocele is strongly related to the epilepsy in all the four patients.

Conclusion: The intracranial encephalomeningocele is a rare aetiology of focal epilepsy. We discuss different epileptogenic mechanism according to the early or late onset of the epilepsy.

E444
EARLY SEIZURES AND SEIZURE RECURRENCE IN PATIENTS WITH AN ACUTE ISCHEMIC CEREBROVASCULAR EVENT

P. Gallmetzer, C. Wehinger*, B. Mamoli*, W. Lalouschek†, and C. Baumgartner**
**Neurological Hospital Rosenhuegel, Vienna, Austria; and*
†Medical University of Vienna, Austria

Purpose: To assess incidence and predictive factors for early seizures after an ischemic cerebrovascular event (CVE) and of further unprovoked seizures after a first early poststroke seizure.

Method: The study was performed within a prospective hospital-based stroke registry. 2581 consecutive patients with an acute ischemic CVE (TIA or stroke) and without previous history of seizures were analyzed. Detailed data on clinical parameters, medical history, technical and laboratory investigations and stroke origin were collected. Seizures occurring within the first 14 days after the CVE were classified as early poststroke seizures, whereas recurrent unprovoked seizures after day 14 were classified as poststroke epilepsy. The mean follow up of seizure patients was 33.3 month. Patients with a follow up of > 12 month were analyzed with regard to risk factors for recurrent seizures.

Results: 2.5% (n = 64) of the patients with an acute CVE experienced early poststroke seizures. A quarter of these patients had seizure recurrence. Initiation of antiepileptic treatment after a first early seizure was not associated with a reduction of seizure recurrence (p = 0.23). None of the analyzed risk factors was significantly associated with early seizures or with seizure recurrence after a first early poststroke seizure.

Conclusion: 2.5% of the patients developed early poststroke seizures and a quarter of these patients had seizure recurrence. AED treatment after a first early seizure did not significantly reduce the risk of seizure recurrence. Clinically useful parameters to predict early seizures and seizure recurrence after early poststroke seizures could not be identified.

E445
PARTIAL SEIZURES PRESENTING AS TRANSIENT GLOBAL AMNESIA

C. Wehinger, P. Gallmetzer, and C. Baumgartner
Neurological Hospital Rosenhügel, Vienna, Austria

Purpose: Transient global amnesia (TGA) is a puzzling neurological syndrome of unclear etiology. Current hypotheses include migraine, transitory ischemic attacks and venous congestion as possible causes.

Method: We present the case of a 61 year old patient admitted to our department due to an acute onset amnestic episode characterized by antero- and retrograde amnesia typical for TGA. Symptoms completely resolved within 24 hours and the patient was discharged under the diagnosis of TGA without medication. Seven months later the patient was readmitted because of two new amnestic episodes that occurred within 48 hours. Neurological examination was normal besides antero- and retrograde amnesia. Cranial MRI and laboratory findings revealed no abnormalities. We performed routine EEG following the first and during the second episode. Video-EEG was performed after the third event and a control EEG before discharge.

Results: EEG performed after the first episode showed a regional right frontal intermittent rhythmic slowing lasting 9 seconds. EEG performed during the second episode disclosed a subclinical EEG seizure pattern consisting of rhythmic theta waves over the right frontal region lasting 40 seconds. Video-EEG monitoring again showed short bursts of regional right frontal intermittent rhythmic slow waves. The patient was put on carbamazepine and no further amnestic episodes occurred since then.

Conclusion: The EEG performed during the second amnestic episode established the diagnosis of focal epilepsy with amnestic seizures. Our findings underline the importance of EEG in patients with suspected TGA, which should be performed as soon as possible, ideally during the attack to differentiate TGA from epileptic seizures.

E446
REPEATED HEAD TRAUMA—DECISIVE FACTOR OF EPILEPSY IN BOXERS

G. Maximov, and K. Maximov
Medical University – Sofia, Bulgaria

Purpose: The repeated application of blows to the boxer's head result in chronic brain lesion. Morphological findings of late traumatic damage include abnormalities (cavitation of rupture) of the septum pellucidum, focal scarring of the cerebral and cerebelar hemispheres, degeneration of the substancia nigra, of the temporal lobe and the hypothalamic structures. One of the sequelae of the repeated blows to the head of boxers is the increased convulsive predisposition and the occurring of epileptic seizures.

Method: Clinical analysis of epilepsy in boxers, in whom history does not reveal any other etiological factors than chronic craniocerebral trauma, was performed.

Patients and Method: A group of 9 boxers suffering from trauma-induced epileptic seizures was examined. The age of boxers range from 21 to 29 years. Neurological examination does not reveal any abnormality. Psychiatric changes include decreased memory and emotional instability.

Results: Generalized seizures of Grand Mal type were identified in 8 boxers (88%), partial seizures with complex symptomatology of temporal lobe – in one boxer. In 2 boxers seizures occurred monthly, in seven – yearly. Regarding the onset of the boxing 7 boxers (77,8%) began boxing at age of 19–20 years. Most frequently seizures occurred two years after the onset of boxing (in 6 boxers – 66,7%).

Conclusion: The younger the boxer the higher the probability of epilepsy. Most frequently generalized tonic–clonic epileptic seizures occurred – usually two years after the onset of boxing. The occurrence of epileptic seizures in boxers following a brain injury depends upon individual predisposition and upon the frequency and severity of repeated head trauma. The possibility of the repeated blows to the head to create potential epileptics raises the question: ''Is the boxing as sport activity really necessary to men?''

E447
RISK FACTORS OF NEUROPSYCHOLOGICAL DETERIORATION IN TEMPORAL LOBE EPILEPSY. DATA FROM PINAR DEL RIO TEMPORAL LOBE EPILEPSY STUDY.

J. Riol Lozano, A. Garcia Medina*, J. Rodriguez Garcia*, E. Cruz Menor*, N. Arteche Diaz*, and J. Garcia Fidalgo†*
**Epilepsy Section, Abel Santamaria University Hospital, Cuadrado, Cuba; and †Epilepsy Section, National Institute of Neurological Disorders, Havana, Cuba*

Purpose: Epilepsy affects 1 to 2% of the whole population. Temporal lobe epilepsy (TLE) represents 40% of all manifestations of the entity. Neuropsychological disorders in TE are frequent and have a multifactory origin.

Objective: This research was aimed at identifying some risk factors related to neuropsychological deterioration in patients suffering from TLE.

Method: A prospective and descriptive study was carried out in 277 patients with TLE having a follow-up treatment at Abel Santamaría University Hospital during January 2000 to January 2007. 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 data-base for its 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 etiologies. 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 efficiency ($P < 0.01$). Disorders of verbal memory when the origen of seizures were located in left temporal lobe and visual-space function with the right temporal lobe were the most frequent ($P< 0.01$).

Conclusion: Definition of some risk factors related to neuropsychological deterioration in TE can play a very important role in selecting the candidates to a presurgical evaluation for surgery in epilepsy.

E448

THE DURATION BETWEEN SEIZURE ONSET AND FIRST TIME DIAGNOSING THE EPILEPSY IN PATIENTS WITH NOCTURNAL SEIZURES VERSUS DIURNAL SEIZURES

I. Pisarenco, S. Crasovschi, V. Chiosa, and A. Hanganu
Laboratory of Neurobiology, State Medical University, Chisinau, Moldova

Purpose: To estimate the time when was first time diagnosed the nocturnal epilepsy versus epilepsy with diurnal seizures.

Method: A total number of 30 patients, between 6–60 years (mean age – 22,4), with nocturnal seizures were reviewed. A control group for comparison consisting of 20 patients, between 7–34 years (mean age-17,6) with exclusive diurnal seizures was selected. The patients were categorized according ILAE classification as localization-related epilepsy, idiopathic generalized epilepsy and symptomatic generalized epilepsy.

Results: Patients with localization-related epilepsy constituted 63, 3% (n=19); idiopathic generalized epilepsy- 26,6% (n=8); symptomatic generalized epilepsy- 10% (n=3). Patients with nocturnal epilepsy associated with diurnal seizures were 30% (n=9). 40% (n=12) patients were early diagnosed, 43, 3% (n=13)- within 1–3 years, 16, 6% (n=5)-within 4–12 years. Diurnal seizures were in 16,6% patients (n=5) with early-diagnosed nocturnal epilepsy, 10% (n=3)-in epilepsy diagnosed within 1–3 years; one patient was in the late diagnosed epilepsy. In the control group of epilepsy with diurnal seizures the following structure was revealed: 70% of patients (n=14) were early diagnosed, 10% (n=2)- within 1–3 years, 20% (n=4)- after 3 years and more.

Conclusion: The early-diagnosed epilepsy is higher in patients with diurnal seizures (70%) versus nocturnal seizures (40%). The presence of diurnal seizures in patients with predominant nocturnal epilepsy favours the possibility to be faster diagnosed and to be treated appropriately. The difference between the groups studied might be explained by several factors such as: un-witnessed, unrecognized, rare frequency of nocturnal seizures etc.

E449

INTERACTION GABA AND GLYCINE RECEPTORS IN CNS'S ANTICONVULSIVE CONTROL

G. Shilau
Republican State Clinical Psychiatric Hospital, Russia

A research in the area of new effective anticonvulsants elaboration is an important part modern Epileptology. It is well known that all negative effects arising from prolong use of any kind anti seizure therapy ultimately realize themselves through basic inhibitory neuromediator system – GABA-benzodiazepine receptors. In the same time it's believed, that glycine inhibitory effect can be mediated not only through its proper receptor anticonvulsants, but also GABA- and NMDA-receptors. In view of that, purpose this investigation has been turned out investigation interaction GABA and glycine receptors and quest on this base of new psychotropic drugs that would not demonstrate untoward aforesaid effects.

Method: In our observation we studied influence intoventrical injection of GABA, glicine and their combination on the cerebral neurophysiological activity in white rats. Electrodes were introduced in the animal's skull, taking of EEG along with chemotrode for intoventrical introduction and preparation under investigation 3 days on all animal were registered bioelectrical activity before and after intoventrical introduction of GABA, glicine and combination of the two. Computer analyses cerebral cortex bioelectric activity was conducted to determine of extend of inhibition of spectrodencity in the area diapasons of 12–18 minutes.

Results: Introducing in same dosage as GABA glycine produces more powerful and prolongs inhibition of the brain cortex bioelectrical activity. Combination GABA and glicine brings about grater inhibition bioelectrical activity as compared the individual components.

Conclusion: It will be prospectively perform antiseizure therapy as combination glicine and modern existing anticonvulsants.

E450

THE ENDOCANNABINOID SYSTEM IS DISREGULATED IN UNTREATED PARTIAL EPILEPSY: CSF FINDINGS

A. Romigi,†, M. Bari*, M. Marciani*,†, F. Placidi*,†, V. Pirazzi*, F. Torelli*, C. Izzi*, A. Prosperetti*, M. Bica*, and A. Maccarrone**
**Università Degli Studi Di Roma Tor Vergata Dipartimento Di Neuroscienze, Rome, Italy; and †Fondazione Santa Lucia Via Ardeatina, Rome Italy*

Purpose: Based on the experimental evidence endocannabinoids seem to possess anticonvulsant properties, since they resulted implicated in regulating both seizure duration and frequency such as block of status epilepticus and acquired epilepsy in neuronal cultures. The primary endpoint of our study was to evaluate the levels of the endocannabinoids anandamide (AEA) and 2-arachidonyl glycerol (2-AG) in the cerebrospinal fluid (CSF) of drug naive patients affected by partial epilepsy in order to test the hypothetical involvement of endogenous cannabinoids system in the pathogenesis of epilepsy.

Method: We collected CSF from 13 untreated inpatients affected by partial epilepsy. Twelve patients were diagnosed as having partial cryptogenic and 1 patients as partial symptomatic epilepsy. The last one patient was excluded from the study because brain MRI, identified a clinically silent small acute infarct on diffusion weighted images. Twelve control subjects matched for age and sex were enrolled between inpatients of the same clinic that underwent lumbar puncture for diagnostic purposes. In all these subjects CSF and blood tests excluded CNS or systemic diseases.

Results: We found a 3-fold decrease of AEA in the CSF of epileptic patients if compared with controls (epileptic patients mean 2.55±1.78 pmol/ml; control subjects 11.65±7.53 pmol/ml) (n= 9 for both group, $P<0.01$), while 2-AG concentration was normal (epileptic patients mean 209.5±146.56; control subjects 159.6±110.2) (n= 6 for both group, $P=0.48$).

Conclusion: Based on our findings, it can be hypothesized that the failure of the inhibitory role of AEA via both GABAergic and antiglutamatergic networks can contribute to pathogenesis of untreated and newly diagnosed epilepsy. The endogenous cannabinoid system might become a promising therapeutic target for the treatment neurological disease with excitoxic events as their hallmarks such as epilepsy.

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E Posters
Alternative Therapies

E451

DIFFERENCES BETWEEN MTHFR C677T AND A1298C ON AFFECTING HOMOCYTEINE IN EPILEPSY

O. Kim, N. Kim*, and W. Kim†*
**Pochon CHA University, Korea; and †Yonsei University, Korea*

Purpose: Hyperhomocysteinemia was occurred by mutation of some methylenetetrahydrofolate reductase (MTHFR) gene loci in various disease. In epilepsy patients, MTHFR C677T mutation affects homocyteine level, but the effect of MTHFR A1298C mutation has not been reported yet. Therefore, we examined to find out whether polymorphisms of two MTHFR gene loci affect homocysteine level in epilepsy patients.

Method: We investigated plasma homocysteine level in 182 patients with epilepsy. And then we analyzed differences of homocysteine levels between MTHFR C677T and A1298C polymorphism.

Results: Homocysteine level of TT genotype (18.84'jmol/L) was significantly higher than CC (11.31'jmol/L) and CT (11.89'jmol/L) in MTHFR 677 gene. In MTHFR 1298 gene, normal type (AA genotype) has higher homocysteine level (13.49'jmol/L) than mutant types (AC; 11.18'jmol/L and CC; 10.67'jmol/L). Homocyteine level was not affected by combination of MTHFR C677T and A1298C.

Conclusion: Our results suggest that homocyteine level was affected by polymorphism of MTHFR C677T, but not A1298C in epilepsy. Therefore, we should pay special attention to hyperhomocyteinemia in epilepsy patients with MTHFR C677T mutation.

E452

PILOTING KETOGENIC DIET IN GEORGIA: COST-EFFECTIVE ALTERNATIVE TREATMENT OPTION FOR PATIENTS WITH INTRACTABLE EPILEPSIES

G. Melikishvili, N. Tatishvili†, G. Javashvili‡, A. Melikishvili§, and D. Grigolia*
**Children's Outpatient Clinic, Iashvili Children's Central Hospital, Tbilisi, Georgia; †Iashvili Children's Central Hospital, Tbilisi, Georgia; ‡Tbilisi State Medical University, Tbilisi, Georgia; and §Higher Medical School, Tbilisi, Georgia*

Purpose: Approximately 30% of epilepsy syndromes are refractory to pharmacotherapy. The burdens from intractability are especially high in developing countries where antiepileptic drugs (AEDs) are commonly the only available treatment modality. The ketogenic diet (KD) is effective in providing seizure control for children with difficult-to-control seizures. The adverse effects of the KD when managed properly are relatively limited. The purpose of our work was KD implementation for patients with intractable epilepsies in Georgia.

Method: Since May 2007 six patients with medication resistant epilepsy (on average 6 AEDs were failed prior the diet initiation) were selected and have started KD using nonfasting diet protocol, with short 4–5 day hospital admission. Families' informed consent was obtained and prediet investigations were performed before the admission. The initiation phase orders were done as well. Follow-up programs were discussed with families. Diet ratios were 4:1 for 3 patients; 2.5:1 for two patients and 1.5:1 for one patient. Average time of the diet duration is 6 months.

Results: 2/3 patients have achieved more than 50% improvement in seizures frequency; one patient has achieved 100% seizures control; one patient > 90% improvement. AEDs were completely weaned-off in two patients; two patients had their number of medications reduced. One patient discontinued the diet due to chronic constipation; episode of metabolic acidosis due to inadequate calories intake was observed in another patient.

Conclusion: Thus, KD appears to be effective, safe and cost reducing alternative treatment option for the patients with intractable epilepsies in developing countries.

E453

EFFECTS OF COMBINING A STATIC MAGNETIC FIELD AND AEDS ON AUDIOGENIC SEIZURE THRESHOLD IN BLACK SWISS MICE

M. McLean, S. Engstrom, Q. Zhang, and M. Zhang
Vanderbilt University Medical Center, Nashville, TN, USA

Pretreatment with a static magnetic field (SMF) prolonged the latency of audiogenic seizures (AGS) and enhanced the efficacy of phenytoin in black Swiss mice (McLean et al., Epilepsy Research, in press). Here we examined effects of pretreatment with five antiepileptic drugs (AEDs), alone and combined with SMF. Animals were handled using methods approved by the Vanderbilt Institutional Animal Care and Use Committee and NIH. All mice were kept in perforated tubes for one hour with/without SMF exposure. A 25 mm x 10 mm x 10 mm neodymium-iron-boron magnet was attached over mouse heads (filling a volume 6–12 mm from magnet surface) for exposure. Five mm from the magnet surface, flux density and perpendicular gradient component were about 220 mT and 40 T/m, respectively. At 15 mm, the values were about 30 mT and 4 T/m. AEDs were administered intraperitoneally at doses that reduced incidence of AGS by 20–50%. For auditory stimulation, mice were removed from tubes and placed in a cylindrical chamber. The intensity of white noise delivered by a speaker in the lid increased stepwise from 70–120 dBA in 11 minutes. Assessments included time to seizure onset (latency) and seizure severity (seizure manifestations, especially clonus). AEDs or SMF alone prolonged seizure latency compared to untreated controls. Combined pretreatment with SMF prolonged latency and reduced severity more than AEDs alone. Enhancement of phenytoin, lamotrigine and diazepam effects was greater than enhancement of levetiractam and pregabalin effects. SMF may enhance effects of AEDs on seizure threshold and severity under certain conditions.

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E Posters
Basic Science

E454

SERUM NEURON SPECIFIC ENOLASE LEVEL AFTER EPILEPTIC ATTACK: 37 PATIENTS CASE REPORTS.

S. Singh, A. Singh, A. Sharma, and R. Kaushal
Epilepsy Care Organization, India

Purpose: Neuron Specific Enolase (NSE) is generally used as marker for neuropathological process in the brain. 37 patients were studied after epileptic attack. NSE in blood was analyzed by enzyme immunoassay. NSE level was obtained in both free epileptic and post epileptic period.

Method: 37 subjects age group 10–50yrs suffering from epilepsy were included in study. Consent for participation in study was given by patient itself. Serum samples were obtained from all subjects within 2 hrs of seizure activity. This group of patients were followed up monthly for 2 yrs. 2yrs after their second sample of serum were taken to find out.

Conclusion: Serum NSE was quantified by EIA kit. Analysis was performed by using a paired *t*–test.

Results: NSE is marker of brain injury after acute neurologic insults. S. NSE was significantly increased as compared with baseline and normal control group after epileptic episode in patients with complex partial seizure and generalized tonic–clonic seizure. Serum NSE was with in normal limit in patients with nonepileptic events. Mean + SD value for NSE

level (ng/ml) was 11.2+ 3.7. There was a significant decrease of NSE level overtime ($p < 0.001$). In most patients the level of NSE remains normal after CPS and GTCS. After 2 hrs of seizure only 43% of the patients had increased NSE.

Conclusion: NSE is not a sensitive marker for seizure and mean NSE level were not increased compared with the normal control group.

E455
PHOSPHORYLATION MYOSIN LIGHT CHAIN AND MYOSIN LIGHT CHAIN KINASE IS FOUND EXTENSIVELY IN THE ANTERIOR TEMPORAL NEUCORTEX OF PATIENTS WITH INTRACTABLE EPILEPSY

J. Yuan, and X. Wang
The First Affiliated Hospital of Chongqing Medical University, China

Purpose: To learn Phosphorylation of Myosin light chain (P-MLC) and Myosin Light Chain Kinase (MLCK) protein expressional levels in anterior temporal Neucortex of Patients with Intractable Epilepsy and the role it plays in mossy sprouting.

Method: Immunohistochemistry, immunofluorescence, western blot were used to check P-MLC and MLCK of protein levels in surgical samples of the anterior temporal neucortex of patients with intractable epilepsy (IE) and the normal samples.

Results: P-MLC was found extensively in the cytoplasm of neurons in all epilepsy specimens; moreover, Western blot showed a up-regulated immunoreactive band of p-MLC in specimens compared with normal samples. Besides, there are no obvious changes of MLCK protein level in specimens compared with normal samples.

Conclusion: The expression in protein of P-MLC and MLCK in anterior temporal Neucortex on patients with IE may play a role in the mossy fiber sprouting process with the development of epileptic seizures.

E456
UPREGULATION OF THE NAV1.6 SODIUM CHANNEL PROTEIN IN TEMPORAL NEOCORTEX IN INTRACTABLE EPILEPSY

P. Rui-Qiang, W. Xue-Feng†, H. Zu-Chun†, and X. Zhi-Qin†*
**The Second Hospital of Xiamen, China; and †The First Affiliated Hospital of Chongqing Medical University, Chongqing, China*

Purpose: Voltage-gated sodium channels (VGSCs) play a critical role in the generation of action potentials in excitable cells throughout the nervous system. The type VI voltage-gated sodium channel (Nav1.6) is widely distributed in neurons of the central nervous systems (CNS). Nav1.6 is the major contributor to sodium current in neurons. Here, we have analyzed the expression of Nav1.6 in the temporal neocortex of the intractable epilepsy (IE) patients and to explore its possible role of Nav1.6 in it.

Method: Surgically resected brain specimens of 40 patients with intractable epilepsy and 15 control cases were collected, then the expression of Nav1.6 protein in the temporal neocortex was evaluated by immunohistochemistry and immunofluorescence technique.

Results: Campared with the control group, the expression of Nav1.6 protein showed a significant increase in the temporal neocortex of patients with intractable epilepsy ($P < 0.05$).

Conclusion: Our results suggest that Nav1.6 overexpression in the temporal neocortex of patients with intractable epilepsy may play a role in the pathogenesis of IE.

E457
EVIDENCE THAT THE PHOSPHORYLATION OF GABAA RECEPTORS REGULATES NEUROSTEROID EFFICACY AFTER KINDLING

M. Kia, and M. Poulter
University of Western Ontario, London, Ontario, Canada

Purpose: Previously, we showed that tetra-hydro-deoxy-corticosterone (THDOC) has reduced efficacy after the induction of stage 5 amygdala kindled seizures. As the phosphorylation modulates THDOC pharmacology, we hypothesized that perhaps kindling induces (long term) changes in the phosphorylation of GABAA receptors.

Method: In order to test this hypothesis we have manipulated phosphorylation state of GABAA receptors by employing agents that activate kinases (PMA, 100 nM) or inhibit phosphatase (FK-506,100 nM). Through patch clamp recordings in layers 1–3 of the piriform cortex prepared from nonkindled male Sprague Dawley rats (200–250 gm),GABAA synaptic responses were isolated by applying 200 nM TTX, 50 μM APV, and 20 μM DNQX. We also carefully monitored the holding current to see if the extrasynaptic transmission may be affected. We applied THDOC (100 nM) for a minimum of 10 minutes, a protocol that has been shown previously to enhance currents by as much as 100%.

Results: We found that PMA (same as Fk-506) prolonged the deactivation of the mIPSCs. The subsequent application of THDOC reduced the amplitude of mIPSCs, but THDOC prolonged mIPSCs further. However, the net affect was that THDOC did not enhance charge transfer, an outcome that was identical to those found in kindled tissue. Both the inactive phorbol (a-PMA, 100 nM) and the PKC antagonist (BIS I, 100 nM) had no effect on the THDOC modulation.

Conclusion: These data suggest that phosphorylation has profound effects on THDOC and kindling may reduce the THDOC efficacy by inducing the phosphorylation of GABAA receptors.

E458
HIPPOCAMPAL MOSSY FIBERS FORM NEW CONNECTIONS WITH INHIBITORY INTERNEURONS IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

T. Freiman, M. Mueller†, J. Zentner*, C. Haas†, and M. Frotscher‡*
**University Hospital, Freiburg, Germany; †University Hospital, Experimental Epilepsy Group, Freiburg, Germany, and ‡University, Institute of Anatomy, Freiburg, Germany*

Purpose: Temporal lobe epilepsy is frequently associated with Ammon's horn sclerosis which is characterized by neuronal death and sclerosis in the hippocampal regions CA1 and hilus. Additionally, there is a reorganization of mossy fibers in the dentate gyrus, known as mossy fibre sprouting. This sprouting is characterized by an abnormal projection of granule cell axon collaterals backwards to the granule cell layer. It has been proposed that sprouting contributes to seizure generation by forming a local excitatory feedback circuit of granule cells. However, data obtained in animal models point to increased connections of sprouted mossy fibers with inhibitory basket cells.

Method: We examined the connectivity of mossy fibers in neurosurgical specimens of patients with temporal lobe epilepsy using a novel tracing technique. In addition, double immunolabeling and electron microscopy were applied to identify putative target cells of the sprouting mossy fibers.

Results: We show that excitatory granule cell axons (mossy fibers) impinge both on excitatory granule cells and inhibitory interneurons. Granule cells were identified by direct tracer application and synaptoporin immunohistochemistry (IHC). Inhibitory interneurons were identified by parvalbumin IHC and GABA-postembedding immunogold electron microscopy.

Conclusion: These results suggest that sprouted mossy fibers do not only lead to an excitatory feedback circuit but also innervate inhibitory basket cells. We hypothesize that this aberrant innervation of interneurons not only results in an increased inhibition of dentate granule cells, but may contribute to the synchronisation of seizures in this network.

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E459

KETOGENIC DIET INCREASES BRAIN-DERIVED NEUROTROPHIC FACTOR EXPRESSION AFTER KAINIC ACID-INDUCED SEIZURES IN MICE

D. Kim, S. Chae†, S. Jeong‡, and Y. Kwon§*
**Inje University Ilsan Paik Hospital, Korea; †Chung-Ang University College of Medicine, Korea; ‡Dongguk University Hospital, Korea; and §Inha University College of Medicine, Korea*

Purpose: The clinical efficacy of the ketogenic diet (KD) has now been well documented. However, little is known about its underlying mechanisms. Calorie restriction (CR) is known to increase brain-derived neurotrophic factor (BDNF) expression. The KD was originally devised to reproduce the biochemical changes seen upon fasting (extreme CR). This study was designed to investigate the effects of the KD on the BDNF expression after kainic acid (KA)-induced seizures in mice.

Method: Thirty-two male ICR mice (P21) were equally divided into four groups: (1) seizure-free normal diet (ND) group, (2) seizure-free KD group, (3) KA-seizure ND group, and (4) KA-seizure KD group. For 4 weeks, the KD groups were fed a KD, while the ND groups were fed a standard rodent chow. Seizures were induced by intraperitoneal injection of KA (30 mg/kg) in the KA-seizure groups. The seizure-free groups were injected with equal volume of physiological saline. After then, we examined the BDNF mRNA expression affected by the KD, using semi-quantitative RT-PCR.

Results: We found that the KD delays the KA-induced seizure onset time. And, a significant (P<0.05) increase of the BDNF mRNA expression was observed in the hippocampus of the KA-seizure KD group (143 ¾ 15% of control) in comparison with other groups (88, 7, 107, 8, 109, 4% of control).

Conclusion: Our results suggest that the KD enhances the BDNF expression after KA-induced seizures in mice, which may be related to its anticonvulsant effects.

E460

VEGF IS A PIVOTAL FACTOR IN ANGIOGENESIS ASSOCIATED WITH EPILEPTOGENESIS

M. Morin, F. De Bock, A. Lebrun, M. Rousset, J. Bockaert, and M. Lerner-Natoli
CNRS UMR5203-Inserm U661- UM1-UM2-IGF, France

Purpose: In human temporal lobe epilepsy and in rat limbic epilepsy, we observed an angiogenesis associated with blood-brain barrier (BBB) disruption. The vascular endothelial growth factor (VEGF) was over-expressed by hippocampal neurons and astrocytes and its receptor VEGFR-2 by endothelial cells. (Rigau et al, 2007). We postulated that VEGF is induced by seizures and triggers neovascularization and BBB permeability. Therefore, we developed an integrative in vitro model to investigate the role of VEGF in angiogenesis during epileptogenesis.

Method: Organotypic hippocampal cultures (OHC) were treated with kainate or bicuculline to trigger seizures with or without lesions, respectively. We compared at different time points the vascular density and we checked the expression of VEGF and VEGFR-2 (mRNA and protein levels) in control and both epileptogenic conditions. Then, we tried to reduce angiogenesis with a monoclonal neutralizing anti-VEGF antibody (developed in cancer therapy).

Results: A few hours after seizure induction, mRNAs of VEGF and VEGFR-2 were enhanced, whereas protein expression was increased from 14h to 24h. At this time point, the vascular density was significantly increased in both models of 'epileptic OHC' compared to controls. Finally, the neutralization of VEGF activity fully abolished the increase of vascularization induced by seizures.

Conclusion: This study demonstrates that seizure itself induces VEGF release and that VEGFR-2 signalling pathways are responsible for the pathological angiogenesis. Their consequences on the epileptic focus are deleterious, since the chronic permeability of the BBB contributes to hypo-perfusion, inflammation and hyperexcitability.

E461

MATERNAL SEIZURES CHANGE THE HIPPOCAMPAL EXPRESSION OF CALCIUM-BINDING PROTEINS IN THE OFFSPRING

T. Vale, E. Lima, A. Cossa, D. Lima, A. Silva, E. Cavalheiro, N. Maria da Graça, and A. Débora
Federal University of São Paulo, Brazil

Purpose: We investigated the effect of untreated epileptic seizures during pregnancy on hippocampal expression of calcium-binding proteins in the offspring.

Method: Adult female Wistar rats were submitted to the epilepsy model induced by pilocarpine, matted and the frequency of epileptic seizures were monitored during all pregnancy. At birth, body weight, length, and skull measures were evaluated in the pups. Animals were perfused at P6 and P13 for the histological study of the brains. Nissl staining and immunohistochemistry for NeuN, calbindin (CB), calretinin (CR) were carried out on P6, and parvalbumin (PV) on P13. Total number of stained cells in the hippocampus was estimated through stereological Method:.

Results: The total number of epileptic seizures during pregnancy was 18.3 ± 4.5. In P1, weight, length, skull measures were reduced in experimental pups when compared to controls. The total number of hippocampal CB-positive cells was reduced (p=0.05), while PV-positive cells was increased (p=0.02) in the experimental group (NCB=35,200±4,856 – NPV=44,437±3,625) when compared to controls (NCB=56,265±2,853 – NPV=32,968±866). The total numbers of hippocampal Nissl-stained and CR-positive cells were similar in experimental and control animals.

Conclusion: Maternal epileptic seizures had important repercussion on growth and development of the offspring. These pups had intrauterine growth restriction, delay in the development and alterations in the number hippocampal interneurons.

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E462

EXPRESSION OF NESTIN IN THE TEMPORAL LOBES OF THE INTRACTABLE EPILEPSY PATIENTS

L. Wang, and X. Wang
Chongqing Medical University, Chongqing, China

Purpose: To investigate the expression of nestin in temporal lobe of patients with epilepsy so as to explore the possible physiopathologic role in epilepsy and intractabl epilepsy.

Method: The temporal lobes of intractable epilepsy patients were used to set up the brain tissue bank of epilepsy according the time of the operation. We selected 36 temporal lobes and tested the expression of nestin by immunohistochemistry and double stain of immunofluorence technic. Nonepileptogenic control brain tissues were used for comparison.

Results: In this study we found some nestin-immuroreactive cells within the normal temporal lobe, but in the intractable epilepsy they were upregulated, increasing with length course. Double staining showed some

nestin-immuroreactive cells coexpresion with glial fibrillary acidic protein (GFAP), while some with microtube associated protein 2 (MAP2).

Conclusion: These findings provided evidences for increased neorogensis and neorogensis in epilepsy, which could be associated with intractable epilepsy.

E463
EFFECT OF AMLODIPINE ON THE BIPHASIC MODULATION OF SEIZURE THRESHOLD BY MORPHINE

T. Gholipour, S. Farough, K. Riazi, A. Noorian, A. Jannati, and A. Dehpour
Tehran University of Medical Sciences, Iran

Purpose: While low doses of morphine could increase seizure threshold, higher doses of this opioid increase seizure propensity. Regarding relationships of opioid and calcium channel blockers in other parts of central nervous system, we investigated the effect of amlodipine on anti- and proconvulsant effect of morphine on pentylenetetrazole (PTZ)-induced seizure in mouse.

Method: PTZ was infused to male Swiss mice until generalized clonus; dose of needed PTZ (mg/kg) was measured as index of seizure threshold. Time course of action and dose response to amlodipine (1,2,5 and 10mg/kg) on seizure threshold were determined. Next, amlodipine (1 or 2mg/kg; i.p.; 120 min prior to seizure) was administered before a subeffective or a proconvulsant dose of morphine (0.5 or 60mg/kg, respectively; s.c.; 45 min prior to seizure).

Results: Amlodipine dose-dependently increased seizure threshold at 2mg/kg and higher ($P<0.01$). Coadministration of subeffective dose of morphine with amlodipine (1 and 2mg/kg) resulted a significant anticonvulsive effect (47.11±2.28mg/kg for 1 and 55.40±4.13mg/kg for 2mg/kg amlodipine; both $p<0.01$ compared to 44.35±2.85mg/kg for control group). The proconvulsive effect of high dose of morphine could be augmented by addition of subeffective or anticonvulsive doses of amlodipine (29.09±1.99mg/kg for 1 and 26.41±1.33mg/kg for 2mg/kg amlodipine; both $p<0.001$ compared to control).

Conclusion: Amlodipine augmented both proconvulsive and anticonvulsive morphine effects, suggesting a synergistic effect with opioid system in both conditions, which are previously shown to be opioid receptor mediated, a dual modulatory effect of calcium channel on neuronal opioid receptor could be claimed. This could be useful in antiepileptic drug research.

E464
EPILEPTIFORM ACTIVITY EXERTS LONG-LASTING EFFECTS ON NMDAR AND AMPAR SUBUNIT EXPRESSION, DISTRIBUTION AND INTERACTION IN NEOCORTICAL CULTURES

Q. Jiang, J. Wang, Y. Wu, X. Wu, and Y. Jiang
Peking University First Hospital, China

Purpose: To explore systematic effects of early epileptiform activity on the formation and function of developing neocortical neurons at the cellular level.

Method: We use in vitro model of early-life seizure, that is, single event of epileptiform activity induced by magnesium-free medium treatment in primary cultured rat neocortical neurons. First we extract total protein and detected the expression of NR1, NR2A, NR2B, GluR1, GluR2 and PSD-95, then by using biochemical sub-cellular fractionation and immunoblot analysis, we further examined alterations of receptor composition and sub-cellular distribution. Coimmunoprecipitation and immunocytochemistry was applied respectively to detect changes in protein (s) interaction, neuronal morphology as well as excitatory synapse formation.

Results: When total neuronal protein was examined, we found a decrease in expression of NR2B NMDAR subunit and PSD-95 ($P < 0.05$) shortly after insult (within 24 hours). With the use of cell fractionation, we found that the cellular location of each NMDAR subunit (NR1, NR2A and NR2B), AMPAR subunit GluR1 and GluR2 and PSD-95 changed after the induced epileptiform activity. Co-IP detection revealed a gradually enhanced interaction between PSD-95 and NR2A compared with NR2B from 7DIV to 21DIV. In addition, early-life seizure-like insults still exert effects on excitatory synapses number, size and distribution.

Conclusion: Epileptiform activity may cumber normal development of neocortical neurons and preserve them at much more naïve period with less matured function and strength. These findings in an in vitro model of early-life seizure may inform rodent models of epilepsy, as well as the pathology of seizures in human neocortical development.

E465
HYPERTHERMIA INDUCED EPILEPTIC SEIZURES IN MICE CARRYING A *SCN1A* MUTATION

H. Ohtani, Y. Takahashi*, S. Ohtani*, I. Ogiwara†, E. Mazaki†, K. Yamakawa†, T. Fujiwara*, and Y. Inoue**
**National Epilepsy Center, Shizuoka Institute of Epilepsy and Neurological Disorders, Japan; and †Neurogenetics Research Group, RIKEN Brain Science Institute, Japan*

Purpose: Severe myoclonic epilepsy in infancy, or Dravet syndrome, is the most severe and intractable form of the SCN1A-associated epileptic syndrome. The seizures of this syndrome are often precipitated by fever. Recently, Ogiwara et al. (2007) succeeded to produce the mice carrying an SCN1A gene mutation. We examined whether hyperthermia really induce seizures in this mouse.

Method: We used heterozygous knock-in mice (SCN1ARX/+) as human disease model. The mouse was put into the small box and heated by hot plate from bottom and by electric light bulb from above with measuring rectal temperature by use of converted body temperature control device (Nihonkohden, Tokyo, Japan). Video and electroencephalogram were recorded simultaneously and we compared the rectal temperature where the seizure was precipitated and the duration of seizures between SCN1ARX/+ and SCN1A+/+. 32 seizures of SCN1ARX/+ (n=12) and 9 seizures of SCN1A+/+ (n=10) were investigated.

Results: All seizures were (clonic-) tonic–clonic seizures or clonic seizures. One SCN1A+/+ mouse did not show seizures even with hyperthermia of 45 Ž. The precipitating temperature (Ž) of SCN1ARX/+ (40.1}0.9) was significantly lower compared with SCN1A+/+ (43.2}0.8) ($p<0.0001$). The seizure duration (seconds) of SCN1ARX/+ (35.1}15.3) was not significantly longer than those of SCN1A+/+ (29.5}8.4). (Values represent means} SD).

Conclusion: We found the seizures of SCN1ARX/+ are precipitated by lower temperature than SCN1A+/+.

E466
EXTRACELLULAR TAURINE LEVELS ARE INCREASED IN MICE HIPPOCAMPUS DURING LATRUNCULIN A-INDUCED SEIZURES.

G. Sierra-Paredes, S. Alonso, and G. Sierra-Marcuño
University of Santiago de Compostela, Spain

Purpose: Taurine is one of the most abundant amino acids in the brain. In several studies, taurine has been reported to activate glycine receptors and to act as a potent activator of extrasynaptic GABA A receptors. Thus, taurine is an interesting candidate for modulating network excitability in the hippocampus via tonic inhibition. We have investigated the changes in extracellular taurine in the mouse hippocampus during seizures induced by latrunculin A microdialysis.

Method: Mouse hippocampus was continuously perfused with a latrunculin A solution (4 microM) through CMA/7 microdialysis probes at a flow rate of 1 microL/min during 7 hours with continuous EEG and videotape recording for 3 consecutive days. Samples from the microdialysate were collected and analyzed by HPLC using precolumn derivatization with 6 aminoquinolyl-N-hydroxysuccinimidyl carbamate (AQC) and fluorescence detection.

Results: All mice studied developed a mean number of 4 ± 2,2 seizures during the third day of latrunculin A microperfusion. Mean seizure duration was 68.3 ± 23 seconds. Hippocampal extracellular levels of taurine were significantly increased during latrunculin A microperfusion (from basal levels of 3.08±0.46 microg/ml to 5.83±0.52 microg/ml).

Conclusion: We have previously reported that no modifications are observed in extracellular GABA levels during acute latrunculin A seizures. The present results suggest that the increase of extracellular taurine levels in the mouse hippocampus during latrunculin A administration may be the mechanism to activate tonic inhibition to protect neurons from increased excitability induced by latrunculin A.

E467

VALPROATE'S ACTION ON PROTEIN KINASE A SIGNALLING

P. Chang, R. Williams, and M. Walker
School of Biological Sciences, Royal Holloway, University of London, Egham, Surrey, UK

Purpose: Valproate acid (VPA) is a short chain fatty acid, widely used as an anticonvulsant and mood-stabilizing drug; however, its mechanism of action is still unclear. Recent evidence indicates that VPA may regulate mitogen-activated protein kinase through modulation of protein kinase A (PKA) signalling. In this study, we investigated whether VPA has an effect on PKA dependent LTP at mossy fibre to CA3 pyramidal cell synapses by having a direct effect on PKA.

Method: We tested the effects of VPA on PKA dependent enhancement of mossy fiber-CA3 synapses in hippocampal slices induced by high frequency stimulation or the adenylyl cyclase activator, forskolin. We next tested the effects of VPA on PKA activity. In vitro assays for PKA activity were obtained by measuring PKA's phosphotransferase activity.

Results: VPA (1mM) reduced mossy fiber fEPSP long term potentiation following high frequency stimulation (fEPSP amplitude as percentage of baseline: control: 231.1±22%, VPA 1mM: 147.9±19%). Further, VPA (1mM) decreased enhancement of mossy fiber transmission by forskolin (fEPSP amplitude as percentage of baseline: control: 435.5±46.3%, VPA 1mM: 353 ± 76%, p=0.02). However, VPA had no direct effect on PKA activity (PKA activity as percentage of control: VPA 50 uM: 96.4± 2.4%, VPA 100 uM: 93.2± 5.7%, VPA 500 uM: 98.7± 4.6%, VPA 1 mM: 97.6± 5.4).

Conclusion: VPA inhibits PKA mediated enhancement of mossy fiber transmission, yet has no direct effect on PKA. This suggests that the effects of VPA are down- or up-stream of PKA activation.

E468

ADVERSE NEUROPROTECTIVE EFFECT OF CYTIDINE-5-DIPHOSPHATE CHOLINE TO THE HIPPOCAMPUS OF PILOCARPINE-INDUCED SEIZURE MOUSE

W. Kim, O. Kim†, S. Lee*, and Y. Choi**
**Yongdong Severance Hospital, College of Medicine, Yonsei University, Korea; and †College of Medicine, Pochon CHA University, Korea*

Purpose: Cytidine-5-diphosphate choline (CDP-choline) is a compound normally present in all cells in the body and has neuroprotective effect when administered exogenously. With oral CDP-choline applying within the first 24hrs after onset of stroke, the positive results were proven in clinical data. However, its precise mechanism of action is not fully known. One possible mechanism is that CDP-choline might be affecting the accumulation of extracellular glutamate caused by ischemia, either inhibiting its release or increasing its uptake. We apply this drug to epilepsy model for evaluating the protective effect of CDP-choline for acute seizure.

Method: We examined male ICR mice after systemic injection of pilocarpine. Two hours after status epilepticus started, we stopped the seizure by injecting diazepam and also injected CDP-choline 1g/kg i.p. We divided the mice only pilocarpine injection group for control and CDP-choline injection group. After 3 days we sacrificed the mice and stained cresyl violet, TUNEL method for cell loss and apoptotic status. After 8 weeks we use Timm's staining for evaluating mossy fiber sprouting of hippocampus.

Results: Neuronal cell loss of whole hippocampus was more prominent in CDP-choline injection group compare with only pilocarpine injection group. Especially the neuronal cell in CA3 region decreased severely than other hippocampal region. Apoptosis also increased and mossy fibre sprouting decreased in CDP-choline injection group than control.

Conclusion: The present results indicate that CDP-choline administration in acute seizure phase is not neuroprotective and even harmful for hippocampal neuron although its inhibitory effect for glutamate.

E469

PHARMACOLOGICAL AND NEUROCHEMICAL CHARACTERIZATION OF THE INVOLVEMENT OF HIPPOCAMPAL ADRENORECEPTOR SUBTYPES IN THE MODULATION OF ACUTE LIMBIC SEIZURES

R. Clinckers, I. Smolders, T. Zgavc, A. Schallier, G. Ebinger, and Y. Michotte
The Vrije Universiteit Brussel, Brussels, Belgium

Purpose: Noradrenaline acts as endogenous anticonvulsant as it exerts profound inhibitory effects on seizure susceptibility. The identification of a universal anticonvulsant adrenoreceptor was impeded by conflicting results from pharmacological investigations in which nonselective agents were used. We here used subtype selective compounds to delineate the role of hippocampal adrenoreceptor subtypes in seizure susceptibility.

Method: Intracerebral microdialysis was used for intrahippocampal administration of all compounds and as neurotransmitter sampling tool. The modulatory effects on pilocarpine-induced limbic seizures were behaviorally assessed. Coperfusion experiments of anticonvulsant concentrations (250nM) of the selective noradrenaline reuptake inhibitor maprotiline were conducted with subtype selective antagonists for alpha-1A (5-methylurapidil), alpha-1D (BMY-7378), alpha-2A (BRL-44408), alpha-2C (MK-912), beta-1 (betaxolol) beta-2 (ICI-118551) and D2 (remoxipride) receptors. Finally, selective agonists for alpha-2 (medetomidine) and beta-2 (salmeterol) receptors were tested to confirm our working hypothesis.

Results: Maprotiline mediated anticonvulsant effects, associated with increases in extracellular hippocampal noradrenaline, dopamine and GABA levels. The anticonvulsant effect was blocked independently by alpha-2 and beta-2 antagonism. Beta-2 antagonism inhibited the dopamine increases, while alpha-1A antagonism blocked the GABA-ergic but not the anticonvulsive effect. Antagonism of hippocampal D2 receptors, which mediate the anticonvulsant effect of dopamine, did not affect the anticonvulsant effect of maprotiline. Combined and not separate alpha-2 and beta-2 agonism inhibited pilocarpine-induced seizures.

Conclusion: Hippocampal noradrenaline increases inhibit limbic seizures via combined alpha-2 and beta-2 receptor activation. The concomitant GABA-ergic and dopaminergic effects are not crucially involved in

this anticonvulsant effect. These data demonstrate that the noradrenergic system is an interesting target for innovative antiepileptic treatment.

E470
DISTRIBUTION OF AQUAPORIN-4 IN CONTROL AND EPILEPTIC HUMAN CEREBRAL CORTEX

V. Medici, R. Garbelli*, L. Tassi†, M. Bramerio‡, M. Cossu†, and R. Spreafico**
**I.R.C.C.S. Foundation Neurological Institute 'C. Besta', Milan, Italy; †Epilepsy Surgery Center 'C. Munari', Niguarda General Hospital, Milan, Italy; and ‡Niguarda General Hospital, Milan, Italy*

Purpose: Aquaporin-4 (AQP4) is the predominant water channel in the central nervous system. Recent data show that it is especially expressed on astrocytic endfeet and this polarized distribution suggests its involvements in brain volume and water homeostasis. Moreover, a functional coupling between water transport and K+ clearance has been proposed. We analyze the distribution of AQP4 in relation to gliosis and vascular endothelium in human cerebral cortex in order to evaluate its possible involvements in epileptic condition.

Method: We apply immunocytochemical methods using antibodies against AQP4, GFAP, and CD34 on human surgical cortices from control nonepileptic patients, patients with cryptogenic epilepsy and with epilepsy secondary to Focal Cortical Dysplasia (FCD) Type IIB. Light microscopy, confocal laser scanning microscopy, quantification of the relative optical density of the immunoreactivities and Western Blotting (WB) technique are performed.

Results: We found that: (1) in control cortex AQP4 is localized in the neuropil, and prevalently concentrated in perivascular and subpial astrocyte profiles; (2) WB and quantification of the relative optical density of the immunoreactivity do not show differences in AQP4 level in epileptic tissues versus nonepileptic control cases; (3) the pattern of AQP4 immunoreactivity is different in FCD Type IIB where an intense labelling around dysmorphic neurons and a loss of perivascular localization is present.

Conclusion: since water flux through perivascular AQP4 is needed to sustain efficient reuptake of K+, we propose that the changes observed in FCD Type IIB in AQP4 localization may affect the K+ buffering capacity and neuronal activity.

E471
MAPROTILINE MEDIATES CONCENTRATION-DEPENDENT ANTICONVULSANT AND PROCONVULSANT EFFECTS AGAINST LIMBIC SEIZURES

I. Smolders, R. Clinckers, T. Zgavc, A. Schallier, A. Massie, and Y. Michotte
Vrije Universiteit Brussel, Brussels, Belgium

Purpose: The neurobiological relationships between epilepsy and depression are receiving increased experimental attention. A key role for limbic monoamines in depression has been established and we recently showed the importance of hippocampal dopamine and serotonin in limbic seizure control. We here evaluated the anticonvulsant effect of the noradrenergic antidepressant maprotiline and screened for associated neurochemical effects on extracellular hippocampal noradrenaline, dopamine, serotonin, GABA and glutamate.

Method: In vivo intracerebral microdialysis was used in rats to administer maprotiline intrahippocampally and to sample the hippocampal extracellular space. Concentration-response experiments were conducted with a wide range of maprotiline perfusion concentrations (1nM-100μM). Following maprotiline pretreatment, acute limbic seizures were induced by intrahippocampal perfusion with 10mM pilocarpine for 40 min. Seizure severity assessment was based on the observation of behavioral manifestations according to an in-home validated seizure severity scoring system.

Results: From 250nM concentration onwards maprotiline potently inhibited limbic seizures. Remarkably, at the highest concentrations (10 and 100μM) maprotiline was proconvulsant as pilocarpine-induced seizure severity was potentiated. Intrahippocampal maprotiline perfusion concentration-dependently increased extracellular hippocampal noradrenaline and dopamine levels from 100nM onwards, and serotonine and glutamate levels from 10μM onwards. GABA-ergic effects were only observed with anticonvulsant maprotiline concentrations.

Conclusion: Within a limited concentration range maprotiline mediates potent inhibitory effects on acute limbic convulsions. These anticonvulsant effects are associated with significant increases in noradrenaline, dopamine and GABA levels. Proconvulsant effects are associated with excessive noradrenaline and dopamine increases, serotonin and glutamate increases and suppression of GABA-ergic activity.

E472
EXPRESSION OF LAYER-SPECIFIC MARKERS IN NODULAR HETEROTOPIA

L. Rossini, R. Garbelli*, R. Moroni*, A. Watakabe†, L. Tassi‡, M. Bramerio§, M. Cossu‡, C. Marras¶, C. Frassoni*, and R. Spreafico**
**Division of Epilepsy Clinic And Experimental Neurophysiology, I.R.C.C.S. Foundation Neurological Institute 'C. Besta', Milan, Italy; †Division of Brain Biology, National Institute For Basic Biology, Okazaki, Japan; ‡Epilepsy Surgery Center 'C. Munari', Niguarda General Hospital, Milan, Italy; §Division of Pathology, Niguarda General Hospital, Milan, Italy; and ¶Division of Neurosurgery, I.R.C.C.S. Foundation Neurological Institute 'C. Besta', Milan, Italy*

Purpose: Heterotopia are malformations of cortical development characterized by the presence of apparently normal cells in abnormal position as result of abnormalities of neuronal migration and they are frequently associated with intractable epilepsy. Despite the increasing number of clinical and neuropathological studies aimed at characterizing these abnormalities, little is known about the aetiology and the composition of the heterotopic nodules. Aim of this work is to study the expression of layer-specific markers in human surgical tissue presenting a neuropathological diagnosis of nodular heterotopia (NH).

Method: We use tissues from epileptic patients with two different types of NH: (1) subcortical heterotopia (5 cases) with characteristic of PNH at the MRI investigation, (2) small subcortical nodules (7 cases) not visible at the MRI. We perform RNA in situ hybridization (ISH) using a panel of cortical layer-specific markers, whose expression covers some cortical layers: Ror-ß, Er81, Nurr1 respectively expressed in layers IV, V and VI. Normal tissues are also used to confirm the specificity of these markers. Moreover, double ISH and immunocytochemistry using NeuN antibody is performed.

Results: In the first group, ER81- and Nurr1-positive cells are prevalently distributed at the borders of the nodules whereas Ror-ß-positive cells are more concentrated within nodules. In the second group, the nodular formations are only composed by Nurr1-positive neurons.

Conclusion: the two types of NH present different neuronal composition, in group 1 a rudimentary laminar arrangement can be suggested whereas in group 2 the nodules are formed of clustered, improperly migrated layer-VI neurons.

E473
THE INVOLVEMENT OF THE SOMATOSTATIN SST2 AND SST3 RECEPTORS IN THE ANTICONVULSANT EFFECT OF CORTISTATIN-14

N. Aourz, B. Stragier, R. Clinkers, Y. Michotte, and I. Smolders
**Vrije Universiteit Brussel, Brussels, Belgium*

Purpose: Several neuropeptides and their receptors are currently studied as possible future neurobiological targets for anti epileptic drugs. Anticonvulsant actions have already widely been proven for somatostatin-14 (SST-14). Cortistatin-14 (CST-14) was shown in one report to protect against kainate-induced seizures (Braun et al. Brain Res. 1998; 803 (1–2):54–60). Although these neuropeptides are products of different genes, they are structurally related. This explains the interaction of CST-14 with the SST receptors. To investigate the possible involvement of the SST2 and SST3 receptors in the anticonvulsant actions of CST-14, we used a selective SST2 receptor antagonist, Cyanamid154806 (CYN), and a selective SST3 receptor antagonist, SST3-ODN-8, as pharmacological tools.

Method: In vivo microdialysis in male albino Wistar rats was used for intrahippocampal drug administration and as neurotransmitter sampling tool. Seizures were evoked by intrahippocampal pilocapine perfusion (10mM, 40min) and seizure severity was assessed using a behavioral scoring system.

Results: Intrahippocampal administration of CST-14 was able to prevent pilocarpine convulsions but did not alter the extracellular hippocampal levels of dopamine, serotonin, GABA or glutamate. Coperfusion experiments of CST-14 with CYN or SST3-ODN-8 could reverse the anticonvulsant actions of CST-14. CYN or SST3-ODN-8 perfusion alone showed proconvulsant actions in the pilocarpine model.

Conclusion: These observations point to an important role of both SST2 and SST3 receptors in regulating independently of each other the hippocampal excitability. It is not yet clear to which extent both receptor types are involved in the anticonvulsant mechanism of action of CST-14.

E474
TRANSIENT ANGIOGENESIS DURING KINDLING DEVELOPMENT: A VASCULAR PRECONDITIONING?

M. Lerner-Natoli,†, A. Lebrun*,†, M. Morin*,†, and J. Bockaert*,†*

**Institut De Genomique Fonctionnelle – CNRS UMR 5203, France; and †INSERM U661, UM1, UM2, France*

Purpose: We reported previously a pathological angiogenesis in human Temporal Lobe Epilepsy and, also, during epileptogenesis in the rat pilocarpine model. From acute to chronic phases, angiogenesis was associated with a persistent disruption of the blood-brain barrier (BBB) which is known to reinforce epileptogenicity. Here, we investigated angiogenesis and BBB impairment in a model of progressive hyperexcitability, kindling induced by pentylenetetrazol (PTZ).

Method: 35 rats were implanted with deep electrodes and cortical screws. They were given 30mg/kg PTZ or vehicle intraperitoneally every second day for 28 days. EEG recording and behavioral score (1 to 5) were performed after each injection. Rats were sacrificed at various stages of kindling, and we investigated the vascular density, VEGF expression, and the integrity of BBB tight junctions by immunohistochemistry or Western blotting.

Results: the VEGF level peaked at stage 1, likely overexpressed by neurons, and decreased rapidly. The vascular density was enhanced in hippocampus, thalamus, cingular and entorhinal cortices at stages 1–2 then was stabilized. The expression of occludin and ZO-1 decreased during stages 1–2, but they rebounded and rebuilt tight junctions as soon as stage 3.

Conclusion: Angiogenesis and BBB permeability are transient in chemical kindling, whereas they are persistent in the pilocarpine model. These results suggest that a vascular preconditioning occurs after the first seizures. The down regulation of VEGF during further kindling seizures likely prevents the degradation of tight junctions. We hypothesize that the consolidation of blood–brain barrier could reduce the probability of spontaneous seizures.

E475
DOUBLECORTIN EXPRESSION PATTERNS IN HIPPOCAMPAL SCLEROSIS AND OTHER FOCAL EPILEPSY PATHOLOGIES

N. Srikandarajah, L. Martinian*, W. Squire†, S. Sisodiya†, and M. Thom**

**Institute of Neurology, London, UK; and †Radcliffe Infirmary, Oxford, UK*

Purpose: Doublecortin is a developmentally regulated microtubule-associated protein that plays an important role in neuronal migration. As many epilepsy-related pathologies have a mal-developmental basis we aimed to study a wide range of pathologies using doublecortin.

Method: Doublecortin immunohistochemistry was investigated and qualitatively assessed on 30 surgical hippocampal sclerosis (HS) cases with varying degrees of granule cell dispersion (GCD), 6 postmortem (PM) HS cases, 5 Focal Cortical Dysplasia type IIB (FCD), 5 mild dysplasias, 5 dyembyoplastic neuroepithelial tumors (DNT) and 4 heterotopias; all these patients suffered from refractory epilepsy. 10 control cases were included.

Results: In PM and surgical controls expression was unique to occasional larger neurones in layer I, small round cells and satellite cells. Surgical HS cases variably displayed immunopositivity of residual CA1 neurones, with enhanced labelling in GCD; this was neither a consistent finding nor age dependent. In FCD IIB, doublecortin-positive dysplastic cell types and multipolar cells were seen. Labelling was noted in layer I and II of DNT and layer II dysplasias. Normal staining patterns were noted in the heterotopias.

Conclusion: Persistent cellular doublecortin expression is confirmed in normal adult cortex. Inconsistent doublecortin expression in GCD cases may reflect a transient up-regulation. The abnormal cell types noted in the cortical dysplasias and DNTs are likely to reflect cell immaturity in a developmental abnormality or alternatively seizure enhanced recruitment of doublecortin expressing cell populations.

E476
HIPPOCAMPAL KINDLING IN RATS WITH ABSENCE EPILEPSY RESEMBLES AMYGDALOID KINDLING

O. Akman, A. Karson*, R. Aker†, N. Ates*, and F. Onat†*

**Kocaeli University Faculty of Medicine Kocaeli, Turkey; and †Marmara University Faculty of Medicine Istanbul, Turkey*

Purpose: Genetic absence epilepsy rats, WAG/Rij and GAERS, show a delay or resistance to secondary generalization of limbic seizures during amygdaloid kindling. We aimed to evaluate hippocampal kindling, and to compare its effects on spike-and-wave discharges (SWDs) with that of amygdaloid kindling.

Method: Stimulation electrodes were placed into the ventral hippocampus and recording electrodes into the skull of WAG/Rij, GAERS and Wistar rats. Animals received kindling stimulation twice daily at their afterdischarge thresholds until they reached stage 5 seizures, or the maximum number of stimulations (50) have been delivered. The spectral changes of SWDs of the WAG/Rij and GAERS after stage 2, 3 and 4 seizures were analyzed by computing the power spectra using the Fast Fourier Transform.

Results: All nonepileptic Wistar rats reached stage 5 by the 34th stimulation. Four of eight WAG/Rij rats showed stage 5 seizures and three of six GAERS rats displayed stage 4 seizures (kindling-prone rats); all the others stayed at stage 2 seizures (kindling-resistant rats) even after the maximum number of stimulations. The cumulative duration and number of SWDs decreased in the poststimulation period after the first stage 2 seizures, whereas these parameters of the SWDs increased in the poststimulation period after the first stage 3 seizures in the kindling-prone

WAG/Rij and GAERS. The spectral characteristics of SWDs after stage 4 seizures differed between the absence epilepsy rat strains.

Conclusion: Hippocampal kindling resembles amygdaloid kindling in showing a resistance to secondary seizure generalization. This demonstrates an interaction between thalamocortical and limbic circuitries.

E477
SELECTIVE Y1 RECEPTOR ANTAGONISTS MAY NOT BE USEFUL IN THE TREATMENT OF LIMBIC SEIZURES.

J. Portelli, A. Meurs*,†, A. Balasubramaniam‡, R. Clinckers*, Y. Michotte*, and I. Smolders**

**Drug Analysis and Drug Information, Research Group Experimental Pharmacology, Vrije Universiteit Brussel, Brussels, Belgium; †UZ Gent, Ghent, Belgium; and ‡University of Cincinnati Medical Center, Cincinnati, OH, U.S.A.*

Purpose: Neuropeptide Y's anticonvulsant activity is generally believed to be mediated by Y2 and/or Y5 receptors. Conversely, Y1 receptors are thought to have a permissive effect on seizures. Two Y1 antagonists, BIBP3226 and BIBO3304, have been shown to inhibit seizures in animal models. Brain-entering Y1 antagonists with good oral bioavailability may therefore be useful treatments of epilepsy. Our aim was to better characterise the role of Y1 receptors in epilepsy using novel, highly selective Y1 receptor ligands.

Method: Freely moving Wistar rats underwent a 3 hour intrahippocampal microperfusion of the Y1 antagonists BIBP3226 (10μM) or BVD10 (40μM) or a 2 hour microperfusion of the Y1 agonist D-His26-NPY (0-20-50-200μM) via a stereotactically implanted microdialysis probe. Pilocarpine (10 mM) was subsequently co-administered in the hippocampus for 40 min, and behavioral changes indicative of seizure activity were scored.

Results: BIBP3226 (10μM) was potently anticonvulsant. An equivalent concentration of BVD10 (40μM) had no effect on pilocarpine-induced seizures. D-His26-NPY had no effect on pilocarpine-induced seizures at low concentrations (20–50μM), and attenuated seizures at high concentrations (200μM).

Conclusion: Y1 receptor antagonists may not be useful in the treatment of epilepsy. Previously reported anticonvulsant effects of BIBP3226 were confirmed, but the more selective Y1 antagonist BVD10 did not suppress seizures, suggesting that BIBP3226 acts through non-Y1 receptors. Moreover, the permissive effect of hippocampal Y1 receptor activation on seizures could not be confirmed. The anticonvulsant effect of high doses of the Y1 agonist D-His26-NPY is probably due to a loss of selectivity.

E478
SINGLE CELL ELECTRICAL ACTIVITY DURING HUMAN SPONTANEOUS INTERICTAL EPILEPTIFORM DISCHARGES AND RESPONSES TO SINGLE PULSE ELECTRICAL STIMULATION (SPES)

G. Alarcon, A. Valentin*, E. Lacruz*, T. Fitzgerald*, R. Quian-Quiroga†, J. Martinez-Gomez†, R. Selway‡, and J. Garcia-Seoane§*

**Institute of Psychiatry, London, UK; †University of Leicester, UK; ‡King's College Hospital, London, UK; and §Universidad Complutense, Madrid, Spain*

Purpose: Simultaneous intracranial EEG and microelectrode recordings have been studied in order to identify the patterns of cell firing associated with spontaneous interictal EEG epileptiform discharges and with EEG responses to single pulse electrical stimulation (SPES) in the human brain.

Method: Behnke-Fried electrodes were inserted in the temporal and frontal lobes of 5 patients being assessed for surgical treatment of their epilepsy with depth electrodes.

Single cells were identified with Wave_Clus software (http://www.vis.caltech.edu/~rodri/Wave_clus/Wave_clus_home.htm).

Results: Four patterns of cellular firing were associated with spontaneous interictal discharges and with early responses to SPES: (1) No change in firing rate (no change). (2) Brief burst (<100 ms) of action potentials (burst-only). (3) Period of suppression of action potentials (suppression-only). (4) Brief burst of action potentials followed by suppression (burst-suppression). Among the 32 cells that were studied during spontaneous epileptiform discharges, 15 showed no change, 10 showed suppression-only, 4 showed burst-suppression and 3 showed burst-only. Among the 95 cells that were studied during early responses to SPES, 39 showed no change, 38 showed suppression-only, 14 showed burst-suppression and 4 showed burst-only. Changes in firing rate were were essentially similar during spontaneous EEG discharges and during early responses to SPES but generally more prominent after stimulation.

Conclusion: Approximately half of the cells did not show changes in discharge rate. Among the cells that showed changes, suppression-only was the most common pattern, probably due to powerful lateral inhibition.

E479
EFFECTS OF ISOFLURANE ON HIPPOCAMPAL SEIZURES IN IMMATURE RATS

E. Isaeva, D. Isaev*, and G. Holmes†*

**Bogomoletz Institute of Physiology, Kiev, Ukraine; and †Dartmouth Medical School, Lebanon, NH, USA*

Purpose: Refractory status epilepticus is an emergency state, which requires immediate suppression of seizures, but conventional drugs may be ineffective. In this case general anaesthesia may be helpful in further management. The response of the immature brain to anaesthesia procedure is more variable, and prolonged exposure to volatile anaesthetic agents may adversely alter brain development. Appropriate treatment requires an understanding of the pharmacokinetics and pharmacodynamics of the drugs used, as well as knowledge of the mechanisms of action anticonvulsive medications applied. The goal of this study is to investigate the efficacy of isoflurane on evoked seizures in the hippocampus of immature rats.

Method: Extracellular field potential recordings from CA3 pyramidal cell layer was performed on unanesthetized rats at ages P8-16. Hippocampal seizures were evoked by injection of high potassium/ low magnesium ACSF. The concentration of isoflurane was regulated by specific vaporizer.

Results: While isoflurane in clinically relevant concentration stops hippocampal seizures, we have revealed that seizures can be evoked by proconvulsant agents while the animal is under isoflurane anaesthesia. The epileptiform activity induced during anesthesia is qualitatively different from that obtained in unanesthetized conditions. This observation suggests that the mechanism by which seizures are terminated differ from the mechanisms responsible for preventing of the initiation of seizures.

Conclusion: Our results show that general anesthesia with isoflurane can be effectively used in the treatment of severe status epilepticus. However prolongation of isoflurane exposure does not prevent the seizure reappearance.

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E480

ANTIEPILEPTIC EFFECT OF HIGH-FREQUENCY STIMULATION AND BILATERAL ANTERIOR THALAMIC NUCLEUS LESIONS ON PILOCARPINE-INDUCED STATUS EPILEPTICUS AND SPONTANEOUS SEIZURES

V. Rooslan, K. Nadezhda, and S. Alexei
State Medical University, Odessa, Russia

Purpose: Previous results indicate that high frequency electrical stimulation (ES) of anterior nucleus of the thalamus cause antiepileptic effects on the pentylenetetrazol kindling model in rats. The aim of this study was to investigate the influence of ES of anterior thalamic nucleus lesions in conditions of pilocarpine model in rats.

Method: Adult Wistar rats underwent bilateral anterior thalamic nucleus ES or their bilateral thalamotomies through implanted electrodes. Seizures were induced by i.p. administration of pilocarpine (320 mg/kg). Electrographic recordings from hippocampal and cortical electrodes were evaluated. Latency for the developing status epilepticus and the first spontaneous seizure, frequency and duration of seizures were monitored.

Results: Bilateral thalamic ES significantly prolonged the latency of status epilepticus development and reduced the frequency and duration of spontaneous seizures. Bilateral thalamotomies reduced the propensity and increased the latency for developing seizures and status epilepticus.

Conclusion: Bilateral anterior thalamic complex stimulation and thalamotomies did not abort epileptogenesis but minimized the expression of seizures induced by pilocarpine.

E481

IDENTIFICATION OF A BRAINSTEM EVOKED POTENTIAL FOLLOWING CERVICAL VAGUS NERVE STIMULATION IN RATS

R. El Tahry, R. Raedt*, V. De Herdt*, L. Waterschoot*, T. Wyckhuys*, A. Van Dycke*, A. Meurs*, K. Vonck*, W. Wadman†, and P. Boon**
**Ghent University Hospital, Laboratory for Experimental and Clinical Neurophysiology, Ghent, Belgium; and †Swammerdam Institute for Life Sciences, University of Amsterdam, Amsterdam, Netherlands*

Purpose: Vagus nerve stimulation is used as an ad-on treatment for patients with refractory epilepsy. Up till now, the exact mechanism of action is still not fully understood. Moreover, there is a lack of objective parameters that reflect effective vagus nerve stimulation.

Method: A cuff stimulation electrode was implanted around the vagus nerve of a Sprague Dawley rat. A four channel depth-recording electrode was stereotactically implanted into the solitary tract nucleus [AP= −13.6 mm, ML= 1mm, DV=−8 mm relative to bregma]. A biphasic stimulus (1 mA, 500 μsec), was applied to the nerve.

Results: Vagal evoked potentials (VaEP) could be recorded consisting of two positive peaks (P1 and P2) and one negative (N1) peak (P1N1P2) Peak latencies were 3.1, 3.8 and 4.6 msec respectively. The VaEP had a threshold at 100μA. Moreover, the amplitude of the VaEP was frequency dependent.

Conclusion: We recorded a vagal evoked potential in the rat brainstem which reflects true stimulation of the vagus nerve. This result indicates that brainstem VaEP characteristics change depending on the VNS parameters used. Further characterisation of the VaEP will be performed to evaluate its usefulness as an objective parameter during VNS trials.

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E482

ACETYLCHOLINE-INDUCED SEIZURE-LIKE ACTIVITY AND CHOLINERGIC MODIFIED GENE EXPRESSION IN CHRONICALLY EPILEPTIC RATS

G. Zimmerman, M. Njunting†, S. Ivens†, M. Gross*, E. Tolner‡, H. Soreq*, U. Heinemann†, and A. Friedman†,§*
**The Institute of Life Sciences, The Hebrew University of Jerusalem, Jerusalem, Israel; †Institute For Neurophysiology, University Medicine Berlin, Berlin, Germany; ‡University of Helsinki, Helsinki, Finland; and §Zlotowski Center of Neuroscience, Ben-Gurion University, Beer-Sheva, Israel*

Purpose: The entorhinal cortex (EC) plays an important role in temporal lobe epilepsy. Under normal conditions, local synchronized oscillatory activity in the EC is modulated by its enriched cholinergic innervation. The current study examines the role of cholinergic innervation in the EC in the initiation and propagation of seizures in chronically epileptic rats.

Method: We examined cholinergic modulations in epileptic tissue and studied molecular and electrophysiological cholinergic responses in the EC of chronically epileptic rats following exposure to pilocarpine or kainic acid.

Results: We confirmed that while the total activity of the ACh hydrolyzing enzyme, acetylcholinesterase (AChE) was not altered, epileptic rats showed alternative splicing of AChE pre-mRNA transcripts, accompanied by a shift from membrane-bound AChE tetramers to soluble monomers. This was associated with increased sensitivity to ACh application: thus, in control rats, acetylcholine (10–100μM) induced slow (<1Hz), periodic events confined to the EC; however, in epileptic rats, ACh evoked seconds-long seizure-like events with initial appearance in the EC, and frequent propagation to neighboring cortical regions. ACh-induced seizure-like events could be completely blocked by the nonspecific muscarinic antagonist, atropine, and were partially blocked by the muscarinic-1 receptor antagonist, pirenzepine; but were not affected by the nonspecific nicotinic antagonist, mecamylamine. Epileptic rats presented reduced transcript levels of muscarinic receptors with no evidence of mRNA editing or altered mRNA levels for nicotinic acetylcholine receptors.

Conclusion: Our findings suggest that altered cholinergic modulation may initiate seizure events in the epileptic temporal cortex.

E483

INCREASED DOPAMINERGIC TONE IN GENETIC ABSENCE EPILEPSY RATS FROM STRASBOURG (GAERS): EVIDENCE FROM QUINPIROLE-INDUCED YAWNING AND MICRODIALYSIS EXPERIMENTS.

C. Deransart, H. Bernard, A. Bertrand, M. Savasta, and A. Depaulis
Grenoble – Institut Des Neurosciences, France

Purpose: In rats with absence epilepsy (GAERS), systemic and intrastriatal dopamimetics suppress seizures, whereas antagonists aggravate them. In addition, D3 receptor transcripts are overexpressed in the nucleus accumbens core (NacC) as compared to inbred nonepileptic control rats (NEC). The hypothesis of an increased dopaminergic tone in GAERS was thus addressed using pharmacology and microdialysis.

Method: In GAERS and NEC (1) spontaneous and quinpirole-induced yawning behavior and (2) changes in intra-accumbens dopamine contents induced by amphetamine and K+ and measured by microdialysis were investigated.

Results: Spontaneous yawning was significantly decreased in GAERS (0.3±0.2 yawn/hr, n=9) as compared to NEC (5.4±1.2, n=8) and Wistar Harlan rats (9.7±2.3, n=7). Quinpirole-induced yawning was significantly increased in GAERS (29.4±4.9) as compared to NEC (10.5±2.7)

and Wistar-Harlan rats (22.6±3.5). Quinpirole also increased the number of absence-seizures in GAERS (+47.4±8.6%). When compared to NEC, basal levels of DA were 40% lower in GAERS whereas amphetamine and K+ produced a higher increase in extracellular dopamine in GAERS.

Conclusion: The increased quinpirole-induced yawning in GAERS may account for an overexpression in D3 transcripts. The increased responsiveness of dopamine transmission observed in GAERS after pharmacological manipulations, as compared to NEC, suggests a 'hyperdopaminergic' phenotype of GAERS. Altogether, these data support that GAERS have an impaired DA tone that may be associated with the development of mechanisms controlling absences seizures.

E484

ATTENUATION OF KINDLING PROGRESSION BY ESLICARBAZEPINE ACETATE, (S)-LICARBAZEPINE, AND OXCARBAZEPINE BUT NOT BY (R)-LICARBAZEPINE IN THE MOUSE CORNEAL KINDLING MODEL

A. Pekcec, P. Winter*, P. Soares-da-Silva†, and H. Potschka**
**Inst. of Pharmacology, Toxicology, and Pharmacy, Ludwig-Maximilians-University, Muncih, Germany; and †BIAL S. Mamede Do Coronado, Portugal*

Eslicarbazepine acetate (ESL; BIA 2-093) is a new sodium channel blocker that is structurally related to the drugs Carbamazepine and Oxcarbazepine (OXC). However, metabolism of ESL differs to CBZ and OXC as it only forms (S)-licarbazepine but not (R)-licarbazepine. These differences are discussed to imply an improved drug efficacy and drug safety. The present study aimed to determine the effect of ESL, OXC and its metabolites on kindling progression and on seizure-induced hippocampal neurodegeneration. Female NMRI mice were kindled by twice daily bilateral corneal stimulation. The different compounds were administered intraperitoneally (100 mg/kg) 15 min before each kindling stimulation. The neuronal density of different hippocampal subregions was stereologically assessed in the treatment groups as well as in nonstimulated and stimulated control groups that received the corresponding vehicle solution. ESL, OXC and (S)-licarbazepine but not (R)-licarbazepine affected the number of stimulations necessary to induce a specific seizure stage and the mean seizure severity during kindling progression in a relevant manner. Compared to the nonstimulated controls kindling resulted in a reduced hippocampal neuronal density in all treatment groups. No significant inter-group differences in neuronal density were observed. The data give evidence for an antiepileptogenic effect of ESL and (S)-licarbazepine but not (R)-licarbazepine. In addition, corneal kindling resulted in hippocampal neurodegeneration that could contribute to hyperexcitability.

E485

KAINATE IS BOTH TROPHIC AND PROLIFERATIVE FOR HIPPOCAMPAL PRECURSORS VIA AMPA RECEPTORS IN VITRO AND HAS DIFFERENTIAL EFFECTS ON PROLIFERATION KINETICS IN THE SUBGRANULAR ZONE AND GRANULE CELL LAYER AFTER SEIZURE INDUCTION IN VIVO

A. Shtaya, A. Pringle, and W. Gray
University of Southampton, UK

Kainate-induced seizures and status epilepticus transiently enhances hippocampal neurogenesis but the mechanisms are unclear. To determine the underlying mechanisms, we examined the effects of Kainate on hippocampal precursor's in vitro and on prelabelled and unlabelled clones of proliferating hippocampal precursor's in vivo. Cultured hippocampal cells were prepared from rats P7-10 and exposed to 5μM Kainate. BrdU and Ki-67 were used to measure cell proliferation while, caspase-3 and Time-lapse microscopy were used to study cell survival. Nestin and TuJ1 were used to label precursor cells and neuroblasts, respectively. To examine Kainate effects in vivo, a clone of proliferating cells in the dentate gyrus was prelabelled with BrdU 24 hours before Kainate-induced status epilepticus and examined 6–72 h later. In vitro, we found that kainate increased the symmetric and asymmetric proliferation rate of nestin-positive precursors, via AMPA receptors. It also enhanced the survival of nestin and TuJ1 cells with a proportional increase in neurogenesis. Consistently, kainate/seizures in vivo increased cell proliferation of both prelabelled and unlabelled clones of precursors in the subgranular zone (SGZ) with increased cell cycle reentry of the prelabelled clone. In the granule cell layer (GCL) there was increased preferential proliferation of the prelabelled clone in addition to increased cell cycle exit, without enhancing cell death. Kainate/seizures increased doublecortin positive cells in the GCL by 72 h. We conclude that Kainate/seizure enhances hippocampal precursor proliferation via AMPA receptors without increasing cell death, and that it has a differential effect on the proliferation kinetics and fate choice of precursors in the SGZ and GCL.

E486

GLIA-DERIVED STEROIDS MODULATE EPILEPTOGENESIS IN A MODEL OF TEMPORAL LOBE EPILEPSY

D. Longo, E. Baldelli*, G. Bertazzoni†, M. Avoli†,‡, and G. Biagini**
**University of Modena E Reggio Emilia, Italy; †University of Rome ''La Sapienza'', Italy; and ‡Montreal Neurological Institute, McGill University, Montreal, Canada*

Purpose: The conversion of cholesterol into pregnenolone by cytochrome P450 cholesterol side-chain cleavage enzyme (P450 scc) is the rate-limiting step in the steroid synthesis. Glial cells and neurons both express P450 scc and synthesize neurosteroids, which are positive modulators of GABAergic transmission. Astrocytes become activated following status epilepticus (SE), but it is presently unclear whether this activation leads to enhanced neurosteroidogenesis.

Method: We studied the time course of P450 scc immunoreactivity changes after pilocarpine-induced SE in adult (8 week-old) and young (3 weeks-old) rats. To evaluate the role of P450 scc upregulation, we used the 5a-reductase inhibitor finasteride (100/kg s.c. for 3 weeks) to suppress the synthesis of neurosteroids.

Results: We demonstrated that P450 scc is upregulated in the CA3 hippocampal region. Moreover the extent of P450 scc induction was directly related to the onset of spontaneous recurrent seizures in adult (8-week-old) rats. In 3-week-old rats compared with adults, higher P450 scc levels and a longer latent period were found. Interestingly, adult epileptic rats, treated with finasteride, compared with a group of vehicle-treated rats, presented anticipated generalized seizures ($p<0.01$). In young rats, finasteride anticipates seizures in approximately 50% of the animals.

Conclusion: These findings suggest that neurosteroids can modulate epileptogenesis in the pilocarpine model of temporal lobe epilepsy.

E487

BLOOD–BRAIN BARRIER DISTURBANCES FOLLOWING HYPERTHERMIA IN RATS WITH CORTICAL DYSPLASIA

C. Gurses, M. Kaya, R. Kalayci, N. Arican, B. Ahishali, O. Ekizoglu, I. Elmas, N. Orhan, M. Kucuk, D. Ustek, B. Bilgic, and G. Kemikler
Istanbul University, Turkey

Purpose: To investigate the influence of hyperthermia on the integrity of blood–brain barrier (BBB) in rats with cortical dysplasia.

Method: In this study, 32 one-month-old baby Sprague-Dawley rats were used for sodium fluorescein (NaFlu) staining.

Method: The pregnant rats were administered gamma irradiation of 145 cGy from the uterus on day E 17. To induce hyperthermia (39.5°C), rats were exposed to an elevated ambient temperature (55–60°C) for 30

minutes. Immunohistochemistry and Western blot methods were used, and electron microscopy was performed to evaluate structural properties of BBB in this experiment.

Results: Blood pressure levels of rats with hyperthermia and rats with hyperthermia as well as cortical dysplasia increased significantly when compared to control values. Seizures the rats had were observed clinically; the longer the duration of hyperthermia was, the more seizures were seen. Both hyperthermia and cortical dysplasia did not change BBB permeability to NaFlu. Hyperthermia induced a generalized increase in BBB permeability to NaFlu in rats with cortical dysplasia and the highest increases (*f*® 130% over control values) were recorded in diencephalon and cerebellum regions. Western blot analysis of brain capillaries showed that the expression of the transmembrane tight junction protein occludin was not changed in response to dysplasia and hyperthermia.

Conclusion: These results indicate that immature rats are resistant to hypertermic BBB disruption. However, hyperthermia may induce significant BBB permeability increase under cortical dysplastic conditions. We conclude that cortical dysplasia as an underlying pathology could increase the disruption of BBB integrity during hyperthermia.

E488
INTRA-AMYGDALOID KAINIC ACID INJECTION IN RATS WITH ABSENCE EPILEPSY

K. Tezcan, A. Gurbonova, R. Aker, and F. Yýlmaz Onat
Marmara University, Turkey

Previous studies of kindling in models of genetic absence epilepsy have shown a resistance to secondary generalization of focal limbic seizures. In order to determine the effect of kainic acid injection on the induction of temporal lobe epilepsy in GAERS, we examined convulsive seizures in Wistar control rats and GAERS during acute and chronic periods after kainic acid-induced status epilepticus. Adult male nonepileptic Wistar rats and GAERS were used in the experiments. A guide cannula was stereotaxically implanted into the right basolateral amygdala. Animals were given a single intraamygdaloid injection of kainic acid (750 ng) disolved in 300 nl of arteficial cerebrospinal fluid. The behavior of rats after the kainic acid injection was evaluated on the basis of a 6-stage scale. In the acute period observations although the number and mean duration of convulsive seizures were not significantly different, the first convulsive seizures during status epilepticus were significantly delayed in GAERS (39.6 ± 10.1 min in Wistar rats and 100.4 ± 13.8 min in GAERS). In the chronic period, the first spontaneous convulsive seizure was observed on the 13.33 ± 0.7 day in the Wistar group and on the 20.14 ± 2.61 day in GAERS. There was no difference between the Wistar and the GAERS groups in the number of convulsive seizures per hour. Thus, the animals in both groups became epileptic although this was delayed for the GAERS relative to the Wistar group. Our findings demonstrate a mutual cross inhibition of circuits underlying absence epilepsy and temporal lobe epilepsy.

E489
ALTERATION IN THE EXPRESSION OF GLIAL FIBRILARY ACIDIC PROTEIN IN KAINIC ACID INJECTED GENETIC ABSENCE EPILEPSY RATS FROM STRASBOURG

D. Akin, S. Ketenci, R. Aker, and F. Yilmaz Onat
Marmara University, Turkey

Genetic absence epilepsy rats from Strasbourg (GAERS) display a resistance to secondary generalization of limbic seizures by kindling electrical stimulations. In order to investigate the underlying mechanisms of this resistance kainic acid injections, another model for limbic epilepsy, were performed in GAERS. The glial fibrillary acidic protein (GFAP) immunostaining was carried out in kainic acid-injected GAERS to study astrocytic modifications in absence epilepsy.

Method: Naïve, sham-operated and kainic acid-injected male Wistar rats and GAERS were used in the experiments for GFAP immunostaining. The brains were removed 7 days after intraamygdaloid kainic acid injection (750 ng) and brain slices (20;m) were prepared. The sections were immunostained using the anti-GFAP and peroxidase activity was visualized by incubation with 0.03% 3–3-diaminobenzidine and 0.003% hydrogen peroxide in 50 mM Tris-HCl.

Results: There was an increase in GFAP staining of cortex in naïve and sham-operated GAERS compared to naïve and sham-operated Wistar animals. Further the increased GFAP staining in GAERS after kainic acid injection was significantly higher than that observed in naïve GAERS. We found no clear differences between kainic acid-injected Wistar rats and GAERS.

Conclusion: The increased GFAP staining in naïve GAERS suggests that astrocytic reactivity plays a role in absence epilepsy. No differences after kainic acid injection show that this modification is not the underlying mechanism of resistance of limbic seizure in GAERS. It can be concluded that reactive astrocytes are involved in some adaptive responses to kainic acid injections in both GAERS and Wistars.

E490
REGIONAL PERFUSION CHANGES DURING PILOCARPINE-INDUCED STATUS EPILEPTICUS IN THE RAT UNDER FENTANYL/MEDETOMIDINE ANAESTHESIA

R. Scott, M. Lythgoe, D. Thomas, J. Wells, D. Gadian, and M. Choy
UCL-Institute of Child Health, London, UK

Purpose: Convulsive status epilepticus (CSE) can cause brain injury, particularly to the hippocampus. Mechanisms include excitotoxicity, although ischaemia, as a result of failure of cerebral autoregulation, may also contribute to injury1. Therefore we investigated whether cerebral blood flow (CBF) changes during CSE differ in the parietal cortex and the hippocampus.

Method: Pilocarpine (n=7) or saline (n=6) was administered to fentanyl/medetomidine anesthetized adult Sprague-Dawley rats. Noninvasive MRI measurements of CBF were performed continuously using arterial spin labelling and grouped into 5 periods: baseline, pre-CSE, early CSE (first 30 mins), late CSE (30–90 mins) and following diazepam. Statistical analyses were performed using 3-way repeated measures ANOVA with contrasts to baseline.

Results: Comparisons between the magnitude of CBF change from baseline of the pilocarpine-injected animals and the saline-injected controls indicated that there were significant differences between the hippocampus and the parietal cortex following pilocarpine injection ($F = 9.45$, $p = 0.014$) and during early CSE ($F = 6.87$, $p = 0.031$), but no significant differences were observed for the late CSE period ($F = 1.76$, $p = 0.221$) or following diazepam injection ($F = 0.162$, $p = 0.698$).

Conclusion: Regional CBF differences occur in vivo during pilocarpine-induced CSE under fentanyl/medetomidine anaesthesia. Cortical perfusion increased significantly more than hippocampal perfusion, supporting the hypothesis that a relative ischaemia may play a role in the selective vulnerability of the hippocampus to CSE.

1. Lothman 1990 Neurology 40:13–23.

E491
CHOLINERGIC STIMULATION OF NUCLEUS BASALIS OF MEYNERT AFFECTS SPONTANEOUS SPIKE-AND-WAVE DISCHARGES IN WAG/RIJ RATS WITH GENETICALLY DETERMINED ABSENCE EPILEPSY

R. Berdiev, G. van Luijtelaar†, and N. Chepurnova**
**Lomonosov Moscow State University, Moscow, Russia; and*
†Nijmegen Institute for Cognition and Information, Radboud University Nijmegen, Nijmegen, The Netherlands

Purpose: A contemporary view on spike-and-wave discharges (SWD) generation in rat models implies a crucial role of somatosensory cortex and thalamus. Nucleus basalis of Meynert (NBM) is an important source of both cortical and thalamic cholinergic afferentation. The aim of this study is to evaluate consequences of NBM stimulation and try to find the main targets of this action.

Method: WAG/Rij rats with genetically determined absence epilepsy were implanted with EEG electrodes in reticular thalamic nucleus, frontal and somatosensory cortex, and guide cannulas above NBM. Carbachol (0.55 and 5.5 nmol), scopolamine (0.55 and 5.5 nmol) and saline (as a control) were injected into NBM in different combinations. Number, mean duration and spectral power of SWD were analyzed.

Results: Cholinergic stimulation of NBM with carbachol dose-dependently decreased number and mean duration of SWD. Unilateral injections of 5.5 nmol of carbachol affected SWD only during 1st postinjection hour while bilateral injections had prolonged (several hours) effect. Fast Fourier Transformation analysis of SWD after carbachol injections revealed a decrease of power spectra amplitude in 8–12 Hz and 12–30 Hz, more pronounced in somatosensory than in frontal cortex. Scopolamine alone had no influence on SWD, but preliminary injection of scopolamine counteracted the effects of carbachol.

Conclusion: Thus, cholinergic activation of NBM inhibits SWD manifestation due to increased excitatory input to the cortex and thalamus where pacemaker cells are located. We can make a prior conclusion that NBM-mediated excitation of cortex has more influence on SWD generation than the same of thalamus.

E492
THE POLARITY OF AQUAPORIN-4 IN ASTROCYTIC ENDFEET IS ALTERED IN THE KAINATE MODEL OF TEMPORAL LOBE EPILEPSY

J. Hammer, S. Alvestad†, U. Sonnewald†, and O. Ottersen**
**University of Oslo, Norway; and †Norwegian University of Science and Technology, Trondheim, Norway*

Hyperexcitability in neuronal networks is a key feature of mesial temporal lobe epilepsy (MTLE). Flux of water through the water channel aquaporin-4 (AQP4) may affect neuronal excitability via perturbation of K+ clearance and changes in the extracellular space volume. A previous study of surgical specimens from patients showed a loss of AQP4 from the perivascular endfoot membrane in MTLE hippocampi compared with non-MTLE hippocampi and no change was found in the astrocytic membrane facing the neuropil. Loss of AQP4 could contribute to increased seizure propensity via impaired clearance of extracellular K+. We investigated AQP4 expression in hippocampus prior to and after development of epilepsy following kainate injection. Western blotting of hippocampus revealed an increased expression of the AQP4 isoform M1 in the latent phase compared with controls, whereas the M23 isoform was unchanged. In the chronic phase, there was no change in the AQP4 isoforms. Immunogold analysis of the CA3 region revealed a 40% reduction ($p = 0.04$) of AQP4 along the perivascular endfoot membrane in animals in the chronic phase as compared with controls. In the astrocytic membrane facing the neuropil there was a 211% increase ($p=0.01$) in AQP4. The altered AQP4 polarity could be due to defects in the anchoring complex or impaired endothelial-glial interaction.

E493
NEUROPEPTIDE Y INCREASES EXTRACELLULAR GLUTAMATE CONCENTRATION IN THE HIPPOCAMPUS

A. Meurs,†, J. Portelli†, A. Balasubramaniam‡, R. Clinckers†, G. Ebinger*, Y. Michotte†, and I. Smolders†*
**UZ Gent, De Pintelaan, Ghent, Belgium; †Research Group Experimental Pharmacology, Vrije Universiteit Brussel, Laarbeeklaan, Brussels, Belgium; and ‡University of Cincinnati Medical Center, Cincinnati, OH, USA*

Purpose: The anticonvulsant activity of neuropeptide Y (NPY) in the hippocampus is generally attributed to an inhibition of glutamate release from presynaptic terminals. This hypothesis, which was advanced on the basis of in vitro observations, has not been verified in vivo. In the present study, we used intracerebral microdialysis to determine the effect of NPY on hippocampal extracellular glutamate concentration in vivo, and to identify the NPY receptor subtype that mediates this effect.

Method: Freely moving male Wistar rats underwent a 2 hour intrahippocampal administration of a known anticonvulsant concentration of NPY (20μM), an equivalent concentration of the selective Y1 receptor agonist D-His26-NPY (20μM) or coadministration of NPY (20μM) and the Y1 receptor antagonist BVD10 (2μM) via a stereotactically implanted microdialysis probe. Changes in glutamate dialysate concentration were monitored.

Results: Intrahippocampal microperfusion of NPY or D-His26-NPY increased glutamate dialysate concentration. Hippocampal Y1 receptor blockade (BVD10) reversed the NPY-induced increase in glutamate dialysate concentration.

Conclusion: Local administration of an anticonvulsant concentration of NPY increases hippocampal glutamate overflow in vivo, through activation of hippocampal Y1 receptors. These findings are at odds with the current hypothesis regarding NPY's mechanism of action in epilepsy. Further experiments are needed to determine the origin and functional relevance of NPY-induced increases in hippocampal extracellular glutamate.

E494
EXPERIMENTALLY INDUCED VARIOUS INFLAMMATORY MODELS AND SEIZURE: UNDERSTANDING THE ROLE OF CYTOKINE IN RAT

B. Medhi, R. Rao, U. Saikia, S. Arora, J. Toor, K. Khanduja, and P. Pandhi
PGIMER, India

Purpose: Aim of study was to produce various inflammatory models and seizure to understand the role of TNF-α in above mentioned models.

Method: Total of 54 male rats were included in the study. Animals were divided into 3 groups of colitis, arthritis, and cotton wool granuloma. Each group had 3 subgroups of control, model and treatment. At the end of three days in colitis, seventeen days in arthritis and seven days in cotton wool granuloma group a subconvulsive dose of PTZ (40mg/kg i.p) was injected to note seizure onset and seizure score. Brain samples were subjected to DNA fragmentation testing. Presence of inflammation was confirmed by morphology and histology. Plasma and brain TNF-α levels were measured.

Results: The models of colitis, arthritis and CWG were effectively produced as evidenced by morphology and histology scores ($p<0.001$). Seizure onset was reduced and grade was increased ($p<0.001$). Thalidomide reduced the morphological, histological ($p<0.002$), DNA fragmentation and seizure grade ($p<0.001$) while increased seizure onset ($p<0.001$) in the arthritis group. TNF-α levels in both plasma and brain were reduced following thalidomide treatment ($p<0.002$) in arthritis group. There were no significant findings in colitis or cotton wool granuloma group.

Conclusion: Inflammation was associated with decreased threshold to PTZ induced seizure. Thalidomide is effective in reducing the extent of arthritis as well as reducing the seizure scoring and increasing seizure onset in the adjuvant arthritis group. Thalidomide was also effective in reducing TNF-α levels thus contributing to its antiepileptic activity.

E495
GENERAL ANESTHESIA FOR REFRACTORY NON-CONVULSIVE STATUS EPILEPTICUS OF COMPLEX PARTIAL TYPE: A CASE REPORT

P. Polychronopoulos
Medical School of Patras University, Greece

Purpose: Nonconvulsive status epilepticus of complex partial type (NCSE-CP) is a relatively common and often underrecognized entity, with hugely variable clinical and electrographic manifestations. Although the response to the treatment is usually good, there is little consensus on how aggressively should be managed. We report a case of a 45 year-old man who, after having an operation for a benign tumor in the left temporoparietal lobe, developed prolonged (25 days) NCSE-CP with predominantly cognitive features, refractory to intravenous treatment with AEDs.

Method: The patient exhibited prolonged episodes of ictal cognitive impairment with selective rather than global neuropsychological deficits. Consciousness was slightly impaired with mild mental slowing, nonfluent speech, perseveration, acalculia, alexia and sporadic tingling sensations in the right arm. MRI showed postoperative porencephalic cavity with glial proliferation in the left temporoparietal lobe. Serial EEGs showed continuous epileptiform discharges restricted to the left temporal lobe with phase reversing at T3. Intravenous loading with various first line AEDs (BZD, PHE, PB, and VPA) was ineffective. The patient admitted to the ITU and general anesthesia was induced with propofol and pentobarbital.

Results: Following general anesthesia seizures were remitted. Cognitive deficits were fully reserved in association with the normalization of EEG, 25 days from the beginning of status.

Conclusion: Little has been reported about refractory NCSE-CP. Although the most documented reports reveal favorable outcome without prompt medical treatment there is still a strong debate regarding the morbidity of NCSE and general anaesthesia is justified for some cases.

E496
EPILEPTOGENESIS IN RABBITS TREATED WITH GINKGO BILOBA

V. Ivetic, M. Popovic†, and V. Vasic**
**Medical Faculty, Novi Sad, Serbia; and †Faculty of Sciences, Novi Sad, Serbia*

Purpose: Epilepsy is the significant health problem worldwide. In order to understand neurophysiological mechanisms of epileptogenesis, methodological approach of animal models is frequently used. The aim of this investigation was analyzing possibly affect of Ginkgo biloba extract (EGb 761) on bioelectric activity and epilepsy in rabbits.

Method: In this research epileptogenic focus was formed in hippocampus by applying repeating electrostimulations on the region. The level of epileptically discharges was determined, as the lowest number of electro stimulations that was indispensable for induction of epilepsy. Graphic elements of EEGs were used in analisis of epilepsy. Three groups of animals were used. In the first group (control) kindling focus was formed. In the second group kindling focus was formed after aplication of EGb 761. In third group epilepsy extract was administrated in rabbits with previously formed kindling epilepsy. In first and second group how many electro stimulation were necessary in order to induct epilepsy was measured.

Results: Obtained results show that the summary bioelectrical activity of brain structures changes during the process of adaptation of animals on experimental conditions. Application of extract of EGb 761 affect on this activity by making it faster. It was noticed that application of extract had proconvulsive effect, which was manifested through the occurrence of spikes in EEGs. Application of extract significantly decreased the number of electro stimulation that was indispensable for induction of epilepsy and increased the level of epileptically discharges. Application of EGb761 in rabbits, in which experimental epilepsy was previously induced, did not change number of epileptic discharges on statistically significicant level.

Conclusion: EGb 761 had proconvulsive effect.

E497
LEUKOCYTE RECRUITMENT IN EXPERIMENTAL EPILEPSY

P. Fabene, G. Navarro Mora*, M. Martinello*, B. Rossi*, F. Merigo*, L. Ottoboni*, S. Bach*, S. Angiari*, D. Benati*, A. Chakir*, L. Zanetti*, F. Schio*, A. Sbarbati*, E. Butcher†, and G. Constantin**
**University of Verona, Verona, Italy; †Stanford University School of Medicine, Stanford, CA, USA; and Palo Alto VA Health Care System, Palo Alto, CA, USA*

Purpose: Epilepsy (E) is a neurological disorder affecting 0.5–1% of the general world population. Experimental and clinical data indicate that inflammatory condition can mediate neurodegenerative mechanisms. It becomes thus imperative to investigate such mechanisms in order to identify any possible pharmacological treatment to prevent that single episode of brain insult can lead to a condition of epilepsy.

Method: Intravital microscopy, as well as telemetry EEG and behavioral observations have been used to validate the hypothesis that leukocyte recruitment is required in pilocarpine-induced epileptogenesis.

Results: We show that in a mouse model of pilocarpine-induced epilepsy, seizures induce elevated expression of vascular cell adhesion molecule-1 (VCAM-1) and selectins on brain vessels. Intravital microscopy revealed enhanced granulocyte and Th1 lymphocyte rolling and arrest in brain vessels after seizures and these leukocyte-vascular interactions were inhibited by blockade of integrin 41or of the leukocyte mucin P-selectin glycoprotein ligand-1 (PSGL-1). Mice treated with anti – 4-integrin mAb reduced acute and chronic seizure events. Genetic deficiency of PSGL-1 or of the 1–3-fucosyltransferases, enzymes involved in the glycosylation of PSGL-1, as well as neutrophil depletion, also inhibited seizure activity. Seizure-induced blood–brain barrier leakage was drastically reduced in anti-4 treated or PSGL-1 or FucT deficient animals, establishing a pathogenetic link between leukocyte adhesion to vascular endothelium, BBB damage and seizure generation.

Conclusion: Our results suggest leukocyte-endothelial interactions as potential targets for the prevention and treatment of epilepsy.

E498
CHRONIC EXPOSURE TO THE POTASSIUM CHANNEL OPENER RETIGABINE (RGB), BLOCKS KINDLING ACQUISITION AND PREVENTS THE DEVELOPMENT OF PHARMACORESISTANCE

A. Srivastava, and H. White
Antiepileptic Drug Development Program, University of Utah, Salt Lake City, UT, USA

Purpose: Voltage gated sodium channels (VGSC) are the primary target for many antiepileptic drugs. Exposure to the VGSC blocker lamotrigine (LTG) during kindling acquisition results in the subsequent development of LTG- (Postma et al., Epilepsia 200041 (12):1514–21), phenytoin-, and carbamazepine-resistance (Srivastava et al., Epilepsia 2003;44:42) but fails to cause resistance to the potassium channel opener retigabine (RGB). In the present investigation, the ability of a minimally effective dose of RGB to produce the development of pharmacoresistant state during kindling acquisition was evaluated.

Method: Adult male Sprague-Dawley rats were kindled via basolateral amygdala stimulation either in the presence of 0.5% methylcellulose or RGB (5 mg/kg, i.p.). Seizure severity and after-discharge duration were recorded after each kindling stimulation. Treatment was continued until all rats displayed four consecutive Stage 5 seizures (Racine RJ, Clin. Neurophysiol 1972; 32:281–294). On the day after the last kindling session, a higher dose of RGB (20 mg/kg i.p) was administered 10 min prior to amygdala stimulation to both groups (vehicle and RGB-treated) .

Results: RGB-treated rats displayed a slower kindling acquisition as compared to vehicle-kindled rats. Furthermore, RGB (20 mg/kg) blocked the expression of fully kindled behavioral seizures in both vehicle- and RGB- (5 mg/kg) treated rats. This dose of RGB also reduced the duration of electrographic after-discharge in both treatment groups. At the doses tested, RGB did not display any significant motor impairment in open field test.

Conclusion: The present findings suggest that unlike Na+ channel blocker LTG the presence of potassium channel opener RGB during kindling acquisition does not carry the risk of developing subsequent pharmacoresistance to RGB. The results from this study also suggest that RGB possesses an antiepileptogenic and anticonvulsant activity which might be helpful in preventing or slowing the progress of pharmacoresistant epilepsy.

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E499
ANALYSIS OF THE DYNAMICS OF HUMAN EPILEPTIC SEIZURES FROM SCALP EEG

N. Mammone, U. Aguglia†, F. La Foresta*, A. Latella†, E. Le Piane†, and F. Morabito**
**DIMET – University of Reggio Calabria, Italy; and †Centro Regionale Epilessie, Università Magna Graecia Di Catanzaro, Presidio Riuniti, Reggio Calabria, Italy*

Purpose: Results in literature show that the convergence of the STLmax (Short Term Maximum Lyapunov Exponent) time series, extracted from intracranial EEG of patients affected by intractable temporal lobe epilepsy, is linked to the seizure onset. Moreover, the trend of the convergence allows for the automatic detection of the electrodes involved in the process leading to the seizure. ATSWA (Adaptive Threshold Seizure Warning Algorithm) is an advance seizure warning algorithm based on STLmax convergence.

Method: In order to test ATSWA over scalp EEG, the technique was implemented and tested over four scalp EEG recordings: three from three patients (A1, A2 and A3) affected by partial frontal lobe epilepsy and two from a patient affected by absence seizures (patient B), the average duration was 37min for patients A1, A2 and B, whereas the duration for patient A3 was 5hours.

Results: The technique succeeded in issuing a warning before every seizure, with a warning horizon of 5min for patient A1, 12 for A2, 4.3min and 7min for the two seizures of patient B, and of 21.8min and 101.8min, for the two seizures of patient A3. The technique automatically selected as critical the electrodes in the focal area, for patient A1, A2 and A3 and in the frontal area, for patient B.

Conclusion: ATSWA seems to be able to detect changes in the dynamics of scalp EEG as well as to infer information about the critical area, however, further work is required in order to test the technique over recordings including many seizures.

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E500
EEG FEATURES IN PATIENTS WITH JUVENILE MYOCLONIC AND JUVENILE ABSENCE EPILEPSIES WITH RESPECT TO ANTICONVULSANT TREATMENT

G. Japaridze, S. Kasradze, G. Lomidze, D. Kvernadze, L. Zhizhiashvili, and O. Toidze
Epilepsy Prevention and Control Centre, Tbilisi, Georgia

Purpose: To analyze EEG features in untreated and treated patients with juvenile myoclonic epilepsy (JME) and juvenile absence epilepsy (JAE).

Method: Out of 1706 subjects diagnosed in the Epilepsy Centre (August 2005 – December 2007) as having epilepsy, EEGs of 103 patients with generalized epilepsy (JME 69, JAE 34), 77 females and 26 males aged 11–56 years have been analyzed. 63 patients were treated (50 adequately, usually by valproate; 13 inadequately, mostly with carbamazepine), and 40 were drug-free.

Results: Generalized discharges were found in 54.4% of all patients (JME – 50.0%; JAE – 61.8%). They occurred in 80.0% of drug-naive and in 38.1% of treated patients ($p < 0.001$). In inadequately treated patients the occurrence of generalized discharges, 69.2%, was almost as high as in untreated patients, essentially higher than in adequately treated patients, 32.0% ($p < 0.001$). Focal epileptiform EEG abnormalities, mostly frontal or frontotemporal, were noted in 45.6% (JME – 42.0%; JAE – 52.9%). In JME certain tendency of higher occurrence of focal changes were seen in treated (48.8%) vs untreated (30.8%) subjects. Besides, focal discharges occurred somewhat more often in inadequately (61.5%) than in adequately (46.0%) treated patients, this trend being noticeable in both JME and JAE patients.

Conclusion: Occurrence of generalized EEG abnormalities in patients with JME and JAE decreases regularly under adequate treatment, whereas inadequate therapy has slight if any influence on generalized discharges and may exacerbate focal abnormalities. Focal EEG abnormalities in JME and JAE are common that may complicate syndromological diagnosis, especially in treated patients.

E501
SURFACE EMG RECORDED DURING GENERALIZED EPILEPTIC SEIZURES

S. Beniczky, C. Hansen, J. Alving, and P. Wolf
Danish Epilepsy Centre, Denmark

Purpose: Recording surface EMG signals during epileptic seizures is a useful method providing a more detailed description of the motor activity than the visual analysis of the video recordings. We attempted to elucidate several aspects previously not specifically addressed in surface-EMG investigations of epileptic seizures: the coactivation of the antagonistic muscles, the latency between the activation of the muscles on the left and the right side of the body, and the within-patient consistency of these findings.

Method: We analyzed surface EMG signals, recorded from 12 muscles, during 23 generalized epileptic seizures in three patients (7 epileptic spasms and 16 generalized seizures with focal start).

Results: In the epileptic spasms EMG signals started almost simultaneously (within 40 ms) in all the muscles (bilaterally, both upper and lower limbs). In the generalized seizures with focal start, the onset of the EMG-activity was markedly asymmetrical and the site of the seizure-start showed a significant within-subject consistency. The EMG signals enabled us to describe in detail the propagation of the motor activity during the seizure. However this was variable from seizure to seizure, even within the same patient. During the epileptic seizures there was a strong coactivation of the antagonistic muscles. However, this was not specific to the seizure activity, as it could be observed also during nonepileptic movements.

Conclusion: Recording surface EMG signals during the epileptic seizures provides additional information for seizure classification.

E502
SYMPTOMATIC GENERALIZED EPILEPSIES- CLINICAL SIGNIFICANCE AND PROBLEMS

Y. Ohtsuka
Okayama University, Japan

According to the 1989 ILAE classification, generalized epilepsies and syndromes are divided into three types: idiopathic, cryptogenic or symptomatic, and symptomatic. The latter two consist of mainly symptomatic cases. Symptomatic generalized epilepsies include epilepsy syndromes such as Ohtahara syndrome, early myoclonic encephalopathy, West syndrome, Lennox-Gastaut syndrome, epilepsy with myoclonic-astatic seizures and epilepsy with myoclonic absences. However, some cases cannot be classified as definite epilepsy syndromes, and thus are categorized as other symptomatic generalized epilepsies. In order to further elucidate these unclassified cases, we proposed a new epilepsy syndrome called severe epilepsy with multiple independent spike foci characterized by generalized seizures such as tonic spasms, although multifocal spike-waves are the main EEG feature. A new proposal by the ILAE Task Force (2001) does not adopt the dichotomies of idiopathic vs. symptomatic, and localization-related vs. generalized, and most epilepsy syndromes previously classified as symptomatic generalized epilepsies are listed as epileptic encephalopathies. Conventionally generalized epilepsies are characterized by generalized seizures with generalized-onset ictal EEGs and diffuse epileptic discharges on interictal EEGs. However, due to various types of brain damage partial seizures are observed in addition to generalized seizures in some cases of generalized symptomatic epilepsies. Thus, the boundary between symptomatic generalized epilepsies and symptomatic localization-related (focal) epilepsies is sometimes blurred. Clinical seizure manifestations and EEG features of symptomatic generalized epilepsies may vary according to age or some other factors. The role of both focal cortical and subcortical mechanisms in the occurrence of symptomatic generalized epilepsies should be further clarified.

E503
MULTIPLE SCLEROSIS AND EPILEPSY: EVIDENCE OF PREFERENTIAL INVOLVEMENT OF UPPER LIMB SOMATOSENSORY EVOKED POTENTIALS

E. Papathanasiou, S. Papacostas, P. Myrianthopoulou, E. Kkolou, and M. Pantzaris
The Cyprus Institute of Neurology & Genetics, Cyprus

Purpose: The prevalence of epilepsy in patients with multiple sclerosis (MS) has been of interest for many years. Electroencephalography has been of limited value in determining the relationship between the two. This analysis focuses on the relationship of evoked potential abnormalities and epilepsy in MS patients.

Method: Patients with MS who have had evoked potentials (EPs) performed (visual, brainstem and upper and lower limb somatosensory) were retrospectively included.

Results: Seventy-four MS patients were divided into three groups. I: Patients (n=34) with no epilepsy and not taking antiepileptic drugs (AED); II: Patients (n=16) with epilepsy and taking AEDs; and III: Patients (n=24) with no epilepsy but taking AEDs for neuropathic pain. No statistically significant difference was found between the groups with regards to symptom severity, age at last follow-up and time since symptom onset and diagnosis. A significant difference in the percentage of patients with upper limb somatosensory EP abnormalities, involving increases in interpeak latencies, was found between Groups I (35.5%) and II (63.6%). No difference between Groups I and III and between II and III was found. The other EPs showed no difference between the groups.

Conclusion: Demyelinating lesions involving the upper limb somatosensory pathway may be triggering the onset of epilepsy in MS patients. Possible confounding factors of AED use were ruled out by the comparison between Groups I and III. However, the similarity between Groups II and III suggests that the latter patients may potentially have seizures, but are protected as they are taking AEDs for neuropathic pain.

E504
3D SOURCE LOCALIZATION APPLIED TO ECOG RECORDINGS: A SIMULATION STUDY

M. Dümpelmann, and C. Elger
University of Bonn, Bonn, Germany

Purpose: Source localization is an established approach in the analysis of EEG and MEG recordings. However little experience exists in the application of source localization methods applied to ECoG (electrocorticogram) recordings. This simulation study addresses the question, whether 3D source localization yields reliable results for recordings obtained by ECoG.

Method: Simulations were based on a boundary element model and electrode positions derived from the MRI of a patient with a subdural grid and strip electrodes covering both hemispheres. For regular distributed source positions potential distributions at the electrodes were computed. These potential distributions, respective a second data set with added noise, were applied to two source reconstruction.

Method: MUSIC (MUltiple SIgnal Classification) using positions covering the 3D brain volume and the linear estimation (minimum norm) approach. A second run was performed using only the electrodes of one hemisphere.

Results: Without noise the maxima of the MUSIC scans were identical to the original source positions. Noise gave small reconstruction errors (error < 15 mm for 98% of the source positions). Linear estimation maxima were attracted to the electrodes. Only source positions close to electrode contacts were accurately reconstructed (error < 15 mm for 31% of the source positions). Electrodes in the hemisphere opposite to the source did not provide a relevant improvement in accuracy for both approaches.

Conclusion: MUSIC analysis derived from ECoG gives accurate source localizations results and can improve source localization in epilepsy diagnosis and cognitive research. Linear estimation needs additional strategies to avoid the attraction of maxima toward the electrodes.

E505
THE BENEFIT OF SUBDURAL ELECTRODES IN THE PRESURGICAL LOCALIZATION OF EPILEPTIC FOCI IN PATIENTS WITH PARTIAL EPILEPSY

F. Chowdhury, N. Mullati, R. Elwes, R. Selway, and C. Polkey
Centre for Epilepsy, King's College Hospital, UK

Purpose: To evaluate the efficacy of subdural electrodes in mapping epileptogenic zone and surgical outcome in patients with refractory partial epilepsy undergoing presurgical evaluation. Definitive localization of epileptic focus correlates with favorable outcome following epilepsy surgery. In approximately 30% of patients noninvasive studies fail to localize the epileptogenic zone and investigation using intracranial electrodes is indicated. There is debate over the relative efficacy and safety of subdural versus depth electrodes. In our unit subdural strip evaluation is used as preliminary less invasive intracranial evaluation.

Method: We retrospectively reviewed patients who underwent subdural electrode recording during presurgical assessment between 1997 and 2005. Data collected (seizure semiology, scalp EEG/ telemetry, MRI, neuropsychometry, intracranial electrode recording, surgical outcome and pathology) were analyzed for indication of intracranial electrodes, efficacy in seizure localization and overall outcome (Engel scale).

Results: Of the 55 cases reviewed, 28 patients had bitemporal strips, 22 had strips and grids and 5 had grids alone. The main indications for subdural electrode evaluation were lateralization of temporal onset (n=18), mapping of epileptogenic zone (n=16), electroclinical discordance (n=13), possible dual pathology (n=11), negative MRI (n=10) and functional mapping of eloquent cortex (n=7). The epileptogenic zone was localized in 43 patients. 39 patients went on to have resective surgery. 33 patients had good postoperative outcome (Engel grade 1/2). There was no significant morbidity related to electrode insertion.

Conclusion: Subdural electrodes aid localization of epileptogenic zone in a significant proportion of carefully selected cases. The majority of these proceed to resective surgery and become seizure-free.

E506
CHARACTERISTICS OF THE EEG PATTERNS OF EPILEPTIC SEIZURES WITH FRONTAL OR TEMPORAL LOCALIZATION OF INTERICTAL DISCHARGES

A. Sobieszek, and B. Swiderski†*
**Medical Center for Postgraduate Education, Poland; and*
†Institute of Biocybernetics And Biomedical Engineering, PAS, Poland

Purpose: EEG patterns recorded from the scalp during epileptic seizures reflect complex signals arising in variable proportions from different interconnected brain sources. They include the pacemaker: neuronal structure responsible for seizure generation and subcortical and cortical structures activated by the primary focus. This investigation was aimed at illustrating relationships between composition of the temporal and spacial EEG patterns of ictal events encountered during different types of seizures, especially during nonconvulsive status epilepticus (SE), in relation to the patterns of interictal discharges (IID).

Method: The EEG analysis was performed on selected EEG records in a group of ten patients with epileptic seizures. The EEG was recorded in 10–20 system of electrode placement and sampling frequency 250 Hz. Distributions of brain potentials and results of current source analysis were obtained using ELMIKO recording system and MATLAB program.

Results: Existence of unilateral IIDs localized in frontal region correlated with rapid or immediate generalization of ictal activity characterized by 2–4/s discharges of spikes and slow waves over both hemispheres with the maximum of discharge amplitude in frontal and central derivations. Localized unilateral temporal IIDs correlated with the appearance of paroxysmal lateralized epileptic discharges. Seizures were expressed as rhythmic spikes or sharp waves within beta, alfa and theta frequency limits, predominantly in temporal and occipital derivations. During nonconvulsive SE they occurred independently over right or left hemisphere.

Conclusion: The results illustrate ictal and interictal EEG patterns reflecting engagement of the different cortical and subcortical generators in different functional configurations.

E507
MOVIE OF ICTAL HIGH-FREQUENCY OSCILLATIONS ON INTRACRANIAL VIDEO EEG IN PATIENTS WITH JACKSONIAN SEIZURES

H. Otsubo, T. Akiyama, A. Ochi, S. Weiss, D. Chan, C. Snead, and J. Rutka
The Hospital For Sick Children, Toronto, Canada

Purpose: High-frequency oscillations (HFOs, gamma frequency) occur at the epileptogenic zone during focal onset seizures. Spatial propagation of HFOs is observed on intracranial video EEGs (IVEEGs) during ictal evolution. We evaluated dynamic changes of ictal HFO powers correlating with EEG and ictal semiology in Jacksonian seizures.

Method: We recorded IVEEGs in two patients with focal sensory-motor seizures with secondary generalization (sampling rate, 1 kHz). We used Multiple Band Frequency Analysis to calculate power spectra of ictal IVEEGs with windows of 50 ms and 2 Hz, and averaged power within the predominant frequency range of ictal HFOs. We pioneered time-locked movie with topographic HFO power, EEGs and digital videos.

Results: Ictal HFOs were observed from the postcentral gyrus to precentral gyrus corresponding to initial focal sensory symptom and consecutive tonic motor symptom of the contralateral arm. Secondarily generalized clonic convulsions coincided with more widespread spike-and-waves on EEG and increase of the power of HFOs, yet remaining HFOs in the Rolandic region.

Conclusion: Jacksonian seizures presented ictal HFOs marching from focal sensory and motor cortices but staying in the Rolandic region while secondary generalization. Time-locked movie of HFO powers and IVEEG reveals evolution of ictal HFO powers from the ictal onset zone to the symptomatogenic zone.

E508
COLOR IN PHOTOSENSITIVE EPILEPSY

L. Cantonetti, M. Piccioli†, P. Parisi*, P. Tisei*, C. Cerminara‡, A. Luchetti*, L. Conti†, C. Buttinelli*, and D. Kasteleijn-Nolst Trenité**
**La Sapienza University, II Faculty of Medicine, Sant'Andrea Hospital, Rome, Italy; †San Filippo Neri Hospital, Rome, Italy; and ‡Tor Vergata University, Rome, Italy*

Purpose: Since we know from the Pokémon cartoon incident and related studies that flickering red light can provoke seizures easily in susceptible persons, we determined whether flickering colors with a long wavelengh (red, green) are more provocative than colors with a middle (yellow, orange) or short wavelength (blue)and whether different eye-conditions influence the effect.

Method: Ten patients (7 F, 3 M; age range 8–56) with a photoparoxysmal response (PPR) to flickering white light, were investigated with standardized colored filters (blue, green, yellow, orange and red) in front of the Grass PS33 photic stimulator at 30 cm distance. Photosensitivity ranges were determined per eye condition and per color. The effect of wearing blue Zeiss lenses was tested also. In addition 10 patients (3 F, 7 M), with a history of photosensitivity, migraine or being a first degree relative were investigated with the colors in a similar way, although they did not show a PPR to IPS with white light.

Results: The sensitivity to the different colors appeared to be remarkable variable, both in terms of PPR response and eye condition, although orange and eye closure appeared to be the most provocative. In two patients, including a daltonic boy, blue flickering light could provoke a PPR. None of the subjects without a PPR to white light showed a sensitivity to any of the colors.

Conclusion: The epileptogenic threshold for colored flickering light in the individual epileptic patient is remarkable variable. It would be best to test the blue Zeiss lenses before prescribing them.

E509
TRACING ORIGIN AND PROPAGATION AREAS OF EPILEPTIC ACTIVITY BY COMBINING TMS AND EEG SOURCE ANALYSIS IN GENERALIZED EPILEPSY

T. Fadini, M. Nitsche, and W. Paulus
University Clinic of Goettingen, Goettingen, Germany

Purpose: One of the challenges in studying the epileptic brain is to identify the source area (s) and the propagation of the epileptic activity in vivo. Purpose of our work is to outline the epileptic network upon non-invasive and painless magnetic stimulation. For this purpose we

combined transcranial magnetic stimulation and electroencephalographic recordings.

Method: Fourteen patients affected by idiopathic generalized epilepsy (IGE) were measured. Seven out of them were stimulated twice for proof of reproducibility and got also sham stimulation. Fourteen healthy volunteers were measured as control group. The recording setup consisted of 62 recording Ag/AgCl electrodes (10–10 system compliant). The signals were sampled at 5 kHz with a DC-1kHz band pass. The stimulating setup consisted of a Magstim Rapid2 stimulator, delivering a biphasic pulse, coupled with a figure-of-eight coil. Six areas over the scalp were targeted for the stimulation: F3/F4, C3/C4 and P3/P4. Thirty pulses (interstimulus interval = 5 seconds) were delivered at each target at 80% of the maximum stimulator output. The individual data acquired were averaged for identifying peaks (in form of event related potentials) and a source analysis of the activity were performed by use of BESA.

Results: The IGE group showed an abnormal long negative current peak starting at 168.57±25.04 ms after the stimulating pulse and with amplitude of 11.98±10.51 μV on the stimulated side (CP5 peak for stimulation over C3, single factor ANOVA $p = 0.02$ vs. healthy volunteers, CP6 for stimulation over C4, $p = 0.03$). The results showed to be reproducible in patients and healthy volunteers. Moreover, it was possible to back trace the different propagation of the source activity in both groups.

E510
RISK OF ADVERSE EVENTS DUE TO ANTIEPILEPTIC DRUG WITHDRAWAL AND SLEEPDEPRIVATION DURING LONG-TERM VIDEO-EEG MONITORING

J. Van Gaalen, and H. van Hemert- van der Poel
Dutch Epilepsy Clinics Foundation Zwolle, The Netherlands

Purpose: Assessment of the occurrence of adverse events during AED withdrawal and sleep deprivation for long-term video-EEG monitoring.

Method: We reviewed our database of patients undergoing long-term monitoring for the questions mentioned above. Over one hundred patients could be included. Associations with seizure frequency before admission and underlying lesion were reviewed.

Results: There was no higher risk of more severe adverse events in the group with AED withdrawal in comparison to the group with no withdrawal. The most frequent adverse event was a de novo occurrence of generalized tonic–clonic seizures in patients with complex partial seizures before admission. In the group with carbamazepine withdrawal there was a higher percentage of severe adverse events, (non-)convulsive status, than in other withdrawal groups (lamotrigine, etc). Adverse events did not occur more frequently in patients in whom two AEDs were tapered instead of one. No irreversible adverse events were reported. Daily or weekly frequency of seizures before admission increased the risk of adverse events during monitoring. The underlying lesion had no influence. Sleep deprivation did not provoke serious adverse events.

Conclusion: AED withdrawal in general did not lead to a higher risk of adverse events. Carbamazepine withdrawal gave more severe adverse events than other AEDs. Sleep deprivation had no influence on the occurrence of adverse events.

E511
COMPARISON OF SELF-SIMILAR PROPERTIES OF EPILEPTIC SEIZURES OF MESIOTEMPORAL/HIPPOCAMPAL AND NEOCORTICAL ORIGIN

B. Weiss, Z. Vágó*, R. Tetzlaff†, P. Halász‡, and T. Roska**
**Faculty of Information Technology, Péter Pázmány Catholic University, Budapest, Hungary; †Institute of Applied Physics, Johann Wolfgang Goethe University, Frankfurt Am Main, Germany; and ‡EPI-HELP BT, Budapest, Hungary*

Purpose: In this study we examined whether self-similar properties of brain electrical activity in human epilepsy could provide useful information about the evolution of epileptic seizures in order to detect and predict them.

Method: Self-similar properties of intracranial electroencephalogram recordings were analyzed by estimation of the Hurst exponent (H). For this purpose we implemented a method based on the R/S statistics and evaluated long-term data containing 104 seizures of twenty-four patients suffering from different types of epilepsy.

Results: A drop of H was observed for 97.1% of the seizures, regardless of their origin, which could allow the detection of the seizures. Moreover, for mesiotemporal/hippocampal seizures it was found that a gradual decrease of H occurred in 72.1% of the cases, gradual increase in 16.3%, and while for 11.6% of seizures no changes could be found in the preictal period. Neocortical seizures, on the other hand, showed the opposite phenomenon in the preictal state. Namely, a gradual increase of H was present in 73.6% of the seizures, while a decrease occurred in only 15.1%.

Conclusion: These findings might imply different seizure generation mechanisms and could propose different models and prediction approaches for seizures of different origin. Other research groups revealed similar duality in the state of vigilance at the seizure onset time. Our next goal is to examine the preictal correlation of H and the state of vigilance after collecting an appropriate database containing information both about the seizures and the state of wakefulness.

E512
SLEEP STRUCTURE IN PATIENTS WITH GENERALIZED AND PARTIAL EPILEPTIC ATTACKS

S. Jankovic, D. Sokic, N. Vojvodic, and A. Ristc
Institute of Neurology, Serbia

Purpose: To determine the sleep structure in epileptic patients with generalized and partial (simple and complex) epileptic attacks.

Method: Fifty five adult male and female patients with generalized and partial epilepsy underwent a whole-night polysomnographic recordings prior to and after the administration of antiepileptic therapy (AET).

Results: In patients without antiepileptic therapy (AET), partial attacks (PA) in respect to generalized attacks (GA) have increased number of episodes for total sleep time (TST) and wake after sleep onset (WASO>120sec), prolonged WASO<120sec and decreased duration of sleep stage III and total recording time (TRT). In the group of patients with AET, PA in respect to GA have increased number of epochs for the sleep stage III, increased number of episodes for TST and sleep stages III and III+IV, prolonged sleep stage III and sleep latency. In patients with PA without AET, partial simple (PS) in respect to partial complex (PC) attacks have shortened TST, increased numbers of epochs and episodes and prolonged duration for WASO>120sec and WASO<120 sec. On the other side patients with PC in respect to patients with PS attacks only have prolonged sleep latency.

Conclusion: In epileptic patients both with and without AET, the degree of sleep disturbance is higher in PA than in GA. In patients with PA, the degree of sleep disturbance is higher in patients with PS than with PC attacks. Sleep structure is more disturbed in patients with PA (more in PS then PC) then in patients with GA.

E513
USEFULNESS OF THE URGENT ELECTROENCEPHALOGRAM IN ALTERED MENTAL STATUS AND IN DIAGNOSIS OF NONCONVULSIVE STATUS EPILEPTICUS – EXPERIENCE FROM OUR CENTRE

N. Ferreira, and P. Breia
Hospital Garcia De Orta, Almada, Portugal

Purpose: Altered mental status is common in hospitalized patients and its cause is often unknown. The EEG helps in differentiating between metabolic, structural or epileptic causes and is therefore a valuable diagnostic tool in these cases. We aimed to identify the results of the EEGs in this population, namely regarding the incidence of nonconvulsive status epilepticus and to determine possible clinical predictive factors for this diagnosis.

Method: We retrospectively analyzed the EEG records from our unit, requested for altered mental status or clinical suspicion of nonconvulsive seizures, from January 2004 to December 2006 and selectively analyzed the clinical records of all the patients with nonconvulsive status epilepticus, comparing them with a control group of 30 patients with other diagnosis, regarding several clinical factors.

Results: We analyzed 190 EEG's of 93 male patients and 97 female patients, with a median age of 65. Forty-six percent were requested for altered status of consciousness, 31% for altered level of consciousness and 24% because of clinical suspicion of nonconvulsive seizures. EEG.

Results: 26% normal, 36% focal or generalized lentifications, 18% suggestive of metabolic derangements and 10% diagnosed nonconvulsive status epilepticus. The only clinical factors statistically different between the two compared groups were the sex and the refractoriness of the epilepsy, if preexisting.

Conclusion: Our results are concordant with other reports, namely regarding the incidence of nonconvulsive status epilepticus and the few clinical predictive factors identified, stressing the difficulty of this diagnosis and the utility of the urgent EEG in altered mental status.

E514
SYNTHETIC APERTURE MAGNETOMETRY-KURTOSIS FOR PRESURGICAL EVALUATION OF TUREROUS SCLEROSIS COMPLEX

I. Sugiyama, K. Imai, Y. Yamaguchi, T. Akiyama, C. Go, A. Ochi, and H. Otsubo
The Hospital For Sick Children, University of Toronto, Canada

Purpose: Synthetic aperture magnetometry (SAM) is an adaptive spatial filtering algorithm for magnetoencephalography (MEG). SAM kurtosis (SAM (g2)) provides source locations of intracranial discharges with excess kurtosis value (steepness). We applied SAM (g2) in children with intractable epilepsy secondary to tuberous sclerosis complex (TSC).

Method: We analyzed SAM (g2) and single dipole model (SDM) in 10 TSC patients (age ranging 1–18 years; mean 7.9 years). We used whole head gradiometer Omega system (151 channels). SAM (g2) calculated kurtosis value (band pass filter, 20–70 Hz) at each voxel (5 mm distance) in the entire brain. In each dataset, we selected active voxels with local peak kurtosis higher than half of maximum value. We applied SDM analysis for equivalent current dipole (ECD) (band pass filter, 10–70 Hz). We defined the cases as concordant when more than 50% of high kurtosis voxels overlapped with clustered ECDs and the cases as partially concordant when less than 50%.

Results: Multiple clustered ECDs were found in 5 patients and single in 5 patients. Locations of high kurtosis voxels overlapped with clustered ECDs between 24.1–95.2%. Eight patients had concordant results (multiple and single 4 each). The remaining 2 patients showed partially concordant results (multiple and single one each).

Conclusion: SAM (g2) clustering analysis succeeded in localizing the single and multiple independent epileptic foci in children with TSC. This systematic SAM (g2) analysis using half of maximum value provided consistent active voxels with valuable spikes in the epileptic zones detected by SDM analysis.

E515
RECORDING EPILEPTIC ACTIVITY WITH MEG USING LIGHT-WEIGHT MAGNETIC SHIELD

X. De Tiège, M. Op de Beeck*, M. Funke†, B. Legros*, S. Goldman*, and P. Van Bogaert**
**ULB-Hôpital Erasme, Brussels, Belgium; and †University of Utah Magnetic Source Imaging, Salt Lake City, UT, USA*

Purpose: To determine if magnetoencephalography (MEG) using a new light-weight magnetic shield technique (LW-MS, MaxShield, Elekta Neuromag) provides sufficient signal to noise ratio (SNR) to accurately detect and localize the magnetic correlates of epileptic abnormalities.

Method: 10 patients (7 women; age range: 10 to 53 years; 6 temporal lobe epilepsies) with symptomatic focal epilepsy were studied with MEG using the LW-MS that combines three interference suppression.

Method: (1) a light-weight magnetic shielded room (MSR) comprising a single shell of interleaved mu-metal/aluminum layers to reduce external magnetic field from reaching the sensors, (2) six internal active feedback compensation coils utilizing a combination of MEG channels to compensate variation of the magnetic field in the sensor array, and (3) the signal space separation algorithm. In all patients, spontaneous magnetic activity (eyes-closed rest, lying position) was continuously recorded during one hour and then visually inspected for epileptic events. Equivalent current dipoles (ECD, g/% >80%) corresponding to epileptic events were fitted in the patients' spherical head model and coregistered on their MRI.

Results: Interictal epileptic abnormalities colocalizing with the presumed localization of the epileptogenic zone were found in all patients. In three patients, additional distinct MEG foci were also found.

Conclusion: This study shows that MEG using LW-MS provides sufficient attenuation of magnetic interference and good SNR to allow accurate detection and localization of single epileptic abnormalities on continuous MEG data. The use of LW-MS, which are cheaper and smaller than conventional MSR, should facilitate the development of MEG in clinical environments.

E516
ICTAL LAUGHTER – A VIDEO-EEG AND SEEG STUDY

C. Badiu,†, C. Adam*, M. Baulac*, and V. Navarro**
**Epilepsy Unit, Pitie Salpetriere Hospital, Paris, France; and †Functional Exploration Department, Bichat- Claude Bernard Hospital, France*

Gelastic seizures are rare ictal manifestations during which laughter is the predominant symptom, classically associated with hypothalamic hamartoma. However, laughter may occur in other types of partial epilepsy.

Purpose: We evaluated the frequency, the semiology of ictal laughter (IL) in patients with partial epilepsies and we analyzed the lateralizing and localizing value of different types of IL.

Method: We reviewed the video-EEG recordings of epileptic patients in presurgical evaluation in our Unit from 2001 to 2008. IL was defined by a sonorous and rhythmic expulsion of air from the lungs modulated by laryngeal muscles, usually associated with movement of the muscles of the face, occurring without provocative external factor.

Results: We identified 32 patients who laughed during their seizures (n = 410 seizures). Sixteen patients had a laugh caused by a nonictal mechanism or presented a vocalisation which did not meet the characters of a laugh. Sixteen patients experienced an IL defined according to our criteria, at least once during their recorded seizures. The video analysis allowed the distinction of: (1) a discreet, non-noising laugh, (2) a noising belly laugh and (3) a sonorous rhythmic, sniggering laugh. One patient presented postictal laugh. The result of the presurgical investigations of

each patient will be presented in order to attempt to correlate the epileptogenic zone to the types of IL.

Conclusion: The lateralizing and localizing value of these clinically different types of IL will be discussed. The networks involved in IL will be discussed and compared with those of physiological laughter.

E517
THE PATHOGENESIS OF IDIOPATHIC GENERALIZED EPILEPSY (IGE): A PHARMACO-TMS STUDY

V. Kimiskidis, S. Papagiannopoulos*, D. Kazis*, G. Vasiliadis*, V. Tsimourtou†, M. Potoupnis*, S. Tryfon‡, and N. Vlaikidis**
**Aristotle University of Thessaloniki, Greece; †University of Larissa, Greece; and ‡A Pneumonological Clinic, Greece*

Purpose: Transcranial magnetic stimulation (TMS) is being increasingly used to explore the pathophysiological substrate of epilepsy. In order to interpret the results of these studies in a biologically meaningful way, one might compare their findings to the effects of CNS-active drugs with well-defined modes of action and thereby make inferences regarding neurotransmitter or ion channel dysfunction in epilepsy. The objective of the study is to investigate excitatory and inhibitory brain mechanisms in patients with IGE.

Method: 18 untreated IGE patients and 13 healthy, age-matched controls. Results were compared to the effects of various drugs, including the GABA-A receptor antagonist imipenem, on key TMS parameters, observed in previous pharmaco-TMS studies by our group. Corticomotor threshold (Thr) was measured at 1% steps. Silent period (SPs) were investigated as recently described (Kimiskidis et al, Exp Brain Res 2005;163 (1): 21–31). SPs were elicited using a wide range of stimulus intensities. The resulting S/R curves were fitted to a Boltzman function, the best-fit values of which were statistically compared between the patient and the control group.

Results: Thr was decreased in epileptic patients compared to the controls (34,92% vs 41,08%, $p<0.001$). The Max value of the patient's SP S/R curve was 263.2 ms vs 218.1 ms in the controls ($p<0.0001$) whereas slope did not differ significantly. These results were similar to the effects of imepenem.

Conclusion: IGE is characterized by reduced Thr and prolonged SPs. These findings are similar to the effects of a GABA-A receptor antagonists. It is therefore suggested that GABA-A receptor hypofunction may be implicated in the pathogenesis of IGE.

E518
COMPARISON OF FUNCTIONAL BRAIN MAPPING OF EPILEPTIC ACTIVITY USING HIGH-RESOLUTION EEG AND EEG-FMRI IN PATIENTS WITH REFRACTORY FOCAL EPILEPSY

A. Leal, M. Secca†, C. Jordão‡, P. Cabral‡, N. Canas‡, P. Breia§, A. Dias¶, J. Vieira¶, and E. Calado¶*
**Hospital Julio De Matos, Portugal; †New University of Lisbon, Portugal; ‡Hospital Egas Moniz, Portugal; §Hospital Garcia Horta, Portugal; and ¶Hospital Dona Estefânia, Portugal*

Purpose: Integration of EEG and functional magnetic resonance imaging (fMRI) has generated expectations of major improvements in spatial and temporal resolution of noninvasive functional brain mapping. In epilepsy significant discrepancies were demonstrated between the spikes BOLD activation and source analysis. We used 64-channel laplacian montages to overcome the uncertainties of source analysis and re-evaluate the EEG-BOLD integration.

Method: High-resolution EEG (HR-EEG) recordings of interictal spikes in 12 patients with focal epilepsy were obtained, processed with an average reference (avg-EEG) and a spline-laplacian algorithm, and integrated with the BOLD activations obtained in simultaneous EEG-fMRI.

Results: BOLD activations were obtained in 75% of patients (N=9). In 5 patients they occurred in the convexity or basal brain areas; in these, avg-EEG and focal laplacian peaks were in the close neighborhood (<3 cm). In 4 patients BOLD activations occurred in the interhemispheric fissure; in those the laplacian failed to show a focal peak, while the avg-EEG showed a nearby maximum in 3. Each method in isolation had major limitations: widespread maximum in avg-EEG; secondary sources and sinks far from the presumed focus for the spline-laplacian; multiple BOLD clusters for fMRI. There is a close spatial relation between BOLD activation and HR-EEG in the brain convexity or basal cortex; BOLD activations in central fissure do not provide focal sources in HR-EEG, but in two operated cases resection including the BOLD cluster rendered the patient seizure-free.

Conclusion: HR-EEG of interictal spikes demonstrates a close spatial relation with the BOLD activation recorded in simultaneous EEG-fMRI.

E519
DECREASE OF CORTICAL EXCITABILITY IN REFRACTORY EPILEPTIC PATIENTS AFTER ONE YEAR OF VAGUS NERVE STIMULATION: A TRANSCRANIAL MAGNETIC STIMULATION STUDY – PRELIMINARY RESULTS

M. Mann, B. Gueguen, E. Landré, C. Francine, M. Bourdel, B. Turak, and F. Roux
Ste Anne Hospital, Paris, France

Purpose: To evaluate prospectively changes in cortical excitability by means of transcranial magnetic stimulation (TMS) after one year of chronic left vagus nerve stimulation (VNS).

Method: 26 consecutive patients with refractory epilepsy and treated with chronic VNS have entered the study between 8/11/2005 and 13/3/2008. 10 patients (3 female, 7 male) completed at least one year of chronic VNS at a minimum intensity of 1 mA and are reported here. The antiepileptic treatment remained unchanged during the study. The motor threshold is the primary outcome measure.

Results: The motor threshold showed after one year of chronic left VNS a statistically significant increase from 61, 4% to 70, 2%. A decrease was found only in one hemisphere in a single patient.

Conclusion: Preliminary results of our study show that chronic VNS is associated with a significant increase of the motor threshold, i.e. with a decreased cortical excitability, as measured by TMS. A significant correlation between this modification and the clinical outcome cannot be established yet.

E520
PAROXYSMAL KINESIGENIC MOVEMENT DISORDERS (PKMD) – A 56 CASES REPORT OF CLINICAL AND ELECTRONEUROPHYSIOLOGICAL STUDIES

Y. Deng, Y. Huang, W. Jiang, and F. Du
Xijing Hospital, China

Purpose: To document the clinical features and changes in electroencephalogram (EEG) of 56 patients with paroxysmal kinesigenic movement disorders (PKMD), analyzing the therapeutic efficacy of antiepileptics and the relationship between PKMD and epilepsy.

Method: Detailed observation of the clinical features, imaging examinations and alterations in EEG of 56 cases of PKMD patients.

Results: The 56 cases were all kinesigenic. Among these 39 were diagnosed to have paroxysmal kinesigenic choreoathetosis (PKC), 17

with paroxysmal kinesigenic dystonia (PKD), while all remained conscious during attacks. Six subjects showed abnormal imaging signs, whereas epileptiform discharges were identified on EEG from 15 cases, and observed particularly in 2 such cases during epileptic attacks. Over half of all cases showed abnormal changes on somatosensory evoked potentials recorded on the afflicted hemisphere of the brain. A 1-17 years follow-up after administration of antiepileptics revealed a complete recession rate of 73.2%, while the rest patients were partially controlled.

Conclusion: The pathological foci in PKMD may be localized to reflex centres bridging input pathways of sensory stimuli and output routes for seizure symptoms. The epileptic features of PKMD suggest some common underlying biological basis with that of epilepsy, thus lending support to a hypothesis of possible pathological mechanisms igniting syndromes of epileptic attacks.

E521
EFFECTS OF ELECTRICAL STIMULATION IN VESTIBULAR CORTEX AREAS IN HUMANS

C. Best, H. Stefan†, R. Hopfengartner†, and M. Dieterich**
**Johannes Gutenberg-University, Mainz, Germany; and*
†Friedrich-Alexander-University, Erlangen, Germany

Purpose: Mapping of vestibular cortex areas has been focussed on recent PET and fMRI studies, where a cortical network activated by vestibular stimulations could be identified. In patients with intracranial electrical stimulation for epilepsy surgery the inferior parietal and superior temporal cortex (STG) were correlated with the perception of vestibular sensations. Nonetheless, the exact organization of vestibular cortex areas remains unclear.

Method: Here, we present the case of a 24-year-old right handed male with a 2-year history of intractable focal epilepsy. In part the epileptic seizures were accompanied by a vestibular aura. Neurological examination revealed overall normal findings in the seizure-free interval. Intracranial electrodes were applied for EEG recording and electrical stimulation was performed to evaluate the epileptogenic areas. Eye movements were simultaneously recorded by means of 3-dimensional video-oculography.

Results: Stimulating the medial part of the STG with high stimulus intensities (14 mA) a 3-dimensional nystagmus occurred: Its slow phase was horizontally toward the nonstimulated hemisphere (i.e., contralateral), vertically upward, and torsionally counterclockwise. In addition, the patient perceived an unidirectional vestibular sensation. Stimulation of other cortex areas at the temporoparietal junction induced a strictly horizontal nystagmus with its slow phase toward the stimulated hemisphere (i.e., ipsilateral).

Conclusion: These results give evidence that the STG is involved in the perceptional correlate of vestibular stimuli and the ocular motor consequence, the nystagmus. Either the local stimulation of a single area induced activation within the whole vestibular cortical network or vestibular perceptions are tightly connected with their ocular motor and postural responses.

E522
REAL-TIME SONIFICATION OF ICTAL EEG DATA

M. Feichtinger, A. Walisch*, T. Urbanic Purkart*,*
A. de Campo†, E. Körner, and E. Ott**
**Medical University Graz, Austria; and †Institute of Electronic Music And Acoustics, Technical University Graz, Austria*

Purpose: The real-time detection of epileptic seizures in a video-EEG Monitoring unit needs intensive attention of the personnel in charge. A tool supporting visual control by auditory signal processing would be of advantage to react immediately in case of an ongoing seizure.

Method: A sound synthesis tool for sonification of EEG data (MATLAB, Super Collider 3) has been generated for both generalized 3/sec spike wave paroxysms and for ictal rhythmic EEG discharges during temporal lobe seizures.

Results: This event based sonification allowed an accurate real-time detection of temporal lobe seizures as well as of generalized spike wave paroxysms. The practical use of this sonification tool was tested using an 'expert user acceptance questionnaire'. Usability of this acoustic support was rated 'very good'.

Conclusion: This new sonification tool can be implemented for online monitoring of epileptic seizures during video-EEG monitoring and can improve visual control of seizure onset. Generalized Spike wave paroxysms can be detected more easily during long-term EEG in patients with absence seizures using acoustic support.

E523
DESCRIPTION OF TWO CASES WITH ICTAL APPEARING DISCHARGES TERMINATED WITH VARIOUS SENSORY STIMULATIONS

M. Bensalem-Owen, and T. Fakhoury
University of Kentucky, USA

Purpose: Stimulus induced rhythmic or periodic ictal appearing discharges have been previously reported. The reverse phenomenon where ictal appearing discharges are terminated by sensory stimulations has been rarely described. We describe two patients with this unusual electrographic pattern.

Method: We prospectively identified patients who underwent continuous video-EEG and whose EEG showed changes with sensory stimulations. We then reviewed these EEG recordings for ictal appearing patterns and reviewed changes associated with stimulation visible on concomitant video recordings.

Results: We identified two patients whose EEGs showed bursts of repetitive or rhythmic epileptiform discharges terminated by various sensory stimulations. Both patients had multiple medical problems, including epilepsy and decreased mental status at the time of continuous video-EEG. Both patients had ictal appearing discharges without any clinical correlate which were aborted with various sensory stimulations. Both patients improved clinically following optimization of baseline antiepileptic drugs but without treatment for subclinical seizures. One patient was discharged to a rehabilitation facility and the other to her nursing home.

Conclusion: The termination of ictal appearing discharges with sensory stimulations is an interesting and rare phenomenon. The clinical significance and pathophysiology of this electrographic pattern remains however unclear.

E524
THE DIAGNOSTIC VALUE AND EFFICIENCY OF EEG REVISION IN A TERTIARY EPILEPSY CLINIC: A COMPARATIVE STUDY

J. Arends, J. van der Linden, S. Ebus, M. Debeij – van Hall, and W. Gunning
Kempenhaeghe, The Netherlands

Purpose: To assess the efficiency and accuracy of EEG diagnosis in 100 patients with revision of previous EEGs from elsewhere.

Method: All EEGs were reclassified and the consequences for epilepsy diagnosis systematically investigated. A matched control group was used to compare the efficiency of the diagnostic process.

Results: In 85 of the 100 patients the initial conclusion was known. In 23 of these 85 patients the conclusion about the presence of epileptic activity was changed: 17 cases with positive EEG elsewhere were

reclassified as negative, 6 patients with negative EEG elsewhere were reclassified as positive. In 15 patients a different localization of epileptic activity was found, 7 of which were elsewhere regarded as having generalized activity and partial by us. In 5 patients the syndrome diagnosis was changed. So in 43 from the 85 patients the reclassification of the EEG lead to a different opinion. The reclassification group was more efficiently diagnosed. The average total amount of technician time spent for the first diagnostic EEG of each patient was 7.96 hours in the matched group and 2.83 hours in the revision group. In 57% of the revision group no further EEG was necessary.

Conclusion: Reclassification of EEGs in a tertiary centre leads to a more efficient diagnostic process and reveals considerable differences in classification between the original and tertiary hospital.

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E525
PREVALENCE OF VISUAL FIELD DEFECTS FOLLOWING EXPOSURE TO VIGABATRIN THERAPY: A SYSTEMATIC REVIEW

M. Maguire, K. Hemming†, J. Hutton†, and A. Marson‡*
**Sunderland Royal Hospital, Sunderland, UK; †University of Warwick, Coventry, UK; and ‡University of Liverpool, Liverpool, UK*

Purpose: Vigabatrin is an efficacious antiepileptic drug licensed as add-on therapy in refractory epilepsy and used in infantile spasms. In recent years, use has diminished as it causes bilateral concentric visual field constriction. We report a systematic review ascertaining the magnitude of risk of visual field defects and any clinical predictors of risk.

Method: Electronic searches of MEDLINE (1966–2007), EMBASE (1974–2007) and CINAHL (1982–2007) were conducted. Fully published reports of observational studies investigating the prevalence of visual field defects by static or dynamic perimetry in epilepsy patients treated with vigabatrin were included. Outcomes were the proportion with an overall and vigabatrin-attributed visual field defect, and a relative risk estimate in controlled studies.

Results: Thirty-two reports (16 longitudinal studies and 16 cross-sectional studies) were identified. Ten studies investigated children, and 18 studies were controlled. There was significant variability in reported prevalence rates among studies. Studies investigating patients with a larger mean cumulative dose, treatment duration and an older mean age reported higher prevalence rates of visual field defects. The random effects estimate for the proportion of adults with a visual field defect was 51% [95%CI 45, 57]. The estimate for children was lower at 36% [95%CI 31, 40]. The relative risk for a visual field defect in vigabatrin-exposed patients was 11.3 [95%CI 8.1, 14.5].

Conclusion: Visual field defects occur in half of adults and a third of children exposed to vigabatrin. Major predictors of risk were not identified. Risk is sufficiently high to warrant referral of all vigabatrin-exposed patients for ophthalmology assessment.

E526
FACTORS ASSOCIATED WITH THE OUTCOME OF LAMOTRIGINE TREATMENT IN JUVENILE MYOCLONIC EPILEPSY

H. Bodenstein, R. Gandelman-Marton†, B. Gidoni-Ben-Zeev*, and I. Blatt**
**Sheba Medical Center, Tel-Hashomer, Israel; and †Assaf Harofe Medical Center, Zrifin, Israel*

Purpose: To characterize a subgroup of juvenile myoclonic epilepsy (JME) patients who have a good clinical response to treatment with lamotrigine (LTG), and in addition, to characterize patients whose myoclonic seizures are exacerbated by LTG.

Method: Records of 62 JME patients were reviewed for: gender, age at seizure onset, time from onset to diagnosis, family history, first seizure type, seizure type combination, EEG parameters, psychiatric comorbidity, maximal LTG dose, rank order of LTG, reason for valproate (VPA) failure (if relevant), classification of treatment (monotherapy / polytherapy). We determined the clinical response to LTG and divided patients into LTG responders and nonresponders, comparing the above parameters between these groups.

Results: There were 35 LTG responders and 27 nonresponders. Patients with combination of seizure types which did not include generalized tonic–clonic seizures (GTCS) responded better to LTG ($p<0.04$). Patients whose reason for failing VPA treatment was adverse effects responded better to LTG ($p<0.069$). Other parameters showing a trend for good response to LTG were: long time to diagnosis ($p<0.08$), absence of psychiatric problems. In 25% of patients myoclonus worsened with LTG; this was associated with LTG administration as polytherapy, but no other association was found.

Conclusion: Combination of seizure types not including GTCS was associated with a good response to LTG, making LTG a good option as first drug of choice. The reason for stopping VPA may predict the subsequent response to LTG. Patients with late diagnosis had a better response to LTG, possibly due to a milder disease severity.

E527
VALIDATION OF THE SPANISH VERSION OF THE SIDE EFFECTS AND LIFE SATISFACTION (SEALS) INVENTORY IN PATIENTS WITH EPILEPSY

V. Villanueva, A. Gil-Nagel†, M. Carreño‡, E. Elices§, J. Salas-Puig¶, J. Sánchez**, J. Serratosa††, E. Luaces‡‡, and J. Porcel§§*
**H. La Fe, Valencia, Spain; †Program For Epilepsy, H. Ruber Internacional, Madrid, Spain; ‡H. Clínic, Barcelona, Spain; §Clínica Rotger, Palma De Mallorca, Spain; ¶H. Univ. Central De Asturias, Oviedo, Spain; **H. Univ. Virgen De Las Nieves, Granada, Spain; ††Fundación Jiménez Díaz, Madrid, Spain; ‡‡Medical Department, EISAI Farmacéutica, S.A., Spain; and §§Biometría Clínica, S.L., Barcelona, Spain*

Purpose: Antiepileptic drug (AED) therapy's side effects influence health related Quality of Life (QoL). Practitioners need a reliable, validated, clinically efficient psychometric instrument to measure QoL in patients with epilepsy. Side-Effect and Life Satisfaction (SEALS) is a 38-item, 5 subscales (cognition, dysphoria, temper, tiredness and worry), patient-completed questionnaire designed to measure satisfaction with AED therapy.

Method: We evaluate the psychometric properties of the Spanish version of SEALS in 595 patients with epilepsy 50.0% female; mean age 41.7 years (range 18 to 90); 41.9% primary, 35.9% secondary and 19.3% university studies, 2.9% no formal education; mean age at diagnosis was 25.2 years with mean of evolution of 16.7 years; 55.6% with single AED therapy. Hospital Anxiety and Depression Scale (HADS) and SF-12 Health Scale were also applied to the patients.

Results: Overall and within subscales mean results for SEALS Spanish version were consistent with those from SEALS French version validation: overall results 60.7 and 58.5 respectively; indicative of a worse QoL in both, worry showed lowest results (38.5 and 34.6 respectively); dysphoria showed highest results (72.3 and 72.1 respectively). SEALS' overall score correlated negatively with HADS so a worse QoL was related to more anxiety or depression symptoms. Correlation between SEALS' overall score and the SF-12's emotional or mental health measures was

over 0.50. Correlation of SEALS with SF-12's physical measures was lower.

Conclusion: The Spanish version of the SEALS inventory is a valid instrument, with similar psychometric properties to the original English version.

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E528

ETOTAL ANTIOXIDANT STATUS (TAS) IN PATIENTS WITH EPILEPSY ON MONOTHERAPY WITH CARBAMAZEPINE (CBZ) AND LAMOTRIGINE (LTG)

G. Nikoloski
Clinic for Neurology, Skpoje, Macedonia

The new facts about patophysiology of epilepsy and potential role of free radicals in this patophysiology are the basic motives of our study.

Purpose: To fortify the values of TAS in patients with epilepsy on monotherapy with CBZ and LTG as indirect indicator of oxidative stress. Data basis had been formed by specific computer program and than we used standard descriptive and analytical variants and multivariant methods, for statistical analyses.

Method: Longitudinal study. The statistical group contains 42 patients with epilepsy, diagnosed by ICD X and EBM criteria, AED free till that moment. Analyze of TAS values in the beginning of therapy and after one month.

Results: Average values of TAS are: 2,13+ 0,63 1st day,; 1,83 + 0,37 after one month at patients who use CBZ (N=23). In the group with LTG (N=19), average TAS value in first analyze is 2,02+ 0,55, and after one month 1,94+ 0,42.

Conclusion: Average TAS values are theoretical expected, but without statistical significance: t<0,66; p=0,05, even we may concluded that CBZ leads to oxidative stress more than LTG. Maybe some greater series of patients can show statistical significant differences.

E529

RELATIONSHIP BETWEEN DRUG RESISTANCE AND NUCLEAR RECEPTORS ACTIVATION IN THE BRAIN MICROVASCULAR ENDOTHELIAL CELLS TREATED WITH CARBAMAZEPINE AND LEVETIRACETAM

A. Pavone, and V. Cardile†*
**Garibaldi Hospital, Catania, Italy; and †University of Catania, Italy*

Purpose: Drug resistance is a complex phenomenon that involves many mechanisms, none of which is well understood. In any case, why some patients with seizures are successfully treated with antiepileptic drugs (AEDs) and others prove medically intractable is still not known. Our work contributes to the understanding of the mechanisms of drug resistance in epilepsy.

Method: This study aimed to investigate (1) the levels of expression of P-glycoprotein (P-gp), and multidrug resistance-associated proteins (MRP)1 and 2, (2) the activation of the pregnane X receptor (PXR) and the constitutive androstane receptor (CAR), and (3) the relationship between increased P-gp and MRPs expression and PXR and CAR activation, in immortalized rat brain microvascular endothelial cell lines, GPNT and RBE4, following treatment with carbamazepine (100 mM), and levetiracetam (300 mM), using Western blotting and immunocytochemistry method.

Results: Carbamazepine induced the highest levels of P-gp and MPRs expression that was associated with increased activation of PXR and CAR receptors as compared to levetiracetam.

Conclusion: We conclude that P-gp and MRPs are differently overexpressed in GPNT and RBE4 by assayed AEDs and both PXR and CAR are involved in the drug-resistant epilepsy induced by carbamazepine. In addition, the results suggest that there is correlation between the nuclear receptors and antiepileptic drugs transport and induction of resistance proteins in the brain endothelial cells. This is confirmed by the decrease of P-gp and MRPs when phorbol 12-myristate 13-acetate (PMA, 100 nM), repressing the PXR activity, and S-5-isoquinolinesulfonic acid 4-[2-[(5-isoquinolinylsulfonyl) methylamino]-3-oxo-3- (4-phenyl-1-piperazinyl)propyl] phenylester1-[N,O-bis (5-Isoq uinolinesulfonyl)-N-methyl-Ltyrosyl] -4-phenylpiperazine (KN-62, 10 mM), repressing the CAR activity, were used with AEDs.

E530

NEUROTOXICITY OF ANTIEPILEPTIC DRUGS – A PATIENT-BASED ASSESSMENT

M. Milovanovic, Z. Martinovic, R. Djokic, and M. Jovanovic
Institute of Mental Health, Belgrade, Serbia

Purpose: To assess the adverse effects of antiepileptic drugs on cognitive functions based on subjective reports of patients with chronic epilepsy.

Method: Patients with proven epilepsy were included in this prospective study and followed up for more then three years. Seizures, epilepsy and epilepsy syndromes were classified according to the proposals of the International League Against Epilepsy. Cognitive functions were assessed with the patient-based Neurotoxicity Scale-II (Aldenkamp A.P. et al. Epilepsy Research 1995; 20: 229–239.).

Results: In 102 patients (mean age 34.5 years, 51% females) there were significantly higher overall scores in: localization-related epilepsies compared to primarily generalized epilepsies (mean 15.37 versus 6.76, p=0.007); in complex partial seizures compared to other seizure types (mean 15.73 versus 8.02, p=0.001); in patients with three seizure types (simple partial, complex partial and secondarily generalized) compared to less then 3 seizure types (only motor coordination subscore: mean 2.5 versus 1.13, p=0.05); in patients with frequent seizures (>5 generalized seizures and/or >13 complex partial and/or >101 simple partial seizures per year) compared to group with low seizure frequency (mean 22.75 versus 9.39, p=0.001). Overall scores were significantly higher in patients using benzodiazepines compared to group without these drugs (mean 18.13 versus 10.13, p=0.006); in polytherapy (n=46) compared to monotherapy (n=55) (mean 16.67 versus 9.27; p=0.01) and in patients using three drugs (n=10) compared to patients using two drugs (n=36) (mean 27.44 versus 14, p=0.016).

Conclusion: Reported cognitive impairment correlated with clinical characteristics and severity of epilepsy, polytherapy and benzodiazepine use.

E531

INFLUENCE OF VALPROATE AND CARBAMAZEPINE ON CONCENTRATIONS OF IL6, TNF ALFA IN THE SERUM IN CHILDREN WITH EPILEPSY

B. Steinborn, J. Mlodzikowska-Albrecht, J. Losy, G. Gramza, M. Wojcicka, and M. Cieslik
University of Medical Sciences, Poznan, Poland

Purpose: The aim of study was the comparison concentrations of IL6, TNF alfa in blood serum before and after 4–6 months of CBZ or VPA treatment in patients treated by the reason of epilepsy in Department of Developmental Neurology University of Medical Sciences in Poznan until January 2006 to May 2007.

Material and Method: The analysis was conducted on group of 21 patients, with generalized epilepsy, at the age of 7.7 ± 4.7 years treated by VPA and 5 children with partial epilepsy at the age of 11.8 ± 2.7 treated by CBZ before and after 4–6 months of therapy. Quantitative determi-

nation of cytokines: Il6, TNF-α were performed with immunoensimatic method (ELISA) in the solid phase. The drug concentration was determined with the use of fluorescence-polarization-immunoassay system (FPIA).

Results: Concentration of IL6) decreased significantly after VPA therapy ($p<0.001$. Concentration of TNF-α ($p=0.079$) after VPA therapy and concentrations of both cytokines after CBZ therapy (TNF-α – $p=0.178$ and IL6 – $p=0.225$) didn't change significant way. Mean concentration CBZ and VPA in the blood serum of patients were in therapeutic range (VPA – 73.53 μg/ml and CBZ – 5.23 μg/ml).

Conclusion: Concentrations of pro-inflammatory IL6 in the blood serum of patients with epilepsy decreased significantly after 4–6 months of VPA therapy. Level of TNF alfa after and before VPA therapy and concentrations of TNF alfa and IL6 after and before CBZ therapy were similar. Antiinflammatory properties and the role inflammation of VPA in epileptogenesis can be suggested. That problem needs investigations on more numerous groups of children and adolescents.

E532
CHANGES OF SPECTRUM ANTIEPILEPTIC DRUG DURING TEN YEARS

G. Odintsova, A. Chugunova, and N. Koroleva
Institute of Human Brain Russian Academy of Science, Russia

Purpose: To compare spectrum antiepileptic drug (AED), practiced in 1996 and 2006 years and to estimate dynamics of changes.

Method: case records of 96 patients suffering epilepsy and taking AED, in the age from 6 to 52, middle age is 21 year, were analyzed. First group consists of 48 patients from a database of 1996 year. Second group consists of 48 patients with similar forms from a database of 2006 year. Quantitative and qualitative analysis of AED of each patient, with computation of average indices of each group was leed. Following parameters were considered: a spectrum of all practiced AED in 1996 and 2006, a percentage parity of AED used in 1996 and 2006, quantity of the patients taking mono- and polytherapy.

Results: There were 12 kinds of AED used in treatment. Valproate was to be one group. In the first group there were used 9 kinds of AED, in the second – 10. In both groups were practiced 7 kinds of AED. On monotherapy in 1996 there were 6 patients -12.5%, on polytherapy there were 42 patients-87.5%. In 2006 29 patients received monotherapy -60.4%, polytherapy received 19 patients -39.6%. In the first group were registered 109 AED, on the average 2.3 AED for 1 person. In the second group were registered 68 AED, in average-1,4 AED. Leaders of AED in 1996: dihpenin-23.1%, benzonale – 21%, valproate-13.2%, carbamazepine-12.4%. Leaders of AED in 2006: valproate-40.6%, carbamazepine -14.5%, topiramate – 13%, levetiracetam and lamotridgin.

Conclusion: Thus the spectrum of used AED has changed on 42% during 10 years. The spectrum of leaders AED has changed on 50%. The increase in percent of base AED and application of new AED has lowered quantity of patients receiving polytherapy in 5 times.

E533
EFFICACY OF RECTAL DIAZEPAM IN STOPPING SEIZURES IN CHILDREN – SINGAPORE EXPERIENCE

H. Ong, L. Dong*, S. Tay†, and P. Low†*
**National University Hospital, Singapore; and †National University of Singapore, Singapore*

Purpose: Pediatric patients with seizure disorder are often affected by acute repetitive or continuous seizures that may last several minutes to hours. Rectal administration of diazepam is one available treatment for these seizures. The purpose of this study was to assess the effectiveness of caregiver administration of rectal diazepam during seizure recurrences, following instructions by a pediatric epilepsy nurse.

Method: This prospective study included 231 patients aged 0 to 15 years old who had either epileptic seizures or febrile seizures in the two year period from 1 March 2006 to 29 February 2008. Caregivers were taught how to identify convulsive seizures and to administer diazepam rectally if the seizures lasted longer than 5 minutes, or if the seizures did not stop by the time they obtain the rectal diazepam tube. Patients who subsequently had seizure recurrence and were managed at our Children's Emergency were recruited into the study.

Results: Forty-two patients were reviewed at the Children's Emergency following subsequent seizure recurrence. Thirty-five patients had seizures that lasted longer than 5 minutes, out of whom 33 (94%) had rectal diazepam administered at home. Of these patients, the seizures stopped after administration of rectal diazepam in 26 (79%); the remaining 7 (21%) required further intravenous treatment at the hospital.

Conclusion: Following education by a pediatric epilepsy nurse, caregiver administration of rectal diazepam is effective in stopping almost 80% of subsequent seizure recurrences lasting more than 5 minutes. It is a reassuring safety net for patients who are prone to prolonged seizures.

E534
LONG-TERM EFFICACY AND TOLERABILITY OF TOPIRAMATE AS ADD-ON THERAPY IN REFRACTORY PARTIAL EPILEPSY: AN OBSERVATIONAL STUDY

B. Lee, Y. Cho, S. Jang, and K. Heo
Severance Hospital, Yonsei University College of Medicine, Korea

Purpose: Topiramate (TPM) is a new antiepileptic drug (AED) with proven efficacy and safety. We evaluated long-term efficacy and tolerability of TPM in add-on therapy of refractory partial-onset epilepsy.

Method: An open label, single center, observational study included patients with refractory partial epilepsy, newly prescribed TPM as add-on therapy at Severance Hospital between Jan 2000 and June 2002. 85.4% of patients had at least five-year follow up duration. All patients had three months baseline periods, at least two-year epilepsy duration, and two or more failed AEDs. Dose adjustments were according to clinical response.

Results: Total 246 patients (112 women, mean age 32.1 years) were included. Starting dose was usually 50mg, and median dose increased to 100mg at three months and 200mg thereafter. At the time of 1-year and 5-year follow up, retention rate was 89.8% and 65.0%. Mean seizure frequency reduction was 73.8% at five years, compared to baseline. Five-year response rate was 46.7% (ITT) and 71.9% (completers), respectively. Seizure free rate was between 17.1% (ITT) and 26.4% (completers) at five years. Adverse events (AE) occurred in 40.4% of patients during the follow up period, but significant AEs leading to AED withdrawal developed in 30 patients (12.2%). Most common AEs were anorexia (17.5%), gastrointestinal symptoms (9.8%), weight loss (8.1%), and cognitive dysfunction (7.7%). Concomitant AEDs were reduced in 24.4% of the completers.

Conclusion: TPM was effective and well-tolerated add-on therapy of patients with difficult-to-treat partial epilepsy in long- term, individualized everyday clinical practice.

E535
CORRELATION OF SERUM LEVEL OF CARBAMAZEPINE WITH SEIZURE CONTROL AND ADVERSE DRUG REACTIONS AMONG EPILEPTICS IN IBADAN, NIGERIA

J. Fadare, C. Falade†, L. Owolabi*, A. Ogunniyi†, and O. Bolaji‡*
**Bayero University, Nigeria; †University College Hospital, Ibadan, Nigeria; and ‡Obafemi Awolowo University, Ile-Ife, Nigeria*

Purpose: Epilepsy is a chronic neurological disorder requiring long-term treatment. Seizure control requires adequate blood levels of antiseizure drugs. Cabarmazepine is one of the first-line drugs used in the treatment of epileptic seizures. This study was carried out to investigate the correlation between serum levels of carbamazepine and seizure control and adverse drug reactions among epileptics in Ibadan, Nigeria.

Method: In a cross-sectional study, 69 patients with confirmed diagnosis of epilepsy who had been on treatment with carbamazepine alone or in combination with phenytoin for at least one month were enrolled into the study and divided into two groups based on seizure control. Drug level in predose venous blood was analyzed by high performance liquid chromatography.

Results: 69 patients (38 male, 31 female) with a mean age of 31.1±13.2 yrs (range 18–72 yrs) were studied. The mean serum concentration of carbamazepine (CBZ) was 13.5±9.3 μg/mL (Range – 1.2–48.9 μg/mL). The mean serum concentration of carbamazepine-epoxide (CBZ-EP) was 6.34±12.61 μg/mL (Range – 0–69.6 μg/mL). Patients with good seizure control had mean serum CBZ concentration of 12.7 ± 9.2 μg/mL versus 15.02 ± 9.7 μg/mL among patients with poor seizure control (P=0.33). The serum concentration of CBZ-EP in patients with good seizure control was 8.05 ± 15.2 μg/mL while it was 3.11 ± 3.5 μg/mL in the second group (P=0.122). Drowsiness was the commonest adverse drug reaction (26.1%). Other adverse effects include difficulty with learning, cognitive impairment and skin rashes.

Conclusion: The study showed that serum level of carbamazepine does not correlate well with seizure control and adverse drug reactions.

E536

THE RELATION BETWEEN MOOD-STABILIZING ANTIEPILEPTIC DRUGS AND USE OF PSYCHOTROPIC DRUGS IN PATIENTS WITH REFRACTORY EPILEPSY AND INTELLECTUAL DISABILITY

F. Tan, L. Leunissen*, T. Rentmeester*, C. Vader*,†, M. Veendrick*, and A. Aldenkamp*,‡*
**Kempenhaeghe, Heeze, The Netherlands; †Sint Anna Hospital, Geldrop, The Netherlands; and ‡University Hospital, Maastricht, The Netherlands*

Purpose: The aim of this study was to investigate whether antiepileptic drugs (AEDs) with known mood-stabilizing properties (carbamazepine, valproic-acid and lamotrigine) lead to a different use of psychotropic drugs, notably antidepressants, in institutionalized epilepsy patients with Intellectual Disability.

Method: We performed a retrospective, cohort study of adults with epilepsy and ID in an epilepsy centre in The Netherlands. 246 residents were included. We gathered demographic data, use of psychotropic drugs, AEDs and drug load. The latter was defined by the PDD/DDD ratio (prescribed daily dose/ defined daily dose).

Results: Mean age was 47 years (range 18–87), M:F ratio was 61:39. 41.5% used psychotropic drugs: antidepressants were used in 14.6%, 30.5% used antipsychotics and 11.8% used anxiolytics. Mean number of AEDs use was 3.3 (range 0–6). In patients using LTG there was a reduced use of antidepressants (9.2% versus 19.8%, p=0.027). Patients using mood-stabilizing AEDs had a significant lower use of anxiolytics (10.2% versus 28.6%, p=0.024). Males use significantly more antipsychotics (36.4% versus 21.1%, p=0.0011) than females and have a higher drug load of mood-stabilizing AED's (1.66 versus 1.31, p=0.010). Most importantly, we found an inverse relation between the drug load of CBZ and/or VPA and/or LTG and the use of psychotropic drugs, for instance patients with a drug load between 2–3 used psychotropic drugs in 28.3%, while patients with a drug load of 0 used psychotropic drugs in 61.9% (p=0.009).

Conclusion: Higher drug loads of mood-stabilizing AEDs (CBZ, VPA and LTG) correspond with reduced use of psychotropic drugs.

E537

THE EFFECT OF OXCARBAZEPINE ON EEG BACKGROUND ACTIVITY IN CHILDREN WITH EPILEPSY

S. Nam, T. Hwang†, and Y. Lee‡*
**Pusan National University Hospital, Korea; †Inje Baek Hospital, Korea; and ‡Pusan National University Hospital, Korea*

Purpose: Reports concerning the electroencephalographic (EEG) findings have revealed that anticonvulsants such as phenytoin and carbamazepine (CBZ) induces slowing of the dominant rhythm and increased slow activity, even in the face of clinical improvement. This study was undertaken to assess the effect on EEG background activity (BA) associated with oxcarbazepine (OXC) monotherapy in the children with epilepsy.

Method: EEG BA was studied in 73 newly treated children with epilepsy (38 boys and 35 girls) who have been administrated OXC monotherapy for more than 3 months between January 2002 and June 2007 at Pusan National University Hospital. EEG was recorded for each patient before and during the follow-up visits after OXC therapy. We evaluated if there are the changes of the posterior dominant rhythm as EEG BA before and after OXC monotherapy.

Results: The mean age of patients at the start of the OXC therapy was 8.8 years old (range, 3.9~16.4) and the mean duration of follow-up after OXC therapy was 7.1 months (range, 4.0~12.0). In total patients' population, the mean frequency of the occipital dominant rhythm on initial EEG before OXC therapy was 9.35 Hz (range, 7.33~11.00) and that of follow-up EEG after OXC therapy was 9.48 Hz (7.83~11.00) (P>0.05). There was no change of posterior dominant rhythm after the treatment in any subgroup classified according to sex, age, underlying cause and dosage.

Conclusion: We concluded that in contrast with the traditional AEDs, OXC didn't result in any significant slowing of the occipital dominant rhythm on EEG BA.

E538

LONG-TERM EFFICACY AND TOLERABILITY DATA ON TOPIRAMATE AS ADD-ON THERAPY IN PATIENTS WITH TREATMENT-RESISTANT EPILEPSY

S. Papacostas, A. Dietis†, A. Flourentzou†, G. Stylianidou‡, R. Koukkoullis§, and E. Kkolou**
**The Cyprus Institute of Neurology And Genetics, Nicosia, Cyprus; †Nicosia General Hospital, Nicosia, Cyprus; ‡Archbishop Makarios III Hospital, Nicosia, Cyprus; and §Cyprus Red Cross Home for Sick Children, Limassol, Cyprus*

Purpose: To investigate the long-term efficacy and tolerability of topiramate (TPM) as add-on therapy in Cypriot patients with refractory epilepsy.

Method: 46 patients were studied retrospectively for five years. 11 patients had generalized epilepsy (GEN). 35 patients had focal onset (FO) epilepsy. Patients received TPM as add-on therapy to 1–4 anticonvulsants. We compared the mean seizure frequency for a 3-month period prior to and 5 years after introduction of TPM. All subjects had physical and neurological examinations, routine baseline hematological, biochemical, and urinary investigations at entry and every 6 months during study period.

Results: Six patients (13%) became seizure free. Six patients (13%) had seizure reduction of by 75% or greater. One patient (2.2%) had seizure reduction by 50% or greater. Nineteen patients (41.3%) discontinued TPM treatment because of lack of efficacy (30.4%), side effects (6.5%) or both (4.4%). Seizure reduction of 50% was seen in 27.3% of GEN patients and in 28.6% of FO patients. There was a decreased chance of the patients responding to TPM as the number of concomitant AEDs and the seizure duration increased. Frequently reported side effects were: headaches (10.9%), dizziness (17.4%), weight loss

(26.1%), body pain (17.4%), ataxia (10.9%) and behavioral complains (41.3%).

Conclusion: Topiramate was effective in both FO and GEN epilepsy. 28.2% of our patients with refractory epilepsy experienced seizure reduction of 50% on Topiramate, sustained for up to 5 years with 58.7% of patients continuing treatment. Topiramate was well tolerated by the majority of our patients.

E539
FIRST EXPERIENCES WITH RUFINAMIDE – TOLERABILITY AND EFFECTIVENESS IN CLINICAL PRACTICE

A. Friedo, K. Bohlmann†, and H. Straub‡*
**Epilepsiezentrum Berlin-Brandenburg, Germany; †Epilepsieklinik Tabor Bernau, Germany; and ‡Universität Potsdam, Germany*

Objective: New options are urgently needed in the treatment of Lennox-Gastaut syndrome (LGS). Since June 2007 rufinamide is available in Germany as adjunctice therapy in LGS. We report our first experiences with rufinamide with respect to effectiveness and tolerability in the context of polytherapy.

Patients and Method: Up to now 22 adults were treated with rufinamide (age 19–48 years, mean 32.5 years, 16 men). All suffered from pharmacoresistant epilepsies (16 patients with LGS), frequent seizures (12 patients with daily seizures) and mild to severe cognitive impairment. 20 patients had antiepileptic polytherapy (2–4 AEDs, mean 2.3 AEDs). rufinamide was titrated slowly (+ 200mg/3–7days, target 1200–3200mg/day), follow up ranges between 2 and 8 months (mean 5.3 months).

Results: 16 patients tolerated rufinamide without side effects, in 6 patients side effects (toxic cerebellar syndrome, sleepiness) occurred. Side effects were intraindividually dose-dependent (not interindividually) and could be abolished either by reduction of comedication or rufinamide. Effectiveness was not assessed in 6 patients (follow up < 3 months), 9 of 16 patients responded to rufinamide (>50% reduction of seizure frequency, 3 patients: >75%). Neither freedom nor worsening of seizures were observed.

Discussion and Conclusion: Rufinamide is well tolerated even in complex polytherapy, pharmacokinetic interactions are insignificant. Side effects seemed to be related to individual doses and cumulative pharmacodynamic phenomena in polytherapy. Influence on seizure frequency is limited- a result not unexpected in LGS. Some worthwhile effects – as well in focal epilepsies – were observed. Further investigations are necessary to assess the role of rufinamide in the treatment of epilepsies.

E540
PROSPECTIVE AUDIT OF ZONISAMIDE IN REFRACTORY EPILEPSY: AN INTERIM ANALYSIS

K. Kelly, L. Stephen, E. Wilson, P. Parker, and M. Brodie
Epilepsy Unit, Western Infirmary, Glasgow, UK

Purpose: Zonisamide (ZNS) was licensed in Europe in 2005 for the adjunctive treatment of focal-onset seizures. We undertook a prospective audit of ZNS in patients with uncontrolled epilepsy attending our epilepsy service.

Method: Following a 3 month retrospective baseline, ZNS was added to the antiepileptic drug (AED) regimen of 121 patients. Endpoints were 6 months ¯seizure freedom, 50% or <50% reduction in seizures compared with baseline, or ZNS withdrawal due to adverse effects or lack of efficacy. An end point has been reached in 69 (57%) [49F:20M, aged 18–80 years (median 37 years)] patients, 46 (66.7%) with localization-related and 23 (33.3%) with idiopathic generalized epilepsy. Ten patients had juvenile myoclonic epilepsy (JME).

Results: Twelve (17.4%) patients became seizure-free for 6 months on a median daily dose of 100mg (range 50–300mg). Eight took one other AED; the remaining 4 received duotherapy. Eleven patients (15.9%) had 50% reduction in seizure frequency; 10 (14.5%) had <50% reduction. There was no statistical difference between patients with focal-onset seizures (8 seizure-free, 3 50% reduction, 8 <50% reduction) and those with idiopathic generalized epilepsy (4 seizure-free [3 JME], 8 50% reduction [3 JME], 2 <50% reduction). ZNS was withdrawn in 36 (29.8%) patients [29 adverse effects, 5 lack of efficacy, 2 both]. Ten patients stopped taking ZNS due to neuropsychiatric problems. Other reasons for discontinuing ZNS were nausea and vomiting (9), sedation (6), weight loss (3) and rash (2).

Conclusion: ZNS is a promising AED for refractory focal-onset and idiopathic primary generalized epilepsies.

E541
BENEFICIAL EFFECT OF ADD-ON LEVETIRACETAM IN PATIENTS TREATED WITH VAGUS NERVE STIMULATION FOR REFRACTORY EPILEPSY

V. De Herdt, E. Vancaester, A. Van Dycke, I. Dewaele, R. El Tahry, A. Meurs, P. Boon, and K. Vonck
Reference Center for Refractory Epilepsy, Ghent University Hospital, Belgium

Purpose: To evaluate additional efficacy of add-on treatment with levetiracetam in patients already treated with vagus nerve stimulation (VNS) and a combination of other antiepileptic drugs.

Method: Medication history of all patients treated with VNS at Ghent University Hospital from 1995 until 2005 was reviewed. In patients who received additional treatment with levetiracetam after at least 6 months of VNS treatment, mean monthly seizure frequency before VNS, after VNS and after start of levetiracetam was assessed.

Results: 30/102 patients treated with VNS between March 1995 and April 2005 were additionally treated with levetiracetam. Data on seizure frequencies were available in 26/30 patients. Mean seizure frequency reduction after VNS was 34%. 9/26 patients (35%) had a seizure frequency reduction of >50%. After add-on of LEV, an additional mean seizure frequency reduction of 25% was seen. 1/26 patients (4%) became seizure-free, 7/26 (27%) had a seizure frequency reduction of >50%. Mean dosage of levetiracetam was 1850 mg. Side effects seen with VNS were mild and stimulation-related. 11/26 patients (42%) eventually stopped levetiracetam treatment because of lack of efficacy or side-effects.

Conclusion: Patients treated with VNS are considered to suffer from the most refractory epileptic seizures. This study showed a worthwhile improvement in seizure frequency in about one third of the patients treated with VNS when levetiracetam was added to their treatment regimen.

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E542
LAMOTRIGINE VERSUS LEVETIRACETAM IN THE INITIAL MONOTHERAPY OF EPILEPSY; FIRST RESULTS OF THE LALIMO-STUDY – AN OPEN RANDOMIZED CONTROLLED HEAD TO HEAD PHASE 3B TRIAL

F. Rosenow, S. Bauer*, P. Reif*, K. Klein*, H. Hamer*, C. Schade-Brittinger†, N. Burchardi†, Y. Weber‡, H. Lerche‡, S. Arnold§, A. Beige§, S. Evers¶, U. Reuner**, G. Winkler††, J. Springub§, M. Niedhammer§, E. Roth§, I. Eisensehr§, M. Schröder‡‡, and J. Berrouschot§§*
**Epilepsy Center Marburg, Germany; †Koordinierungszentrum Für Klinische Studien Marburg, Germany; ‡University Hospitals Ulm, Germany; §Neurological Private Practice,*

*Germany; ¶University Hospitals Münster, Germany; **University Hospitals Dresden, Germany; ††Leopoldina Krankenhaus Schweinfurt, Germany; ‡‡University Hospitals Regensburg, Germany; and §§Kreiskrankenhaus Altenburg, Germany*

Purpose: Immediate seizure control is important to prevent injury and deterioration of the patients socio-economic situation. Patients are likely to take AEDs for several years. The purpose of this study was to compare efficacy and tolerability of LTG and LEV in the initial monotherapy of patients aged 12 or above with epilepsy or a first seizure with high risk of recurrence.

Method: Open, prospective, randomized multicenter comparative 26 week study. Patients were titrated to an initial dose of 2000mg of LEV reached on day 22 or 200mg of LTG reached on day 71. Dose adjustments in up to two 500/50mg steps were allowed. The Primary endpoint: proportion of patients seizure free at 6 weeks. Secondary endpoints: seizure free patients during the last 16 weeks, time to first seizure, quality of life, safety/tolerability. The confirmatory analysis was based on ITT-population (primarily) and per-protocolpopulation using a two-sided Fisher's exact test (a=0.05).

Results: 410 patients were included by 58 centers. Data of 368 patients are currently available. Demographic data for the LEV/LTG groups were: n=187/181, mean age: 38.8/39.1; age 12–18: 16/14, age 18–60: 142/136; age≥60: 28/30, female: 87/89, male: 98/92; focal: 91/90, generalized: 63/67 or unclassified: 27/23 epilepsy; 1st seizure: 38/35 vs. epilepsy: 139/129.

Conclusion: This is the first randomized, prospective trial comparing LEV and LTG in the initial monotherapy of patients with newly diagnosed epilepsy or a first seizure and high recurrence risk. No differences in groups regarding population characteristics were present. Results regarding efficacy and safety will be presented.

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E543
LEVETIRAZETAM (LEV) AS ADJUNCTIVE THERAPY IN MYOCLONIC EPILEPSIES: EFFECT ON EEG ABNORMALITIES

S. Carrasco, C. Torres, M. Gallardo, M. Gudín, and J. Vaamonde
Ciudad Real General Hospital, Spain

Purpose: A retrospective, long-term, open study to evaluate the effects of LEV on electroencephalogram (EEG) abnormalities and photo paroxysmal response (PPR) of patients affected by different myoclonic epilepsies (ME).

Method: A retrospective open trial reviewing clinical histories and EEG of 13 (7/6:F/M) patients diagnosed of ME treated with LEV for more than 6 months was performed. The diagnoses of the patients were as follows: 5 patients had Janz syndrome, 2 Undverricht Lundborg syndrome, 2 other genetic ME, 1 ME postencephalitis, 1 ME post anoxia, 1 ME due to congenital toxoplamosis. 1 focal ME of cryptogenic origin. Patients EEGs pre and post LEV treatment were reviewed in order to evaluate changes on interictal epileptiform activity (IEA). Efficacy parameters were based on the comparison and analysis of EEG interictal abnormalities classified as spikes-and-waves, polyspikes-and-waves, and presence of PPR.

Results: Mean daily dosage of levetiracetam was 2220 mg/day. Prior to LEV treatment interictal EEG abnormalities were detected in 10/13 patients and PPR was determined in 5/13 of patients. After LEV treatment, 7/13 of patients had a normal EEG. Three out of 5 patients showed suppression of PPR. The patients improved the number of seizures and their myoclonic condition.

Conclusion: LEV appears to be effective in decreasing epileptiform EEG abnormalities, and suppressing the PPR in ME patients. This effect, along with a good efficacy and tolerability profile in this population further supports a first-line role for levetiracetam in the treatment of ME.

E544
PHARMACOKINETICS OF ESLICARBAZEPINE ACETATE AT STEADY-STATE IN ADULTS WITH EPILEPSY

E. Perucca, A. Falcão†, J. Maia‡, L. Almeida‡, and P. Soares-da-Silva‡*
**University of Pavia, Italy; †4Health Ltd, Cantanhede, Portugal; and ‡BIAL – Portela & Co, SA, S Mamede Do Coronado, Portugal*

Purpose: To evaluate the pharmacokinetics of eslicarbazepine acetate (ESL) at steady-state in adults with partial epilepsy participating in a 2-year open label extension of a phase III study.

Method: Blood samples for the pharmacokinetic assessment were taken at predose, and 1, 2, 3, 4, 6, 8, 12 and 24 postdose in 51 patients stabilized on chronic treatment with ESL 400 mg (n=7), 800 mg (n=26) or 1200 mg (n=18) once-daily. Patients were receiving one (n=21) or two concomitant AEDs (n=29), and one was on ESL monotherapy. Most frequent comedications were carbamazepine (n=34), valproate (n=19) and lamotrigine (n=8). Plasma concentrations of ESL and its metabolites were determined by liquid chromatography coupled to mass spectrometry.

Results: Plasma ESL concentrations were below the limit of quantification (50 ng/mL). The major compound in plasma was the active metabolite eslicarbazepine, which reached maximum concentrations between 1–6 h postdose (median=2h) and declined thereafter with mean apparent half-lives of 13h, 14h, and 20h in the groups treated with ESL 400, 800, and 1200 mg, respectively. Geometric mean (median) maximum plasma eslicarbazepine concentrations were 8.8 (7.6), 14.1 (15.8) and 22.3 (23.4) μg/mL, and area under the plasma concentration-time curve over the dosing interval were 113.8 (85.4), 184.7 (195.6) and 327.3 (323.0) μg.h/mL at ESL 400, 800 and 1200 mg once-daily, respectively. Eslicarbazepine Cmax/dose and AUC0-24/dose ratios showed dose-proportionality ($p>0.05$, Kruskall-Wallis test). R-licarbazepine and oxcarbazepine were minor metabolites, accounting for <10% of the molar sum of active compounds in plasma.

Conclusion: ESL showed approximately dose-proportional pharmacokinetics following oral administration of ESL 400 mg, 800 mg and 1200 mg once-daily to patients co-treated with 1 or 2 AEDs. ESL is rapidly converted to the active metabolite eslicarbazepine, which is the primary active compound found in plasma.

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E545
ANTICONVULSANT PROFILE AND TERATOGENICITY OF UREA DERIVATIVES OF BRANCHED ALIPHATIC ACIDS

J. Shimshoni, B. Yagen*, N. Pessah*, B. Wlodarczyk†, R. Finnell†, and M. Bialer**
**School of Pharmacy, The Hebrew University of Jerusalem, Jerusalem, Israel; and †Institute of Biosciences And Technology, Texas A&M Health Science Center, Houston, Texas, USA*

Purpose: The purpose of this study was to evaluate the anticonvulsant activity and teratogenic potential of branched aliphatic acylureas represented by isovaleroylurea (IVU), pivaloylurea (PVU) and 3,3-dimethylbutanoylurea (DBU), as potential second-generation drugs to valproic acid (VPA).

Method: The anticonvulsant activity of IVU, PVU and DBU was determined in mice and rats utilizing the maximal electroshock seizure (MES) and the pentylenetetrazole (scMet) tests. DBU was further examined in

the psychomotor 6Hz model and the hippocampal kindled rat model. The induction of neural tube defects (NTDs) by IVU, PVU and DBU was evaluated after i.p. administration at day 8.5 of gestation to a mouse strain susceptible to VPA-induced teratogenicity. The pharmacokinetics of DBU was studied following i.v. administration to rats.

Results: DBU emerged as the most potent compound having an MES-ED50 64mg/kg (55–74) and an scMet-ED50 and 26mg/kg (23–28) in rats. DBU underwent further evaluation in the hippocampal kindled rat (ED50=35mg/kg), the psychomotor 6Hz mouse model (ED50=80mg/kg (55–104) at 32mA and ED50=133mg/kg (108–172) at 44mA). In contrast to VPA, DBU, IVU and PVU did not induce a significant increase in NTDs as compared to control. DBU was eliminated by metabolism with a half-life of 4.5h.

Conclusion: DBU's broad spectrum and potent anticonvulsant activity, along with its high safety margin and favorable pharmacokinetic profile, make it an attractive candidate to become a new, potent and safe AED.

E546
PREGABALIN IN REFRACTORY LOCALIZATION-RELATED EPILEPSY: INITIAL FINDINGS FROM A PROSPECTIVE AUDIT

L. Stephen, K. Kelly, E. Wilson, P. Parker, and M. Brodie
Epilepsy Unit, Glasgow, UK

Purpose: Pregabalin (PGB) has been licensed recently in the UK for partial seizures with or without secondary generalization. We monitored its use as adjunctive treatment for refractory localization-related epilepsy.

Method: PGB was added to the antiepileptic drug (AED) regimen of 126 patients following a 3 month retrospective baseline. Patients reached an end point when one of the following occurred: seizure freedom for at least 6 months; 50% or <50% seizure reduction at optimal dosage; withdrawal of the drug due to adverse effects, lack of efficacy or both.

Results: Eighty-seven patients (69.0%; 44F:43M, aged 18–76 years, median 44 years) have completed the audit to date (36 on 1 AED, 38 on 2 AEDs, 11 on 3 AEDs, 2 on 4 AEDs). Ten (11.5%) patients became seizure free on a median daily PGB dose of 300mg (range 225–600mg). Sixteen (18.4%) had a 50% seizure reduction and 8 (9.2%) patients had a <50% seizure reduction. Only one of 10 patients, who had previously taken gabapentin, was controlled on adjunctive PGB. PGB was discontinued in 53 (42.1%) patients (28 adverse events, 15 lack of efficacy, 10 both). Commonest adverse events leading to withdrawal were weight gain (13); median 4.6kg, range 2.4–11.1kg), sedation (12) and ataxia (8). Of the 20 (15.9%) patients who gained weight, 7 elected to remain on PGB (median gain 6kg, range 3.4–9.2kg). Fifteen (11.9%) patients lost weight (median loss 2g, range 1–6kg).

Conclusion: PGB is an effective AED for refractory focal-onset seizures. Weight gain was the commonest side effect leading to withdrawal.

E547
OBSERVATIONAL LONGITUDINAL STUDY ON LATE SEIZURES IN NEUROSURGICAL PATIENTS

E. Bartolini, B. Lenzi*, P. Maritato*, R. Vannozzi†, A. Iudice*, L. Murri*, and G. Parenti**
**University of Pisa, Italy; and †University Hospital, Pisa, Italy*

Purpose: Late seizures are a frequent complication in patients who undergo neurosurgery, and can deteriorate postoperative quality of life. Evidence on the prophylactic anticonvulsant therapy after craniotomy is still limited.

Method: A 24- to 42-month observational longitudinal study was undertaken in patients with neurosurgical interventions and routinely treated with a prophylactic antiepileptic therapy, to evaluate late seizures onset or persistence and therapeutic response.

Results: To date, a total of 82 patients (median age 51.5 years) have been enrolled. Subjects underwent neurosurgery for gliomas (24), meningiomas (21), cerebral aneurysms (9) or metastasis (6), and other lesions. After discharge 95,1% subjects (n=78) were on antiepileptic monotherapy (52 phenytoin, 10 phenobarbital, 8 carbamazepine, 6 valproate, 1 clonazepam, 1 levetiracetam) and 4 (4,9%) patients on AEDs polytherapy. Six and twelve months after neurosurgical procedure all patients continued AEDs (polytherapy 10, monotherapy 72), but 51,2% (n=42) switched to an alternative monotherapy, due to inefficacy (20), intolerance (6), or both. At 32-month follow-up, 28 patients (34,1%) presented seizures; among them 14 subjects had had seizures before surgery, and 6 had presented early seizures.

Conclusion: This ongoing observational study shows that 17% of neurosurgery patients routinely given AEDs treatment develop late onset seizures, and a 17% continue to show seizures already present presurgically. In the large majority of patients (59%) the initial antiepileptic therapy has been changed to either alternative drugs or regimen (polytherapy), mostly due to lack of seizure control.

E548
STIRIPENTOL OPEN STUDY IN JAPANESE PATIENTS WITH DRAVET SYNDROME

Y. Inoue, Y. Ohtsuka†, H. Oguni‡, Y. Takahashi*, J. Tohyama§, H. Baba¶, K. Fukushima**, H. Ohtani*, and S. Ikeda††*
**Shizuoka Institute of Epilepsy and Neurological Disorders, Japan; †Okayama University, Okayama, Japan; ‡Tokyo Women's Medical University, Tokyo, Japan; §Nishiniigata Chuo Hospital, Niigata, Japan; ¶Nagasaki Medical Center, Nagasaki, Japan; **Yakumo Hospital, Hokkaido, Japan; and ††International University of Health And Welfare, Tokyo, Japan*

Purpose: On the background that only 15% of the treatment trials with 15 conventional antiepileptic drugs (AEDs) for 112 patients with Dravet syndrome succeeded to reduce seizures more than 50% (investigated in the 6 institutions of the Japan SMEI study group for the year 2006), we examined the effectiveness of stiripentol in an open label multicenter study to see whether it contributes to the treatment of this syndrome in Japan.

Method: Stiripentol (compassionate use) 50mg/kg was added upon at least one antiepileptic drug in 25 patients older than 1 year with more than 4 convulsive seizures per month. The seizure status of the second month after stiripentol add-on (early period) and of the long-term treatment period after dose adjustment was compared with that of the prestiripentol period. We checked also the adverse effects observed.

Results: In the early period, the seizures of 16 patients reduced more than 50%, including 3 patients who became seizure free. Moreover, the duration of the seizure shortened in 8 patients and status epilepticus disappeared in 2 patients. These effects continued in the long-term period though in less degree. The most often encountered adverse effects were loss of appetite, sleep disturbance, ataxia and hyperactivity that in most cases disappeared after dose modification of other AEDs.

Conclusion: We found stiripentol more effective than conventional AEDs in Japanese patients with Dravet syndrome and the adverse effects were manageable. An early introduction of this drug into Japan is desirable.

E549

PRESCRIPTION PATTERNS OF ANTIEPILEPTIC DRUGS IN SWEDEN

P. Mattsson, O. Eriksson†, G. Ringbaumlick†, and T. Tomson‡*
**Uppsala University Hospital, Sweden; †Center for Epidemiology, Swedish National Board of Health and Welfare, Sweden; and ‡Karolinska University Hospital, Sweden*

Purpose: The conditions for use of antiepileptic drugs (AEDs) have changed considerably with the introduction of several new drugs and with the extension of indications for some to include neuropathic pain, bipolar disorders, and migraine. The objective of this study was to analyze prescription patterns of AEDs in the Swedish population utilising the recently established national drug prescription register.

Method: We utilized the Swedish Prescribed Drug Register (SPDR), a nationwide database established in July 2005, which contains patient identities for all dispensed prescribed drugs to the entire Swedish population (9 million inhabitants). Data on prescribed individual AEDs was extracted from the SPDR for the whole population in the year 2007and analyzed for different age groups.

Results: Out of the entire population, 1.8% (n=160,825) was exposed to an AED. The proportion exposed was lowest among the youngest, 0.21% up to 4 years of age, and increased gradually by age. The highest exposure, 3.8%, was seen among the elderly, 75 years of age. However, prescription of AEDs measured as defined daily doses (DDD) per 1000 inhabitants daily was similar in middle-aged and older inhabitants. The type of prescribed AED also varied with age. Gabapentin, followed by carbamazepine, phenytoin, and pregabalin were the most prescribed AEDs in DDDs in people 75 years.

Conclusion: The proportion of the population exposed to AEDs varies with age. The high exposure among the elderly probably largely reflects prescribing for nonepilepsy indications, an interpretation supported by the high usage of gabapentin and pregabalin in this age group.

E550

ANTIOXIDANT THERAPY FOR DRUG RESISTANT POSTTRAUMATIC EPILEPSY PATIENTS, WHO HAD MODERATE TO SEVERE HEAD TRAUMA

M. Odinak, D. Dyskin, and M. Estuti
Kirov Military Medical Academy, Russia, St. Petersburg, Russia

Purpose: Efficacy for treating posttraumatic epilepsy (PTE) in patients who were with a history of moderate to severe head trauma.

Method: The analyzed group comprised 52 patients aged from 20 to 55 y/o with PTE (Temporal- 26, Frontal-13, Parietal-6, Occipital-7), who had a direct history of moderate to severe head trauma, and who were characterized of being drug resistant to pharmaco-treatment (partial and generalized epileptic seizures once a month and frequently) on the following basis: Cytaflavin – (I/V)10ml /24hrs. Mexidol- (I/M) 300 mg / 10 days. Later mexidol in tablet from, 250 mg / TID for 6 weeks. Espa-lipon-600 mg /OD for one month . All of the patients under went EEG and Neuro-visualization, also studied blood antioxidant results before and after the course of antioxidant treatment.

Results: After repeated EEG examination, we fond that their was a positive clinical effect in 65% patients had remission and curtailment of epileptic seizures (Accordingly 19% and 46%), they had a positive EEG results in the form of decreased or absent paroxsismal epileptic activity at rest. (Accordingly 10% and 37% of the patient had no positive in EEG after functional load. After this treatment there was positive result of certain activitics of the antioxidant system (TBARS,Glutatone erythrocyte, Glutathione Peroxidase, total antioxidant status serum) and decreased intensity of change for repeated neuro-visualization investigations while focusing in the epileptic activity, we registered positive dynamics at 3 natural metabolite levels (N-acetylaspartate,cholin,creatin) at proton magnetic resonance spectroscopy (MRS) and reliable decrease in the hypometabolism of the radionuclide glucose during positron emission tomography (PET).

Conclusion: (1) Complex antioxidant therapy allows substantial increase in effectiveness of the therapy in PTE patients, who had a history of moderate to severe head trauma. (2) Positive neuroprotective effect after antioxidant therapy in PTE patients, who had a history of moderate to severe head trauma. (3) Decrease in epileptic seizures after a course of antioxidant therapy, which reliably correlates with positive dynamic results of repeated MRS and PET.

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E551

LONG-TERM EFFICACY OF PREGABALIN TREATMENT IN PATIENTS WITH PARTIAL-ONSET EPILEPSY: POOLED ANALYSIS OF SIX LONG-TERM, OPEN-LABEL CLINICAL STUDIES

B. Emir, C. Bazil†, B. Uthman‡, and T. Leon**
**Pfizer Global Pharmaceuticals, New York, NY, USA; †College of Physicians And Surgeons, Columbia University, New York, NY, USA; and ‡Malcolm Randall VA Medical Center and University of Florida College of Medicine, Gainesville, FL, USA*

Purpose: Evaluate efficacy of long-term (LT) add-on pregabalin treatment in 6 open-label (OL) studies.

Method: 2061 patients from 6 LT studies received OL pregabalin (BID/TID) as add-on treatment for refractory partial-onset seizures. Inclusion criteria: males or females 12 years old, diagnosis of epilepsy with partial-onset seizures with or without secondary generalization. Primary efficacy parameter was percentage of patients with 50% reduction in frequency of all partial seizures during OL phase compared with baseline period for double-blind (DB) cohort. Adverse events were recorded.

Results: Median average of baseline seizures was approximately 9/28 days. 576 patients completed one of 6 OL studies. Total pregabalin exposure was 3877 person-years. 33.2% of patients withdrew due to lack of efficacy. Responder rate for all patients with prospective baseline seizure counts (n=1467) was 39.2% during first 3 months of OL treatment. During last 12 weeks of OL treatment, responder rate was 43.2%. For patients treated with pregabalin during DB trials and who were 50% responders (n=346), responder rate during first 3 months of OL treatment was 63.9%. For those not responding to pregabalin at end of DB trials (n=588), responder rate was 21.4% during first 3 months of OL treatment. 24%, 12%, and 6% of patients were seizure-free for 3-, 6-, and 12-month periods at any time during treatment. The most common AEs were dizziness and somnolence.

Conclusion: Long-term, add-on pregabalin treatment showed sustained efficacy for controlling partial-onset seizures in a highly refractory population. No new safety concerns emerged.

Study funded by Pfizer Inc.

E552

THE EFFECTIVENESS OF OXCARBAZEPINE AFTER SWITCH FROM CARBAMAZEPINE IN THE TREATMENT OF PARTIAL EPILEPSY EVALUATED IN DAILY ROUTINE MEDICAL PRACTICE IN POLAND. RESULTS OF A NATIONAL, OBSERVATIONAL 'E-PILL STUDY'

B. Majkowska-Zwoliñska‡,§, J. Jêdrzejczak, P. Zwoliński†, and M. Miczka¶*
**Medical Center For Postgraduate Education, Warsaw, Poland; †Neuronet Foundation, Warsaw, Poland; ‡Medical University of Warsaw, Poland; §Foundation of Epileptology, Poland; and ¶Novartis, Poland*

Purpose: An open-label, observational study has been conducted for assessment of safety and tolerability of oxcarbazepine (OXC) in 16 weeks after switch from carbamazepine (CBZ) in the treatment of partial epilepsy in routine clinical practice.

Method: The study based on a review of ambulatory records in 723 patients. Population consisted of:117 children (6–14 yrs), 37 adolescents (15–18 yrs) 506 adults (19–60 yrs) and 77 elderly (> 60 yrs), in whom adverse effects and/or unsatisfactory seizures control during CBZ therapy leaded to switch to OXC. Duration of epilepsy was > 1 year in 89% of patients and < than 1 year in 11%.

Results: The diagnosis of seizure type (based on 1989 ILAE classification) was: IA – 13%, IB- 27%, IC- 50% and combination of seizures – 10% of patients. The median dose of CBZ was 800 mg and the most frequent reason for switching was the unsatisfactory seizures control (70%). After 16 weeks from switching to OXC mean number of seizures during last 3 months was reduced from 8,5 to 2,8 per month* (67%) (* p=0,001) and the highest reduction was in group with IA type of seizure (80%). The median dose of OXC was 1200 mg. Adverse events were reported in 58 patients (8%) and were primarily headache, dizziness, and fatigue. Seven patients (1%) required treatment discontinuation.

Conclusion: This observational study provided data of the effectiveness of oxcarbazepine after switching from carbamazepine.

The study was supported by the Neuronet Support Foundation for People with Epilepsy an Novartis Polska.

E553
COGNITIVE AND EMOTIONAL EFFECTS OF PREGABALIN ADD ON THERAPY IN REFRACTORY EPILEPSY

E. Pauli, F. Kerling, and H. Stefan
**Epilepsy Center, University Hospital Erlangen, Germany*

Purpose: Chronic epilepsy is frequently associated with cognitive impairment and behavioral disturbances and thereby iatrogenic factors like negative side effects of medication are of importance. But also positive effects of medication on mood and behavior are possible. Pregabalin (PGB) is labelled for adjunctive therapy in partial epilepsy and also has anxiolytic and analgesic properties. In our study we examined emotional-affective and cognitive effects of PGB in 36 patients with partial epilepsy.

Method: We performed neuropsychological evaluation before treatment and four weeks after the target dose (300 mg twice a day) was reached. Tests included measurements for depression, anxiety, aggressiveness, short-term and long-term memory, selective awareness and cognitive speed.

Results: Twenty three patients finished the study, thirteen dropped out because of adverse events (n=6), compliance problems (n=5) and other reasons (n=2). There were no significant changes in the cognitive parameters and in emotional-affective variables, but persons with increased aggression scores at baseline showed a significant decline and patients with elevated anxiety at baseline showed a tendency to lowered scores.

Conclusion: We found no evidence for deterioration of cognitive or emotional-affective parameters during PGB-treatment. Patients with psychiatric co-morbidity may benefit from PGB add on therapy.

E554
PRELIMINARY DATA OF OPEN-LABEL STUDY ON LEVETIRACETAM MONOTHERAPY IN BRAIN TUMOR-RELATED EPILEPSY: SEIZURE CONTROL AND QUALITY OF LIFE

L. Dinapoli,†, M. Maschio*,†, B. Jandolo*,†, A. Fabi‡, A. Pace†, F. Sperati§, H. Schunemann§, and P. Muti¶*
**Center for Tumor-Related Epilepsy, National Institute for Cancer 'Regina Elena', Rome Italy; †Department of Neuroscience and Cervical-Facial Pathology, National Institute for Cancer 'Regina Elena', Rome Italy; ‡Department of Oncology, National Institute for Cancer 'Regina Elena', Rome Italy; §S.C. Epidemiology, National Institute for Cancer 'Regina Elena', Rome Italy; and ¶Scientific Direction of National Institute for Cancer 'Regina Elena', Rome Italy*

Purpose: To investigate the efficacy and safety of levetiracetam (LEV) monotherapy on seizure control and to assess quality of life and neurocognitive performances in patients with brain tumor-related epilepsy over 12 months.

Method: Twenty-nine patients with brain tumor and epilepsy were recruited. We present here preliminary data of 18 patients. Assessment of haematological parameters, frequency of seizure per month in the 2 months preceding the study, physical and neurological examination, neurocognitive and QoL tests were performed. Patients were evaluated by mini Mental State Examination (MMSE), Karnofsky Performance Status (KPS) and Barthel index (BI). Then they completed these tests: QOLIE 31P (V2), EORTC QLQ C30 and Adverse Events Profile. Conversion from other antiepileptic drugs to LEV monotherapy was initiated by introduction of LEV 250 mg BID. Dose was increased to 1000–3000 mg/day depending on seizure control and adverse events. Follow-up visit was at 6 months interval.

Results: Regarding seizure control, after 6 months sixteen patients were seizure free and 2 had reduction in seizure frequency >50%. This improvement was statistical significant (p=0.000). Compared to baseline we observed a worsening of performance (KPS p=0.011; BI=0.008) and lower global cognitive performance (MMSE p=0.011). Patients reported a significantly lower distress related to seizure frequency (p=0.003) and lower medication effects (p=0.046). We observed only mild and reversible side effects.

Conclusion: LEV monotherapy induced a good seizure control without significant side effects. Patients reported significantly lower distress related to seizures and lower medication effects of AEDs, despite a worsening of physical and neurological performances probably due to neoplastic progression.

E555
SEIZURE RISK ASSOCIATED WITH NEUROACTIVE DRUGS: A REPORT FROM WHO COLLABORATION CENTRE FOR INTERNATIONAL DRUG MONITORING

P. Lundberg, J. Strandell†, and E. Kumlien**
**Neurology, Uppsala University, Sweden; and †WHO Collaborating Centre for International Drug Monitoring, Uppsala, Sweden*

Purpose: Many drugs, especially neuroactive compounds, are known to reduce the seizure threshold and provoke epileptic seizures. A Collaborating Centre for International Drug Monitoring was set up by WHO in 1968 following the thalidomide disaster, and since 1978 the programme has been carried out by the Uppsala Monitoring Centre (UMC). The WHO database reports of Adverse Drug Reactions (ADRs) from healthcare providers in 79 member countries throughout the world. The purpose of this study was to make a survey of the WHO database concerning seizures events for a number of neuroactive drugs.

Method: A search for case reports of ADRs classified according to WHO adverse reaction terminology as convulsions, convulsions grand mal, convulsions local and convulsions neonatal was collected and compared to the total number of ADRs. Convulsion ADRs were further analyzed for drugs within the category nervous system according to the Anatomical Therapeutic Chemical (ACT) system. Thus neuroleptic, atypical neuroleptic, antidepressant, triptanes, anti-Parkinson, anxiolytic and miscellaneous neurotropic drugs were included.

Results: The total number of all kinds of ADRs was 7.375.325. Convulsion reactions reported was 71 469, i.e. 1% of all ADRs. The ten drugs most frequently reported to be associated with convulsions relative total number of ADRs were maprotilene (14.42%), escitaloprame (9.78%), clozapine (9.0%), chlorprothiexene (8.74%), amoxapine (8.74%) and donezepil (8.4%), rivastigmin (6.41%), quetiapine (5.9%), trimipramine (5.69%), and clomipramine (5.6%).

Conclusion: Epileptic seizures are rare ADRs of therapy of neuroactive drugs. Antidepressant and antipsychotic drugs are associated with the highest seizure susceptibility. Cholinomimetic drugs may also cause seizures.

E556

AMBIGUOUS RESULTS OF AN ATTEMPT TO WITHDRAW BARBITURATES IN EPILEPSY PATIENTS WITH INTELLECTUAL DISABILITY

B. Huber, M. Bocchicchio, I. Hauser, V. Horstmann, G. Jokeit, T. May, T. Meinert, E. Robertson, H. Schorlemmer, L. Schulz, W. Wagner, and M. Seidel
VBA Bethel, Germany

Phenobarbital and primidone frequently have adverse effects on mental functions. Therefore, an attempt was made to taper barbiturates in 85 patients out of a resident population with epilepsy and intellectual disability. The patients to undergo the tapering were carefully selected out of a sample of 191 patients on phenobarbital or primidone identified in 2004. Clinical criteria used for selection included, amongst others, a revision of treatment history, outcome of earlier taper attempts, an estimation of the patient's individual risk for seizure relapse or increase, and pharmacokinetic interactions between PB and concomitant medication. 4 months after complete withdrawal changes in seizure frequency were assessed as well as changes in cognitive abilities, psychological state and behavior (using the Clinical Global Impression Scale). In 13 patients (15.3%) the tapering failed due to complications. In many patients the tapering procedure actually lasted longer than originally planned (mean duration: 393 days). 25 patients (29.4% of the initial 85) showed improvement of cognitive abilities and/or seizure decrease after complete barbiturate withdrawal. 31 patients (36.5%) remained unchanged while 12 patients (14.1%) deteriorated in cognition or showed seizure increase. Stepwise logistic regression revealed a history of an attempt to withdraw phenobarbital/ primidone (p=0.017; OR 3.8), age (p=0.012) and seizure frequency (marginally significant: p=0.097) as independent outcome predictors. Older age was associated with better outcome. A high seizure frequency before tapering was related to good outcome, while seizure freedom was associated with negative outcome (failure or deterioration). Outcome did not depend on duration of barbiturate therapy, barbiturate dosage or serum concentration, comedication, reduction rate, degree of intellectual disability, or epilepsy syndrome.

E557

SCN1A IVS5N + 5 G-A POLYMORPHISM IN PATIENTS WITH EPILEPSY FROM MACEDONIA

Z. Sterjev, G. Kiteva†, A. Kapedanovska Nestorovska*, N. Matevska*, Z. Serafimoska*, A. Doneva‡, A. Dimovski*, and L. Suturkova**
**Institute for Pharmaceutical Chemistry, Faculty of Pharmacy Skopje, Republic of Macedonia; †Clinic of Neurology, Faculty of Medicine, Skopje, Republic of Macedonia; and ‡Clinical Hospital D-R Trifun Panovski, Bitola, Republic of Macedonia*

Epilepsy is a common neurological disorder, affecting approximately 1 to 2% of the world population. Approximately 30 X40% of adult patients remain refractory to antiepileptic drug, which is a major health problem. The mechanisms underlying treatment-resistant epilepsy are complex and each individual or group of individuals will undoubtedly display one or more unique reasons for their pharmacoresistance. Polymorphisms in genes that encode metabolic enzymes and drug transporters, are in some instances associated with result of drug therapy. In particular, the IVS5N+5 G'_A variant in the sodium channel gene (*SCN1A*) was implicated as a marker for individual response to carbamazepine therapy of epilepsy. Moreover, several studies indicated that mutations in the *fÑf*unit of the *SCN1A* gene are associated with familial and sporadic epilepsies. In order to investigate the influence of SCN1A IVS5N + 5 G'_A polymorphism on susceptibility and to the efficacy of carbamazepine therapy, we analyzed the allelic frequency and genotype distributions of this variant in 107 patients with epilepsy and 84 normal controls from the R. Macedonia. The SCN1A IVS5N + 5 G'_A polymorphism (rs3812718) was analyzed by allelic discrimination TaqMan assay. No statistically significant difference in the allelic frequency (0.49 and 0.54 for A allele, p=3097) and genotype distribution (0.25, 0.48, and 0.26, and 0.27, 0.54 and 0.17 for AA, AG and GG genotypes, p=0.1689) was determined between patients and controls, respectively. The influence of this variant on the efficacy of carbamazepine therapy in our group of patients is being currently evaluated and will be presented at the Congress.

E558

RETROSPECTIVE CASE SERIES OF BIRTH DEFECTS CAN PREDICT MALFORMATION PATTERNS ASSOCIATED WITH PRENATAL ANTIEPILEPTIC DRUG EXPOSURE

K. Flipsen-Ten Berg, C. van Oppen*, N. Wentges-van Holthe†, S. Bulk*, and D. Lindhout*,‡*
**University Medical Center Utrecht, Utrecht, The Netherlands; †Teratology Information Service, National Institute for Public Health and The Environment, Bilthoven, The Netherlands; and ‡Epilepsy Institute of Netherlands SEIN, Heemstede, The Netherlands*

Purpose: Pregnancy registers use prospective data to assess the risk of congenital malformations after prenatal exposure to antiepileptic drugs (AEDs). Retrospectively ascertained pregnancies may be used to study malformation patterns associated with specific exposures. We compared malformation patterns in retrospectively and prospectively ascertained pregnancies.

Method: We studied all cases with congenital malformations after prenatal AED exposure from the Dutch AED & Pregnancy Registry (1963–2007), classified according to ICD-10. This registry includes prospectively (<16th gestational week) and retrospectively ascertained cases.

Results: The Dutch AED & Pregnancy Registry included 3,052 pregnancies with AED exposure. The malformation rate was 76/731 (10.4%) in the prospective and 360/2,321 (15.5%) in the retrospective series. The mean number of malformations per malformed fetus was 1.7 in the prospective and 1.9 in the retrospective series. The relative frequency (RF) of malformations in this study differed from the pattern in the general population. Nervous system, ear and limb malformations were relatively more frequent. The increased RF of nervous system malformations was mainly due to spina bifida associated with valproate. Notably, there was no difference between the retrospective and prospective series with respect to the RFs of birth defects, including nervous system and limb malformations. Urinary system malformation were relatively more frequent with lamotrigine compared to other AEDs.

Conclusion: Retrospectively ascertained case series may help to detect an abnormal distribution of malformation patterns and thereby predict or add to prospective studies. Postmarketing studies of prenatal AED exposure should include rather than neglect retrospective data.

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E559

LONG-TERM SAFETY OF PREGABALIN TREATMENT IN PATIENTS WITH PARTIAL-ONSET SEIZURES: POOLED ANALYSIS OF SIX OPEN-LABEL CLINICAL STUDIES

A. Schulze-Bonhage, B. Uthman†, C. Bazil‡, E. Whalen§, T. Leon§, B. Emir§, and R. Benabou§*

**Epilepsy Centre, University Hospital, Freiburg, Germany; †Malcolm Randall VA Medical Center and University of Florida College of Medicine, Gainesville, FL, USA; ‡College of Physicians and Surgeons, Columbia University, New York, NY, USA; and §Pfizer Global Pharmaceuticals, New York, NY, USA*

Purpose: To evaluate the safety and tolerability of long-term (LT) add-on pregabalin treatment in open-label (OL) studies.

Method: 2061 patients in 6 LT studies received OL pregabalin (BID or TID) as add-on treatment for refractory partial-onset seizures. Males or females 12 years old, with a diagnosis of epilepsy with partial-onset seizures with or without secondary generalization, were included. All spontaneously reported or observed adverse events (AEs) were recorded.

Results: 576 patients completed one of 6 OL studies; 513 were de novo patients. Total pregabalin exposure was 3877 person-years. Of the 2061 patients who received OL pregabalin, 1891 (91.7%) experienced at least 1 AE, and 1590 (77.1%) experienced a treatment-related AE. 262 patients (12.5%) withdrew due to AEs; for 217 patients (10.5%), AEs leading to withdrawal were considered treatment-related. The most common AEs by frequency were dizziness (30.0%), accidental injury (25.3%), somnolence (22.8%), weight gain (20.8%), infection (20.2%), headache (18.2%), asthenia (17.6%), pain (14.6%), ataxia (12.1%), amblyopia (11.0%), and diplopia (10.0%). These were mild to moderate in intensity. The most common AEs causing discontinuations were somnolence (2.0%), dizziness (1.6%), weight gain (1.6%), and asthenia (1.3%). The most common AEs were observed within the first few months of OL treatment and tended to be transient. 28 patients died during these studies, but no deaths were considered related to pregabalin.

Conclusion: LT add-on pregabalin treatment for refractory partial-onset seizures was safe and well tolerated. No new safety concerns emerged.

Study funded by Pfizer Inc.

E560

INTRAVENOUS LEV AS THE FIRST-LINE TREATMENT OF STATUS EPILEPTICUS IN THE ELDERLY

J. Fattouch, C. Di Bonaventura*, E. Rosati‡, F. Bonini*, S. Petrucci*, G. Ricciardo Rizzo*, L. Lapenta*, M. Manfredi*,†, M. Prencipe*, G. Muscas‡, and A. Giallonardo**

**University of Rome 'La Sapienza', Italy; †Neuromed Institute of Pozzilli (IS) – University of Rome, Italy; and ‡Careggi Hospital, Florance, Italy*

Purpose: Status epilepticus (SE) is a serious condition of prolonged or repetitive seizures often occurring in the elderly. In old people its treatment can be complicated by serious side effects of traditional first-line drugs (cardiovascular/respiratory complications). Levetiracetam (LEV) i.v., a safe/well tolerated AED, can be considered an effective option in the therapy of SE. The objective of this study is to analyze the short-term efficacy and safety of LEV i.v. as the first choice in the treatment of SE in the elderly.

Method: We included in the study 10 consecutive old patients (8 women and 2 men, mean age 73 years) with SE which referred to our unit in the last 6 months. Since BDZ, PHT and PB were considered unsafe because of concomitant medical diseases, LEV i.v. was used as first-line therapy with a load dose of 1500 mg followed by a maintenance daily dose of 3000 mg.

Results: In all the cases SE was symptomatic in 8/10 (stroke in 6/10, tumor in 1, subdural haemorrhage in 1), two patients had a previous diagnosis of partial epilepsy. SE was convulsive in 7 patients, nonconvulsive in 3. Relevant medical conditions included arrhythmias, respiratory distress, hepatic disease. In all the patients LEV was effective in treating SE and determined a disappearance/significant reduction of the epileptic activity in few minutes after the administration. No serious adverse events were observed.

Conclusion: LEV is an effective and safe option in the therapy of SE in the elderly.

E561

PATIENTS 50 AND OLDER IN ADD-ON PREGABALIN EPILEPSY TRIALS: POOLED ANALYSIS

E. Ramsay, S. Giordano, T. Leon, and B. Emir

Pfizer Global Pharmaceuticals, New York, NY, USA

Purpose: Evaluate efficacy and safety of pregabalin as add-on treatment for partial seizures in patients over 50 years old.

Method: Data were pooled from 6 randomized, double-blind, placebo-controlled trials of add-on pregabalin treatment in patients with partial seizures (dosages: 150–600 mg/d, flexible- or fixed-dosage regimens, BID or TID). Patients were males or females ≥50 years old, with a diagnosis of refractory partial epilepsy. Percent change from baseline, responder rates, and seizure-freedom rates were evaluated for all pregabalin treatment groups combined vs placebo (all partial seizures considered). Assessed treatment-emergent adverse events (AEs).

Results: 335 intent-to-treat patients were ≥50 years old (n=31: pregabalin 150mg/d, 46: pregabalin 300mg/d, 101: pregabalin 600mg/d, 46: pregabalin flexible-dosage, 111: placebo). Mean age (56; range: 50–82) was similar across groups. Median baseline seizure rate (8) was similar across treatment groups. For percent change from baseline in seizure frequency, Hodges-Lehman estimate for treatment difference between pregabalin and placebo (-46.3%) favored pregabalin (95% CI: -56.9, -35). Proportion of 50% and 75% responders in the pregabalin treatment group (54.9%, 30.8%) was significantly larger vs placebo (15.3%, 2.7%; both $P<0.0001$). Significantly more pregabalin patients (16.9%) achieved seizure freedom during the last 28-day treatment period compared with placebo (4.7%, $P=0.0018$). Most common treatment-emergent AEs for pregabalin were: dizziness (35.3%), ataxia (21.9%), somnolence (21.0%), asthenia (15.2%), weight gain (13.8%). For placebo: asthenia (16.2%), dizziness (15.3%), headache (13.5%), somnolence (11.7%), nausea (6.3%).

Conclusion: Pregabalin as add-on treatment for partial seizures is safe and effective in patients over 50 years old.

Study funded by Pfizer Inc.

E562

POSTTRAUMATIC EPILEPSY: POOLED ANALYSIS IN ADD-ON PREGABALIN EPILEPSY TRIALS

T. Leon, S. Giordano, and B. Emir

Pfizer Global Pharmaceuticals, New York, NY, USA

Purpose: Evaluate efficacy and safety of add-on pregabalin treatment for partial seizures in patients with posttraumatic epilepsy in clinical trials.

Method: Data were pooled from 6 randomized, double-blind, placebo-controlled trials of add-on pregabalin treatment in patients with partial seizures (dosages: 150–600mg/d, flexible- or fixed-dosage regimens, BID or TID). Patients were males or females ≥12 years old with a diagnosis of epilepsy with partial seizures, posttraumatic etiology. Percent change from baseline, responder rates, and seizure-freedom rates at endpoint were evaluated in all treatment groups combined vs placebo (all partial seizures considered). Assessed treatment-emergent adverse events (AEs).

Results: 203 intent-to-treat patients had a posttraumatic epilepsy etiology (n=25: pregabalin 150mg/d, 26: pregabalin 300mg/d, 76: pregabalin 600mg/d, 11: pregabalin flexible-dosage, 65: placebo). Median age was 42.0 years (range: 16.0–82.0 years). Median baseline seizure rate ranged from 7.8–15.8. For percent change from baseline in seizure frequency, Hodges-Lehman estimate for treatment difference between pregabalin and placebo (-39.9%) favored pregabalin (95% CI: -54.9, -24.4). Proportion of 50% or 75% responders in pregabalin group (43.5%, 18.8%) was significantly greater compared with placebo (16.9%, 6.2%; p=0.0002, p=0.0125). More patients in pregabalin group (16.2%) achieved seizure freedom during the last 28-day period compared with placebo (5.4%, p=0.0504). Most common treatment-emergent AEs for pregabalin were dizziness (31.9%), somnolence (22.5%), ataxia (19.6%), asthenia (13.8%), accidental injury (12.3%); for placebo: somnolence (18.5%), dizziness (18.5%), asthenia (15.4%), headache (12.3%), accidental injury (10.8%).

Conclusion: Pregabalin as add-on treatment for partial seizures is safe and effective for patients with posttraumatic epilepsy.

Study funded by Pfizer Inc.

E563

THERAPY WITH SECOND-LINE ANTIEPILEPTIC DRUGS IN STATUS EPILEPTICUS: A RETROSPECTIVE REVIEW

D. Garcia-Alvarez, R. Marrero-Abrante, A. Gutierrez-Fernández, M. González-Lopez, Z. Mendoza-Plasencia, H. Pérez-Pérez, C. Croissier-Elías, J. Rojo-Aladro, M. Pueyo-Morlans, J. Pérez-Labajos, and P. De Juan-Hernández
Hospital Universitario Canarias, Tenerife, Spain

Purpose: Status epilepticus (SE) is a medical emergency requiring prompt diagnosis and early treatment. Benzodiazepines are a well established first-line therapy, but patients usually require a second-line anticonvulsivant. Phenytoin is the most frequently recommended but prospective data for second-line antiepileptic drugs (AEDs) are lacking. For refractory SE, continuous e.v. midazolam and propofol, separately or in combination, are rapidly effective. Our aim is to evaluate AEDs effectiveness and safety in SE management.

Method: We retrospectively studied clinical record of 27 patients who were admitted in our neurology department in last seven years (2000–2007).

Results: Most SE were convulsive (88%), refractory in 9 cases (33,3%). 74% presented a prior history of epilepsy. Infection and low serum drug levels were the most common risk factors. E.v. valproate was used as second-line AED in 18 patients and phenytoin in 11; seizures were aborted in 73% in both groups. Two patients treated with Valproate and phenytoin suffered hiperamoniemic encephalopathy. No other severe complications were recorded. Oral adjunctive medications were added in 51,8% (nine levetiracetam, three topiramate, two carbamazepine and one gabapentine). Nine patients required intensive care management with e.v. midazolam and propofol and 4 needed ventilator support.

Conclusion: In our study we did not find difference in SE seizures control between valproate and phenytoin. Both were effective in 73%. Tolerability between both groups did not differ, excepting valproate hepatotoxicity. Other case series suggest good efficacy of e.v. valproate in the treatment of different types of SE as second-line AED.

E564

LONG-TERM FOLLOW-UP STUDY ON EFFICACY AND SAFETY OF TOPIRAMATE (TPM) IN CHILDHOOD EPILEPSIES

P. Rasmini, and D. Besana
Neuropsichiatric Child Unit, Italy

Purpose: To evaluate efficacy and safety of topiramate in a open retrospective controlled observational survey.

Method: 67 patients (mean age 9.1 years, range 1 month to 18 years) treated with TPM in our Epilepsy Centre were retrospectively evaluated after a period ranged between 2 and 5 years. In 37 subjects TPM was added on for refractory epilepsies, 18 received TPM as first AED and 12 were converted to monotherapy. Efficacy was valuated in term of seizures free or >50% seizures reduction. Epilepsy types were classified according to I.L.A.E criteria. Retention to TPM treatment was examinated at 2 and 5 years and reasons of discontinuation were analyzed.

Results: 53 patients were initial responders; retention rate at 2 years was 49% and 35% at 5 years. 25 subjects are still receiving TPM and seizures free. Main group of patients discontinued the drug because of inefficacy and usually in course of comedication, side effects determined the drug discontinuation in a very small number of cases.

Conclusion: In our experience topiramate confirmed efficacy and good tolerability also in long term retention particularly in monotherapy.

E565

HABITAUTION IN FETUSES EXPOSED TO ANTIEPILEPTIC DRUGS

C. Lynch, P. Hepper, and J. Morrow
Queens University, UK

Purpose: Selected antiepileptic drugs have been associated with higher risk of congenital anomalies and with impaired cognitive development. Since behavior directly reflects neural function and integrity, observation of the behavior of the fetus provides insights into the functioning of its brain. Habituation may be one technique that, requiring the participation of sensory and motor processes and the involvement of the cerebral cortices, enables the performance of the fetus's brain to be evaluated.

Method: Mothers taking antiepileptic drugs carbamazepine (n=13), lamotrigine (n=11), valproate (n=13). were referred from the UK Epilepsy and Pregnancy Register Mothers not taking antiepileptic drug (n=16) were recruited from clinics at RJMS. Fetal habituation was examined using a Corometrics vibroacoustic stimulator as the stimulus sound.

Results: At 31 weeks gestation there was a significant effect of group [f, (3, 54) =70 3.214, p=0.030). Post hoc tests showed that fetuses exposed to carbamazepine took significantly longer to habituate (p=0.004) than fetuses of mothers not exposed to carbamazepine. Post hoc tests also revealed that fetuses in the carbamazepine group were significantly different (p=0.029) than those in the lamotrigine group and habituation scores in the valproate group were almost significantly different (p=0.074) than those in the carbamazepine group.

Conclusion: Habitaution performance is affected by antiepileptic drugs, and these effects are drug-specific.

E566

INTRAVENOUS LEVETIRACETAM IN SEIZURE EMERGENCY SITUATIONS INCLUDING STATUS EPILEPTICUS.

J. Dobesberger, G. Brössner, I. Unterberger, G. Walser, R. Ehling, K. Seppi, E. Schmutzhard, and E. Trinka
Innsbruck Medical University, Germany

Purpose: Status epilepticus (SE) and seizure clusters are emergency situations, which require immediate and effective treatment. To date, intravenous (IV) benzodiazepines (BZD), IV phenytoin (PHE) and IV

valproic acid (VPA) are widely used antiepileptic drug (AED) therapies in these situations. This study aimed to investigate the efficacy and tolerability of IV levetiracetam (LEV) in the treatment of SE and seizure clusters.

Method: All patients treated with IV LEV between August 2006 and February 2008 were retrospectively analyzed. Indications for IV LEV were (1) premonitory SE with seizure clustering in 18 patients, (2) nonconvulsive SE (NCSE) refractory to first-line therapy in 12 patients, and (3) IV LEV rapid loading after successful treatment of NCSE in ten patients. Dose, responsiveness and adverse events were evaluated.

Results: Forty patients (21 men, median age 54±29 years) treated consecutively with IV LEV were analyzed. The mean loading dose was 962±177mg IV LEV, the mean maintenance dose over the next 24 hours was 1000±623mg IV LEV. Outcome: In 17/18 patients, IV LEV was effective in terminating seizure clusters. NCSE could be terminated successfully with IV LEV in 7/12 patients, in three patients, SE was terminated with other IV AED therapies, two patients were resistant to all therapeutic attempts. In ten patients with rapid loading of IV LEV after NCSE, no relapses occurred. No side effects were observed.

Conclusion: These data suggest that IV LEV can be used as a safe and effective alternative to standard IV AED treatments for seizure emergency situations, although larger studies are required to confirm these findings.

E567
EFFICACY OF LEVETIRACETAM IN THE TREATMENT OF DRUG RESISTANT RETT SYNDROME

N. Specchio, M. Cilio*, R. Nardello†, G. D`Orsi‡, S. Patanè§, M. Margiotta¶, P. Striano**, S. Striano**, S. Russo††, L. Fusco*, D. Claps*, and F. Vigevano**

**Division of Neurology, Bambino Gesù Children's Hospital, Rome, Italy; †Child Neurology and Psychiatry, University of Palermo, Palermo, Italy; ‡Epilepsy Center, Opera Don Uva, Biseglie (BA), Italy; §Child Neurology and Psychiatry, ASL LE/1, Lecce, Italy; ¶Child Remedial Service, ASL LE/2, Lecce, Italy; **Epilepsy Center, Federico II University, Napoli, Italy; and ††Medical Genetics, Italian Auxetic Institute, Cusano Milanino (MI), Italy*

Purpose: Epilepsy is reported to occur in 50 to 90% of patients with Rett Syndrome (RTT). The aim of this study is to report the efficacy of levetiracetam (LEV) in drug resistant patients with RTT.

Method: This was a prospective, pragmatic, open-label study consisting of an 8-week baseline period and six months of evaluation period. Adverse events were recorded. Efficacy variable was the mean monthly seizures frequency before and after LEV.

Results: Eight female patients, aged 7.5–19 years (M12.8"b5), entered the study. Mean age at the epilepsy onset was 29.6 ± 21.2 months. All patients showed MEcP2 mutation. Patients have been treated with a mean of 3.4 AEDs (2–7) before LEV. Two patients had been previously treated with Hydrocotison. The mean LEV dose was 1780+795 mg/day. Concomitant AEDs were: valproate in 4 cases, carbamazepine in 1, topiramate in 1, valproate plus oxcarbazepine in 1, and lamotrigine plus carbamazepine in 1. The mean monthly seizure frequency for all seizures type during the baseline period was 21.3+8.1 (range 10–35), and after LEV treatment was 1.5+1 (range 0–5) $p<0.01$. The mean follow-up duration was 20.2+13 months. EEG evaluations showed multifocal and diffuse abnormalities in all patients. Interictal EEG epileptiform abnormalities were reduced in 5 out of 8 patients. Mild sleepiness occurred in two patients, one reported intermittent agitation.

Conclusion: Levetiracetam seemed to be effective in our series of drug resistant RTT patients. All of them reported a reduction of seizures frequency, an improvement of attention and consequently a better quality of life also for caregivers.

E568
EFFECTIVENESS OF LEVETIRACETAM AS ADD-ON THERAPY IN PATIENTS WITH PARTIAL REFRACTORY EPILEPSY

I. Kuzmanovski, E. Cvetkovska, and D. Petrovska Cvetkovska

Clinic of Neurology, Skopje, Macedonia

Purpose: Levetiracetam (LEV) is new generation antiepileptic drug, currently used as add-on therapy for partial-onset seizures. To evaluate the effectiveness of LEV in patients with partial refractory epilepsy.

Method: Twenty-one patients with refractory partial onset-epilepsy, who received LEV as an add-on treatment, were evaluated in this open, prospective study. Group consisted of 13 females and 8 males, aged 15–45y., mean 27,1y. The average duration of epilepsy was 14, 7 years; the average seizure rate was 25 per month. The patients were treated for 9, 5 months with an average dose of 1760 mg LEV per day.

Results: One (4, 8%) patient became seizure free, more than 50% reduction in seizure frequency occurred in nine (42, 8%) patients after introduction of LEV. In 47, 6% no significant changes occurred and in one patient (4, 8%) aggravation was observed. Most frequent side effects were: drowsiness in 9, 6% and aggression and agitation in the same proportion of patients.

Conclusion: The results of our study are concordant with the previous ones, suggesting that LEV is effective new generation antiepileptic drug, who improves seizure control in significant percent of patients with intractable epilepsy.

E569
THE ROLE OF LEVETIRACETAM IN TREATMENT OF STATUS EPILEPTICUS: REVIEW OF 77 PATIENTS

B. Feddersen, M. Einhellig, C. Vollmar, J. Remi, C. Stoyke, and S. Noachtar

University of Munich, Klinikum Grosshadern, Germany

Purpose: Status epilepticus (SE) is a medical emergency which can lead to significant morbidity and mortality and requires prompt diagnosis and treatment. We wished to assess the efficacy of the new antiepileptic drug levetiracetam (LEV) in SE.

Method: We reviewed the database of the Department of Neurology of the University of Munich from 1/2000 to 10/2007 for all patients with SE who received LEV. We evaluated patients with 'severe' SE, which required ICU treatment and 'moderate' SE, which were treated at general neurological wards.

Results: We identified 410 patients with SE, 77 of these were treated with LEV (12% iv application). The status treatment included benzodiazepines and phenytoin prior to LEV in all patients, unless these drugs were contraindicated in selected patients (n=17).) In 63 of 77 patients (82%) SE ceased with treatment; in 32 patients (42%) LEV was considered the antiepileptic drug leading to SE cessation (mean dose of 3 g/d). The rate of succesfull status cessation was significantly higher in moderate SE (24 from 36 (66%)) than in severe status treated at the ICU (8 from 41 (21%)); $p<0,05$. The rate of status cessation was not significantly higher in patients with de novo SE (19 from 38 (50%)) than in patients with a known history of epilepsy (13 from 39 (33%). The response of NCSE vs CSE to LEV treatment was not significantly different in our patient group (39% vs 54%).

Conclusion: LEV seems to be efficacious in SE particularly in patients with SE not requiring ICU treatment.

E570
ERECTILE DYSFUNCTION INDUCED BY TOPIRAMATE: AETIOLOGY AND TREATMENT

C. Civardi, A. Collini*, P. Gontero†, R. Cantello*, and F. Monaco**
**Università Del Piemonte Orientale 'A. Avogadro', Novara, Italy; and †Urology Unit. Università Degli Studi Di Torino, Torino, Italy*

Purpose: Topiramate (TPM), is a new and effective antiepileptic drug. Recently reversible erectile dysfunction (ED) induced by TPM has been reported. Its mechanism of action has not been explored yet. We describe a patient who complained of ED during TPM treatment and we studied its possible mechanism of actions.

Method and Results: 48-year-old patient with drug resistant temporal lobe epilepsy. TPM was added to carbamazepine. After one month at dosage of 300 mg/daily patient complained about ED. He never had experienced ED before. During TPM therapy, Sildenafil on demand, temporarily reverse ED. After TPM discontinuation sexual function was completely restored within two weeks. Sexual hormone serum levels did not changed before and after the interruption of TPM.

Conclusion: This unusual side effect of TPM was previously explained as a direct actions of the drug on sexual hormones level. Unfortunately none of the authors performed these determination. In our patient TPM did not influenced sexual hormones blood profile. Thus TPM reversible ED is a relatively rare and unrelated to changes in sexual hormones level. We propose two mechanisms: (1) impaired neurotransmission, which may be responsible for the dampening of the sexual response. (2) As other carbonic anhydrase inhibitor TPM could induce ED acting on VIP and nitric oxide through a peripheral reduction in genital blood. Thus the impaired tumescence could be related to a vasogenic erectile dysfunction, the positive response to Sildenafil may support this view.

E571
ELECTROCARDIOGRAPHY PARAMETERS IN PATIENTS WITH LAMOTRIGINE AND VALPROATE MONOTHERAPY OR DUOTHERAPY-INTERIM REPORT

M. Spasic, M. Mihajlovic, and S. Lukic
Clinical Centre Nis, Serbia

Purpose: To explore electrocardiography (ECG) parameters in patients with monotherapy or duotherapy with lamotrigine (LTG) and valproate (VPA).

Method: Prospective analysis of standard resting 12- leads ECG parameters in patient with LTG) and VPA monotherapy as well as LTG and VPA combination therapy.

Results: We analyzed ECG parameters in 8 patients with VPA monotherapy (V group), 4 patients with LTG monotherapy (L group) and 11 patient with LTG and VPA duotherapy (VL group). Patients age were 36.00 ± 11.48, 42.50 ± 16.50 and 43.45 ± 9.19 for V, L and VL groups respectively. Mean daily doses of VPA were 687.50 ± 221.60 mg and 1500.00 ± 813.94 mg for V and VL group respectively. Mean daily doses of LTG were 262.50 ± 75.00 mg and 272.73 ± 125.23 mg for L and VL group respectively. Main differences was notify for duration of PQ interval: 137.25 ± 17.63 ms, 152.00 ± 22.45 ms, and 138.80 ± 13.54 ms for V, L and VL group respectively. Also there're similar subsequent differences for QRS, QT and QTC intervals of ECG in investigated groups.

Conclusion: Our findings could indicate potential difference effects of VPA and LTG on ECG findings, but clinical, diagnostic and therapeutic significances must not be considerate without respects to confounding variables. Further studies are warranted for definitive conclusions.

E572
PATIENT-PERCEIVED DRUG RELATED COGNITIVE IMPAIRMENT OF LOW-DOSE TOPIRAMATE MONOTHERAPY IN EPILEPSY PATIENTS: A 1-YEAR FOLLOW-UP

S. Lukic, and M. Spasic
Clinical Centre Nis, Serbia

Purpose: The present study was conducted to evaluate the long-term effects of low dose topiramate (TPM) monotherapy on the patient- perceived drug related cognitive impairment.

Method: Prospective open study in patients with newly diagnosed cryptogenic epilepsy on monotherapy with TPM. Patients had to be >18 years, of normal intelligence, with adequate clinical, neurophysiologic and neuroradiology assessment. Exclusion criteria were psychiatric history or current psychiatric treatment; treatment with other antiepileptic drugs or other concomitant medication. Neurotoxicity scales II testing was performed twice, at baseline and 1 year after starting medication.

Results: Thirty seven epilepsy patients received TPM monotherapy, with daily doses of 50, 75, and 100 mg/day. Twenty six patients completed the follow up questionnaire assessment. After a year of treatment, sixteen patients (61.54%) complained of cognitive problems. Although it improved seizure frequency and EEG abnormalities, TPM had meaningful negative impact on the patient-perceived drug related cognitive impairment. These cognitive influence were dose related and consequential improved after withdrawal from TPM and substitution with older antiepileptic drugs.

Conclusion: Even at a low dose, TPM has long term, negative effects on patient- perceived drug related cognitive impairment.

E573
ONE YEAR EXPERIENCE WITH ZONISAMIDE; EFFICACY AND TOLERATILITY IN OUTPATIENT CLINICAL PRACTICE

A. Oliveros Cid, J. Mauri†, V. Bertol Alegre‡, A. Oliveros Juste§, and I. Perez Lopez-Fraile‡*
**Servicio De Neurologia, Clínica Quiron, Zaragoza, Spain; †Servicio De Neurologia, Hospital Clinico Universitario, Zaragoza, Spain; ‡Servicio de Neurologia, Hospital Miguel Servet, Zaragoza, Spain; and §Servicio De Neurologia, Policlinica Sagasta, Zaragoza, Spain*

Purpose: Antiepileptic drugs (AEDs) suppress seizures by selectively modifying the excitability of neurons and blocking seizure firing with minimal disturbance of nonepileptic activity, through several mechanisms of action: modulation of voltage-gated ion channels, enhancement of synaptic inhibition, and inhibition of synaptic excitation. Zonisamide is a novel AED that has a broad combination of complementary mechanisms of action, which may offer a clinical advantage over other antiepileptic agents. Therefore, it seems that from the multiple pharmacological actions observed, zonisamide should contribute to similar seizure reduction in clinical practice as observed in controlled studies.

Method: 162 adult neurology patients (83 men, 79 women) treated with zonisamide were recorded through an analysis chart; all them received zonisamide, initially as adjunctive therapy, for at least 12 months. The addition of zonisamide was decided because of lack of efficacy or tolerability with previous AEDs. The average duration of treatment was 13.3 months (range, 12–16 months), and the average zonisamide dosage was 314 mg/day (range, 100–600 mg/day).

Results: 38 patients (23.45%) were seizure-free, 34 (20.98%) had >75% seizure frequency reduction, and 42 (25.92 %) had a 50 – 75 % seizure frequency reduction at the last follow-up visit. 44 patients (27.16%) reported mild to moderate adverse events, such as weight loss (5.55%),

fatigue (6.79%), and sedation (8.64%). No severe adverse effects were reported. 10 patients (6.17 %) discontinued zonisamide due to adverse effects.

Conclusion: Zonisamide, as adjunctive therapy, is a safe, effective, and well-tolerated long-term treatment option in refractory patients with various seizure types.

E574
DO THE SIDE EFFECTS OF TOPIRAMATE CAUSE SPECIFIC LEARNING DIABILITIES?

H. Mayer
Epilepsy Centre, Germany

Purpose: Topiramate is one of the newer antiepileptic drugs, which has shown its efficacy not only in adults but also in children. There are a lot of convincing data of high rates of clinical side effects like dizziness, drowsiness. Neuropsychological and behavioral disorders has been reported especially in adult patients. In children such data are lacking. The objective of this study, based on single case analysis, was to identify neuropsychological side effects in children and adolescents.

Method: The study group comprised 16 children up to 16 years of age (6 males, 10 females) with different types of epilepsy. TPM was administered as add-on therapy to the baseline treatment. Patients has been investigated neuropsychologically with different measures at least 2 times, i.e. before treatment and after target dose was reached or in the course of the treatment and after the withdrawal because of clinical side effects (drowsiness, speech problems and s.o.). The neuropsychological assessment comprises the following tests test: WISC III, KAB-C, language-test (HSET), digit combining test, digit cancelling test, digit-symbol-test. The collected data were analyzed in a single case manner, that means each patient was its own control.

Results: The pre-post comparisions of IQ-scores show a significant decrease (1SD) after introducing or an increase in the case of a withdrawal. The main changes were observed in speed dependent subtests, language subtest and working memory (WISC/KAB-C). Also attentional functions including mental speed were adversely affected by the treatment with TPM. The pattern of side effects are different between the young patients. Twelve of 18 patients had a previous history of behavioral and neuropsychological deficits. The side effects do not appear to be related to the dosage.

Conclusion: TPM has an important adverse impact on different neuropsychological functions, which are very important for school performance. These changes are reversible after discontinuation, that means, the side effects cause only transient learning disabilities.

E575
RECURRENT PLANTAR FIBROMATOSIS CAUSED BY ONGOING PHENOBARBITAL TREATMENT

A. Strzelczyk,†, H. Vogt*, H. Hamer†, and G. Krämer**
**Swiss Epilepsy Centre, Zürich, Switzerland; and †Philipps-University Marburg, Germany*

Purpose: Despite contrary recommendations by expert opinion and international guidelines phenobarbital remains the most widely prescribed anticonvulsant worldwide. However, not only in developing countries where it is a cost-effective and affordable anticonvulsant but also in industrialized countries it remains a popular choice for epilepsy treatment. Connective tissue disorders associated with phenobarbital and later its derivative primidone were described timely after introduction of phenobarbital, yet, the association between plantar fibromatosis – also called Ledderhose's syndrome – and phenobarbital seems not be well known in general.

Method: We present three cases with phenobarbital induced plantar fibromatosis seen in our department from 2000 to 2007. All patients were analyzed regarding epilepsy syndrome, seizure type, AEDs and outcome after discontinuation of phenobarbital. Risk factors and susceptibility to develop fibromatosis were reported and compared to literature.

Results: Our case series uniquely demonstrates that ongoing PB treatment leads to recurrent plantar fibromatosis and may result in long-term disability and numerous unnecessary operations. In view of the ongoing important role of PB in treatment of epilepsy we aim to draw attention to this rare side effect. In general, the association between connective tissue disorders and phenobarbital most prominently appears in adult patients of northern European descent. However our case series and data from the literature suggest that patient groups less susceptible to connective tissue disorders as children and non-Caucasians may as well develop Ledderhose's disease or other associated syndromes as Dupuytren's contractures, frozen shoulder, Peyronie's disease or complex regional pain syndrome in the course of phenobarbital treatment.

E576
CONGENITAL MALFORMATIONS IN CHILDREN OF EPILEPTIC MOTHERS. DATA FROM PINAR DEL RIO EPILEPSY PREGNANCY OUTCOMES MULTICENTER STUDY

J. Riol Lozano, A. Garcia Medina*, J. Rodriguez Garcia*, E. Cruz Menor*, N. Arteche Diaz*, and J. Garcia Fidalgo†*
**Epilepsy Section, Abel Santamaria University Hospital, Pinar Del Río, Cuba; and †Epilepsy Section, National Institute of Neurological Disorders, Havna, Cuba*

Background: Incidence of congenital malformations (CM) in children of epileptic mothers (EM) is higher than general population having multifactorial origen.

Objective: Know frequency of CM in children of EM some risk factors related.

Method: Prospective study 370 children of EM carried out Jan 1997 – Jan 2007, a form designed to register demographic, clinical and genetic data final results were recorded on data base to make statistical analysis, results were compared to a control group of 500 children from nonepileptic mothers (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%) ($P < 001$). 37.5% of MC were diagnosed in children from EM with toniclonic seizures during first trimester of pregnancy.

Conclusion: CM more frequent in children from EM use of DAEs in pregnancy, polytherapy, high doses and seizures during first trimester are some risk factors of CM in children from EM.

E577
NONCONVULSIVE STATUS EPILEPTICUS IN CHILDREN, ELECTROCLINICAL PROFILES, EVALUATION OF ORAL AND IV TREATMENT IN 40 CHILDREN AT DHAKA SHISHU (CHILDREN'S) HOSPITAL

S. Banu,‡, M. Mahbub†, A. Mosiul†, S. Rani‡, and N. Khan†*
**Institute of Child Health, Mirpur, Dhaka, Bangladesh; †Dhaka Shishu (Children's) Hospital, Bangladesh; and ‡Comfort Diagnostic Center, Dhaka, Bangladesh*

Introduction: Nonconvulsive status epilepticus (NCSE) is an underdiagnosed neurological condition. We are reporting the electroclinical profile and the result of a protracted treatment in forty children.

Method: Cases were identified at the EEG laboratory from 2004 to 2007. Initially treated with oral or conventional IV antiepilepsy drugs (AED) in some cases. Daily EEG recording for 30 minutes was performed for each till over 80% of epileptiform discharges removed and the baseline functional states were achieved. In absence of electro-clinical response to conventional treatment a protracted management with infusion diazepam or midazolam for 12 hours was introduced on hospital admission. Oral AED was continued, children were followed up at the epilepsy clinic for 3 months to 3year.

Results: All presented with altered psychomotor, speech or behavior state lasting for 1 wk to several months, over 80% were on oral AED (s) during diagnosis. Unprovoked seizure was reported in 37%. Generalized (80%) or localized (18%) slow spike-wave discharges were found on the first EEG records. Conventional treatment was not sufficient in 34, protracted treatment introduced in 28, six families denied IV treatment. Target was achieved in 73% on discharge, during follow ups recurrent NCSE occurred in 18%.

Conclusion: NCSE is common in children, may occur de novo. Protracted treatment with slow infusion DZP or MDZ and titration based on electro-clinical evaluation by daily EEG may be a solution for the resource poor countries to monitor treatment effect. Further study with RCT is needed.

E578
COMPLIANT; A SURVEY COMPARING NEWER AND CLASSIC ANTIEPILEPTIC DRUGS IN 907 EPILEPSY PATIENTS IN GERMANY

A. Haag, S. Kühne†, G. Lippert‡, and F. Rosenow**
**Epilepsy Center Marburg, Germany; †Sanofi-Aventis Deutschland GmbH, Germany; and ‡Practice for Neurology and Psychiatry, Lahnstein, Germany*

Background: Data comparing classic and newer AEDs regarding compliance, quality of life (QoL) and occupational status are sparse. These aspects of epilepsy treatment were assessed in a prospective survey conducted in 2006.

Patients and Method: Data regarding 907 epilepsy outpatients, 45.9% female, mean age 44.8 years, were ascertained by 95 neurologists filling in data entry forms in the patients presence. Participating physicians were also involved in a noninterventional study of Ergenyl ChronosphereÒ by Sanofi-Aventis Deutschland GmbH. Epilepsy and treatment duration, seizure type, AED-doses, occupational status and the patients acceptance of the AEDs and QoL were documented.

Results: 51.0% had generalized tonic–clonic, 30.9% complex and 11.4% simple partial seizures. Epilepsy duration was 15.3years. 69.7% of the patients received monotherapy. 25.4% received two, 4.5% three and 0.4% four AEDs in combination. Partial seizures were treated more frequently with combination therapies (34.1%) as compared to generalized tonic–clonic seizures (27.2%). Mean treatment duration was longest for carbamazepine (8.4yrs) and valproate (5.4yrs). For other drugs it was between 1.6 (topiramate) and 2.7 (lamotrigine and oxcabazepine) years. 58.9% were working for a mean of 34.7 hours/week. The patient's acceptance of the AEDs was rated by the physicians to be; good or very good; independent of the medication. Patients QoL was between good and satisfying (2.34). I t was worse on combination therapy than on monotherapy.

Conclusion: The classic AEDs with the longest treatment durations were associated with the same acceptance and quality of life as compared to the newer AEDs.

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E579
THE TIME COURSE OF DEINDUCTION OF LAMOTRIGINE AND TOPIRAMATE WITH CARBAMAZEPINE AND PHENYTOIN

E. Ramsey, S. Marino†, A. Birnbaum†, B. Gidal§, R. Nemire‡, J. Cloyd†, and F. Pryor**
**Int'l Center for Epilepsy, University of Miami, Miami, FL, USA; †University of Minnesota, Minnesota, USA; ‡Touro University, California, USA; and §University of Wisconsin, Milwaukee, USA*

Purpose: Two commonly used enzyme inducing AEDs (EIAEDs) are carbamazepine (CBZ) and phenytoin (PHT). Primary metabolic pathway for TPM is CYP 3A4/5 and for LTG is UGT. Enzyme induction is the increase in quantity or activity of a cytochrome (CYP) enzyme. This results in increased drug clearance and a lower drug plasma level. Induction requires 2–4 weeks to achieve maximum effect. Deinduction is the lost of this effect with drug clearance returning to baseline. The purpose of this project is to determine the time course and the dose at which the induction effect is lost for drugs metabolized via the P450 and UGT pathways.

Method: Patients selected for the study were on stable doses of one of the enzyme inducing AEDs (CBZ or PHT) and were also taking either LTG (20 patients) or TPM (20 patients). Patients were included who were to have the EIAED discontinued. Unit dose reduction was done biweekly (PHT 100 mg, CBZ 200 mg) and plasma samples were obtained biweekly during the taper. Plasma samples were collected three times a week for two weeks after the inducer was stopped and then weekly for three more weeks. Plasma concentrations were assayed using HPLC.

Results: Mean clearances values for LTG/TPM were 127.4/85.1 L/day at baseline, 73.1/61.3 L/day on last day of de-induction and 48.2/40.0 L/day at the end of study. The percent change and time course for the de-induction was similar LTG and TPM and no difference in effect was noted between CBZ and PHT.

Conclusion: CBZ and PHT are strong inducers of metabolism of LTG and TPM. Approximately 50% of induction is lost during the taper and de-induction is complete by two weeks after the inducer clears the system.

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E580
IMMUNOTHERAPY IN CHILDREN WITH RASMUSSEN ENCEPHALITIS

R. Kravljanac, N. Jovic†, M. Djuric*, and D. Zamurovic**
**Institute for Mother and Child Health of Serbia,Belgrade, Serbia; and †Clinic for Neurology and Psychiatry for Children and Youth, Belgrade, Serbia*

Purpose: To evaluate response to immunotherapy in children with Rasmussen encephalitis (RE).

Method: The study included 10 children with RE according diagnostic criteria of a European consensus statement (2005). In addition to antiviral and antiepileptic drugs, the patients were treated by immunotherapy: corticosteroids (10), IVIG (7), plasma exchanges followed by ciclophosphamide (1), thalidomide (3) and tacrolimus (1). In three patients neurosurgery was performed. The response to immunotherapy was clinically assessed according seizure frequency, neurological function, duration of effect (short- and long-term) and side effects.

Results: Long-term response to corticosteroids was in 3 and short-term in 6 patients concerning seizure frequency and neurological functions, but one developed Cushing syndrome. IVIG showed transient improvement in 4 patients with no side effects. Thalidomide was very effective in two patients but was ineffective in one girl with very fast course of disease. The patient treated by tacrolimus had reduction of seizure frequency for several months but had diabetes mellitus as side effect.

Conclusion: RE is rare and catastrophic syndrome of childhood. Immunotherapy has played a major role in treatment of RE especially in cases at risk of functional deterioration by hemispherectomy. In our study the most effective immunotherapy was with corticosteroids. IVIG, thalidomide and tacrolimus were also effective in some patients and should be given if corticosteroids failed. In the treatment of children with RE it`s necessary to have individual approach and think about positive but also side effects of therapy.

E581
EPILEPSY SECONDARY TO HYPOTHALAMIC HAMARTOMAS: CLINICAL MANIFESTATIONS AND DIFFICULTIES IN ITS TREATMENT IN A DEVELOPING COUNTRY.

C. Papayannis, D. Consalvo, G. Seifer, M. Kauffman, W. Silva, and S. Kochen
Ramos Mejía Hospital, Buenos Aires, Argentina

Purpose: Clinical features, treatment and prognosis in a series of patients with epilepsy secondary to hypothalamic hamarthomas (HH) in a developing country are described.

Method: Between 1997–2006, 8 patients with epilepsy and HH were included. We analyzed gender, age, age at seizure onset (ASO), seizure types (ST), mental retardation (MR), precocious puberty (PP), EEG-MRI features, and response to treatment.

Results: Mean age 25.1 y, 2/6 female/male, none had PP, ASO 4.5 y. Complex partial seizure were the most frequent (100%), similar to those seen in temporal (62.5%) o frontal lobe epilepsy (37.5%). 87.5% developed gelastic seizures (GS). Half of patients showed MR. Mild to severe MR was associated with the presence of multiple ST including atonic and complex partial seizures with frontal semiology. Interictal EEG was abnormal in 87.5% patients. Video EEG was done in 3 cases with unspecific findings. HH were small and sessile in 7 patients and large and pedunculated in one. All patients were refractory to medical treatment. In five an additional procedure was done without any significant improvement. Mean age at additional procedure was of 19 years (12–32 y) with a mean duration of epilepsy (MDE) of 16 years (10–24 y).

Conclusion: These series shows the heterogeneous spectrum of this entity and the difficulties in its treatment in a developing country. The delay in diagnosis in our patients was probably because they were first seen in nonspecialized centres where the knowledge of this syndrome is low. In addition, there was a difficulty in access to treatment options after correct.

E582
CLINICAL COURSE OF LAFORA DISEASE ASSOCIATED WITH EPM2B GENE MUTATIONS IN PATIENTS OF SERBIAN/MONTENEGRIN ORIGIN

N. Jovic, and M. Kecmanovic†*
**Clinic of Neurology and Psychiatry for Children and Youth, Belgrade, Serbia; and †Molecular Genetics, Faculty of Biology, Belgrade, Serbia*

Lafora disease (LD) is inherited progressive myoclonic epilepsy with unfavorable clinical course leading to severe clinical condition and fatal prognosis. At least two genes (EPM2A and EPM2B) are associated with LD. Possible genotype-fenotype differences are rarely studied.

Patients: A group of 15 patients with LD associated with mutations in EPM2B (NHLRC1) gene, from 13 families of Serbian/Montenegrin origin was studied for clinical course. Additional two siblings from different families are homozygous carriers of EPM2B mutations.

Results: Onset of LD ranged between ages 12 and 16.5 (mean 13.4) after the normal development in all but one case. Diagnosis was made 0.5 – 3.5 years later. Generalized tonic–clonic seizures in 6, occipital lobe seizures in 5 and sporadic myoclonus in 4 patients, preceded myoclonic jerks from 1 to 25 months. Previous history of headache was reported in 5 patients. Insidious cognitive decline in 9 and/or behavioral disorders occurred from 5 to 17 months after the seizure onset. Almost constant myoclonus and tremor occurred for 6 to 26 (mean 16 months), while intractable generalized seizures began for 2 to 14 months after the disease onset. Dementia was diagnosed after 2.1 to 4 years in 12 patients, while inability to walk occurred for 7 to 32 months after the first seizure. Five patients died after 2.5 to 7 years following LD onset. Despite of giant SEPs and bilateral EEG discharges, two siblings, carriers of EPM2B mutations, are without clinical LD phenotype and presenting only with periodical headache.

Conclusion: Constant myoclonus and intractable seizures, inexorable neurological and cognitive deterioration were observed in majority of patients of Serbian/Montenegrin origin, with LD due to mutations in EPM2B gene.

E583
MALIGNANT MIGRATING PARTIAL SEIZURES IN INFANCY; ADDITIONAL THREE CASES FROM TURKISH POPULATION

A. Tosun, G. Serdaroglu, M. Polat, H. Tekgul, and S. Gokben
Ege University Medical School, Izmir, Turkey

Purpose: Malignant migrating partial seizures in infancy is an unusual but often overlooked epilepsy syndrome that begins in the first six months of life. It is characterized by virtually continuous multifocal seizures, no identifiable immediate or remote causes, intractability to antiepileptic drugs, and developmental delay. This report adds three cases to the 27 previously described cases in English literature.

Method: Three female infants aged between 2 and 4 months old referred to the hospital with multifocal motor seizures with secondary generalization and refractory to antiepileptic treatment. Their neurodevelopmental delay was near normal at the beginning, but worsened with refractory seizures. Electroencephalograms of the infants had characteristic features of malignant migrating partial seizures in infancy. Etiologic factor couldn't identified with an extensive metabolic work-up and neuroradiologic examinations. Magnetic resonance imagines revealed progressive cortical and subcortical atrophy.

Results: The seizures were refractory to antiepileptic drug treatment. All of the cases had no seizure control with phenobarbital, diphenylhidantoin, valproate, carbamazepine. In first case, the seizures were partially controlled between 6–9 months of age concomitant with minimal improvement in her developmental status. Second case had partial control of seizures with potassium bromide therapy. Third case was born premature and had a twin. Her twin had a normal development and no seizures. She had partial response to potassium bromide and high dose topiramate therapy.

Conclusion: Additional case report may lead to more frequent diagnosis of malignant migrating partial seizures in infancy and further opportunities to accurately assess the full meaning of this epileptic condition.

E584
THE SPECTRUM OF ABSENCES IN ADULT LIFE

R. Ribacoba, J. Salas-Puig†, M. Gonzalez*, and V. De la Vega**
**Hospital Alvarez Buylla, Mieres, Spain; and †Hospital Universitario Central de Asturias, Spain*

Purpose: Typical absence consist of a sudden, mild or severe, impairment of consciousness concomitant with the abrupt occurrence of bilateral synchronous 3 Hz spike-and-wave discharges (SWDs). Idiopathic generalized epilepsies are listed in 2001 ILAE Classification in accordance with age at onset. Attending it, juvenile absence epilepsy can appear between the ages 7 to 17. We analyzed the absence seizures that had begun later in three patients.

Method: We studied three previous healthly subjects, without family antecedence of epilepsy. Case 1. Is a female who at the age of 18 suffered a tonic–clonic seizure. In the previous six months she had spontaneously 5–6 events per day with a stoppage of conversation and impairment of consciousness. She suffered another GTCS during the puerperium. Case 2. A 24 year old male began with several daily events similar to typical simple absences. Case 3. A male when he was 20 years old he began with isolated fits with myoclonic jerks in his arms and transient loss of consciousness. He was put on topiramate 200 mg per day. Six years later he began to have typical simple absences when he was tired or he felt sleepy. They never suffered status.

Results: In all cases we recorded on video-EEG, short disconnection events with surprise faces, and concomitant bilateral SWDs. Hyperventilation did not provoke absences. MRI was normal in all three cases. In all of them absences disappeared with VPA.

Conclusion: We considered that the spectrum of age in absences could be wider in some unusual cases.

E585
FRONTAL LOBE COGNITIVE FUNCTIONS IN PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY

D. Vucinic, N. Jovic*, P. Ignjatovic*, M. Borkovic*, and S. Jelic†*
**Clinic of Neurology and Psychiatry for Children and Youth, Belgrade, Serbia; and †Special Hospital for Cerebral Palsy and Developmental Neurology, Belgrade, Serbia*

Purpose: Some neuropsychological and behavioral studies suggest frontal lobe dysfunctions in patients with juvenile myoclonic epilepsy (JME). It correlates with mesiofrontal and prefrontal dysfunctions confirmed with recent neuroimaging studies.

Method: Frontal cognitive functioning in 49 JME patients was investigated. Adolescents (male 21, female 28), aged 15–34 years, treated mainly with VPA are divided into two groups: A-35 patients with JME duration > 5 years, and B-14 patients with epilepsy lasting <5 years. No inter-group difference in mean seizure onset was shown. Complete long-term seizure freedom was noted in 72,4% (A) vs. 66,3% (B). Battery of seven neuropsychological tests sensitive to frontal dysfunction was administered.

Results: The performance of our patients was not homogenous. No strong association of clinical parameters (including AED and seizure control) with results was concluded. The number of impaired test results per patients ranged from 0–7. One third of patients scored within normal limits on all tests. One fifth of JME patients showed impairment on ≥ 4 tests. Approximately half of the patients was impaired on ≤ 3 tests. The highest number of deficits was seen on tests measuring mental flexibility, cognitive speed and perseverative tendencies. No inter-group differences regarding to JME duration were found. However, it was noticed better verbal fluency and TMT B achievements in group of patients with epilepsy duration more than 5 years.

Conclusion: JME in adolescents is associated with selective impairment of frontal lobe functions in sizable number of patients. Test performance was not significantly related to the JME duration.

E586
TRANSIENT ANTERIOR OPERCULAR SYNDROME IN A CHILD WITH BENIGN EPILEPSY WITH CENTRO-TEMPORAL SPIKES COMPLICATED WITH CONTINUOUS SPIKE-WAVES DURING SLEEP

P. Dimova, and V. Bojinova
University Hospital of Neurology and Psychiatry 'St. Naum', Sofia. Czech Republic

Transient anterior opercular syndrome has been rarely described in the course of benign epilepsy with centrotemporal spikes (BECTS) with continuous electrographic focal or bilateral seizure activity with rolandic predominance. The condition of continuous spike-waves during slow wave sleep (CSWS) is also known as a relatively rare complication of BECTS. Here, we report on a 6-year old child with the diagnosis of BECTS who developed transient oro-motor deficit. After a 6-month period of poorly controlled right-sided rolandic seizures with typical centrotemporal spikes on the left in the electroencephalogram (EEG), magnetic resonance imaging revealed a temporo-polar angioma on the right. The child was operated on, and shortly thereafter experienced a progressively worsening speech difficulties and drooling, while some increase in seizure frequency. Awake EEG demonstrated bilateral independent rolandic discharges. The condition deteriorated further with unceasing facial, mainly perioral myoclonia more prominent on the right, and sleep EEG revealed CSWS. After a short-term IV treatment with corticosteroids, the condition improved dramatically with complete resolution of CSWS and gradual neurological normalization shortly thereafter. Antiepileptic drug therapy was continued adding levetiracetam to the baseline valproate and resulting in seizure freedom. This case confirms that transient anterior opercular syndrome is a possible, although rare complication in BECTS and could be related to an increase in the epileptiform EEG activity up to CSWS.

E587
INFANTILE SPASMS: ETIOLOGY, INVESTIGATION, CLINICAL OBSERVATIONS

N. Smulska, L. Chepiga, A. Nechay, and V. Ryslyayeva
Pediatric Hospital, Kiev, Ukraine

Infantile spasms (IS) are a severe epileptic encephalopathy with heterogeneous aetiology that occurs in infancy and early childhood. We had in to the Department of Neurology 25 patients with IS – 15boys (60%), 10 girls (40%). Seven patients had perinanatal problems – after born they had treatment in to the Emergency Department; 2 had cardiac rhabdomyomas since born, and we think about tuberous sclerosis; 2 had Down syndrome; 1 had meningitis at the 20-days-old; 1 had congenital toxoplasmosis; 1 had stroke after vaccination. They had development problems before starting seizures. 11 patients were born in time, had normal delivery, but 3 patients had abnormal development before starting seizures. Infantile spasms have begun along early period between the third and nine month (middle 6 month). MRI scans: 5 children (20%) had normal; 18 patients (72%) had different brain abnormalities: periventricular atrophy, pachygyria, lissencephaliy, cysts degeneration, disgenesiy corpus collosum, subarachnoid haemorrhage, cortical tubers, sudependymal nodyles; 2 patients (8%) didn't make MRI. EEG: 8 patients had hypsarrhythmia, 9 patients had multifocal asynchronous pattern of spike, 8 patients had asymmetry, focal high waves. Treatment: all patients took VPA in to the different doses (min 25 mg/kg/per day). Unfortunately, in Ukraine we haven't license to use VGB. Nine patients didn't have seizures. Theirs EEG going to be normal. Only 2 patients (8%) had normal development after seizures stopped. Nine had partial effect: jerks per cluster and clusters per day were reducing. Seven patients didn't have any effects. About 36% patients had control for IS from VPA.

E588
FROM EPILEPTIC SPASM TO WEST SYNDROME, CAN TIME, FREQUENCY AND SEMIOLOGY BE A PREDICTIVE FACTOR

S. Arcieri, F. Formicola, A. Pascotto, and G. Coppola
Second University of Naples, Italy

Purpose: To analyze the time at onset, frequencies and semiology of epileptic spasms can to explain the outcome to West syndrome.

Method: We selected 10 infants with age (3–9 months) with epileptic spasms at onset. All the babies have a normal clinic history prior to the diagnosis. A long-term polygraphic-video-EEG recordings and neurological examination was performed. We analyzed the time at onset, the frequencies of spasms, the duration (in ms) and the semiology with a specific nonstandardized scale.

Results: Our results suggest that babies who had had spasm from less <3 months, have major possibility to develop in West syndrome. Still, the presentation of spasms in cluster >30/day is associated a highly characteristic features of West syndrome, and a semiology, in particular asymmetrical spasms with focal EEG predominance is related with symptomatic spasms that in 95% of cases evolved in West syndrome.

Conclusion: It is possible to consider the spasm phenotype like a predictive factor for outcome to West syndrome. That can suggest to start a adeguate therapy.

E589
FOCAL SEMIOLOGICAL ABNORMALITIES ASSOCIATED TO THE SPECTRUM OF IDIOPATHIC GENERALIZED EPILEPSIES

R. Fernandes Cury, and R. França Fernandes
Ribeirão Preto School of Medicine, University of São Paulo, Brazil

Idiopathic generalized epilepsies (IGEs) are characterized by absences, myoclonic jerks, generalized tonic–clonic fits (GTC) or a mixture of them, accordingly to ictal semiology, whereas the EEG shows bilateral and synchronous typical spike-wave or polyspike-wave disharges. Focal ictal features have been described in those patients, particularly amongst bearers of juvenile myoclonic epilepsy. This has not been approached in a systematic way in the literature, resulting in uncertainties regarding its clinical significance. In order to investigate this topic, we have preselected 128 patients with IGEs based upon EEG and further allocated them into two groups: typical IGE (n=84) and atypical IGE (n=44) patients, according respectively to the absence or presence of focal semiological manifestations. The following issues were significantly associated to the atypical group: antecedent of initial precipitating insult, independent focal spikes (IFS) on EEG, structural abnormalities detected by MRI, presence of GTC, brain CT scan alterations, polypharmacy and less frequent valproate intake; a trend toward longer time of active epilepsy was also noticed. The first three variables could predict the focused characteristic in an independent way through binary logistic regression. Subgroup analysis (absence-type epilepsy), with or without focal semiological manifestations, confirmed the previous findings. Considering only typical IGEs, the presence of IFS is correlated to a longer time of active epilepsy and the presence of structural abnormalities is linked to previous febrile seizures and possibly to worse clinical outcome. The interplay between inherited factors and environmental injuries modifies the phenotype of IGEs, with implications for their diagnostic, therapeutic and prognostic approaches.

E590
A POLYGRAPHIC EEG AND ELECTROMIOGRAPHIC CHARACTERISTICS IN A PEDIATRIC POPULATION WITH ASTATIC AND ASTATIC MYOCLONUS SEIZURES

E. Barragán, and M. Hernández
Hospital Infantil de México, Mexico

Purpose: To classified the astatic and astatic-myoclonus seizures depending to the clinical and poligraphic EEG characteristics.

Method: We analyze a new epileptic peadiatric patients with astatic and astatic-myoclonic seizures in a prospective clinical trial in the neurology department of the Hospital Infantil de México. After a clinical and neurologic examination we proceed to realize a poligraphic and electromiographic video-EEG during 3 hours.

Results: A total of 15 patients (6 males and 9 females) between 2 to 6 years were evaluated, 11 patients had an impact over the neurodevelopment and the total of correlation with a positive electromiographic study, correlated with the severity of the clinical and neurological manifestations.

Conclussions: The video-EEG is a diagnostic method in those patients with astatic seizures, but the correlation with electromiographic activity its very important for the differentiation with the astatic-myoclonic seizures which impact over the severity and treatment of the epilepsy.

E591
DISTRIBUTION OF DIAGNOSIS AND MAIN EPILEPSY SYNDROMES IN PATIENTS REFERRED FOR THE EVALUATION OF CHRONIC EPILEPSY IN A LARGE COHORT OF ADULT PATIENTS WITHIN A PERIOD OF TEN YEARS (1998–2007)

D. Sokic, N. Vojvodic, S. Jankovic, and A. Ristic
Institute of Neurology Clinical Centre of Serbia, Serbia

Purpose: To determine the proportion of confirmed diagnosis of epilepsy and the distribution of main epilepsy syndromes in patients referred for the evaluation of chronic epilepsy.

Method: The setting of investigation is outpatient clinic for adults (>12 years) of one of the authors (DS) in the university hospital in Belgrade, Serbia. Period of investigation was ten years (1998–2007). All patients were referred for the presumed diagnosis of chronic epilepsy. Detailed clinical history, physical and neurological examination, ECG, blood chemistry, at least 1 wake EEG and CT scan of the brain were performed in all patients. MRI of the brain and sleep EEG were performed in majority of patients. Other investigations were performed when necessary.

Results: We examined 2004 patients during a 10-year period. The diagnosis of epilepsy was established in 1665 (83.1%) patients; in 23 (1.4%) of them epilepsy was associated with psychogenic nonepileptic seizures. There were 1275 (76.6%) patients with focal epilepsy, 256 (15.3%) with generalized epilepsy, 133 (7.9%) with nonclassifiable epilepsy and 3 (0.2) with reflex epilepsy. Diagnosis of pure psychogenic nonepileptic seizures was established in 55 (2.7%), recurring provoked seizures in 49 (2.5%), recurring syncope in 35 (1.7%) and various paroxysmal recurring disorders (panic attacks, drop attacks, hypoglycemia, or TIA) in 177 (8.8%) patients.

Conclusion: Our estimate is that in patients with recurring seizures one fifth of them do not have epilepsy. However, in patients who have epilepsy approximately 5 in 6 have focal and 1 in 6 generalized epilepsies, while nonclassifiable and reflex epilepsies are rare.

E592
ZONISAMIDE ADD-ON FOR DRUG-RESISTANT PARTIAL EPILEPSY

S. Anfosso, M. Ricca*, A. Ferrari†, and C. Serrati**
**Imperia Hospital, Italy; and †Savona Hospital, Italy*

Introduction: Zonisamide is sulfonamide antiepilepsy drug with sodium and calcium channel-blocking action. Previous studies have demonstrated the efficacy of zonizamide as adjunctive treatment in patients with drug-resistant partial epilepsy.

Case report: We used zonisamide as an add-on treatment for six patients with refractory partial epilepsy, criptogenetic or synthomatic ethiology, range age 25–65 years, receveing a stable regimen of one to three antiepileptic drugs, with frequent seizures (3–4/week). After a 4–6 week titration phase the patients received a fixed dose of 300–400 mg/day. Follow up at six months demonstrated a significantly greater decrease in complex partial seizures frequency from baseline.

Conclusion: Zonisamide has efficacy as an add-on treatment in our patients with drug-resistant partial epilepsy.

E593

SEIZURE AGGRAVATION AFTER BENZODIAZEPINE IV. DURING THE NONCONVULSIVE STATUS EPILEPTICUS IN THREE CASES WITH LENNOX GASTATUT SYNDROME – IS IT SYNDROME SPECIFIC?

Z. Rener-Primec, and N. Zupancic
University Children's Hospital, Ljubljana, Slovenia

Purpose: Benzodiazepines with valproate are the first drugs of choice in Lennox-Gastaut syndrome (LGS). The nonconvulsive status epilepticus (the status of atypical absences) occurs frequently in LGS, along with increased tonic seizures in sleep. In status epilepticus (SE) benzodiazepines iv. are the first drugs of choice. A paradoxical effect of seizure aggravation after the iv.benzodiazepine occurs in some LGS cases.

Method: EEG and seizure deterioration immediately after the i.v.benzodiazepine use in three LGS patients is described.

Results: Three patients with Lennox-Gastaut syndrome were admitted to our department with a status of atypical absences (nonconvulsive status epilepticus). The EEG showed nearly continuous diffuse slow spike-waves of very high amplitude, marked anteriorly. Each patient received treatment by the standard protocol: benzodiazepines (diazepam 0, 03 mg/kg BW) intravenously, which turned out unsuccessful. After a repeated dose and additional fenition, the aggravation was observed, with frequent tonic seizures in sleep. EEG on the next day demonstrated diffuse bursts of multiple spikes at 16/sec and low voltage fast rhythms in sleep, along with short tonic seizures. Therapy was changed to dexamethasone, manitol and phenobarbitone, with no more use of benzodiazepines. The condition in all three patients improved over the next days.

Conclusion: Paradoxical effect of benzodiazepines on tonic seizure aggravation was first described by Tassinari et al. (1972). The exact mechanism is unknown. Though rare, the early recognition of such patients may avoid aggravation of the condition; the awareness of appropriate treatment choice can shorten the duration of nonconvulsive and tonic status epilepticus.

E594

MERRF WITHOUT RAGGED RED FIBERS: AN UNUSUAL CASE OF A PROGRESSIVE MYOCLONIC EPILEPSY

C. Reinsberger, T. Fortwaengler†, G. Winkler†, C. Monoranu‡, and J. Classen**
**Julius-Maximilians-University, Wuerzburg, Germany; †Leopoldina Hospital, Schweinfurt, Germany; and ‡Insitute of Pathology, Julius-Maximilians-University, Wuerzburg, Germany*

Purpose: Progressive Myoclonic Epilepsies (PME) are a heterogenous group of diseases with genetic background and share a symptomatic generalized epilepsy as a common feature. Among the PMEs, myoclonic epilepsy with ragged red fibers (MERRF) has the highest incidence. Between the PMEs, the exact syndromal diagnosis is of therapeutic importance as the use of valproic acid may worsen the clinical course in MERRF, but may be useful in other forms, such as Unverricht-Lundborg's disease. However, the clinical diagnosis of MERRF is frequently not possible based on clinical features alone. The diagnostic hallmark of MERRF lies in the demonstration of structurally altered mitochondrias, as seen in the modified Gomori trichrome stain, and negative cytochrome-c-oxidase reaction in muscle fibers.

Method and Results: We report an unusual and instructive case of a 22 year old Caucasian female with progressive cerebellar ataxia, myoclonias, rare generalized tonic–clonic seizures and in the progress of the disease progressive hearing impairment, lactacidosis and dementia. After the demonstration of a normal muscle biopsy all investigative efforts concerning other causes of PME yielded normal.

Results: Subsequent genetic testing identified a mtDNA mutation m.8344A>G in the tRNALys gene (MTTK) along with a balanced translocation 46,XX,t (8;18) (p23.1;q21.3).

Discussion: Our case illustrates the role of genetic testing and cautions against using muscle biopsies as the sole diagnostic marker in MERRF. This appears to be the first case of MERRF with m.8344A>G mutation with a balanced translocation of chromosomes 8 and 18.

E595

EPILEPSIAE – EVOLVING PLATFORM FOR IMPROVING LIVING EXPECTATION OF PATIENTS SUFFERING FROM ICTAL EVENTS

A. Dourado, M. Le Van Quyen†, B. Schelter‡, G. Favaro§, A. Schulze-Bonhage¶, S. Sales**, and V. Navarro††*
**University of Coimbra, Portugal; †LENA-CNRS UPR640, UPMC, 47, Bd De L'Hôpital, Paris, France; ‡Center For Data Analysis And Modeling, Albert Ludwigs University, Freiburg, Germany; §MICROMED, SpA, 31020 Zerman Di Mogliano Veneto, Treviso, Via Giotto 4, Italia; ¶Universitätsklinikum Freiburg, Freiburg, Germany; **Hospitais Da Universidade De Coimbra, Praceta Mota Pinto, Coimbra, Portugal; and ††Unité Epilepsies, CHU Pitié-Salpêtrière, Hôpital De La Salpêtrière, 47 Boulevard De L'Hôpital, Paris, France*

The FP7 project EPILEPSIAE, with a total budget of 4 million euros and an European Union support of 3 million (grant 211713), is previewed to run for the next three years. We intend to develop an intelligent alarming system, transportable by the patient, measuring on-line the brain dynamical activity, aiming to predict the seizures, and by this allowing the patient to assess the risk of his actual situation and acting accordingly to improve his safety, privacy and social integration. The system is based on multisignal information (EEG, ECG), intelligent data processing and wireless communications. The project will develop knowledge (in data analysis), algorithms (for seizure prediction) and technologies (of data acquisition and Bluetooth wireless transmission) that integrate into an intelligent system. This will provide an important step forward in economical affordable personal healthcare systems for neurological applications. Seizure prediction will be faced through multialgorithm approaches, exploring multifeatures extracted from multichannel bio signals, classified by computational intelligence techniques and personalized to each patient. A multinode European Epilepsy Database will also be built by the project, including all the available information about epileptic patients in the three participating hospitals, allowing semantic mining based on multimodal, multisignal and multidimensional data. The members of the multidisciplinary consortium are: University of Coimbra-Portugal, Centre National de la

Recherche Scientifique (LENA-CNRS UPR640) and CHU Pitié-Salpêtrière- France, Albert-Ludwigs University Freiburg-Germany, company Micromed SpA-Italy, Freiburg University Hospital-Germany, Hospitals of the University of Coimbra-Portugal, covering the whole value chain from theoretical conception to market products and final users. More on www.epilepsiae.eu.

E596
COMPUTATIONAL INTELLIGENCE ALGORITHMS FOR SEIZURE PREDICTION

B. Direito, R. Martins*, R. Costa*, A. Dourado*, F. Sales†, and M. Vieira**

**Centro de Informática e Sistemas da Universidade de Coimbra, Department of Informatics Engineering, Polo II, Pinhal de Marrocos, Coimbra, Portugal; and †Epilepsy Monitoring Unit, Hospitals of the University of Coimbra, Praceta Mota Pinto, Coimbra, Portugal*

Purpose: To develop computational intelligence algorithms for seizure prediction to embed in a transportable device to support refractory epileptic patients.

Method: Firstly a set of features is extracted from the EEG, measuring energy, time-frequency and nonlinear dynamic contents. These features are then used for classification of the brain state into four classes: inter-ictal, preictal, ictal, postictal. Two approaches from computational intelligence are applied: (1) artificial neural networks in the original 14 features space (several architectures are compared: feedforward, with and without memory, radial basis function, Elman), (2) multidimensional scaling to reduce the 14th dimensional space to 3-dimensional space where classification may be done in an easier way.

Results: The used data is from the Freiburg University Database (Germany) and from the Coimbra University Hospital Database (Portugal). It was impossible to find a solution for all cases from the point of view of both the sensitivity and the specificity criteria. If only one of these criteria is considered, then it is relatively simple to find several solutions. For each patient there exists an architecture with the potential of a good predictor, detecting the preictal period almost without false alarms, giving some optimistic perspective and leading to the concept of customization of the predictor system.

Conclusion: Seizure prediction systems must be personalized, finding a good algorithm for each patient. More extensive studies are needed but artificial neural networks and multidimensional scaling have the plasticity to support the research of such personalized systems.

This study is supported by FP7 EU project EPILEPSIAE (www.epilepsiae.eu).

E597
TRENDS IN MANAGING SEVERE EARLY ONSET EPILEPSIES IN SLOVENIA

I. Ravnik, M. Krzan, G. Tretnjak, N. Krajnc, B. Lorber, N. Zupan, N. Peari, and D. Gosar

Centre for Epilepsy, University Pediatric Hospital Ljubljana, Slovenia

Purpose: From epidemiological data about 600 pharmacoresistant patients (0–18) with epilepsy would be expected in Slovenia. A similar number of multidisciplinary Seizure Conferences for pediatric/adolescent patients with difficult-to-treat epilepsy have been performed from 1995 to 2007 at the tertiary Epilepsy Centre for children and adolescents.

Method: To assess trends in managing difficult to treat early onset epilepsies.

Results: The number of patients discussed by the Centre's multidisciplinary team at regular Seizure Conferences has been constant at about 50 cases/year, with very rare referrals below age 3. Videotelemetry with narrow capacity is regularly available since 2004, averaging 25 evaluations/year. Weekly neuradiology staff meetings (mean 2–3 cases/week) are performed with a dedicated neuroradiologist. From Phase I investigations only ictal SPECT is not available on a regular basis. Smallness of our population has precluded development of a multidisciplinary team for surgical management of pediatric epilepsies, so 37 patients have been referred since 1988 for epilepsy surgery to various foreign epilepsy centres. 22 have had surgery (15 intracarotid Wada tests were performed in patients' mother-tongue by a neuropsychologist accompanying patients abroad), 14 were declined after Phase I and 1 was declined after Phase II. About 10 are at this time considered for referrals and/or waiting at various administrative stages of the procedure. Waiting time from the suggestion by the Epilepsy Centre to actual admission has been considered too long (months to years).

Conclusion: Favourable trends: Our multidisciplinary team has seen most of the pediatric resistant epilepsy cases. The number of surgical referrals has been increasing over time with patients referred for surgery at a younger age. Introduction of videotelemetry has contributed to an earlier age of Phase I completion. Duration of epilepsy before surgery has dropped from 16.5 to 7.5 years.

Suggestions: Though mean age at referral has dropped, many could be referred earlier. The very young are seldom referred for multidisciplinary work-ups. Referrals from some regions and specialists are rare compared to general referral patterns. International networking in managing severe epilepsies brought additional workload on the referring and on the receiving side that should be recognized and accompanied by respective increase in manpower. Waiting for surgery could be shortened by staffing in home institutions and more international facilities for severe epilepsy patients, including those referred from small countries.

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E598
FAMILIAL GENETIC LINKAGE STUDY OF MESIAL TEMPORAL LOBE EPILEPSY

C. Lo

Institute of Neurology, UCL, UK

Purpose: The purpose of this study is to identify possible susceptible genes of mesial temporal lobe epilepsy.

Method: A large family with mesial temporal lobe epilepsy (MTLE) and pain syndrome was identified through epilepsy out patient clinic at the NHNN and peripheral blood samples were taken from consenting participants. DNA was extracted from whole blood and a genome wide linkage scan using 546 microsatellite markers was carried (DeCode Genetics). Linkage analysis was carried out using the FASTLINK version of MLINK to obtain LOD scores. Haplotype analysis was carried out using Cyrillic 2.1 and by visual inspection of genotypes.

Results: The initial linkage analysis parameters assumed that one gene causes both the pain syndrome and MTLE yielded a LOD score of 2.4 at 6p22.2 – 6p22.3. However, further fine mapping and haplotypes analysis excluded this region. Applying stricter criteria in the definition of the phenotype to include only 7 affected individuals generated a LOD score of 2.35 at 3p23-3p24 and 2.33 at 7q11.22 – 7q11.23.

Conclusion: Although small in sample size, a LOD score of 2.35 is the maximum that can be obtained with 7 affected individuals. Thus the region in chromosome 3 will be further investigated together with other regions not yet excluded.

E599

POSTMORTEM DIAGNOSIS OF POLG MUTATION IN A SIBLING WITH FATAL STATUS EPILEPTICUS

T. Dorn, A. Schaller†, S. Gallatt†, and G. Krämer**
**Swiss Epilepsy Center, Bleulerstrasse 60, CH 8008 Zürich, Switzerland; and †Division of Human Genetics, University Hospital for Children, CH 3010 Bern, Switzerland*

Purpose: To contribute to description of the epileptological phenotype of POLG mutations.

Method: Case report.

Results: After an unremarkable personal history a 17-year-old girl developed serial focal seizures and status epilepticus in 8/00. There were two seizure semiologies, namely (1) elementary and complex visual hallucnations, (2) clonic seizures of the left half of the body corresponding to two different seizure patterns in ictal EEG. Interictally left sided hemiparesis and left sided heminaopsia were observed. In MRI two hyperintense lesions were visible right occipital and right frontal, respectively corresponding to hypermetobolic areas in the FDG-PET. Analysis CSF including lactate and virology, screening for inherited metabolic diseases, muscle biopsy including COX and Gomori staining, screening for mtDNA mutations in blood cells yielded no significant results.10/00 seizures emerging from the left hemisphere also occurred. The seizures were pharmacoresistant to a wide range of antiepileptic drugs. 10/00 resection/biopsy in the right parietal lobe guided by electrocorticography did not influence seizure frequency and revealed diffuse gliosis. 12/00 the patient died due to liver failure under valproate therapy. 2007 post mortem analysis of mtDNA of blood and liver cells showed no deletions. Analysis of the POLG gene, however, disclosed a compound heterozygosity with p.Gly588Asp in Exon 10 and p.Trp748Ser in Exon 13. The sister had died at the age of 10 due to pharmacoresistant status epilepticus.

Conclusion: In status epilepticus with an etiology remaining unknown after MRI and CSF analysis POLG mutations should be considered. This should guide choice of antiepileptic drugs.

E600

VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) POLYMORPHISMS IN IDIOPATHIC GENERALIZED EPILEPSY

Y. Kim, I. Lee*, B. Choi*, S. Chung*, H. Kim†, K. Lee*, and S. Yim‡*
**The Catholic University of Korea, Seoul, Korea; †Neuroscience Genome Research Center, The Catholic University of Korea, Seoul, Korea; and ‡College of Medicine, Kyung Hee University, Korea*

Purpose: The increases of VEGF after seizures may reflect a connection between these genes and the excitabililty of hippocampal neurons in seizure disorders. The single nucleotide polymorphisms markers may provide a new way to identify complex gene-associated diseases such as idiopathic generalized epilepsy (IGE). We further tried to evaluate whether these VEGF polymorphisms are useful markers for predicting susceptibility to IGE in children.

Method: 50 IGE and 378 healthy control subjects were selected throughout a collaborative study of Catholic Child Neurology Research Group. VEGF_p2488_CT, VEGF_p634_GC, VEGF_p7_CT, VEGF_q3436_GC, VEGF_q6112_CA, VEGF_q6594_CT, VEGF_q9374_GA, VEGF_q13125_CT and VEGF_q13553_CT were screened by DHPLC. DNA fragments showing variant chromatograms were subsequently sequenced. Genotypes and allelic frequencies for VEGF gene polymorphism in both groups were compared.

Results: Genotype proportions for the VEGF_p2488_CT polymorphism in both groups were significantly different (P=0.044). The Proportions of VEGF_p2488 genotypes (CC, CT. TT) are 62.5%, 27.1%, and 10.4% in IGE group, 49.5%, 45.0% and 4.9% in healthy control group. The most common genotype for VEGF_p2488_CT in both groups were C/C homozygote. The allele C and T frequencies for VEGF_p2488-CT in IGEs group were 76.0% and 24.0%, respectively, and in healthy control group, 72.0% and 28.0%, respectively. But genotype proportions and allele frequencies for other VEGF polymorphisms in both groups were not significantly different.

Conclusion: This data suggest that genomic variations of VEGF might not be one of the susceptibility factors for IGEs in the Korean population.

E601

CLINICAL AND GENETIC STUDY OF A NEW LARGE SARDINIAN FAMILY WITH IDIOPATHIC GENERALIZED EPILEPSY AND FEBRILE SEIZURES

T. Pisano, M. Falchi, M. Meloni, G. Gaspa, and D. Pruna
Childhood Epilepsy Unit University of Cagliari, Italy

Purpose: A new four-generations Italian family from Sardinia with idiopathic generalized epilepsy (IGE) and febrile seizures (FS) is presented.

Method: Clinical information, neurological examination, EEG studies and blood samples were obtained. in the 14 affected family members. Screening of the *SCN1A* gene was performed and SCN1B, GABRG2 are in progress, followed by genome-wide linkage analysis.

Results: Eight family members had only febrile seizures between 1 months and 3 years of age. Three patients had febrile seizures in the first months of life and then absences, myoclonic, generalized tonic–clonic and atonic seizures. Three patients had only generalized tonic–clonic seizures. In four patients generalized tonic–clonic seizures were triggered by emotion or sudden pain. In two of these occasional syncope occurred, sometimes followed by true epileptic seizures. SCN1A mutations analysis was negative.

Conclusion: This four generations IGE and FS family with 14 affected members showed a clinical spectrum different from the other GEFS+ families previously described. In fact none of our patients had febrile seizure over 5 years of age, moreover in some patients seizures were triggered by emotion or sudden pain and syncope occurred in others. Absence of SCN1A mutations suggested to examine the other genes known to be involved in GEFS+ (analysis is actually in progress). The family pedigree is large enough for linkage analysis, which will start soon after molecular analysis of SCN1B and GABRG2.

E602

IDENTIFICATION OF MULTIPLE QUANTITATIVE TRAIT LOCI FOR FEBRILE SEIZURE SUSCEPTIBILITY

E. Hessel, P. Stienen†, I. Wolterink*, C. Fernandes‡, M. de Krom*, M. Kas*, and P. de Graan**
**Rudolf Magnus Institute, University Medical Center Utrecht, The Netherlands; †Division Anaesthesiology & Neurophysiology, Utrecht University, Utrecht, The Netherlands; and ‡Social, Genetic and Developmental Psychiatry Research Centre, Institute of Psychiatry, King's College London, UK*

Purpose: Febrile seizures (FS) are the most common seizure type in children affecting 2–5% of the population and occurring between the age of 6 months and five years. Recent association, family and twin studies indicate a genetic component in FS susceptibility. The aim of this study is to identify quantitative trait loci (QTL's) for FS susceptibility using a forward genetic strategy employing a panel of mouse chromosome substitution strains (CSS) based on the A/J (donor) and C57BL/6J (host) strain.

Method: Fever was induced by a hot-air stream of 500 C for 900s at postnatal day 14. EEG recording confirmed that the start of tonic–clonic

seizure coincides with the onset of spike wave discharge in the hippocampus. Tonic–clonic seizure latency was determined in both genders of the host strain (C57BL/6J, n=40), the donor strain (A/J, n=9) and each of the 21 CSS (n=9/strain) as a phenotypic measure for FS susceptibility.

Results: Five CSS carrying a QTL were identified. Behavioral phenotyping and genetic mapping of a F2-progeny (n=144) from one of these CS-strains resulted in a significant peak with a LOD-score > 5 (using MapQTL software).

Conclusion: Screening the CSS panel showed that FS susceptibility is defined by multiple loci, confirming that FS is a genetically complex disorder. Our data indicate that febrile seizure susceptibility is carried by a set of genes distinct from those previously implicated in susceptibility for chemically induced seizures.

E603
INTERSTITIAL DELETIONS OF CHROMOSOME 20: A COMMON CAUSE OF BENIGN FAMILIAL NEONATAL CONVULSIONS AS DETECTED BY MLPA AND HIGH RESOLUTION SNP ARRAY

N. Verbeek, M. Swinkels*, W. Arts†, W. Gunning‡, P. Callenbach§, M. Poot*, D. Lindhout*, and M. Van Kempen**
**University Medical Centre Utrecht, The Netherlands; †Erasmus University Medical Centre, The Netherlands; ‡Epilepsy Centre Kempenhaeghe, The Netherlands; and §University Medical Centre Groningen, The Netherlands*

Purpose: Genetic factors contribute to the aetiology of epilepsy in about 70% of cases. Most of the currently known genetic factors are small mutations in single genes (for example KCNQ2 in Benign Familial Neonatal Convulsions (BFNC), *SCN1A* in GEFS+ and Dravet syndrome, and CHRNA4 in autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE)). In the past decade high resolution techniques have become available to detect submicroscopic chromosomal abnormalities (i.e. deletions/duplications) and have been used mainly to identify causes of mental retardation and congenital abnormalities. Recently, interstitial deletions of chromosome 2 encompassing the *SCN1A*-gene were identified as a rare cause of Dravet syndrome. We hypothesized that interstitial deletions of chromosome 20, including KCNQ2, are a frequent cause of BFNC.

Method: MLPA and Infinium humanhap300 SNP array were applied to detect deletions of the KCNQ2 region of chromosome 20.

Results: In three out of four families with normal KCNQ2 sequence, we detected deletions ranging from 49 to 479 kb, containing two to fifteen genes. The CHRNA4-gene involved in ADNFLE was also deleted in two families (without an ADNFLE phenotype). The majority of affected family members had a normal development.

Conclusion: (1) BFNC with a normal developmental outcome can be caused by large submicroscopic chromosomal deletions of contiguous genes including KCNQ2. (2) The lack of nocturnal seizures in CHRNA4 deletions is in agreement with the proposed gain-of-function change of known mutations for ADNFLE in this gene. (3) The use of high resolution techniques may contribute to the detection of new genes for epilepsy syndromes.

E604
GEFS+: A NOVEL SCN1A MUTATION IN TWO AFFECTED SIBLINGS WITH DIFFERENT CLINICAL PICTURE

P. Dimova, I. Yordanova†, V. Bojinova*, and A. Jordanova†*
**Clinic of Child Neurology, St. Naum University Hospital of Neurology And Psychiatry, Sofia, Bulgaria; and †National Genetic Laboratory, Molecular Medicine Center, Sofia Medical University, Sofia, Bulgaria*

Generalized epilepsy with febrile seizures plus (GEFS+) is a rare idiopathic generalized epileptic syndrome with heterogeneous phenotype. Most common phenotypes are classical febrile seizures (FS) and FS+, and rare forms are myoclonic-astatic epilepsy (MAE) and syndrome of Dravet (severe myoclonic epilepsy of infancy, SMEI). We present two brothers, aged 11 and 4 years, diagnosed as having SMEI and MAE, respectively. The clinical course and electroencephalographic (EEG) findings are typical for each epilepsy type carrying different prognosis. The father experienced one probably simple FS in infancy and two generalized tonic–clonic seizures (GTCS) after head traumas in adulthood, but had abnormal EEGs with generalized spike-wave and polyspikes-wave paroxysms. Unfortunately, he died as a consequence of severe sport accident before genetic testing to be performed. The genetic analysis of both siblings identified a point mutation (c.3925 C>T) in exon 20 of the *SCN1A* gene, that was absent in the mother. This is an unreported missense mutation and might lead to truncated protein, which is a common finding in SMEI. The two available affected members of the family present GEFS+ phenotypes with completely opposite severity. The first child has SMEI, which is among the severest childhood epileptic encephalopathies. The second child is now seizure free for two years and belongs to MAE with benign course. We assume that this mutation is inherited from the father, who had a very mild clinical picture with occasional GTCS only. These cases illustrate the broad intrafamilial variability of the *SCN1A* gene mutations that represent a challenge in the clinical practice.

E605
INTERINDIVIDUAL DIFFERENCES IN PHENYTOIN ORAL BIOAVAILABILITY: INFLUENCE OF VARIANTS IN ABCB1 AND CYP2C9

P. Kijsanayotin,§, J. Cloyd*, R. Brundage*, W. Oetting*, A. Birnbaum*, E. Ramsay†, J. Rarick*, J. White‡, and I. Leppik*,‡*
**University of Minnesota, Minneapolis, MN, USA; †University of Miami, Miami, FL, USA; ‡MINCEP Epilepsy Care, Minneapolis, MN, USA; and §Chulalongkorn University, Bangkok, Thailand*

Purpose: Oral bioavailability is a measure of the extent of drug absorption that escapes efflux and metabolism in the intestine and liver into the systemic circulation. Phenytoin is a substrate of P-glycoprotein efflux transporter (ATP-binding cassette (ABC) B1) and initially metabolized by cytochrome P450 (CYP) 2C9 and CYP2C19. Absorption variability might contribute to differences in patients' response to phenytoin. This study aims to investigate the associations of variants in ABCB1 and CYP genes with area under the plasma concentration-time curve (AUC) which assesses the extent of drug absorption.

Method: Forty-eight adult Caucasian American patients with epilepsy on phenytoin maintenance therapy were included in this cross-sectional genetic association study. Candidate variants: ABCB1c.3435C>T, CYP2C9*2 (c.430C>T), CYP2C9*3 (c.1075A>C) and CYP2C19*2 (c.861G>A) were genotyped. Steady-state AUC 0–12 hr was determined from phenytoin plasma concentrations at 0, 0.08, 0.25, 0.5, 1, 2, 4, 6 and 12 hours after an oral dose by using WinNonlin. Stepwise multiple linear regression analysis was used.

Results: In a regression model (N=48), Dose (mg) (standardized coefficient, Beta = 0.356, $p<0.001$), ABCB1c.3435T/T (Beta = 0.469, $p<0.001$), ABCB1c.3435C/T (Beta = 0.344, $p<0.001$) and CYP2C9*3 (Beta = 0.186, $p=0.015$) were independent predictors and associated with increased mean of phenytoin AUC 0–12 hr. The model explains 76% of variability in AUC 0–12 hr (adjusted R square = 0.760, $p< 0.001$).

Conclusion: This study reveals the associations of ABCB1 c.3435C>T and CYP2C9*3 with increased phenytoin oral AUC and suggests their influence on interindividual differences in phenytoin oral bioavailability.

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E606
POLYMORPHISM IN *SCN1A* GENE IS NOT ASSOCIATED WITH DRUG RESISTANCE IN EPILEPSY

K. Handoko,†,‡, M. Majoie‡, M. Hermans§, J. Zwart*, W. Hermens†, T. Egberts*, and C. Hekster¶*
University Medical Centre Utrecht, Utrecht, Netherlands; †Hospital Pharmacy 'Ziekenhuisapotheek Noordoost-Brabant', 's-Hertogenbosch, The Netherlands; ‡Epilepsy Center Kempenhaeghe, Heeze, The Netherlands; §Jeroen Bosch Hospital, 's-Hertogenbosch, The Netherlands; and ¶University Medical Centre Nijmegen, Nijmegen, The Netherlands

Purpose: Many antiepileptic drugs (AEDs) act by binding to the subunit of voltage-gated sodium channels in neurons. One of the genes encoding this subunit is *SCN1A*, that is also implicated in many hereditary forms of epilepsy. Earlier research has shown that a polymorphism in the *SCN1A* gene was associated with use of higher doses of carbamazepine and phenytoin. [1] We hypothesized that the AA genotype of the *SCN1A* IVS5-91 polymorphism, which is associated with lower sensitivity in the ? subunit sodium channels, influences the response to AED treatment.

Method: *SCN1A* IVS5-91 was genotyped in 287 patients with epilepsy, 127 were classified as drug-resistant and 160 as drug-responsive. Drug resistance was defined as less than 30% reduction in seizure frequency in the year prior to the date of inclusion in patients who were treated with more than two established AEDs at the maximally tolerated doses. Drug-responsiveness was defined as seizure freedom or a 50% or more reduction in seizure frequency in the year prior to the date of inclusion. Allele frequencies between the two groups were compared with use of the chi-square test.

Results: The frequency of the AA (31.3% versus 25.6%), the GA (52.3% versus 58.9%) or the GG genotypes (16.4% versus 15.6%) did not differ significantly between the drug-resistant and the drug responsive group (x2=1.028, p=0.598).

Conclusion: In this study we showed that the SCN1A IVS5-91 G>A polymorphism is not associated with drug resistance in epilepsy.

References

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E607
NOVEL DE NOVO MUTATION OF MONOZYGOTIC TWINS WITH BORDERLAND SEVERE MYOCLONIC EPILEPSY IN INFANCY

L. Chen, Y. Shi†, W. Deng†, M. Yu†, and W. Liao†*
**1st Affiliated Hospital of Guangzhou Medical College, China; and †Neuroscience Institute, 2nd Affilaited Hospital of Guangzhou Medical College, China*

We report on a case of 3-year-old monozygotic twins with epilepsy both involving febrile seizures within one year old, partial and generalized tonic clonic seizures, no myoclonic seizures, mental retardation and medication resistance. Their clinical manifestations were strikingly similar, and fit the criteria of borderland severe myoclonic epilepsy in infancy (SMEB). Genetic screening revealed a novel de novo mutation in the *SCN1A* gene (c.5348C>T, A1783E). De novo mutations are commonly found in cases with severe myoclonic epilepsy of infancy (SMEI), and same *SCN1A* gene mutations found in monozygotic twins with SMEI were also reported before, but never found in monozygotic twins with SMEB. In this case, same *SCN1A* gene mutation was found in these twins with SMEB, providing support that SMEB, same as SMEI, is an epilepsy syndrome caused by gene mutation and there is a close relationship between genotype and phenotype.

E608
MILD GENERALIZED EPILEPSY AND PAROXYSMAL EXERCISE INDUCED DYSTONIA DUE TO GLUT1 DEFICIENCY

Z. Afawi, A. Suls†, D. Ekstein‡, S. Kivity§, P. Jonghe¶, W. Paesschen**, A. Korczyn††, and S. Berkovic‡‡*
**Tel Aviv Sourasky Medical Center, Israel; †University of Antwerp, Division of Neurology, University Hospital of Antwerp, Belgium; ‡Hadassah Ein Kerem University Medical Center, Jerusalem, Israel; §Epilepsy Unit, Schneider Children's Medical Center of Israel, Petach Tikvah, Israel; ¶Division of Neurology, University Hospital of Antwerp, Belgium; **University Hospital Gasthuisberg, Katholieke Universiteit Leuven, Leuven, Belgium; ††Sieratzki Chair of Neurology, Tel Aviv University, Israel; and ‡‡University of Melbourne (Austin Health), Heidelberg West, Australia*

Purpose: Paroxysmal exercise induced dystonia and epilepsy have recently been recognized as part of the spectrum of deficiency of the glucose transporter Glut1, due to mutations in the gene SLC2A1. Here we describe the clinical features of an Israeli family with this disorder.

Method: The family was ascertained as part of a systematic study of the genetics of epilepsy in Israel. The family was assessed clinically. SLC2A1 was examined by direct sequencing.

Results: This Ashkenazi Jewish family had 6 definitely affected members in 2 generations with an autosomal dominant mode of inheritance. Two had epilepsy and paroxysmal dystonia, two had just dystonia and two had epilepsy alone. A seventh member appeared to be a phenocopy with probable benign partial epilepsy of childhood. The mean age of epilepsy onset was 15 years (range 6–30 years) and the seizure types were generalized tonic–clonic in 3 and myoclonic in 1. Interictal EEGs were normal. The mean age of dystonia onset was 13 years (range 10–15 years). The symptoms were predominantly experienced in the legs after walking or exercise, relieved by rest, with a cramping sensation and dystonic movement of the toes and feet. A missense mutation in SLC2A1 (c.950A>C; p.N317T) was detected in four living affected members.

Conclusion: The clinical picture of a mild apparently generalized epilepsy with exercise induced dystonia and onset in the first two decades should raise suspicion of Glut1 deficiency.

E609
EPILEPSY IN THE POPULATION OF NEUROMUSCULAR PATIENTS

S. Todorovic, V. Milic-Rasic*, N. Jovic*, and S. Romac†*
**Clinic for Pediatric and Adolescent Neurology and Psychiatry, University of Belgrade, Serbia; and †Biological Faculty – PCR Center, University of Belgrade, Serbia*

Purpose: Pointing out the rare association between hereditary neuromuscular diseases (NMD)with recognized molecular-genetic mutations and epilepsy.

Method: More than 3000 sufferers of various NMD were diagnosed through biochemical, electrophysiological (EMNG, EEG, ECG, EP), pathological (histochemistry of the muscle) and (around 1/10 of them) molecular-genetic investigations.

Results: Only 13 out of more than 3000 NM patients from our series had some kind of epilepsy. Among these 13 patients 11 had some hereditary NM disorder of which the diagnosis has been established through all classical and molecular-genetic investigations: Duchenne muscular

dystrophy (1 sporadic case), merozin negative congenital muscular dystrophy (1 sporadic case), spinal muscular atrophy type III (2 brothers), hereditary motor and sensory neuropathy type 1A (7 sporadic cases) and 2 unrelated female patients with autoimmune myasthenia gravis. 11 of them had focal epilepsy with or without secondary generalization and 2 brothers suffered of baltic myoclonus.

Conclusion: Although it is well known that the involvement of the central nervous system do exist in some hereditary NMD, epilepsy is a rare associated problem in this population of patients. Regarding the fact that molecular genetic basis of many epileptic conditions has been recognized, rare patients with associated problems (epilepsy + autoimmune or hereditary NMD with proved genetic defect) might be the 'owners' of the genetic clues for better understanding of possible interaction between the mutated genes in NMD and epilepsy.

E610
THE ATTRIBUTION OF GST-PI SINGLE NUCLEOTIDE POLYMORPHISM IN IDIOPATHIC EPILEPSY PATIENTS AND THE ASSOCIATION BETWEEN GENOTYPES AND EEG

H. Zuchun, Y. Juan†, X. Zhengxiang‡, and W. Xuefeng†*
**Chongqing Medical and Pharmaceutical College, China; †The First Affiliated Hospital of Chongqing, China; and ‡Chongqing University of Medical Sciences, China*

Objective: To study the frequency distribution patterns of the SNPs for the three sites (Ile105Val ¢Ala114Val ¢Asp147Tyr) of glutathione S-transferase Pi (GST-Pi) in epilepsy patients. And the possible relationship of GST-Pi gene mutation to the vulnerability of drug-resistant epilepsy, drug-responsive epilepsy and EEG feature were explored.

Method: The SNPs of GST-Pi for healthy people, drug-responsive epilepsy patients and drug-resistant epilepsy patients were genotyped by sequence-specific primers (SSP)-based PCR technologies (PCR-SSP).

Results: Frequency distribution for three sites of mutated SNP of GST-Pi was 59.62% ¢55.32% ¢50.94% in drug-responsive epilepsy group, and 58.33% ¢51.19% ¢45.92% in drug-resistant epilepsy group respectively. The difference of genotype and allele between normal group and foregoing epilepsy group was significant (P<0.0001), but there was no difference between drug-responsive epilepsy group and drug-resistant epilepsy group (P>0.05). There was difference in different feature of EEG group for different genotypes.

Conclusion: The results indicate that the SNPs of GST-Pi were associated with an increased risk of epilepsy, and EEG is easy to come out normal fitful, but not associated with an increased risk of drug-resistant epilepsy.

E611
MUTATION SCREENING OF THE CDKL5 & ARX ARISTALESS-RELATED HOMEOBOX (ARX) GENES IN EARLY ONSET SEIZURES SMEI

C. Depienne, R. Nabbout†,‡, M. Chipaux†,‡, E. Leguern*, C. Beldjord§,¶, T. Bienvenu§,¶, and N. Bahi-Buisson**
**INSERM U679 GH Pitié Salpetriere, France; †Neuropédiatrie Epilepsies Rares GH Necker Enfants Malades, France; ‡Inserm U663, Université Paris Descartes, France; §Génétique Moléculaire Pavillon Cassini Hopital Cochin AP-HP, Université Paris Descartes, France; and ¶Inserm U567, Institut Cochin, Université Paris Descartes, CNRS (UMR 8104), France*

Background: SMEI is a distinctive syndrome with seizure onset in the first year of life, beginning with prolonged febrile hemiclonic or generalized tonic–clonic seizures. A large majority of SMEI are associated with de novo mutations in the *SCN1A* gene. However, 30% patients with SMEI are negative for *SCN1A* mutation screening, suggesting that other molecular mechanisms may account for these disorders. Among the few monogenic of symptomatic epilepsies, CDKL5 and ARX genes are both responsible for X-linked epileptic encephalopathies that can be associated with early onset seizures and refractory myoclonic epilepsy. Given the overlapping yet heterogeneous clinical features of these epilepsy syndromes, we postulated that CDKL5 mutations in females and expansion in poly-Alanine tracts in ARX gene in males may be associated with early onset seizures forms of SMEI.

Method: 29 sporadic SMEI patients negative for *SCN1A* mutational screening were selected and screened for ARX expansions for males (n=15) and CDKL5 mutations in females (n=14).

Results: No mutations in either genes were found. All these patients presented with atypical forms of SMEI starting within the 3 first months, with normal interictal EEG, evolving into myoclonic epilepsy. No patient ever exhibited West Syndrome, dystonia, or Rett-like features.

Interpretations: Our results illustrate that ARX and CDKL5 mutations screening is not effective in patients selected on the basis of clinical signs associated to atypical forms of SMEI. In addition, they might reflect that other phenotypic features associated with CDKL5 mutations (Rett-like features, West syndrome) or ARX mutations (dystonia, familial occurrence) are more distinctive.

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E612
OBSERVATION OF N-ACETYLASPARTATE OF BRAIN TISSUES IN PATIENTS WITH EPILEPSY

X. Zou, and W. He
West China Hospital, Sichuan University, China

Objective: (1) To observe the changes of NAA, Cho and Cr in the brain tissues of patients with epilepsy. (2) To discuss the role of these changes on localization, diagnosis and pathology of epilepsy.

Method: 56 patients with typical epileptic symptoms, video-EEG monitoring expressions (25 patients with TLE 31 patients with no-TLE) and 22 normal subjects had been investigated by multivoxel 1H-MRS examinations. The metabolites of N-acetylaspartate (NAA), Choline-containing compounds (Cho), creatine and phosphocreatine (Cr) were detected.

Results: The signal of NAA in patients was decreased in 1H-MRS examination. The intensity of NAA of abnormal area (1.51 ± 0.22) was obviously lower than that of the contralateral (1.64 ± 0.17, P<0.05) and the control (1.82 ± 0.19, P<0.01). The ratio of NAA/ (Cho+Cr) in abnormal area (0.55 ± 0.11) was obviously lower than that of the contralateral (0.70 ± 0.16, P<0.01) and the control (0.776 ± 0.10, P<0.01). The NAA signal of patients with no-TLE was also decreased. The signal intensity of NAA (1.59 ± 0.16) was lower than those of the control (1.82 ± 0.19, P<0.05). Ratio of NAA/ (Cho+Cr) in abnormal area (0.62 ± 0.11) was lower than those of the control (0.776 ± 0.10, P<0.05).

Conclusion: (1) Signal intensity of NAA in patients with epilepsy were decreased in 1H-MRS detection. (2) The ratio of NAA/ (Cho+Cr) in patients with epilepsy was decreased. (3) 1H-MRS may be helpful in clinical diagnosis pathologic research and preoperative evaluation of patients with epilepsy.

E613

HISTORY OF SIMPLE FEBRILE SEIZURES IS ASSOCIATED WITH HIPPOCAMPAL ABNORMALITY IN HEALTHY ADULTS

T. Auer, P. Barsi*, B. Bóné*, A. Angyalosi*, M. Aradi*, C. Szalay*, R. Horváth*, N. Kovács*, G. Kotek*, A. Fogarasi†, S. Komoly*, I. Janszky‡, A. Schwarcz*, and J. Janszky**
**University of Pécs, Pécs, Hungary; †Bethesda Children's Hospital, Budapest, Hungary; and ‡Karolinska Institute, Stockholm, Sweden*

Background: It is unclear, whether the hippocampal abnormality in temporal lobe epilepsy (TLE) is the consequence or the cause of afebrile or febrile seizures. We investigated whether any hippocampal abnormalities can be present in healthy adults >15 years after simple febrile seizure (FS).

Method: Eight highly educated healthy subjects (5 men) with a history of simple FS (FS+ group) and 8 sex- and aged-matched control subjects (FS- group) were investigated by three MRI methods (1) blind visual inspection of the MRI pictures (2) automatic voxel-based volumetry, and (3) T2 relaxation time measurements.

Results: The mean volume of the two hippocampi was 5.36±1.33 cm3 in the FS+ group and 6.63±1.46 cm3 in the FS- group (p=0.069). The T2 values in the anterior part of the left hippocampus (p=0.036) and in the middle part of the right hippocampus (p=0.025) were elevated in the FS+ subjects. The mean volume of the right hippocampus was 3.05±0.8 cm3 in FS+ men and 4.05±0.48 cm3 in FS- men (p=0.043). The total mean volume of the two hippocampi was 5.38±1.4 cm3 in FS+ men and 7.48±1.14 cm3 in FS- men (p=0.043). There were three FS+ male subjects in whom hippocampal abnormalities including hippocampal sclerosis and dysgenesis were present by visual inspection.

Conclusion: Simple febrile seizures in childhood can be associated with hippocampal abnormalities in healthy highly-educated adults. These abnormalities are more probably pronounced in men.

E614

EEG-FMRI STUDY OF THE ICTAL AND INTERICTAL EPILEPTIC ACTIVITY IN PATIENTS WITH EYELID MYOCLONIA WITH ABSENCES

T. Yang, Y. Liu*, X. Yang*, D. Zhou*, W. Liao†, H. Chen†, and Q. Gong**
**West China Hospital, Si Chuan University, China; and †School of Life Science and Technology/School of Mathematics, University of Electronic Science and Technology of China, China*

Purpose: To investigate the BOLD signal changes correlated to ictal and interictal epileptic discharges with EEG-fMRI in patients with Eyelid Myoclonia with Absences and then to explore the pathophysiological mechanisms of epileptic discharges and their effect on brain function.

Method: Four patients with EMA were investigated through the method of EEG-fMRI. The characteristics of BOLD signal changes linked to ictal and interictal epileptic discharges under different states of consciousness were explored.

Results: Seven sessions of EEG-fMRI scanning in the four patients were obtained. The main regions of activation included thalamus, mesial frontal cortex, middle parietal lobe, temporal lobe, insula, midline structures and cerebellum. Deactivations were mainly in the anterior frontal lobe, posterior parietal lobe and posterior cingulate gyrus. Thalamic BOLD change was predominantly activation in most of our cases. The distribution of activation associated with ictal epileptic discharges was wider and the distribution of deactivation was closer to pericortex compared with the BOLD change linked with interictal epileptic discharges.

Conclusion: The activation in thalamus may be associated with generalized spike wave in EMA; the combination of different patterns of activation with consistent pattern of deactivations (°default ± pattern) in patients with EMA may prognosticate different states of consciousness in response to ictal and interictal epileptic discharges.

E615

VOXEL-BASED MORPHOMETRY (VBM) SUPPORTS NEURODEVELOPMENTAL HYPOTHESIS REGARDING EARLY ONSET TEMPORAL LOBE EPILEPSY (TLE)

S. Kaaden, C. Quesada, J. Schramm, H. Urbach, and C. Helmstaedter
University Hospital Bonn, Germany

Purpose: Childhood onset of epilepsy has been associated with an adverse impact on cognition and brain morphology. We propose a developmental framework for TLE, with the age at onset of epilepsy (AOE) representing a hindrance factor, which should become evident in morphometric analyses. Recent VBM research in TLE patients consistently revealed grey matter reduction in temporal as well as extra-temporal regions.

Method: We performed VBM analyses of T_1-weighted images obtained in a 1.5 Tesla scanner using the SPM5 software and compared early (≤7 years; N=32) versus late (>15 years, N=52) AOE groups. To assure completion of brain development, patients had to be older than 16 years. We focused on extra-temporal lobe abnormalities only and corrected for duration, age and gender.

Results: Onset dependent grey matter abnormalities were obtained in the medial superior frontal gyrus and anterior cingulum, indicating that the early onset patient group exhibits more grey matter in these regions compared to the late AOE group. Correlational analysis with the onset as continuous variable furthermore shows an increase of frontal grey matter with an earlier AOE.

Conclusion: Increased grey matter is not a usual finding in TLE. However, taking the onset of epilepsy into consideration, areas of increased grey matter may well indicate a distant hindrance of the development of anterior brain structures in TLE. This parallels findings of retained neurons in focal cortical dysplasia. The relevance of the affected structures for normal intellectual development has recently been shown in longitudinal evaluations on cortical thickness.

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E616

PROMINENT BRAINSTEM, THALAMIC AND AMYGDALA INVOLVEMENT IN ABSENCE SEIZURES WITH PERIORAL AUTOMATISMS AS REVEALED BY EEG-fMRI

M. Pugnaghi, F. Benuzzi, G. Monti, V. Farinelli, P. Nichelli, and S. Meletti
University of Modena And Reggio Emila, NOCSAE Hospital, Modena, Italy

Purpose: To describe BOLD dynamics in patients with idiopathic generalized epilepsy (juvenile absence epilepsy) and frequent absence seizures who underwent functional MRI with simultaneously acquired EEG (EEG-fMRI).

Method: We studied two patients without antiepileptic therapy at the time of scanning. They performed video-EEG monitoring the same day of EEG-fMRI study demonstrating frequent long runs of typical 3 Hz generalized spike-wave discharge (GSWD) lasting from 4 to 8 seconds, clinically associated with loss of consciousness and followed by discrete oral automatisms (lip smacking, deglutition). Scalp EEG was recorded by means of a 32 channels MRI-compatible EEG recording system

(Micromed S.p.A, Italy). Functional data were acquired with a 3T Philips Achieva system (TR=3000 ms) from 30 axial contiguous 4 mm slices (64 x 64 matrix) over two 10-min sessions per patient with continuous simultaneous EEG recording. Event-related analysis was performed on functional data with SPM2 software, using standard hemodynamic response function (HRF) and its time-derivates (TD).

Results: Seven and 13 absence seizures (mean duration 5 sec.) were recorded in the two patients. FMRI data showed bilateral activations in the thalamus, amygdala/hippocampus, temporal pole, and prefrontal cortex. Deactivations were observed in brainstem (pontine reticular formation), caudate nuclei and in bilateral widespread cortical areas including precuneus, posterior parietal and prefrontal cortex.

Conclusion: We found BOLD dynamics involving sub-cortical regions, not previously described in GSWD of IGE patients. Prominent brainstem and medial temporal involvement could account for the occurrence of brief postictal perioral automatisms in absence seizures.

E617
EFFECTS OF LEVETIRACETAM ON CEREBRAL BLOOD FLOW IN DE NOVO EPILEPSY PATIENTS

E. Joo, M. Lee, S. Kim, J. Lee, J. Kang, and S. Hong
Samsung Medical Center, Sungkyunkwan University School of Medicine, Korea

Purpose: To investigate the effects of antiepileptic drug, Levetiracetam, on regional cerebral blood flow (rCBF),.

Method: Interictal 99mTc-ethylcysteinate dimer (ECD) single photon emission computed tomography (SPECT) was performed before levetiracetam was administered and then repeated after levetiracetam monotherapy for 12 weeks in 16 drug-naïve epilepsy patients (M/F=11/5, mean age 25.5 years). Seizure types were generalized tonic–clonic seizure in 4, myoclonic seizures with secondary generalization in 4 patients, and partial seizures with left side onset in 5 or with right side onset in 3 patients. The mean levetiracetam dose used was 1203.1mg/day (range 1000 – 2000). For SPM analysis, all SPECT images were spatially normalized to the standard SPECT template and then smoothed using a 12-mm full width at half-maximum Gaussian kernel. The paired t-test was used to compare pre- and postlevetiracetam SPECT images.

Results: SPM analysis of pre- and postlevetiracetam brain SPECT images showed decreased rCBF in bilateral superior frontal gyri, left middle and inferior frontal gyri, left precentral gyrus, right orbital gyrus, left caudate nucleus, left superior temporal gyrus, bilateral middle temporal gyri, left insular gyrus, right amygdala, and bilateral cingulate gyri and corpus callosum after long-term levetiracetam administration at uncorrected $p < 0.005$. There was no brain area showing rCBF increase after levetiracetam administration.

Conclusion: Our study demonstrates for the first time the effect of levetiracetam on interictal rCBF in drug naive patients with idiopathic generalized and partial epilepsy.

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E618
CONTINUOUS EEG-FMRI IN PATIENTS WITH PARTIAL EPILEPSY AND FOCAL INTERICTAL SLOW-WAVE DISCHARGES ON EEG

M. Avesani, E. Formaggio*, R. Cerini†, F. Milanese*, A. Gasparini†, L. Bongiovanni‡, S. Storti*, R. Pozzi Mucelli†, A. Fiaschi*, and P. Manganotti**
**Dp Neurological and Visual Sciences-Section of Rehabilitative Neurology, Italy; †Dp of Morphological and Biomedical Sciences-Section of Radiology, Italy; and ‡Dp Neurological and Visual Sciences-Section of Clinical Neurology, Italy*

Purpose: To verify whether in patients with partial epilepsy and routine EEG showing focal interictal slow-wave discharges without spikes, combined EEG-fMRI would localize the corresponding epileptogenic focus, thus providing reliable information on the epileptic source.

Method: Eight patients with partial epileptic seizures whose routine scalp EEG recordings on presentation showed focal interictal slow-wave activity underwent EEG- fMRI. EEG data were continuously recorded for 24 min (4 concatenated sessions) from 18 scalp electrodes while fMRI scans were simultaneously acquired with a 1.5 Tesla MRI scanner. After recording sessions and MRI artifact removal, EEG data were analyzed offline. We compared blood oxygen-level dependent (BOLD) signal changes on fMRI with EEG recordings obtained at rest and during activation (with and without focal interictal slow-wave discharges).

Results: In all patients, when the EEG tracing showed the onset of focal slow-wave discharges on a few lateralized electrodes, BOLD-fMRI activation in the corresponding brain area significantly increased. We detected significant concordance between focal EEG interictal slow-wave discharges and focal BOLD activation on fMRI. In patients with lesional epilepsy, the epileptogenic area corresponded to the sites of increased focal BOLD signal.

Conclusion: Even in patients with partial epilepsy whose standard EEGs show focal interictal slow-wave discharges without spikes, EEG-fMRI can visualize related focal BOLD activation thus providing useful information for presurgical planning.

E619
IN VIVO QUANTIFICATION OF INTRACEREBRAL GABA BY SINGLE VOXEL 1H-MRS – HOW REPRODUCIBLE ARE THE RESULTS?

T. Hammen, W. Bogner†, S. Gruber†, M. Doelken‡, T. Engelhorn‡, A. Mennecke*, A. Stadlbauer§, O. Ganslandt§, C. Nimsky§, S. Trattnig†, A. Doerfler‡, and H. Stefan**
**Epilepsy Center Erlangen (ZEE), Clinics of Neurology, University of Erlangen; †MR Center of Excellence, Medical University Vienna, Austria; ‡University of Erlangen, Germany; and §Clinics of Neurosurgery, University of Erlangen, Germany*

Purpose: Gamma-aminobutyric acid (GABA) is an inhibitory neurotransmitter with anticonvulsive character. Because of an increased interest in GABA metabolism of patients with epilepsy we tested the reliability of a special editing sequence for noninvasive intracerebral GABA measurement in healthy adults.

Method: We determined the reproducibility of results obtained with a J difference editing sequence using MEGA suppression on a 3T-TIM-Trio (Siemens) by single voxel spectroscopy (SVS) with regions of interest (ROIs) in the left and right occipital lobe of subjects. Intra and inter-subject reproducibility was evaluated. 11 volunteers were measured in total, 3 probands repeatedly on 4 different days. Comparison of side differences between left/right hemispheres was calculated. Results of GABA/Cr and GABA/H2O ratios were compared. A detailed comparison of 2 different postprocessing routines for the evaluation was accomplished. Signals of GABA/Cr/H2O were integrated using MestreC, compared to time domain line fitting routine (AMARES-jMRUI). Mean, standard deviation (SD) and coefficient of variation (CV) were calculated among groups.

Results: Using data from all subjects lower CVs were observed for line fitting compared to integration. GABA/Cr ratio performed better than GABA/H2O or GABA alone (GABA/Cr: 13.6% and 21.6%; GABA/H2O: 14.8% and 21.7%; GABA: 20.6% and 26.4%). 4 day measurements on 3 subjects showed better intra- than intersubject reproducibility (GABA/Cr 12.1%).

Conclusion: With a CV of about 14% for intersubject- and 12% for intrasubject variability of GABA/Cr, the technique turns out to be a precise and promising tool for intracerebral GABA determination. GABA/

Cr and GABA/H2O ratios showed comparable reproducibility, significantly better than GABA alone. Automated line-fitting performed better than integration.

E620

A COMPARISON OF ICTAL-INTERICTAL SPECT ANALYZED BY SPM (ISAS) AND SUBTRACTION ICTAL SPECT COREGISTERED WITH MRI (SISCOM) IN PATIENTS WITH INTRACTABLE EPILEPSY

Y. Cho, E. Lee*, S. Yi*, S. Zeon*, and G. Motamedi†*
**Dongsan Medical Center, Keimyung University, Korea; and †Georgetown University Hospital, Washington, DC, USA*

Background: Subtraction ictal SPECT coregistered with MRI (SISCOM) has become an important noninvasive method for localizing the epilepsy onset zone in epilepsy surgery candidates. ISAS (ictal-interictal SPECT analyzed using SPM) is a newly developed analysis technique for ictal-interictal SPECT analysis. We studied the usefulness of ISAS as compared to SISCOM in epilepsy surgery candidates.

Method: In 20 epilepsy surgery candidates (age 11- 63 years, mean 31.1 ¾15.5 years) the ictal scan was compared with a corresponding interictal scan using ISAS and SISCOM. A blinded epileptologist reviewed the ISAS results to identify overall localization, and overall lateralization. The SISCOM results were also evaluated for overall localization, and overall lateralization. True seizure localization was based on concordance of EEG, MRI, and postresection Engel Class I or II outcome after a minimum of 1 year follow up.

Results: Seizure localization was mesial temporal in 13 and lateral temporal in 7 patients. Overall, ISAS correctly identified the lobe of seizure onset in 85% of the patients (17/20) and correctly lateralized in 95% (19/20), while results for SISCOM were 55% and 90% respectively. With ISAS the highest significance voxel of the highest significance cluster correctly identified the lobe of seizure onset for 75% (15/20) of the entire group.

Conclusion: These results demonstrate the higher sensitivity of ISAS for lateralizing and localizing temporal epilepsy compared to SISCOM scan pairs. ISAS is a freely available technique which is useful for seizure localization in epilepsy surgery candidates.

E621

SLOW WAVE DIPOLE DENSITY (SWDD) LOCALIZATIONS USING MAGNETOENCEPHALOGRAPHY (MEG) IN PATIENTS WITH FOCAL EPILEPSY: SIGNIFICANT SWDD-PEAKS EVEN IF SPIKE ANALYSIS FAILS

M. Kaltenhäuser, T. Ehrenfried, S. Rampp, and H. Stefan
Epilepsy Center (ZEE), Erlangen, Germany

Purpose: Magnetoencephalography (MEG) has become a useful tool in preoperative epilepsy diagnostics. Up to now, MEG-investigations have been based on the localization of interictal spikes. The newly developed method called slow wave dipole density (swdd) allows to calculate local increases in slow wave brain activity (Kaltenhäuser et al., NeuroImage 2007;34 (4):1466–72). In this study swdd is used in MEG data of patients without spikes in the MEG.

Method: Spontaneous MEG was recorded in 9 patients with pharmacoresistant focal epilepsy and 5 healthy subjects. Patients were included, if postoperative 1 year outcome was seizure freedom, and if no spikes were detected in the MEG and a MEG measurement had been performed with the 37-MEG-channel-sensor above the brain area later resected. Visual spike inspection was done manually by experienced MEG-investigators. Other investigations in the preoperative epilepsy diagnostic allowed the localization and the decision to resect the epileptogenic focus. 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 slow wave dipole density were displayed on MR-images. Comparison of slow wave dipole density localizations with the resected brain area according to surgery report was done visually.

Results: 67% of the patients showed local slow wave activity increase in or around the brain region which was resected afterwards on the basis of other investigations of presurgical evaluation. In comparison, data of five healthy subjects showed no local increases in slow wave dipole density.

Conclusion: Swdd correctly identified the epileptogenic region and is independant of the occurence of spikes. In this study the detection rate was 67% of those cases in which spike analysis failed. Swdd method is a useful tool in MEG localization routine.

E622

F-MRI-EEG COREGISTRATION IN NONKETOTIC HYPERGLICEMIC SEIZURES

A. Del Felice, P. Manganotti†, M. Avesani†, E. Formaggio†, T. Zanoni†, and G. Moretto†*
**University of Verona, Italy; and †Ospedale Civile Maggiore, Verona,Italy*

Purpose: Epileptic seizures are rare manifestations of nonketotic-hyperglicemia (NKH), sometimes seen as the sole prodromic symptom. Frontal motor seizures are the most common, although occipital seizures have exceptionally been described. We report the first case, to our knowledge, of NKH related occipital seizures studied by fMRI-EEG coregistration.

Method: An obese, undiagnosed diabetic 50yrs-old female patient, with negative medical history, was admitted to hospital complaining of visual disturbances – i.e.'looking through water', diplopia and flashing lights in the right visual field. A simple partial seizure, with conjugated deviation of eyes and head to the right, was witness. Patient reported red flashing lights in the right visual field. Critical EEG showed left posterior spikes and sharp-waves, with bilateral diffusion. Antiepileptic treatment (Carbamazepine) was of minor benefit; seizures subsided after insulin therapy was started.

Results: Cranial CT-scan, ophtalmologic control and 3-Tesla MRI were negative. Laboratory data revealed hyperglicemia (261 mg/dL; HbA1c 10,6%). Urine analysis was negative for ketone bodies. EEG-fMRI continous coregistration was performed before antidiabetic therapy was started. BOLD activation was identified in the left Brodmann's area 18 (visual association area).

Conclusion: To our knowledge, less than 10 cases of occipital seizures during NKH are reported. Occurence of occipital seizures can be explained by reduced Kreb's cycle activity and glucose use in an area with higher metabolism, leading to activation of the GABA-shunt metabolic pathway and consequentely to GABA depletion. This is the first case where the use of a new diagnostic technique permits the precise identification of the involved cerebral area and the likely correlation with the patient's metabolic disturbance.

E623

VOXEL-BASED MORPHOMETRY OF TEMPORAL LOBE EPILEPTIC PATIENTS

A. Labate, A. Cerasa†, E. Colosimo†, R. Ambrosio*, U. Aguglia‡, A. Quattrone*, and A. Gambardella**
**Institute Neurology, University Magna Græcia, Catanzaro, Italy; †Institute of Neurological Sciences, National Research Council, Mangone (CS), Italy; and ‡Regional Epilepsy Centre, Hospital of Reggio Calabria, Reggio Calabria, Italy*

Purpose: In refractory temporal lobe epilepsy (rTLE) gray (GM) and white (WM) matter abnormalities are not confined to the hippocampus but also are found in extrahippocampal structures (Keller SS et al. Neuroimage 2002;16:23–31). Less is known about mild TLE (mTLE). In this study, we used optimized voxel-based morphometry (VBM) to identify GM abnormalities beyond the hippocampus in rTLE and in mTLE with evidence of hippocampal sclerosis (HS).

Method: Brain MRI and VBM of GM with modulation was performed in 30 unrelated patients with mTLE (56% women; mean age 35.6 + 15.2 years), 19 patients with rTLE (52% women; mean age 38.4 + 17.4 years) and 37 healthy controls (25 women, mean age 37.3 + 10.6 years). MRI diagnosis of MTS was based on the atrophy of the hippocampal formation and/or mesial temporal hyperintensity on FLAIR or T2 images, or both.

Results: All patients (rTLE and mTLE) did not have any generalized tonic–clonic seizures for at least three weeks before the scanning. Respectively, mTLE patients showed GM volume reduction of the bilateral thalamus and left hippocampus (FWE < 0.05) whereas rTLE in the thalamus bilaterally (FWE < 0.05) when compared with controls. Conversely, no differences of GM concentrations were found between rTLE and mTLE.

Conclusion: In either rTLE and mTLE, VBM shows GM reductions not confined to the hippocampus but mainly in the thalamus bilaterally. Moreover, no GM differences were found between the two groups. This supports the hypothesis that mTLE and rTLE might lie along a biological continuum.

E624
NEUROPSYCHOLOGICAL DETERIORATION AFTER ABSENCE STATUS CORRELATED WITH DRAMATIC REDUCTION OF FRACTIONAL ANISOTROPY (FA) IN DIFFUSION TENSOR IMAGING (DTI)

G. Möddel, W. Schwindt, N. Meinhardt, H. Lohmann, M. Dogan, S. Kovac, M. Fischera, S. Evers, and M. Deppe
University Clinics of Muenster, Germany

Purpose: To demonstrate that cognitive deterioration due to long-lasting absence status may be correlated with dramatically impaired white matter integrity as assessed by fractional anisotropy (FA).

Method: Clinical case report including EEG documentation, neuropsychological testing, conventional MRI, and assessment of FA using diffusion tensor imaging (DTI). FA maps were compared with 63 age- and gender-matched healthy controls on a regions of interest (ROI) basis. DTI was acquired at 3 T, with 20 diffusion directions.

Results: A 22 year old male with idiopathic generalized epilepsy was admitted due to obtunded-aggressive behavior lasting two weeks. EEG revealed generalized spike-waves and delta slow, supporting diagnosis of Absence status. The patient suffered a series of generalized tonic–clonic seizures before status was terminated by lorazepam and valproate. However, behavior remained severely impaired. Conventional MRI was normal except for a linear left frontal gliotic lesion. In contrast, FA was below 1st percentile in 5 out of 15 ROIs, compared with controls, with exceptionally severe decrease in the frontal lobes. At 2-month follow-up, FA was even further reduced, with 12 out of 15 ROIs below 1st percentile. Neuropsychological testing on that day revealed verbal and figural memory, processing speed, and executive function scores below 10th percentile. The patient remained unable to work and to continue his technical apprenticeship.

Conclusion: Despite its generally good prognosis, prolongated Absence status lasting weeks may cause decline of intellectual functioning. This case demonstrates that FA assessed with DTI may reveal dramatic diffuse white matter changes although conventional MRI shows merely minimal lesions.

E625
EEG-FMRI OF TEMPORAL LOBE EPILEPSY: SOURCE LOCALIZATION USING BOLD AND ICA

M. Sercheli, E. Bilevicius†, H. Ozelo*, A. Alessio†, F. Pereira†, J. Rondina†, F. Cendes†, and R. Covolan**
**Neurophysics Group, Instituto De Física 'Gleb Wataguin', Unicamp, Campinas, Brazil; and †Neuroimaging Laboratory, Faculdade De Ciências Médicas, Unicamp, Campinas, Brazil*

Purpose: Patients were studied by EEG-fMRI aiming to investigate the spatial correspondence between epileptiform spikes and BOLD responses. In order to do that, we have compared the dipole source locations through ICA with the BOLD statistical maps.

Method: We have studied thirty patients with mesial temporal lobe epilepsy. All patients were under clinical investigation (EEG, video EEG, neuropsychological evaluation, SPECT, and MRI). EEG-fMRI measurements were acquired in a 2T Elscint Prestige MR scanner using a cap with 32 scalp MRI-compatible electrodes. The EPI images were analyzed with the SPM2 software package in order to search for corresponding BOLD responses. For EEG source localization, we have used the EEGLAB v6.01b toolbox by fitting dipole models to the ICA components.

Results: From thirty EEG-fMRI studies, five did not present any spike. IEDs were identified in the EEG of twenty-five patients, being that twenty four of them showed BOLD responses. This result corresponds to 80% of the total patients investigated, which is considerably higher than the usual rates found in others studies that laid in the range of 50–63%. From the patients that presented BOLD responses (twenty-four), sixteen exhibited good agreement in terms of spatial localization by comparing the previous clinical investigation, the fMRI outcomes, and the dipoles modeling.

Conclusion: This study has shown, even imposing stringent statistical limits, an elevate rate of effective BOLD responses associated with focal epileptic activity. In 55% of the cases a good spatial agreement has been found among previous clinical investigation, BOLD responses, and dipole modeling.

E626
CRISS-CROSSING THROUGH BAND HETEROTOPIA: A PROBABILISTIC DIFFUSION TENSOR TRACTOGRAPHY STUDY

S. Kreisel, M. Mertens, and F. Wörmann
Epilepsiezentrum Bethel, Germany

Purpose: Patients with band heterotopia (BHT) rarely present with neurological deficits. It has been previously shown using diffusion tensor imaging (DTI) that large white matter tracts traverse BHT. Here we demonstrate that fibers associated with the sensory-motor system cross through BHT using a probabilistic tractography approach.

Method: A female patient with focal epilepsy without sensory-motor abnormalities presenting with BHT was studied Structural and DTI (12 noncollinear directions, b=900mm/sec2) images were acquired on a 1.5 T Siemens Symphony scanner. Structural postprocessing was performed using a previously published algorithm automatically masking regions likely to correspond to band heterotopia using SPM software. Probabilistic tractography was calculated using the BEDPOST and PROBTRACKX routines (FSL software).

Results: Sensory-motor white matter tracts seeded in the internal capsule seemingly cross through bands of heterotopic grey matter unaffected, physiologically terminating in corresponding areas of the sensory and motor cortex.

Conclusion: The lack of sensory-motor deficits in this patient may be associated with physiologically appearing white matter tracts, albeit the presence of BHT. Probabilisitc tractography, though computationally demanding, provides a robust framework to investigate the course of

white matter tracts in regions of decreased anisotropy such as those associated with BHT.

E627

S1 CORTEX LOCALIZATION BY INTRACRANIAL SEP, ELECTROCORTICOGRAPHY AND ESI WITHIN THE CONTEXT OF PRESURGICAL WORKUP

L. Spinelli, A. Lascano†, C. Michel†, and M. Seeck**
**Presurgical Epilepsy Unit – Neurology, University Hospital of Geneva, Geneva, Switzerland; and †Functional Brain Mapping Laboratory, University Medical School, Geneva, Switzerland*

Purpose: To compare the localization of the S1 cortex by somatosensory evoked potentials (SEP), electrocorticography and Electrical Source Imaging (ESI) based on high resolution EEG recordings within the context of presurgical workup.

Method: SEP induced by pneumatical stimulation were recorded first preoperatively using a high-density 256 EEG system and during phase II evaluation. Stimulation was achieved by using fingerclips with balloon diaphragms, placed on the thumb, producing nonpainful tap-like stimuli driven by compressed air. Using realistic head model, ESI was applied to the second SEP component. Direct cortical electrical stimulations were delivered between two adjacent intracranial electrodes with a frequency of 50Hz, a pulse length of 300μs for 2s. Pulse strength was increased gradually starting from 1mA. Postimplantation CT was performed and co-registered to the patient's MRI to achieve spatial correlation between the cortex and electrode position.

Results: Preliminary results showed that pneumatic stimulation is able to accurately delimitate the central sulcus. This is translated as an electrical phase inversion between two adjacent intracranial electrodes. Contrarily, direct cortical electrical stimulation suggested a vaguer mapping of the sensory cortex. ESI, associated with realistic head model, indicated similar localization of S1 cortex on the patient's individual MRI.

Conclusion: Intracranial pneumatic SEPs are feasible within the context of presurgical workup. Preoperative ESI and intracranial pneumatic SEP could be considered as complementary noninvasive tools, to the usual electrocorticography, for localizing S1 cortex. Pneumatical SEP presents the advantage of being a more objective (non-patient dependent), easy to use and precise stimulation.

E628

INVOLVEMENT OF SUPPLEMENTARY SENSORIMOTOR AREA IN STARTLE EPILEPSY: A SISCOM STUDY

S. Fernández, M. Carreño, A. Donaire, I. Maestro, J. Setoain, and E. Seres
Hospital Clinic de Barcelona, Spain

Purpose: Startle epilepsy is a relatively rare form of epilepsy triggered by unexpected stimuli, generally a sudden noise or a somatosensory stimulus. The aim of this study was to get insight into those mechanisms and brain structures involved in startle-induced seizure generation. For that purpose we determined those regions that experiment a relative increase in blood flow during the perictal period using SISCOM studies.

Method: We present three patients with startle epilepsy secondary to sudden noises. One patient also had touch-induced seizures. All of them underwent a comprehensive presurgical evaluation including long-term video-EEG, MRI and ictal SPECT/SISCOM. Two patients had extense hemispheric lesions secondary to perinatal ischemic infarcts. The aetiology in the third remained cryptogenic. In order to inject the radioisotope as soon as possible seizures were induced by sudden and unexpected noise in 2 patients and by rubbing the left foot in the other one.

Results: Seizure semiology was invariably consistent with bilateral asymmetric tonic seizures. Ictal EEG showed a paroxysmal fast activity over the left centro-parietal or over the right fronto-central region in two patients respectively. In the third patient the ictal pattern showed a non-localizing diffuse slowing. Radioisotope injection was performed 6 to 7 seconds after clinical seizure onset. SISCOM showed a significant and well-localized activation over the mesial fronto-central cortex, consistent with the supplementary somatosensory motor area (SSMA).

Conclusion: Our study shows evidence that SSMA is directly involved in the seizure generation process in those patients with startle-induced and touch-induced seizures.

E629

NEURONAL NETWORK ACTIVATION ASSOCIATED WITH CONTINUOUS SPIKES AND WAVES DURING SLOW SLEEP (CSWS) – AN EEG-FMRI STUDY

M. Siniatchkin, F. Moeller*, K. Groening*, R. Boor†, R. Rodionov‡, L. Lemieux‡, C. Michel§, S. Wolf¶, A. Rohr¶, O. Jansen¶, and U. Stephani**
**Hospital of Paediatric Neurology, Christian-Albrechts-University, Kiel, Germany; †Northern German Epilepsy Centre for Children and Adolescents, Raisdorf, Germany; ‡Institute of Neurology, University College London, London, UK; §Functional Brain Mapping Laboratory, University Hospital, Geneva, Switzerland; and ¶Christian-Albrechts-University, Kiel, Germany*

Purpose: Epileptic syndromes with CSWS are characterized by the presence of spike and wave discharges during at least >85% of non-REM sleep and cognitive deficits associated with this EEG pattern. Pathogenetic mechanisms of CSWS are insufficiently investigated. Here we investigate hemodynamic correlates of the CSWS using fMRI and EEG source imaging.

Method: Simultaneous recordings of 32-channel EEG (BrainProducts Co.) and functional MRI (Philips 3T, TR=2.25s, 540 scans) were performed in 9 children (5–11 years old, all sedated) with symptomatic (n=6) and cryptogenic focal epilepsies and CSWS. After the routine MR-artifact correction (BrainVision-Analyser), automated spike detection based on spike topography was performed using BESA. Analysis of generation and propagation of epileptic activity was carried out using distributed linear inverse solution LAURA (Local-Auto-Regressive-Average model). Both results of EEG-driven fMRI analysis and results of the EEG source reconstruction were superimposed on T_1*-weighted images.

Results: Significant positive and negative BOLD responses ($p<0.05$, family wise error-corrected) have been observed in all cases. In every patient positive BOLD responses were individually distributed and matched well both lesional areas and EEG sources corresponding to generation and propagation of CSWS. Negative BOLD responses were consistently found in frontoparietal cortex corresponding with the default mode neuronal network.

Conclusion: Despite of etiologic inhomogeneity, CSWS pattern was associated with activation of individual network of focal epileptic activity and deactivation in the default mode brain areas. The deactivations may reflect the impact of epileptiform discharges on normal brain function which might cause the neuropsychological deficits by inducing repetitive interruptions of neurophysiological function.

E630

MULTIMODAL DIAGNOSTIC PROCEDURE (EEG-FMRI, PET AND ICTAL SPECT) IN CHILDREN WITH FOCAL EPILEPSY

K. Groening, R. Boor†, F. Moeller*, A. Rohr‡, S. Wolff‡, O. Jansen‡, U. Stephani‡, and M. Siniatchkin**
**University Hospital of Paediatric Neurology, Christian-Albrechts University, Kiel, Germany; †Northern German Epilepsy For Children, Raisdorf, Germany; and ‡Christian-Albrechts-University, Kiel, Germany*

Purpose: In presurgical evaluation of pharmacoresistent focal epilepsies, an unambiguous focus identification by a comprehensive diagnostic workup with a number of neuroimaging techniques is required. Simultaneous recordings of EEG and functional MRI have been recently developed to characterize neuronal networks associated with interictal epileptiform discharges. However, the significance and validity of EEG-fMRI technique in the diagnostic workup of pediatric focal epilepsies are insufficiently studied.

Method: EEG (32 electrodes, BrainVision@-amplifier, 5000Hz sampling) and functional MRI (3 Tesla Philips scanner, TR=2.25s, 20min aquisition) were simultaneously recorded in 12 children (1–16 years old, all sedated with chloral hydrate) with symptomatic and cryptogenic focal epilepsies. Positive and negative blood oxygenation level dependent (BOLD)-responses were analyzed using SPM-5 software. Results of fMRI analysis were compared with results of PET and ictal SPECT.

Results: Significant positive and negative BOLD responses ($p<0.05$, FDR corrected) were found in all children. In most children, positive BOLD responses corresponded well with results of PET and ictal SPECT studies. However, the BOLD responses tended to be more distributed than areas of PET hypometabolism and SPECT hyperperfusion. Negative BOLD responses were identified mostly in distant brain areas.

Conclusion: EEG-fMRI is a promising tool to characterize epileptogenic regions in the preoperative workup in children with pharmacoresistant focal epilepsy. In most children, at least one part of the identified neuronal network was localized in areas of interictal hypometabolism and/or ictal hyperperfusion. The distributed BOLD responses outline a weakness of the EEG-fMRI technique which is unable to differentiate between generation and propagation of epileptic activity.

E631
BILATERALLY INCREASED VOLUME OF AMYGDALA IN PATIENTS WITH CRYPTOGENIC ADULT-ONSET TEMPORAL LOBE EPILEPSY

C. Quesada,†, B. Weber*,†, C. Elger*,†, and C. Bien**
**University of Bonn, Bonn, Germany; and †Life & Brain Research Center, Bonn, Germany*

Purpose: This study aims to identify potential structural brain abnormalities in adult patients with recent-onset temporal lobe epilepsy (TLE) who were MRI-negative by conventional criteria.

Method: 50 in-patients with recent-onset (<5 years) TLE and no MRI lesions were selected. 50 age- and gender-matched healthy subjects (recruited for different fMRI studies) were included as control group. T1-MPRAGE images with an isotropic resolution of 1mm obtained in a 3 Tesla MRI with a standard 8 channel head-coil (Siemens, Erlangen) were processed on SPM5 using a modified 'optimized voxel-based morphometry' pipeline (Good et al, Neuroimage 2001) with modulation for nonlinear normalization. A two-sample *t*-test was used to compare both groups, with gender and age as covariates. Results were corrected for multiple comparisons using a very conservative (family-wise) method applying random field theory.

Results: The patient group showed bilaterally a higher volume on both anterior mesiotemporal poles. No structure had a significantly higher volume on the controls group, compared to the patients (even with a less conservative thresholding).

Conclusion: These results show for the first time increase in the volume of limbic structures in recent-onset TLE in adults. This finding is striking because (1) in TLE, there is frequently a progressive atrophy seen, and (2) because no other structures are altered. It may be speculated that a proportion of those cases will evolve into a chronic TLE with mesial atrophy (as described by Bien et al., Neurology 2007, for cases of definite or possible limbic encephalitis).

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E632
LANGUAGE AND MEMORY ASSESSMENT WITH FUNCTIONAL MAGNETIC RESONANCE IN TEMPORAL LOBE EPILEPSY PATIENTS

S. Oddo,†,‡,§, P. Solis*,†,§, C. Lomlomdjian*,†,§, M. Benitez*,†,§,¶, D. Consalvo*,†,§, J. Princich*,†,‡,§,¶, M. Eleta¶, and S. Kochen*,†,‡,§*
**Epilepsy Center. Ramos Mejia Hospital, Buenos Aires, Argentina; †Celular Biology And Neuroscience Institute Prof. Dr. Eduardo De Robertis, Argentina; ‡CONICET, Buenos Aires, Argentina; §CEFYBO, Buenos Aires, Argentina; and ¶Jaime Roca Foundation (TCBA), Buenos Aires, Argentina*

In mesial temporal lobe epilepsy patients, Functional Magnetic Resonance Images (fMRI) contributes to establish the dominant hemisphere for language and it is considered a valuable tool for memory assessment. The aim of the present study is to apply the proper methodology to analyze memory and language. We selected 27 patients (p.) with refractory temporal lobe epilepsy, surgical candidates. All patients presented a mesial lesion on MRI. They were evaluated before surgery. Paradigms used: Language: pictures naming, and verbal fluency.
Memory: We evaluated episodic memory. We included figures learning, new condition recognition, and a semantic decision task. Evaluations were performed in two sessions with a previous training. Language localization was obtained on 100% of cases. Seventy seven percent (21 p) has left fronto-temporal activation and 22.2 % of cases (6 p), presented bilateral activation.
Memory: On 18.5% (5 p). we could not obtained activation with the paradigm used. On 33.3% (9p.) we observed unilateral activation on the mesial region, in 3 cases was correlated with the epileptogenic zone, and on the rest 6 p, activation was contralateral to the lesion. On 48.1% of cases (13 p.), we observed activation of both hemispheres. With the used paradigms we achieved to localize language areas, memory function was less defined. It is essential to have greater number of patients to obtain more determining.

Results: This noninvasive method is promissory for human cognitive functions research.

E633
THE USE OF ARTIFICIAL NEURAL NETWORKS IN PREDICTING THE YIELD OF COMPUTED TOMOGRAPHY (CT) BRAIN STUDY IN GENERALIZED EPILEPTIC SYNDROME (GES) PATIENTS

L. Saadah, R. Ayyanar†, M. Saadah‡, and P. Elaiyan†*
**Tawam Hospital C Johns Hopkins Medicine, Al Ain, United Arab Emirates; †Madurai Medical College, Madurai, India; and ‡Rashid Hospital, Dubai, United Arab Emirates*

Purpose: We used artificial neural networks (ANN) to predict the result of and defer the need for CT scan in patients with generalized epilepsy Syndromes (GES).

Method: We used our database of 1947 consecutive epilepsy patients referred to an outpatient epilepsy clinic in Madurai medical college, Madurai, India. Only 274 and 38 patients with normal and abnormal CT results, respectively, met inclusion criteria. Significant predictors (P value Ü 0.05) in domains such as patient demographics, precipitating factors, prodrome and aura, medical and family history, postictal phenomena, personality traits, and physical examination served as input variables for probabilistic configurations in NeuralTools v1.0.1 (Palisade, London, UK). We validated the networks externally with 5 cases, 1 abnormal and 4 normal CT scans and used a ratio of 4:1 for testing and training in the remainder of cases. We assessed performance using prevalence of CT abnormalities (12.2 %) and predicted outcomes in the study sample.

Results: Networks converged within 12 seconds in less than 250 trials. The best model used 51 input nodes. Highest impact variables were personality traits and postictal personality changes (> 32%), duration of aura (16 %), and abnormal conscious level (>15%). Internal validation and external specificity were <30% and 100%, respectively. At the 99% level of confidence, ANN identifies 259 normal and 21 out of 25 abnormal CT results with a sensitivity, specificity, and positive and negative predictive values of 89%, 100%, 100%, and 99%, respectively.

Conclusion: ANN can defer CT imaging in 84% of patients presenting with generalized seizures.

E634
MULTIMODAL QUANTITATIVE INVESTIGATION OF EEG FOCALITIES IN IDIOPATHIC GENERALIZED EPILEPSIES

L. Betting, M. Morita, C. Yasuda, I. Lopes-Cendes, M. Guerreiro, C. Guerreiro, and F. Cendes
UNICAMP, Brazil

Purpose: EEG is supportive of idiopathic generalized epilepsies (IGE) diagnosis when it shows typical generalized spike and wave (GSW) discharges. Despite of this finding, sometimes focal discharges are disclosed by the EEG investigation. The aim of this research was to combine quantitative techniques to investigate the focalities present in the EEG of patients with IGE. To achieve this objective, voxel-based morphometry (VBM), volumetry and EEG source detection were exploited.

Method: All patients had at least one GSW and one focal epileptiform discharge at the EEGs for evaluation. Focal discharges were used for quantitative source detection. A volumetric MRI sequence was used for VBM and volumetry analysis. For VBM analysis, the images of each patient were processed and individually compared with a group of 20 controls. Statistical analysis was conducted searching for differences of gray matter volumes. The localization of the focal discharges on the quantitative EEG was compared to the VBM.

Results: Automatic volumetry was used to reinforce the findings.

Results: Twenty-two patients with IGE diagnosis were evaluated. Seven had juvenile myoclonic epilepsy, eleven absence epilepsy and four generalized tonic–clonic seizures only. 77% presented areas of gray matter abnormalities in the VBM investigation. EEG source analysis showed that the focalities had 94% of agreement with the VBM analysis in these patients.

Conclusion: This study supports that structural abnormalities are associated with focal epileptiform discharges observed in the EEG of IGE patients.

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E635
NUCLEAR MAGNETIC RESONANCE OF THE BRAIN IN DIAGNOSING NEUROLOGICAL DISORDERS IN CHILDREN ACCOMPANIED WITH EPILEPTIC ATTACKS

O. Jotovska
Institute for Mental Health of Children and Youth, Macedonia

Purpose: To present NMR images of the brain in 10 children, patients with cerebral palsy, brain tumors, children with perinatal traumas, hereditary diseases, childhood stroke and different developmental anomalies of CNS (most of them cortical dysplasias) accompanied with epileptic attacks. Most of the children clinically manifest mental and psychomotor delay and speech disturbances, intellectual deterioration, behavior disorders, seizures and other diverse symptoms.

Method: Due to up-to-date computer methods and techniques, the images from NMR of the brain are transmitted to a poster in order to present the different kinds of alteration of brain structures when confronting different pathological conditions and persistence of epileptic attacks.

Results: The huge technical possibilities and combinations which NMR of the brain possesses, give an extremely clear and precise presentation on most of the different kind of pathological conditions of CNS, enabling the doctor to understand the clinical symptomatic, etiology, and clearing the possible unclarities in précising the definite diagnosis and causes of epileptic attacks and realization of adequate therapy (medications, surgery, radiation etc.) The results of NMR of the brain at our 10 children show directly the causes for the epileptic seizures which correlate to the present morphologic changes of CNS.

Conclusion: NMR of the brain as a very helpful, unaggressive, nonionizing method with high sensitivity which possesses an essential potential in pediatric practice, providing information to the pediatrician that is not available when using CT and ultrasonography of the brain.

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E636
FREQUENCY AND PATTERNS OF FOCAL EEG ABNORMALITIES IN CHILDREN

Z. Ahmed, A. Akhter*, S. Taj*, A. Bano*, A. Malik*, F. Khan*, and K. Siddiqui†*
**Liaquat National Hospital, Karachi, Pakistan; and †King Fahad Medical City, Riyadh, Saudi Arabia*

Purpose: There are varying patterns of EEG abnormalities in pediatric age group. There are few studies looking at frequency of these abnormalities, in our region.

Method: We retrospectively observed all pediatric EEG data from 2002 to 2006, from our 'Pediatric EEG database' age range between 1–14 years. We recorded; reason for referral to the lab, EEG findings, if abnormal; type of abnormality, frequency and patterns of epileptiform discharges. All this information was analyzed by SPSS version 13.

Results: There were 3744 EEG's carried over four and a half years, in pediatric age group. 67.5 % (n=2527) were normal and 32.5% (n=1217) were abnormal. Commonest reason for EEG referral was seizures with and without loss of consciousness, 72.5 % (n=883). Of the abnormal EEG's 78.4 % (n=954) had epileptiform discharges. Epileptiform discharges that were recorded showed that 24.1% (n=230) had focal spike and slow waves discharge, 19.3% (n=185) had focal sharp and slow wave discharge, 19.2% (n=184) had focal spikes, 8.8% (n=84) had focal sharp waves and rest had generalized epileptiform discharges.

Conclusion: We conclude that 71.4% of patients had focal epileptiform discharges, out of that 24.1% of our patients had focal spike and wave discharges. There is a high probability that partial epilepsy is the commonest epilepsy in this age, in our cohort. We feel that our data is different from the series reported in literature where generalized epilepsy is more common in this age group. We also speculate that our cohort has either different genetic makeup or its secondary to acquired structural etiology.

E637
EFFECT OF MEDICATION WITHDRAWAL ON INTERICTAL EEG IN PRESURGICAL EVALUATION: A RETROSPECTIVE STUDY

N. Andersen Becser, J. Alving, and S. Beniczky
Danish Epilepsy Centre, Denmark

Purpose: To evaluate changes in seizure frequency and interictal EEG pattern related to medication withdrawal in patients with focal epilepsy in presurgical evaluation.

Method: Clinical data and video-EEG recordings of 30 episodes of withdrawal from 25 consecutive patients (mean age 38 y) were analyzed retrospectively (2006–2007). Video-EEGs were recorded (1–4 days) after individually planned medication withdrawal in order to localize the epileptic focus. Seizure frequency and epileptiform activity in interictal EEG localization were compared before and after withdrawal.

Results: There was a significant increase in seizure (sz) frequency after medication withdrawal (mean 2,47 sz/day) as compared to a period of 5 days preceding withdrawal (0,2 sz/day) (p=0.003). Change in interictal EEG localization was observed in 13/30 cases (43%) after withdrawal as compared to those before the withdrawal. In six of these discordant cases the localization of the seizure-onset coincided with the interictal EEG localization after the withdrawal, and in none of them with the EEG before the withdrawal (p=0.03). The neuroimaging focus (MRI, SPECT and PET) was concordant with the interictal EEG pattern after withdrawal in five cases and with those before the withdrawal in two of the discordant cases. In two cases, drug withdrawal-related nonconvulsive status epilepticus with good outcome, was seen.

Conclusion: Antiepileptic drug withdrawal is an effective seizure provoking method confirmed by our.

Results: Interictal EEG localization after medication withdrawal correlated better with the seizure-onset region than those recorded before withdrawal.

E638
THE ROLE OF ENDOGENOUS NEURAMINIDASE IN CONTROL OF NEURONAL AND NETWORK EXCITABILITY

D. Isaev, I. Lushnikova, G. Skibo, and E. Isaeva
Bogomoletz Institute of Physiology, Kiev, Ukraine

Purpose: It has been well documented that seizures and mental retardation are common clinical features of inherited disorders of deficiency of lysosomal neuroaminidase (NEU) (sialidosis, galactosialidosis) and free sialic acid storage disorders (infantile sialic acid storage diseases and Salla disease). However underlying mechanisms of increased seizure susceptibility in patients with these disorders remain largely unknown. These disorders characterized by an extremely large excretion of sialic acid. The purpose of this study was to investigate the role of endogenous NEU, a key enzyme that regulates amount of terminal sialic acid, in control of neuronal and network excitability.

Method: Extracellular field potential recordings were made from pyramidal CA1 layer from cultured hippocampal slices. The level of sialylation and morphological characteristics of synapses were estimated using conventional and electron microscopy.

Results: Two hour incubation of slices with N-Acetyl-2,3-dehydro-2-deoxyneuraminic acid (NEU blocker) lead to highly significant increase in the level of sialylation of the hippocampal tissue and increased quantity of simple and perforated of CA1 stratum radiatum synapses. Also NEU-blocker treatment aggravated hippocampal seizures induced by gabazine increasing their frequency and duration.

Conclusion: In summary, manipulation with level of endogenous neuraminidase leads to changes in excitability of nervous system and seizure susceptibility and increased of the level synaptogenesis in the hippocampal formation. This observation may be important in clarification of the mechanisms responsible for epilepsy in patients with defective or deficient NEU activity and disorders of free sialic acid storage.

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E639
GABAA RECEPTOR-DEPENDENT FIELD POTENTIALS REVEALED BY 4-AMINOPYRIDINE IN THE HIPPOCAMPAL-PARAHIPPOCAMPAL CORTEX OF THE IN VITRO ISOLATED ADULT GUINEA PIG BRAIN

L. Uva, M. Avoli†,‡, and M. de Curtis**
**U.O. Epilettologia Clinica E Neurofisiologia Sperimentale, Fondazione Istituto Neurologico Carlo Besta, Milano, Italy; †Montreal Neurological Institute and McGill University, Montreal, Quebec, Canada; and ‡Università Di Roma La Sapienza, Roma, Italy*

The origin of hyper-synchronous epileptiform discharges has been often explained as an imbalance between glutamatergic and GABAergic transmission. It was demonstrated that the enhancement of synaptic inhibition and excitation with 4-aminopyridine (4-AP) leads to the appearance of synchronous GABAergic potentials that contribute to the generation of epileptiform activity (Perreault and Avoli, J Neurophysiol 1991;65:771–785, Lopantsev and Avoli Neurosci lett 1996;210:5–8).

Purpose: we investigated the effect of a simultaneous increase of excitation and inhibition in a preparation with the entirely preserved synaptic connections.

Method: we administered 4-AP (50μM) to in vitro isolated guinea pig brains and recorded field potentials in piriform cortex (PC), entorhinal cortex (EC) and hippocampus (HIPP).

Results: 4-AP enhanced the propagation of responses evoked by afferent stimulation and potentiated the feedback inhibition along the PC-EC-hippocampal pathway, as demonstrated by paired pulse test. 4-AP induced seizure-like activity in EC and HIPP that was abolished by co-perfusion with the glutamate receptors antagonists. Co-perfusion of 4-AP-CNQX-APV unveiled two types of field potentials that either remained isolated in HIPP or propagated within the EC-HIPP region, even bilaterally. The second type of potential were observed either in hippocampus (CA3 and CA1 region) or in the m-EC, as demonstrated by current-source-density analysis of the field potential profiles recorded with 16-channels silicon probes. These potentials were abolished by the application of GABAa receptors antagonist, bicuculline (50μM).

Conclusion: our data confirmed in the adult guinea pig brain that the convulsant agent 4-AP induces GABAa mediated population events that could support or modulate temporal lobe ictogenesis.

E640
GABA MODULATION OF EVOKED NEURONAL RESPONSES IN THE MEDIAL SEPTUM IN THE EPILEPTIC BRAIN

A. Malkov, I. Popova, and V. Kitchigina
Institute of Theoretical and Experimental Biophysics of the Russian Academy of Sciences, Russia

Purpose: Study of GABA role in synaptic interactions of medial septal (MS) neurons during epilepsy.

Method: Effects of GABA (5mM) and its blockers (phaclofen, 2mM; picrotoxin, 5mM) on the septal neurons responses to electrical stimulation were analyzed in slices taken from control and epileptic guinea pigs. Epilepsy was produced by intrahippocampal injection of kainic acid (0.6 μg).

Results: All MS neurons (41 control, 39 epileptic) responded to electrical stimulation by initial period of inhibition. It was observed an extension of inhibition duration range in epileptic group: 24.0 – 674.4 ms (mean 110.0±19.52) compared to control value from 26.7 to 249.1 ms (mean 87.23±9.98). After inhibition, 29% of control neurons displayed a second activation phase, but only 8% in epileptic group. GABA extended

the initial inhibition on 85% in both groups, but in epileptic one the number of reacted neurons increased up to 86% compared to 79% in control. GABAA and GABAB receptors blockers induced twofold stronger shortening of inhibition in epileptic group (61%) compared to control one (31%).

Conclusion: The extension of the inhibition duration range and reduction of activation components number in MS neurons responses indicate a weakening of intraseptal synchronization in epileptic brain. Enhancement of GABA blockers efficiency can signify compensatory increasing of the number and/or affinity of synaptic GABA receptors in MS during epilepsy. The data show the reorganization of intraseptal GABAergic system. This can influence the synchronization process within the epileptic hippocampus.

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E641
VIABILITY OF HIPPOCAMPAL SLICES DOES NOT DEPEND ON THE ANESTHETIC USED DURING THE EPILEPSY SURGERY

L. Leite Antonio, C. Martins, R. Silva Centeno, E. Ueda, A. Nascimento, A. Cesar da Silva, E. Targas Yacubian, and E. Abrão Cavalheiro
Universidade Federal De São Paulo, Brazil

Purpose: This work aimed to observe if viability of in vitro human hippocampal formation (HHF) during electrophysiological recordings is dependent on the protocol anesthesia maintenance applied at the epilepsy surgery (ES).

Method: Refractory temporal lobe epilepsy patients submitted to ES were divided into two groups. Patients received a balanced anesthesia (BA: sufentanil citrate 20 μg; 1/3 of atracurium besylate induction dosage; isoflurane 1% maximum), or a total intravenous anesthesia (TIA: sufentanil citrate 20 μg; 1/3 of atracurium besylate induction dosage; propofol 80 to 200 μg.kg-1.min-1). After HHF resection and slicing viability of hippocampal slices was assessed by observing the induction of population spikes (PSs) in the granular cell layer of the dentate gyrus triggered by hilar electrical stimulation. The impossibility to obtain PS following different stimulus parameters lead us to consider the slice dead and therefore not viable for electrophysiological studies.

Results: Single or multiple PSs were obtained in hippocampal slices of 50 out of 62 patients submitted to surgery under BA anesthesia. Hippocampal slices from the remaining 12 patients from the BA group were irresponsive to the same electrophysiological protocol. In the TIA group, PSs could be observed in hippocampal slices from 12 patients while the other 3 were considered irresponsive.

Conclusion: These data show that viability of human hippocampal slices submitted to in vitro electrophysiological studies is not dependent on the anesthetic protocol used during ES.

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E642
THETA ACTIVITY OF THE MEDIAL SEPTAL REGION DURING THE PREICTAL AND INTERICTAL EPILEPTIC PHASES: THE SAME FREQUENCY, BUT DIFFERENT SIGNIFICANCE?

V. Kitchigina
Institute of Theoretical and Experimental Biophysics Russian Academy of Sciences, Pushchino, Moscow District, Russia

Purpose: To analyze the relationship between the neuronal theta activity in the medial septal region (MSDB) and hippocampal theta waves in the control and during preictal and interictal periods.

Method: Experiments were performed on awake rabbits. Seizures were evoked by the kindling stimulation of the perforant path.

Results: In the control, the bursts of spikes in one group of rhythmic MSDB neurons phase-locked to the negative peak of theta waves recorded at the hippocampal fissure (group 1), and in the other group, they phase-locked to the positive peak of theta waves (group 2). When seizure after discharges were generated in the hippocampus, dense bursts of spikes separated by periods of inhibition appeared in the MSDB aftera 5-7-s delay. In group 1, bursts of spikes mostly coincided with discharges in the hippocampus. On the contrary, in group 2, the bursts of spikes were mostly observed during inhibitory periods. Acute seizures were often followed by spontaneous secondary epileptiform discharges. The secondary discharges were usually preceded by neuronal oscillations at the theta (6–7 Hz) or 'twice theta' frequency (12–14 Hz). The phase relationships between MSDB theta bursts and hippocampal theta waves could change before seizure generation. When the seizure locus formed in the hippocampus, interictal spikes were recorded in the EEG. Theta oscillations, spontaneous or evoked by sensory stimuli, abolished these pathological spikes.

Conclusion: Evidently, the theta activity during preictal and interictal periods is of different significance for the generation of epileptiform discharges.

E643
ATYPICAL SPIKE – WAVE DISCHARGES IN DIFFERENT EPILEPSIES

G. Kiteva-Trencevska
Clinic of Neurology, Skopje, R. Macedonia

Purposes: Although atypically, there are reports of focal and regional than generalized spike-wave (S-W) discharges and polyspike-wave discharges in idiopathic generalized epilepsies (IGE) and generalized S-W and poly S-Wdischarges in focal symptomatic epilepsies. These atypical EEG findings interfere with the concept of IGE with generalized bilateral symmetric S-W discharges and focal epilepsies with focal or lateralized epileptic discharges. The aim is to present the atypical S-W activity in patients with IGE. The aim is to present that atypical generalized S-W discharges could be found in focal symptomatic epilepsies.

Method: EEG and wake-sleep EEG after sleep deprivation was performed in 103 patients with IGE. EEG was performed in 15 patients with focal symptomatic epilepsy with different etiologies (poststroke, neoplastic, posttraumatic). The patients were with the age range of 13–75 ys. Brain computerized tomography and/or magnetic resonance imaging was performed with normal findings in the patients with IGE.

Results: EEG and wake-sleep EEG after sleep deprivation showed bilateral, synchronous S-W and poly S-W discharges in 98 patients with IGE, with frontocentral or generalized appearance, with frequent occasional lateralization. Atypical focal appearance of S-W and poly S-W discharges was found in 4 patients with IGE. These findings as well as lateralized S-W discharges were one of the reasons for misdiagnosis on first referral of IGE as focal epilepsy and for starting the improper antiepileptic drugs (AEDs). Atypical generalized S-W discharges and poly S-W discharges were found in 2 patients with focal symptomatic epilepsy, suggesting IGE, but neuroimaging showed poststroke and neoplastic etiology.

Conclusion: Focal and lateralized S-W and poly S-W discharges in IGE and generalized S-W and poly S-W discharges in focal epilepsies could lead to misdiagnosis of IGE and focal symptomatic epilepsies. Analyzing the atypical EEG findings in different epilepsies could help for proper

epilepsy classification and diagnosis and contribute to the understanding of the patophysiology of different epilepsies.

E644

MAKING SENSE: TEMPORAL LOBE AUDITORY PROCESSING OF THE NOVELTY RESPONSE IS ABNORMAL IN INFANTILE SPASMS (A TIME FREQUENCY VIEW)

T. Fosi,†, S. Boyd*,‡, R. Scott*,†,‡, and B. Neville*,†,‡*

**Neurosciences Unit, UCL Institute of Child Health, London UK; †National Centre For Young People With Epilepsy (NCYPE), Surrey UK; and ‡Great Ormond Street Hospital For Children NHS Trust, London, UK*

Purpose: To assess if the normal Novelty Response (NR) occurs in babies with cryptogenic West syndrome and its spectral dynamics. This study is motivated by the observation that children with West Syndrome typically lose interest in new environmental stimuli which in normal infants elicit a characteristic NR electrographically.

Method: Fifteen patients (8 female) aged 3–11 months old with cryptogenic West syndrome participated. Cognitive score on the Bayley-III test was age-scaled, classifying infants into Group A (10th – 49th centile: 3 patients) or Group B (below 10th centile:12 patients). ERPs were obtained during normal sleep to a pseudo- random sequence of three sounds (1000Hz, 2000Hz, and variable environmental novels).

Results: The P300 response was identifiable in Group A patients, but not in Group B patients. At 100–200msec Group A patients showed synchronous event-related spectral power (ERSP) increase in the >40Hz gamma band over frontal and temporal lobes ipsilaterally (bootsrap p=0.05). Between 100–300msec they showed ERSP increase and phase-coherence in the 10–15Hz band over the medial temporal region (bootsrap p=0.05).

Conclusion: The novelty detection network within the temporal lobe is more impaired in infants with a worse cognitive outcome from West syndrome (Group B). Paucity of temporal-frontal gamma-synchronisation in this group may suggest diminished long-range interaction of novelty network components between the temporal and frontal lobes. This decreased processing capacity of the network may explain their auditory agnosia. Further investigations aim to establish if the identified spectral features can be improved by treatment and whether they may have a prognostic role.

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MEMORY PROBLEMS IN EVERY DAY ACTIVITIES AS PERCEIVED BY PATIENTS WITH EPILEPSY UNDER TREATMENT. SPANISH NATIONAL STUDY

J. Salas-Puig, J. Álvarez-Carriles*, M. Carreño†, E. Elices‡, A. Gil-Nagel§, J. Sánchez¶, J. Serratosa**, V. Villanueva††, E. Luaces‡‡, and J. Porcel§§*

**H. Univ. Central De Asturias, Oviedo, Spain; †H. Clínic, Barcelona, Spain; ‡Clínica Rotger, Palma de Mallorca, Spain; §H. Ruber Internacional, Madrid, Spain; ¶H. Univ. Virgen de Las Nieves, Granada, Spain; **Fundación Jiménez Díaz, Madrid, Spain; ††H. La Fe, Valencia, Spain; ‡‡EISAI Farmacéutica, Spain; and §§Biometría Clínica, S.L., Barcelona, Spain*

Patients with epilepsy tend to cognitive and behavioral disorders owed both to epilepsy and to antiepileptic drug (AED) therapy. These patients' most frequent complaints are memory problems, psychomotor retardation and attention deficits. Regarding memory, objective and patient's perception scales scores are not always consistent with each other for a given patient. Mood is not ruled out as a possible influence. Aiming to know epileptic patients' perception of their memory and how this relates to social, demographic, clinical and mood characteristics, this epidemiological transversal study was carried out with outpatients from 70 neurologists. Questionnaire of Memory Efficiency (QME) and Hospital Anxiety and Depression Scale (HADS) were completed. 661 patients were included: mean age of 42,1 years (SD=15,2); 56,0% were women. Clinical characteristics: mean evolution time: 17,3 years (SD=12,5); frequency of seizures (last 12 months) 13,8 (SD=43,8); 73,2% were partial seizures; monotherapy 56,3%. Anxiety and depression symptoms were present in 33,4% and 16,0% respectively. QME mean score was 110,0 points (SD=18,6) [In Giovagnoli et al (1997), mean score in control group was 110,7 (SD= 12,7)]. QME's lowest scores were observed in older patients (p=0,001), lower level of studies (p=0,049), unemployment (p=0,001), patients with partial seizures (p= 0,001), in politherapy (p< 0,001) and with anxiety and depression symptoms (p<0,001). Patients related good memory functioning for every day activities. Indicative of worse perception of memory functioning, older ages, lower level of studies, unemployment, partial seizures, politherapy and anxiety and depression symptoms associated with QME's lower scores. Sponsored by EISAI Farmacéutica, S.A.

E646

NEUROPSYCHOLOGICAL PROFILE OF DRUG-RESISTANT NOCTURNAL FRONTAL LOBE EPILEPSY PATIENTS

B. Cascardo, P. Scarpa*, L. Nobili*, G. Zanardi†, G. Lo Russo*, and G. Bottini**

**Niguarda, Ca' Granda Hospital, Milan, Italy; and †University of Pavia, Pavia, Italy*

Purpose: The aim of this work is to investigate the neuropsychological profile of a sample of drug-resistant Nocturnal Frontal Lobe Epilepsy (NFLE) patients, candidate to surgery.

Method: Subjects 1) NFLE PATIENTS: enrolled at the 'Claudio Munari' Epilepsy Surgery Center of Niguarda – Ca' Granda Hospital, Milan. Seven females, 5 males; mean age: 26.8 years; mean education: 11.7 years. 2) Control subjects: seven females, 5 males; mean age: 26.4 years; mean education: 11.3 years. Neuropsychological assessment: The following cognitive functions were explored: language, short- and long-term verbal memory, short- and long-term visuo-spatial memory, constructional motor functions, attention, executive functions, visuo-perceptive discrimination, abstract reasoning. Statistical analysis: a *t*–test for independent samples was performed (p-values <.01).

Results: A significant deficit of semantic fluency (p <.01) and verbal episodic memory (p <.001) has been found in NFLE patients.

Conclusion: This study explores the neuropsychological profile of drug-resistant NFLE patients, not already specifically investigated in the literature. In our patients we found an impairment of semantic fluency, a deficit already signalled in Frontal Lobe Epilepsy (FLE) subjects (Drane DL et al. Epilepsy Behav 2006;9:339–344). Interestingly the most significant result is a NFLE impairment of episodic verbal memory, that is a cognitive function not frequently investigated in FLE patients as it is considered more related to the temporal structures. A speculative hypothesis takes into consideration that sleep fragmentation due to nocturnal seizures (Terzaghi M et al. Epilepsia 2007;48 (2):335–41) could alter the explored (Yoo SS et al. Nat Neurosci. 2007;10 (3):385–92) sleep-related mechanisms in memory consolidation.

E647

LANGUAGE OUTCOME IN BENIGN EPILEPSY WITH CENTROTEMPORAL SPIKES (BECTS)

C. Monjauze, C. Hommet†, M. Barthez‡, J. Motte§, and L. Tuller¶*

**UCL, Institute of Child Health, London, UK; †CMRR center, Tours University Hospital, Tours, France; ‡Hopital Gatien De Clocheville, Tours University Hospital, France; §American Memorial Hospital, Reims University Hospital, Reims, France; and ¶Laboratoire Langage et Handicap, Universite Francois Rabelais, Tours, France*

Purpose: We had previously demonstrated in a cross-sectional study (T1) that the prevalence of language impairment in the BECTS population is significantly higher than that found in a general population (Monjauze C et al Psychologie Francaise 2007;52:107–22). We report here on a follow-up study (T2; mean follow up time = 24.1 months, SD = 1.1) of a subgroup of this population.

Method: Eighteen BECTS participants aged 11 to 18 (13;9 yrs; 11/18 in remission) underwent standardized language assessment in addition to a spontaneous language sample analysis, using measures shown to be relevant in detecting language disorders in school-aged children and adolescents. We compared the spontaneous language samples with samples of the same length (about 60 utterances per participant) from typically developing 11- and 14-year-olds (N = 24, 12;9 yrs).

Results: The proportion of participants with language impairment as measured by standardized tests decreased at follow up (T2) but still remained higher than in the general population (33% with 2 Z scores < -1 SD; 16% with 2 Z scores < -1.65 SD), affecting particularly written language. Moreover, we found that the use of complex sentences was significantly lower in the BECTS group than in the control group: 22.7% vs 30.9% of all verbal utterances ($U = 124.5$, $p < .05$). In addition, the BECTS participants produced significantly more morphosyntactic errors (9.8% vs 1.6%, $U = 80.5$, $p < .001$) although most of them were in remission.

Conclusion: These results support the hypothesis of linguistic sequalea in this so-called benign epilepsy.

E648

A BATTERY FOR SCREENING CHILDREN AFFECTED WITH EPILEPSY IN CLINICAL PRACTICE

G. Ben-Bashat, B. Ben Zeev Ghidoni, and M. Levav

The Chaim Sheba Medical Center, Hashomer, Israel

Purpose: To develop a short and valid battery to assess the neurocognitive functions as a routine in clinical practice with children affected with epilepsy. To evaluate the added value of this procedure to the physician's decisions and management of the patients' compliance with therapy.

Method: 118 children [62 females], age of epilepsy onset [6.6±3.4 years], age of testing [10.3; ±3.3years], 53 of those with generalized and 65 with partial epilepsy were recruited through the Comprehensive Epilepsy Clinic. Eighty percent of the children attended regular schools and 20% received educational support within the school. Participants were assessed with a short neuropsychological battery which included: Attention [visual/verbal/visual search]; Memory [verbal]; Motor [visuomotor/fine motor coordination]; Verbal abilities [naming/ verbal fluency]. Parents filled out the Child Behavior Checklist and Quality of Life questionnaires. Medical diagnoses were reviewed by the neurology staff. Participants were divided according to: epilepsy diagnosis, seizure type and number of AED's (Antiepileptic drugs) reported at time of testing. Standard scores were transformed into Z's to allow for comparisons among the groups.

Results: No differences among age of epilepsy onset and age of testing between the different groups. Cognitive impairments were observed in motor, attention and verbal abilities. Children affected with partial seizures of all types showed a marked deficit in verbal fluency tasks, whereas the affected with generalized seizures showed visual inattention deficits.

Conclusion: This screening battery enabled the physicians to obtain individual and group neurocognitive profiles of the children and guided subsequent interventions and educational recommendations.

E649

THEORY OF MIND IN TEMPORAL AND FRONTAL LOBE EPILEPSY

A. Giovagnoli, F. Reati, A. Aresi, A. Riva, F. Villani, M. Casazza, R. Spreafico, and S. Franceschetti

'C. Besta' National Neurological Institute, Italy

Purpose: Theory of mind (ToM), the ability to understand mental states, is a multifaceted function dependending on the integrity of different neural systems. We assessed ToM in temporal (TLE) and frontal lobe epilepsy (FLE) patients aiming to explore specific deficits and their relationships to cognitive and epilepsy-related variables.

Method: Eighty-eight patients with TLE (n=64) or FLE (n=24) and 70 healthy subjects were assessed using the Faux Pas task (FPT) and other neuropsychological tests. The FPT evaluated ToM by requiring the recognition or exclusion of social gaffes in 20 stories. Each story provided one detection score (the number of FP correctly recognized or rejected), four quality scores relating to story contents, and one control score.

Results: With respect to healthy subjects, TLE and FLE patients were impaired in the recognition and comprehension of gaffes, and FLE patients were also impaired in story control compared to healthy subjects and TLE patients. In epilepsy patients, factor analyses generated two factors (Comprehension, Control) from eight FPT scores and four factors from other test scores (Attention, Language, Executive functions, Working memory). In TLE patients, ToM Comprehension was related to Attention and Language factors, age, and disease duration. In FLE patients, ToM Control was only related to Attention.

Conclusion: Both TLE and FLE patients may be significantly impaired in ToM, showing altered comprehension of others' mental states. Although such impairment may be related to different variables, it might contribute to determine altered social behaviors, thus deserving special attention in these patients.

E650

THE DEVELOPMENTAL PROFILE OF CHILDREN FOLLOWING CSE

M. Martinos, S. Patil, M. Yoong, R. Scott, and M. de-Haan

Institute of Child Health, University College London, UK

Introduction: Convulsive status epilepticus (CSE) is the most common medical neurological emergency in childhood. The developmental profiles of children following CSE have not been systematically investigated. The aims of this study were: (1) to assess whether infants with prolonged febrile seizures (PFS) are performing better than infants with CSE associated with other aetiologies, (2) to assess whether children with PFS have normal function, soon after the event.

Method: 19 infants were assessed using the Bayley Scales of Infant and Toddler development (Bayley-III).

Results: The infants were assessed within a mean of 28 days (8–85) from the CSE. The two groups were similar in gender and age. A Mann-Whitney U test revealed that the PFS group performed significantly better than the non-PFS group in the language scaled score ($p=0.035$) and the fine motor ($p=0.022$) and gross motor ($p=0.043$) scales. There was

also a clear trend for superior performance of the PFS group on the cognitive scale (p=0.090). A one sample *t*–test revealed that the PFS group show impaired performance relative to the norm (standard score of 10) in the language scaled score (p=0.017). A clear trend was obtained in the cognitive scale where the PFS group seem to be performing below the norm (p=0.084).

Conclusion: The PFS group are performing significantly better than the non-PFS group. However, within approximately a month following the CSE, the PFS group show impaired performance relative to the norm. More research is warranted to track the developmental profile of children following CSE.

E651
THE EFFECTS OF LEVETIRACETAM ON COGNITION – A NONINTERVENTIONAL SURVEILLANCE STUDY

J. Witt, and C. Helmstaedter
University Clinic of Epileptology, University of Bonn, Germany

Purpose: To evaluate the effects of levetiracetam (LEV) on cognition in a multicenter noninterventional surveillance trial.

Method: Practitioners prospectively acquired cognitive data from 401 outpatients prescribed LEV. Cognition was assessed before (T1) as well as three (T2) and six months (T3) after administration of LEV applying two screening tools which focus on executive functions and memory (EpiTrack, EpiScope) and two subjective measures – a patient (EpiQuest) and doctor rating.

Results: At baseline, cognitive impairments were indicated in 32% (doctor rating), 37% (EpiScope), 44% (EpiTrack), or 67% (EpiQuest) of the patients. With LEV, 87% initially untreated patients changed to monotherapy, 94% changed from mono- to polytherapy. Retention rate of LEV was 97%, 7% adverse events were reported. Of 293 patients on LEV with complete seizure records and with seizures at T1, 36% achieved seizure control at T2, 25% later at T3, 33% continued to have seizures, and 7% had a relapse between T2 and T3. Ratings indicated excellent tolerance in up to 68%, and cognitive improvements in 58% of the patients. Repeated testing indicated cognitive improvement between T1 and T3, which was significant in 20–23% of the patients, 5–6% deteriorated. Improvements between T2 and T3 depended on successful seizure control. Better baseline scores, shorter epilepsy (EpiTrack), less antiepileptic drugs at baseline (EpiTrack) and seizure control (EpiQuest) were predictive for better cognitive outcome.

Conclusion: LEV was well tolerated and efficacious, and despite an increase of the total drug load, treatment with LEV was accompanied by a general subjective and objective cognitive improvement.

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E652
WADA TEST IN A DEAF EPILEPSY PATIENT: A CASE REPORT

K. Zaar, T. Urbanic Purkart, E. Körner, M. Feichtinger, and E. Ott
Medical University Graz, University Clinic For Neurology, Austria

Purpose: A deaf 25-year-old patient suffering from drug refractory right temporal lobe epilepsy with hippocampal sclerosis underwent presurgical evaluation. He had been profoundly deafened by meningitis at the age of 6 months with epileptic seizures starting at the age of 7 years. Although lateralization of language abilities has been reported to be comparable in deaf and nondeaf persons, there were factors pointing towards a possible atypical speech lateralization in our patient. He was ambidextrous, had an early disease onset and no cognitive deficits including a normal visual and spatial memory.

Method: To ensure that the patient would not have speech deficits after resection of the seizure focus, we performed a Wada test. He was fluent in sign language and able to speak and read aloud rather slowly and not very clearly. After numerous pretests, left and right unilateral cerebral anaesthesia was performed. In order to evaluate the function of the unanesthetized hemisphere, an interpreter communicated signs, and showed signed pictures, words and figures. The patient answered directly in sign language using only one hand due to temporary hemiparesis.

Results: Both under anesthesia of the left and of the right hemisphere, the patient(s performances were comparable to that under pretest conditions. This indicates that speech and memory functions were represented bilaterally in both hemispheres. Surgery improved the patient's seizure situation and did not affect his language abilities.

E653
PSYCHOMOTOR DEVELOPMENT IN BABIES WITH EPILEPSY AND NEONATAL SEIZURES BACKGROUND AT 2 YEARS OLD AFTER A NEUROHABILIATION THERAPY

J. Barrera, E. Porras-Kattz, T. Harmony, J. Ricardo-Garcell, and D. Martinez
Universidad Nacional Autonoma De Mexico, Mexico

Purpose: To compare the psychomotor development in babies with epilepsy and neonatal seizures background at 2 years old after a neurohabiliation therapy.

Method: 77 babies were evaluated at 24 months corrected age (CE) by motor subscale of the Bayley Scale Infant Development: 12 with epilepsy, 12 have neonatal seizure background (NSB) and haven't developing epilepsy, 52 have perinatal risk factor for neurodevelopmental deficits (PRFND) and 15 babies were controls. All babies get into the neurotherapy younger than 4 months CE until 18 months CE. The results were analyzed with the nonparametric Kolmogorov-Smirnov test for comparing two samples.

Results: We observed significant difference in psychomotor development index (PDI) results between babies who develop epilepsy and those who didn`t but have NSB (p=0.03). We also observe difference between the control group and the epilepsy group (p=0.01), but we didn't find not difference between controls and the group with NSB (0.6). We then compared the group with epilepsy and those with PRFND with a significant difference of p=0.01. The group with PRFND haven't significant difference (p=0.8, p=0.5) with the NSB and control group respectively.

Conclusion: The early developing epilepsy it's a conditioning factor for motor development, even if the babies were trained in a neurohabilitation motor therapy for at list 12 months. The neonatal seizures background and perinatal risk factors for neurodevelopmental deficits seems not to be a conditioning factor for motor development and those babies have a normal psychomotor outcome.

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E654
MEMORY CHANGE AFTER EPILEPSY SURGERY

I. Tyrlikova, R. Kubikova, R. Kuba, M. Brazdil, and I. Rektor
St. Anne University Hospital, Czech Republic

Purpose: Our study sought to explain differences in memory changes in the course and after an epilepsy surgery.

Method: Patients (30 males, 14 females; aged 17–49) with refractory temporal lobe epilepsy were followed for five years. We collected surgery data, MRI, hemisphere dominancy and Engel's classification. We used the Wechsler Memory test to assess memory three times: before the surgery; 1 and 5 years after the surgery.

Results: We classified the patients according to changes in the memory score between the presurgical and postsurgical assessments and the assessment after five years. We distinguished unchanged, worsened and improved cases. Group a: 22 patients unchanged in both periods. Group b: 8 patients unchanged in the first and worsened in the second period. Group c: 7 improved in the first and unchanged in the second period. Group d: 7 patients got worse in the first and improved in the second period. The improvement correlated negatively with age in the second period (p=0,012). Group b is more frequent in amygdalo-hippocampectomy (50%) and less in AMTR, whilst the group three is more frequent in AMTR (72%) and is absent in amygdalo-hippocampectomy. High frequency of patients with MTS finding in group b (75%) and group c (71%), compared to a significantly lower frequency of these patients in group d (14%). Low frequency of patients who underwent dominant hemisphere surgery in group a (23%).

Conclusion: Dominant hemisphere surgery, type of such surgery and MTS distinguishably influence the progress of memory changes after surgery.

E655
FLASHBULB MEMORIES IN TEMPORAL LOBE EPILEPSY

B. Metternich, R. McCarthy†, P. McKenna‡, A. Kühn*, K. Wagner*, and A. Schulze-Bonhage**
**Universitätsklinikum Freiburg Neurozentrum, Germany; †Wessex Neurological Centre Southampton General Hospital, UK; and ‡University of Glasgow, Section of Psychological Medicine, UK*

Purpose: Flashbulb memories (FM) belong to the class of autobiographical memory. FM are memories for the circumstances under which an item of surprising news with a high degree of importance and emotional impact were received. FM are vivid and rich in detail, often accompanied by visual images, and maintained over time with great accuracy and confidence. Patients with temporal lobe epilepsy (TLE) have been shown to have deficits in episodic autobiographic memory, but so far, no study has investigated FM in temporal lobe epilepsy.

Method: A group of healthy controls (15), a sample of patients with epilepsy (12) matched for age and gender, and a sample of schizophrenic patients (14) were tested and compared on an especially designed FM test including an eight-week retest procedure. The test contained a questionnaire, probing for various memory features of the reception event. Apart from questions referring to the chosen FM event of the death of Lady Diana Spencer, a control event of ordinary news was included. Scores of memory consistency were obtained by comparing the answers on both tests. It was reasoned that a single-time measure of FM performance would not be sufficient to assess FM quality or filter out confabulation. FM performance was compared across the events and across the groups/subgroups of subjects.

Results: TLE patients and schizophrenic patients displayed significantly lower mean scores than healthy controls on FM consistency ($p < 0,05$). Subgroup analyses revealed that both right- and left-TLE patients were impaired on the test compared with the control group ($p < 0,05$).

Conclusion: The present pilot study indicates that patients with temporal lobe epilepsy have flashbulb memories of lower quality (consistency) than healthy control subjects. Replication attempts with larger samples are desirable.

E656
ELECTRIC STIMULATION OF PERIVENTRICULAR HETEROTOPIAS: PARTICIPATION IN HIGHER CEREBRAL FUNCTIONS

J. Wagner, C. Elger, and C. Bien
University of Bonn, Germany

Purpose: Periventricular heterotopia is among the most frequent malformations of cortical development and often associated with medically intractable epilepsy. Several studies have shown a participation of these heterotopias in lower cerebral functions such as motor tasks, somatosensory processes and visual tasks. Here, we present a case demonstrating a participation of heterotopias in higher cognitive processes such as language or complex visual and acoustic processing.

Method: The patient, a 35-year-old man, suffering from pharmacoresistant epilepsy, showed periventricular heterotopias in both hermispheres. During presurgical diagnostics electric stimulation of the heterotopias and the overlying cortex was performed.

Results: Electric stimulation revealed a functional role of heterotopias in higher cerebral functions such as language, complex visual and acoustic hallucinations. Furthermore, stimulation of the overlying left temporolateral cortex led to unusually intense positive-phenomena such as complex acoustic hallucinations and language production probably due to a reduced GABAergic transmission.

Conclusion: This case description provides evidence of a functional role of heterotopias in higher cerebral functions. Interestingly, the anterior-to-posterior representation of these functions is comparable to the normal anterior-to-posterior representation in normal neocortex, the presumptive target of the 'arrested' heterotopic neurons. This suggests that developing neurons have a specified arrangement in the periventricular zone before starting migration towards the neocortex (like a periventricular 'mini-cortex' in early developmental stages).

E657
OUTCOME AND PREDICTION OF MEMORY PERFORMANCE AFTER SURGICAL TREATMENT FOR TEMPORAL LOBE EPILEPSY

F. Oltmanns, A. Mies, H. Haettig, T. Lehmann, and H. Meencke
Epilepsy-Center Berlin-Brandenburg, Berlin, Germany

Introduction: Besides determination of cognitive status neuropsychological testing in patients with medically intractable temporal lobe epilepsy who are candidates for surgical treatment attempts to predict postoperative cognitive outcome. The aim of this study was to look for preoperative neuropsychological characteristics to render outcome prediction more individual especially in the memory domain.

Method: 155 patients who underwent surgical treatment between 1999 and 2006 for TLE and have been neuropsychologically tested pre- and one year postoperative could be included. After assessment of postoperative changes in verbal and nonverbal memory preoperative data and postoperative control of seizures as well as subjective judgements of memory performance were analyzed to predict postoperative memory outcome.

Results: The analysis revealed no significant differences between L-TLE and R-TLE preoperatively and around 2/3 of the patients remained unchanged postoperatively independent of side of surgery. Only in the verbal memory domain effects could be observed. For the L-TLE group we found slight losses, whereas for the R-TLE group there were significant gains with side of surgery as main influencing factor. This effect was not present in the domain of figural memory. We then divided the sample into three subgroups according to their preoperative T-scores. Higher preoperative performance leads to significant losses after surgery with no correlation to side of surgery x time. In contrast the group with lowest performance showed significant gains irrespective of side of surgery. Surprisingly R-TLE patients in the lower average group had high benefits whereas the L-TLE patients showed modest losses.

E658
MEMORY IN A GROUP OF CHILDREN WITH TEMPORAL LOBE EPILEPY

A. Lopes, M. Simões*, C. Robalo†, I. Fineza†, and O. Gonçalves†*
**University of Coimbra, Portugal; and †Coimbra's Paediatric Hospital, Portugal*

Purpose: The objective of the current investigation is to estimate the clinical utility of the Coimbra's Neuropsychological Battery Assessment memory tests – examining its potential to discriminate the performance of children with temporal lobe epilepsy from that of children with no health problems.

Method: Neuropsychological status was examined in 24 children with temporal lobe epilepsy (14 males, 10 females), aged 7–15 years with epilepsy and compared with 24 control children of the same age and sociocultural level. Children with epilepsy were selected based on the following inclusionary criteria: (1) they were administered the Wechsler Intelligence Scale for Children (WISC-III; Wechsler, 2003) and obtained a Verbal or Performance IQ > 70, and (2) they had an EEG that confirmed the diagnosis of epilepsy. Exclusionary criteria were the following: (1) they did not have a comorbid diagnosis of any other neurological or psychiatric disorder, and (2) they were receiving no more than two antiepileptic medications. Subjects were administered the following tasks of memory assessment: List Learning, Stories, Rey Complex Figure, Corsi Test and Memory for Faces.

Results: Children with temporal epilepsy present deficits in memory performance: verbal memory, working memory, visual memory (only on delayed trials).

Conclusion: This empirical research underlies the importance of assessing, in a systematic way, children and adolescents with temporal lobe epilepsy, with neuropsychological assessment protocols that include several measures of memory assessment. So that we can establish adequate and timely school intervention plans namely for those with school difficulties.

E659
MESIAL TEMPORAL LOBE EPILEPSY-HIPPOCAMPAL SCLEROSIS (MTLE-HS): IS THERE ANY CORRELATION BETWEEN COGNITION AND BILATERAL ICTAL DISCHARGES?

I. Santana, C. Cunha, R. André, C. Bento, and F. Sales
University Hospitals of Coimbra, Portugal

Purpose: Epileptic dysfunction of hippocampal structures is important on cognition, with bilateral lesions inducing severe episodic-memory deficits. In unilateral mesial sclerosis, the observation of bitemporal activity on ictal scalp- EEG has an uncertain significance. Our aim was to compare neuropsychological performance in patients with unilateral vs. bilateral patterns, to evaluate the impact of epileptic propagation on cognition.

Method: We enrolled 43 MTLE-HS patients, 23 with left HS (L-HS) and 20 right-sided (R-HS). A bilateral discharge was defined whenever a synchronous/asynchronous ictal pattern was observed on the scalp Video-EEG monitoring. Of this cohort, 8 (35%) of the L-HS and 11 (55%) of the R-HS patients had bilateral patterns. All underwent a neuropsychological comprehensive assessment where the main cognitive functions (attention, motor-psychomotor speed, executive, memory, language and visuo-spatial abilities) were evaluated.

Results: There was a dissociation in episodic-memory performance between left and right patients, with higher scores of L-HS on visual-memory tests, and R-HS patients on verbal-memory tasks. In this group (R-HS) we couldn't find significant differences between patients with unilateral or bilateral ictal discharges in any cognitive test. For the L-HS group the comparison of these two EEG sub-categories revealed that patients with a bilateral pattern had a worse performance in tests of working memory, mainly in Stroop C (66.43±12.78 vs. 85.28±23.40; p=0.0025) and CW (148.28±27.06 vs. 195.14±63.73; p=0.030), as well as on a verbal fluency task (16.0±6.76 vs. 8.33±8.04; p=0.035).

Conclusion: Our results suggest that H.S.-left-sided patients are particularly susceptible to bilateral discharges, with a negative impact on initiation and working memory.

E660
COGNITIVE REHABILITATION IN TEMPORAL LOBE EPILEPSY

M. Quartuccio, S. Pontecorvo, M. Morreale, M. Prencipe, and A. Francia
Umberto I, La Sapienza University of Rome, Italy

Temporal lobe epilepsy is the most important focal epilepsy due to its high prevalence, drug resistance, and commonly disabling effects on memory functions.

Seizures concern hippocampal and parahippocampal structures,which mediate declarative memory. The aim of this study was to investigate the effects of cognitive rehabilitation on memory disorders.

Method: Thirty patients with partial epilepsy due to temporal lobe epilepsy. Sixteen patients suffered from left temporal lobe epilepsy and fourteen from right temporal lobe epilepsy. A normal control group consisted of sixteen persons matched with the TLE groups for age, educational level, and gender. Patients and control group underwent to: neurological assessment, EEG, and neuropsychological tests. The rehabilitation training focused on the memory functions, in particular processing, elaboration, and encoding specificity (kind of retrieval) of the information operative at the two memory stages, encoding and retrieval.

Conclusion: Our results show that both groups benefited from cognitive aids such as deep processing, elaboration, or cued recall. The ANOVA revealed the global effect of each of these factors. Furthermore, the groups interaction revealed that the effect of the retrieval aid differed from one group to another. Moreover further studies have been required to disclose the rehabilitation efficacy in this patients.

E661
FACE RECOGNITION IN CHILDREN WITH EPILEPSY

E. Mojs, E. Gajewska, and M. Glowacka
Poznan University of Medical Sciences, Poland

Epilepsy is a risk factor of the occurence of emotional disturbances as well as cognitive ones. The origin of these disturbances may be multifactorial. They could be divided into two groups: primary and secondary. The aim of the study was to estimate the level of face recognition in children with epilepsy. 40 pts with epilepsy – partial and generalized epileptic seizures participated in the study. The mean of age was 10,8 yrs, time of duration of the disease was appr. 5,3 yrs. Pts were treated wit conventional and novel antiepileptic drugs. The Benton Facial Recognition Test used in the study. The results show lower scores in this test in comparison to healthy population. There was no statistical correlation between kind of seizures and results of Benton test as well as correlation to time of duration of the disease. In conclusion the problems in facial recognition test may have primary character.

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E662
SOME PECULIARITIES OF FAMILY HISTORY AND EEG FINDINGS AS RISK FACTOR FOR EPILEPSY DEVELOPMENT IN CHILDREN

L. Tantsura, D. Tretjakov, S. Salo, A. Shatillo, O. Pylypets, V. Grokhovsky, O. Lukjantzeva, and O. Trembovetzka
Institute of Neurology, Psychiatry and Narcology of AMS of Ukraine, Ukraine

Objectives of study were to find out methods and criteria for preclinical diagnosis and risk group determination for epilepsy in children. Natural history, neurological status and EEG of 314 children of age between 1 and 16 years with different epilepsies and epileptic syndromes were studied. EEG of their close relatives (parents and siblings) were analyzed too. Also 26 children without epilepsy were studied in the same way. Family history of all children was studied in depth of 3–4 generation. The prevalence of psychiatric disorders was 3,7 times, of paroxysmal disorders 1.8 times and of epilepsy 3,5 times higher among relatives from mother's side of children with epilepsy then in control group. Another interesting practical finding was a high predictable value of siblings' EEG. Spike-waves, photoparoxysmal reactions and high amplitude generalized slow wave activity in EEG of two or more siblings associated with high risk of epilepsy in these offsprings. Such abnormalities in EEG of parents had much less predictable value. Data about epilepsy in mother and here relatives, mentioned above EEG abnormalities and MRI pathology could be considered as risk factors for epilepsy development. Combination of two factors demands frequent monitoring of such children and AED therapy should be started if three factors are present. Also AED therapy should be considered in case of preclinical spike-waves, photoparoxysmal reactions and high amplitude generalized slow wave activity in EEG of two siblings.

E663
DEECTION OF ANTI CARDIOLIPIN ANTIBODY IN CHILDREN WITH EPILEPSY AND COMPARING IT WITH HEALTHY CHILD

S. Inaloo, B. Yavary, and A. Hagh Talab
Shiraz University of Medical Science, Iran

Purpose: Evidence of immune system aberrations in patients with epilepsy includes antiphospholipid antibody positivity in adult patients with epilepsy with a prevalence of 19% and in children with epilepsy with prevalence of 13%, lead us to detect anticardiolipin antibody in children to evaluate correlation between immune system and epilepsy.

Method: We conducted a prospective study on 135 pediatric patients. We categorized the patients into three different groups. Group 1: Children who had epilepsy and received anticonvulsants, group 2: children with new onset convulsion who didn't receive anticonvulsants, group 3: healthy children as control group. In our study we also evaluated correlation between anticardiolipin antibody (ACLA) positivity and factors such as age and sex distribution, onset, type, frequency and duration of epilepsy, type of anticonvulsants used, abnormal physical findings, brain abnormal radiological and electroencephalographical (EEG findings).

Results: Prevalence of IgM ACLA in groups 1, 2 and 3 were 8.9, 6.7 and 2.2% respectively. Prevalence of IgG ACLA in group 1, 2 and 3 were 11.1, 4.4% and 2.2% respectively. There was no significant difference between these three groups. There was no correlation between positivity of ACLA and age and sex distribution, onset, duration, type, cause and frequency of epilepsy and type of drugs used.

Conclusion: However prevalence of ACLA in patients with epilepsy was higher than control group but it was not such significant and in compared with other study was low. Stimulation and promotion of relevant researches would serve as a perquisite for reaching exact results.

E664
EFFICACY AND SAFETY OF TOPIRAMATE MONOTHERAPY COMPARING WITH CARBAMAZEPINE AND LAMOTRIGINE IN TREATMENT OF RECENTLY DIAGNOSED EPILEPSIES WITH PARTIAL SEIZURES

V. Martyniuk, V. Kharytonov, and T. Yarmolyuk
Ukrainian Medical Rehabilitation Center For Children With Organic Injuring of Nervous System of Ministry of Public Health of Ukraine, Ukraine

Purpose: To evaluate the efficacy and safety of topiramate monotherapy comparing with carbamazepine and lamotrigine in treatment of recently diagnosed epilepsies with partial seizures.

Method: 80 patients with different forms of epilepsy had been chosen. 49 (61.3%) of patients had partial seizures. All patients in partial seizures group were divided on three groups according to drug of treatment – topiramate, carbamazepine and lamotrigine. Efficacy of the treatment had been estimated. In the second part of the study the safety of treatment of these drugs had been estimated too.

Results: The efficacy of monotherapy of topiramate was 62.5%, carbamazepine 58.8% and for lamotrigine 50%. Frequency of side effects for topiramate was 19.2%, carbamazepine – 29.4% and lamotrigine – 28.5%.

Conclusion: Topiramate is effective and safe for monotherapy of epilepsies with partial seizures recently diagnosed.

E665
ELECTROENCEPHALOGRAPHY ABUSE IN PEDIATRY

M. Knezevic Pogancev, N. Jovic, M. Pavlovic, and T. Redzek Mudrinic
Child and Youth Neurology and Psychiatry Institute, Beograd, Serbia

Electroencephalography (EEG) is a standard diagnostic method of assessment used after any consciousness disorders in children with the dominance of the normal EEG findings as the result of the fact that a large number of EEG was done in order to 'exclude epilepsy'. The aim of this study was to show that EEG has been applied too often in the process of getting the information it cannot obtain. Study was conduced in period from 1993 to 2003 year in Institute for Child and Youth Health Care Of Vojvodina in 2000 first time hospitalized children aged 11 hours to 18 years (middle age 4 year 3 months 27 days). The initial neurophysiological examination was completed with a standard EEG check-up in a conscious state for 42,2% of children. In 7,9% of cases, an EEG check-up was carried out in a state of a spontaneous sleep, while in 49,9% of cases it was carried out during the sleep, after a partial deprivation of sleep. An EEG check-up was carried out during the sleep in 33,5% of cases due to the age and unwillingness to cooperate, and in 16,4% of cases because of the inability to record a specific epilepsy-forming EEG result in a conscious state, which was in opposition to expectations based on the anamnesis and clinical results. Starting from the fact that EEG check-up is expected to confirm the presence of a change (epileptic activity), and having in mind that the absence of the latter does not necessarily mean excluding it, it has been found that 75% of the EEG findings does not meet the expectations.

E666
SOCIAL ANXIETY IN NORWEGIAN CHILDREN WITH EPILEPSY. A POPULATION BASED STUDY – THE AKERSHUS HEALTH PROFILE STUDY

K. Alfstad, J. Clench Aas†, B. Van Roy‡, H. Kristensen§, L. Gjerstad¶,**, and M. Lossius**

**National Centre For Epilepsy, Sandvika, Norway; †Norwegian Institute of Public Health, Division of Mental Health, Norway; ‡University of Oslo, Institute of Psychiatry, Norway; §Regional Centre for Child and Adolescent Mental Health, Oslo, Eastern and Southern Norway; ¶Division For Clinical Neuroscience, Rikshospitalet, Norway; and **Faculty of Medicine, University of Oslo, Norway*

Purpose: We have previously published data showing a higher prevalence of psychiatric symptoms in youths with epilepsy compared to controls. The aim of this presentation was to assess social anxiety symptoms in children with epilepsy (CWE) aged 8–13 in a Norwegian County.

Method: The study was cross-sectional and based on questionnaires from parents of CWE aged 8–13. 13,228 questionnaires were filled in (response rate 78%). Logistic regression analysis was performed with social anxiety as the dependent variable. Gender, age, having or having had epilepsy, family affluence and living with single parent were independent variables. The definition of social anxiety was based on scores corresponding with criteria A-D for social anxiety disorder, according to DSM- 4.

Results: Social anxiety was significantly more prominent among CWE compared to controls (14.2% % vs. 7.7% %, p= 0.047). The finding was more profound in girls, where 17.8% of girls with epilepsy reported social anxiety compared to 7.6% in controls (p= 0.015). Having or having had epilepsy was an independent predictor for social anxiety (OR= 2.1, p= 0.09). Family affluence was also a predictor of social anxiety, but not as strong as epilepsy (OR 1.1, p= 0.004).

Conclusion: We found that having or having had epilepsy was an independent predictor of social anxiety in CWE aged 8–13. The effect was more profound in girls than in boys. Awareness and early discovery of this in parents, teacher and health professionals could help prevent these problems from developing or allow proper care to be given.

E667
EMERGENCY DEPARTMENT VISITS OF CHILDREN WITH NONFEBRILE SEIZURES

Y. Landau, Y. Waisman, S. Rosenthal, and A. Shuper

Schneider Children's Medical Center of Israel, Israel

Purpose: Emergency department (ED) visits and hospitalizations for the diagnosis and treatment of seizures are not unusual. The need for the unexpected, acute ED visit and potential hospitalization affects quality of life of the child and his family. Reasons for ED visits were studied, looking for a possible role of the neurology outpatient clinic in decreasing hospital admissions of children with epilepsy.

Method: Charts of children aged <18 years, who visited ED during 4 months period due to nonfebrile seizure, were analyzed and the pertinent data were retrieved.

Results: Forty-four boys (52%) and 41 girls (48%) were included; they visited ED 104 times. Reasons were: new-onset seizures (30%), seizures in epileptic child (38%) or status epilepticus (4%), recurrent seizure, not-yet defined etiology (16%), and others. The epileptic syndromes included: benign focal epilepsy, 14%; juvenile myoclonic epilepsy, 1%; infantile spasms 4%; and undefined (39%). The rest causes were: developmental disorders, 14%; pre- or perinatal complications, 12%; brain lesion, congenital (5%) or acquired (3%); and others. Seventy one percent of the children were hospitalized, in 29% an antiepileptic drug was initiated, in 18% the dose was increased. Twenty eight percent underwent a diagnostic work-up only.

Conclusion: Close to 40% of ED visits were due to seizure in an epileptic child, most of them were hospitalized. This fraction can potentially be decreased with improved patient and parent education combined with greater availability/accessibility of neurology clinics. This can improve family quality of life as well as decrease the in-patient load of children with epilepsy.

E668
EFFICACY AND SAFETY OF LEVETIRACETAM IN EPILEPTIC CHILDREN WITH COEXISTENT MEDICAL ILLNESS

J. Lara-Herguedas, J. García-Peñas, M. Rodrigo, L. López-Marín, M. Ruiz-Falcó, and L. González Gutiérrez-Solana

Pediatric Neurology Unit, Hospital Infantil Universitario Niño Jesús, Madrid, Spain

Purpose: To describe the efficacy and safety of Levetiracetam (LEV) in epileptic children with coexistent medical illness.

Method: We retrospectively analyzed data from 35 consecutive children aged 7 days to 18 years treated with LEV. Medical records of these patients were reviewed for demographic data, underlying medical disorders, changes in seizure frequency, seizure freedom and adverse events. We used LEV as first line therapy in 15 patients or as an add-on therapy after failing prior antiepileptic drugs in 20 patients. Starting dose of LEV was 10 mg/Kg/day, increased every 1–2 weeks by 10 mg/Kg up to a maximum of 100 mg/Kg/day, depending on efficacy and tolerability.

Results: Underlying medical disorders included falciform cells anemia (2 cases), systemic vasculitis (2 cases), isolated central nervous system vasculitis (1 case), oncological diseases (14 cases), inherited metabolic disorders (10 cases), Renal Impairment (3 cases) and Hepatic Impairment (3 cases). Seven patients were classified as having generalized epilepsy. Epilepsy was localization-related in 25 patients. Three patients had epileptic encephalopathy. Twenty patients (57%) showed a seizure frequency reduction of more than 50% including 15 patients (43%) who became seizure-free. LEV was generally well tolerated although 10 patients (28%) reported side effects. Somnolence was the most commonly reported adverse event (25%). LEV was withdrawn in 7 patients (20%) because of side effects like irritability and aggressive behavior.

Conclusion: LEV is a safe and effective alternative in patients with associated medical conditions that require long-term polypharmacy because of the lack of hepatic enzyme metabolism and drug to drug interactions.

E669
ABSENCE SEIZURE: GENERALIZED OR PARTIAL EPILEPSY?

G. Pilina

Pediatric Regional Clinical Hospital, Izhevsk, Russia

Purpose: It is well known that absence epilepsy is a form of generalized epilepsy mainly affects children. Sometimes neurologist see patients with absence whose EEG does not fit the typical absence pattern, but with focal epileptiform discharges; it makes us doubt that absence primary generalized seizure. The purpose of this study is to examine EEG abnormalities in children with typical absence clinical features.

Method: We studied 56 children with typical simple absence seizures (just few seconds staring without consciousness) and complex absence seizures (staring with eyelid myoclonia, automatisms, changes in tone, face redness and so on); ranging in age from 4 to 17 (main age 10,73±3,69). The investigation included interictal EEG, neurology status, neurovisualization (MRI or CT of brain).

Results: Family history was positive for epilepsy in 18 (32%) children; neurology status examination was intact in all children; neurovisualization showed asymmetric hydrocephaly in 2 (3,5%) children, retrocerebellar cyst in 4 (7%) children and focal brain abnormalities in 6 (11%). EEG demonstrating just generalized spike/wave discharges of 3–4 Hz in 8 (14%) children and local epileptiform activity in 48 (86%) children: 14/48 (29%) cases in frontal lobe, 22/48 (46%) cases in temporal lobe, 12/48 (25%) cases in parietotemporal or centroparietal part. Retrospectively in 20 (36%) children appeared partial seizure.

Conclusion: The results of our study allow supposing that absence can be a clinical feature of partial epilepsy or secondary generalized seizure with a primary focal epileptogenic abnormality.

E670
EFFECTS OF TOPIRAMATE ON CASPASE-3MRNA EXPRESSION IN ELECTRICAL KINDLED EPILEPSY RAT HIPPOCAMPI

X. Chen, Z. Wang*, G. Bao†, Y. Li*, and X. Zhang‡*
**Children Hospital Affiliated to Suzhou University, China;*
†Baogang Hospital Affiliated to Shanghai Jiaotong University, China; and ‡Biotechnology Research Institute of Suzhou University, China

Purpose: To observe Caspase-3mRNA expression in the basolateral amygdale (BLA) electrical kindled epilepsy rats hippocampi, and the effect of topiramate on the expression.

Method: Bipolar electrodes were implanted in BLA of rats, through which the rats received chronic electrical stimuli for kindling. Their seizure processes and behavior were observed, and electroencephalogram (EEG) recording were performed during kindling and after kindled. Then, hippocampi were extracted and Caspase-3mRNA in hippocampi were analyzed with semiquantitative RT-PCR. Topiramate treatment groups were arranged for comparison.

Results: Mean stimuli needed for kindling was (13.50 À3.99) times. Their afterdischarge duration (ADD) recorded was between 21,450 ms and 119,720 ms. Marked increase of Caspase-3mRNA expression was found in kindled rats hippocampi, while expression of Caspase-3mRNA was decreased in Topiramate treatment groups.

Conclusion: In seizures induced by electrical kindling, Caspase-3 possibly participate in the process of kindling. Topiramate might inhibit the apoptosis of neurons in epilepsy.

E671
RARE CAUSE FOR REFRACTORY EPILEPSY AND COGNITIVE DECLINE

C. Sirbu, R. Popoiu, I. Caloianu, and L. Ionescu
Central Clinical Emergency Military Hospital, Bucharest, Romania

Purpose: By our knowledge there are no data concerning DNTs, epilepsy and cognitive deficits. DNTs described first in 1988 represents 27% of the surgical cases for medically intractable epilepsy. They must be early diagnosticated in order to prevent the neuropsychiatric consequences of the chronic epilepsy and the evolving tumor complications.

Method: We dynamically analyze with the same tests (Bourdon-Antimov, Rey, Wecslar and Raven), the cognitive status of a female diagnosticated with Dysembryoplastic Neuroepithelial Tumor (DNT's), first at the age of 11, at onset of disease and second at the age of 24.

Results: We'll show the procentual difference between the results obtained for each parameter, the first related to the first examination and the second made after a diagnostic had been given. For the mnesic activity – memory and reproduction 30%, -memory and recognition 29%, the cognitive efficiency general index – (exactness) 29%, the cognitive efficiency general index – (quickness) 63% vocabulary (exactness) 35%, vocabulary (quickness) 38%, operational efficiency of thinking (exactness) 23% and for the prosexic activity for focus (exactness), the prosexic activity: the attention mobility (exactness) and operational efficiency of thinking (quickness) the results are the same.

Conclusion: Assessment of the mnesic activity, operational efficiency, vocabulary, cognitive capacity after 13 years of evolution show a significant decrease, preserving the prosexic function. An early and complete exeresis of the DNTs must be done, as the cure rate of the epilepsy in these cases is 85%.

E672
BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) VAL66MET POLYMORPHISMS IN FEBRILE SEIZURES AND GEFS+

I. Lee, S. Kim, B. Choi, Y. Kim, and S. Chung
The Catholic University of Korea, Korea

Purpose: Various studies have shown that brain-derived neurotrophic factor (BDNF) increased neuronal excitability. In the present study, to determine whether or not the functional val66met polymorphisms within the gene encoding BDNF are associated with susceptibility to febrile seizures (FSs), the frequencies of the polymorphisms were investigated in children with FSs and GEFS+, and normal control subjects.

Method: A total of 79 children selected throughout a collaborative study of Catholic Child Neurology Research Group were divided into three groups: (1) FSs (n=30); (2) GEFS+ (n=19); (3) normal control subjects (n = 30). A single base pair polymorphism SNP6265 (Val66Met) at position 196 was analyzed.

Results: Genotype proportions and allele frequencies in children with FSs and GEFS+, and healthy control subjects were not significantly different. The most common genotype for BDNF gene in FSs and healthy control subjects is A/A, but that in GEFS+ is A/G. The allele A and G frequencies for BDNF in FSs were 65.0% and 35.0%, respectively, in GEFS+ 50% and 50%, and in healthy control subjects 88.3% and 31.7%.

Conclusion: Our data suggest that genomic variations of BDNF might not be one of the susceptibility factors for FSs in the Korean population.

E673
INFANTILE AND EARLY CHILDHOOD MASTURBATION: CLINICAL AND SEX HORMONES PROFILE

A. Daoud, S. Ajlouni†, M. Kateeb‡, and K. Ajlouni‡*
**Jordan University of Science and Tecnology, Jordan;*
†King Hussein Medical Center, Jordan; and ‡Jordan University, Jordan

Purpose: To study the clinical and sex hormones profiles among infants and young children presented with masturbation.

Method: This is a prospective study of infants and young children diagnosed to have masturbation at three referral pediatric neurology clinics between September 2004 and September 2007. Detailed history regarding the demographic characteristics, the clinical description, full physical, neurological and neurodevelopmental examination was performed. Before referral, basic laboratory blood Investigations was performed to all children. The level of sex hormones as a possible predisposing factors including, DEHAS, OH_PROG, Free Testosterone, Estradiol, DHGA, SHBG, Androstendin was measured in all the cases and was compared to that age, and sex matched controls.

Results: Thirteen children were diagnosed to have masturbation (10 females and 3 males). The median age at first symptoms was 19.5 months (ranging from 4-36 months). The median frequency of events was 4 times per day and the median length of event was 3.9 minutes. Events occurred

in prone position in 10 of them, and in supine in the remaining three. Knee-chest position in two, flushing and redness of the face was seen in all the children, friction of the thighs in six, sweating in five, sleeping after the event was seen in nine, disturbed if interrupted in 12, abnormal EEG was reported in one and normal in 7, while brain neuroimiges were normal in 9 cases. Sex hormone levels were normal in all the cases and the control group.

Conclusion: Gratification disorder (infantile and childhood masturbation), is one of the paroxysmal movement disorders included in the differential diagnosis of many paroxysmal disorders. Sex hormone seems to play no role in the predisposition of infantile masturbation.

E674
A PROSPECTIVE STUDY OF RECURENCE AFTER A FIRST UNPROVOKED SEIZURE IN CHILDREN

Z. Martinovic, J. Stanisic†, and Z. Cvorovic†*
**Institute of Mental Health, Belgrade, Serbia; and †Pediatric Clinic of Clinical Center, Podgorica, Montenegro*

Purpose: To evaluate the risk factors for recurrence after a first unprovoked seizure in children.

Method: This prospective study was conducted at one tertiary hospital between January 2004 and December 2006. Children were enrolled in the study if they had a first unprovoked epileptic seizure and maximal interval to the enrollment no longer than 30 days. EEG during wake and sleep and computerized brain tomography were performed in all patients. Mean duration of follow-up was 2.4 years. Survival analysis was performed using the Kaplan-Meier curves. Potential predictors of seizure recurrence were compared using the Cox proportional hazards regression. The significance level was set at $p<0.05$.

Results: Sixty-four children (54.7% girls) were included in the study. Their age at first seizure ranged from 1–15 (mean 8.125±3.747) years. Recurrence occurred in 47 (73.4%) patients. Mean time for recurrence was 9.23 (standard error 1,23) months. Abnormal EEG after first seizure was statistically highly significant predictor for seizure recurrence ($p=0.0195$, confidence interval 0.7875–41.7175), in particular epileptiform EEG ($p=0.0008$, confidence interval 1.9442–12.7645). Sleep state reached statistical significance for seizure recurrence ($p=0.0754$, confidence interval 0.9378–3.2293). The etiology was not statistically significant for seizure recurrence, probably due to small number of patients (13 or 20.3%) with symptomatic etiology.

Conclusion: The results suggest that abnormal EEG and sleep state after first unprovoked seizure are significant risk factors for seizure recurrence in children.

E675
USE OF LEVETIRACETAM FOR THE TREATMENT OF INFANTILE SPASMS

R. Gaggero, M. Mancardi, and M. Baglietto
Epilepsy Unit, Gaslini Institute, Genoa, Italy

Purpose: Efficacy of levetiracetam (Lev) has been shown in child epilepsy. This open trial evaluates the efficacy of Lev used in add-on treatment of Infantile Spasms (IS).

Method: a) patients affected by IS both in typical West syndrome and in other epileptic encephalopathy, aged 1 month – 12 years; b) video-EEG, MRI, genetic and metabolic studies; c) count of the IS for 3 weeks; d) introduction of Lev (dosage from 10 to 60 mg/Kg/day); e) control visits every 2 weeks for 3 months and subsequently each 6th month. Frequency of the seizures and side effects were assessed by caregivers diaries.

Results: 12 patients were enrolled, 5 male 7 female, mean aged 4 yrs 5m. IS were associated with partial szrs. in 8pts. Clinical efficacy: 100% control in 2, reduction > 50% in 4, reduction < 50% in 2, < 25% in 4. Side effects (behavior and sleep disorders) in 3. Duration of the treatment ranged from 2 weeks to 30 mths; Lev was discontinued in 7 cases, in other 5 therapy is ongoing. Positive clinical effect persisted for period ranging from 3 mths to 12 mths.

Conclusion: Our results show that Lev can be efficacious in some cases with IS. Side effects are moderate. So Lev seems to be a useful add-on treatment in patients with IS.

E676
INCIDENCE AND PROGNOSIS OF EPILEPTIC SEIZURES FOR CHILDREN WITH HIDROCEPHALUS

D. Georgeta, G. Ioana, B. Marin, and T. Laura
University of Medicine, Iasi, Romania

Purpose: To evaluate the incidence, characteristic and prognosis of epileptic seizures in children with hydrocephalus.

Method: We included in the study 24 children diagnosed, in the first year of life, with hydrocephalus due to varying causes (29,16% cerebral malformations, 33,33% posthemorhagic, 20,83% postinfections, 16,68% unknown). 70,84% of children were treated by ventriculoperitoneal shunt and 29,16% presented not progressive hydrocephalus without shunt implantation. The follow-up period was 3 years. The study protocol included: general physical and neurological examination, clinical and electroencephalographic features of epileptic seizures, CT follow-up. The children with epileptic seizures were treated employing carbamazepine, sodium valproate, phenobarbital, clonazepam single or add-on. Therapeutic efficacy was estimated by percentage of patients who had been achieved significant clinical response.

Results: Nine (37,50%) children (4 with not progressive hydrocephalus, 5 with hydrocephalus with shunt implantation) had epileptic seizures. 2 children suffered from seizures before the shunt implantation. 33,33% of the children present generalized epileptic seizures and 66,67% present simple and complex partial seizures. The EEG was abnormal for all children with epileptic seizures, the epileptiform discharges were multifocal or focal in 6 cases and generalized spike-wave discharges in 3 patients. Seizure control was achieved in 44,44% patients.

Conclusion: Epilepsy is particularly common in the children with hydrocephalus and our data suggest that the risk for seizures depends more by etiology of hydrocephalus rather than by surgical intervention. Therapeutic efficacy was variable depending on type of seizures and antiepileptic drugs used.

E677
THE EFFECT OF OXCARBAZEPINE AND VALPROATE THERAPY ON GROWTH IN CHILDREN WITH EPILEPSY

A. Cansu, A. Serdaroðlu†, E. Yesilkaya†, O. Çamurdan†, T. Hirfanoglu†, and P. Cinaz†*
**Karadeniz Tecnical University Faculty of Medicine, Department Of Pediatric Neurology, Turkey; and †Gazi University Faculty of Medicine, Turkey*

Purpose: This study aimed to evaluate the effect of monotherapy with valproate (VPA) or oxcarbazepine (OXC) on physical growth in children with idiopathic epilepsy.

Method: Seventy six patients (2 years 8 months-16 years 7 months) who were started to medical treatment for epilepsy (36 patients with OXC, 40 patients with VPA) were included in the study. They were examined at baseline and on the 3rd, 6th and 18th months of therapy for calculation of standard deviation of height (Z-score) and body mass index (BMI). Blood samples were collected for the measurement of serum ghrelin, insulin-like growth factor (IGF)-1 and insulin-like growth factor binding protein (IGFBP)-3 levels.

Results: The standard deviation of height increased statistically significantly during the study period in the prepubertal patients on OXC therapy. BMI values of prepubertal patients on VPA therapy showed statistically significant elevations in the 3rd, 6th, and 18th months of therapy compared to baseline values. Serum ghrelin levels of VPA groups showed statistically significant decreases as the BMI values increased throughout the study or vice versa. In prepubertal OXC patients, standardized serum IGF-1 levels showed a statistically significant increase during the study period while standardized serum IGFBP-3 levels showed statistically significant increases in the same patients in the 6th and 18th months of therapy compared to baseline values.

Conclusion: Medication with OXC of prepubertal patients with epilepsy stimulated linear growth via mechanisms which seemed to involve IGF-1 and IGFBP-3 release independent of ghrelin secretion.

E678
FRACTURES IN EPILEPSY CHILDREN IN MY STUDY

A. Gniatkowska-Nowakowska
Outpatient Clinic of Child Neurology and Epileptology, Kielce, Poland

Purpose: To describe a greater risk of fractures (about 2–6 times more often) in epilepsy children then in the children without epilepsy.

Method: We examined 126 children with epilepsy in age 7–16 who were treated with AEDs in mono- and add-on therapy during 5 years. In the control group we included 132 children in age 7–16, without epilepsy and not treated with AEDs, observed in Outpatient Clinic due to headache. In children were measured the calcium and phosphate levels in blood and urine and a densitometry was performed. We analyzed both groups using statistical method.

Results: The frequency of fractures is 2–3 times greater then in general healthy children population. Osteoporosis and osteopenia is about 30% more often in children who has taken AEDs during 5 years. The results are statistically significant.

Conclusion: Fracture in children with epilepsy are important adverse effect in children who were taking AEDs.

E679
LONG-TERM SURVIVAL IN SUBACUTE SCLEROSING PANENCEPHALITIS: LOOKING FOR PROGNOSTIC FACTORS

C. Nobrega, S. Oliveira, and R. Almeida
Centro Hospitalar de Lisboa Central, Portugal

Purpose: Subacute sclerosing panencephalitis (SSPE) usually has a rapid deterioration with death occurring within 3 years from diagnosis. However, there are cases with long term survival. Given the small number of cases in published series, prognostic factors are lacking. The authors describe a case of SSPE with 6.5 years survival up to now and possible prognostic factors are discussed.

Case report: Male, 22 years, diagnosed with SSPE at 16 years of age, after a subacute onset of cognitive deterioration and refractory epilepsy (atonic, generalized tonic–clonic and myoclonic seizures). He had normal psychomotor development, vaccination status was up to date and clinical occurrence of measles was unknown. The electroencephalogram showed type II periodic complexes and slow background activity. Elevated titres of antibody to measles virus were found in blood and cerebrospinal fluid and magnetic resonance imaging was normal. We started antiepileptic drugs and inosiplex and during the first 2 years it was administered interferon by subcutaneous and intraventricular route. After an initial period of progressive deficits with severe cognitive and motor deterioration, the patient regained minimal autonomy in daily living activities and EEG showed improvement in background activity.

Conclusion: The late onset and electroencephalogram background activity improvement might be good prognostic factors in SSPE. Therapeutics might augment remissions and stabilizations, and even improve survival, but this effect is lost for longer periods of follow up. Investigators are looking for immunitary factors. SSPE has clinical evolution extremely variable and prognostic factors should be determined for better counseling of patients and their families.

E680
PREVALENCE OF EPILEPSY IN SHANGHAI CHILDREN AND ADOLESCENTS

S. Zhou, Q. Guo, P. Qiu, and D. Sun
Children's Hospital of Fudan University, China

Purpose: To explore the characteristics of epilepsy in children, focus on prevalence and etiology.

Method: Children with epilepsy (based on ILAE classification in 2001) were under 18 years of age and recorded in our hospital from July 2005 to February 2006. A questionnaire study was conducted among subjects and follow-up by phone or department of neurology.

Results: 1. Characteristics of prevalence: male 541 (65.5%) ¢female 285 (34.5%), male/female rate was 1: 0.53. Average onset- age of epilepsy was 3.74 ± 0.12 years (0.01~15.29y). 53.6% seizures less than 3 years, less than 1 year old was the peak of start-age (27.5%). Average internal of the first and the second seizure was 4.72 ± 0.37 months (1d~95.4m). The ratio of relapse within the first years was 92.4%. 2. Etiology: The etiology of epilepsy was idiopathic in 44.2% of the children, possibly symptomatic in 9.3%, and symptomatic in 43.1%. Prenatal or perinatal factors were the most frequently found cause of epilepsy (78.1%). Additional neuroimpairments affected 29.5% of our epileptic children. 3. Seizure types: 806 (97.6%) were classified into three major categories by ILAE classification. They consisted of 438 (54.3%) with localization-related epilepsy, 347 (43.1%) with generalized epilepsy, and 21 (2.6%) with undetermined epilepsy. Generalized seizures were more prevalent in children less than 3 years of age. 261 (32.4%) were classified into epileptic syndrome categories.

Conclusion: Most childhood epilepsy began less than one year old. Prenatal or perinatal factors may be the role risk factors of epilepsy in children. Diagnostic Scheme for People with Epileptic Seizures and with Epilepsy applied by International League in 2001 enhanced the classification system and can be applied successfully to epileptic children.

E681
POLYTHERAPY IN TREATMENT OF EARLY AGE CHILDREN EPILEPSY

E. Balakireva, and A. Neretina
Burdenco State Medical Academia, Bucarest, Romania

Purpose: We assessed necessity and acceptability of polytherapy for epilepsy treatment of early age children.

Method: 108 children hospitalized in connection with epileptic seizures were monitored during 1 to 5 years starting at age 1 month – 3 years. In all cases the antiepileptic therapy started from valproate (VPA) dose selection. In cases of insufficient effect of the VPA during the dose selection, a monotherapy with topiramate (TPM) or levetiracetam (LEV) was applied. LEV was administered to the early age children with permission of parents and the Ethical Committee. If the therapy did not allow to control the seizures, a combination of two or more medications was applied and optimized accounting the synergistic and side effects. If a patient was resistant to the therapy, ethosuximide, clonazepam, and/or hormones were applied.

Results: The monotherapy was effective for all patients with idiopathic forms of epilepsy (6 cases), in 17 out of 34 cryptogenic form cases, and in 6 out of 51 symptomatic forms cases. In all cases of epileptic

enthephalopathy (17) the best possible effect was achieved with polytherapy including a combination of 3 drugs (9 cases).

Conclusion: The investigation revealed a high efficiency of the applied polytherapy for difficult (nonidiopathic) cases of epilepsy. Combination of the medications provided the therapeutic effect in 64% of the cases – compared with 27% for monotherapy (p=0,05) – and allowed a control of seizures with minimum side effects.

E682
EFFICACY OF ZNS IN HIGHLY REFRACTORY EPILEPSY IN CHILDREN: A MONOCENTRE CLINICAL EXPERIENCE

A. Liava, and P. Bonanni
Epilepsy and Neurophysiology Unit, Paediatric Neurorehabilitation and Research Centre of E Medea Scientific Institute, Italy

Purpose: To evaluate the efficacy of zonisamide in the treatment of pharmacoresistant epilepsy in childhood.

Method: From February 2007, till March 2008 (follow up range: 3–13 months) 17 children (9 boys), aged between 2–17 years, received ZNS as adjunctive therapy for refractory epilepsy at a range dose of 2–10 mg/kg/day. At the time of ZNS addition, 13 children (81%) presented an electroclinical picture of epileptic encephalopathy: 2 Lennox-Gastaut syndrome, 1 Dravet's syndrome, 3 myoclonic status in nonprogressive encephalopathy associated with partial tonic seizures, 1 CSWS. Etiology: 2 Aicardi syndrome, 3 encephalitis, 1 traumatic brain injury, 3 cerebral palsy, 1 Angelman syndrome, 1 Dravet syndrome. Seizure types: 47% symptomatic partial, 43% cryptogenic partial, 6% idiopatic generalized, 30% mixed. Two patients discontinued ZNS after 2 weeks treatment because of side effects (worsening of agitation and loss of appetite).

Results: All the patients are responders: 12% are seizure free, 41% and 29% with reduction of seizure number > 50% and <50% respectively. No loss of efficacy was observed. A dose depended efficacy was observed and tolerability remained satisfactory. Efficacy was observed at lower dosages in comparison to various studies (2–18 mg/kg/day). Interestingly, two patients affected by myoclonic status in nonprogressive encephalopathy experienced the complete absence of the tonic seizures, at a dose of 9 and 10 mg/kg/day respectively.

Conclusion: Our experience not only encourages the use of ZNS in children but also provides promising results regarding its efficacy in epileptic encephalopathies.

E683
RELATION BETWEEN THE SHORT-TERM NEUROPHYSIOLOGIC FINDINGS AND CLINICAL OUTCOME IN PEDIATRIC PATIENTS WITH KETOGENIC DIET

M. Aberastury, M. Vaccarezza, W. Silva, C. Maxit, and G. Agosta
Hospital Italiano de Buenos Aires, Argentina

Purpose: The use of electroencephalographic studies as an indicator of clinical outcome in patient receiving ketogenic diet is not clear. Analyze and relate the terapeutic efficacy of KD with the electroencephalographic findings.

Material and Method: In a prospective study we analyzed the electroencephalographic characteristics (EEG before and 2 months after treatment with KD) of 10 patients between 6 months and 10 years. These changes were quantified analyzing the background, presence of physiologic elements during sleep, changes in the electric camp of the discharges and the percentage of the interictal epileptic activity.

Results: 10 patients were divided in 4 groups according the reduction in number of seizures: Group 1: > 90% reduction, Group 2: 50–90%, Group 3: < 50% and Group 4: no reduction. Considering the EEG: Group 1: 2/4 showed an improvement in background and in the interictal epileptic discharges (IED) and 1/4 on the IED only. Group 2: 1/3 showed an improvement in background and in IED. Group 3: 1/2 showed an improvement in IED. Group 4: 1/1 showed an improvement in background.

Conclusion: We did not observe a clear correlation between the improvement in the number of clinical seizures and the changes in the EEG in a short term. But we highlight that the patients that had an excellent response to KD improved the EEG in a high percentage. Further prospective studies assessing the importance of the EEG as a predictor of clinical efficacy in ketogenic diet are needed.

E684
THE LANDAU-KLEFFNER SYNDROME RESPONSIVE TO LEVETIRACETAM I.V.

E. Cesaroni, N. Zamponi, S. Cappanera, and C. Cardinali
Children's Hospital G. Salesi Ospedali Riuniti, Ancona, Italy

Purpose: The Landau-Kleffner syndrome (LKS) is rare epilepsy syndrome with continuous spike-waves during slow sleep on the EEG (CSWS) associated with various seizure types. The CSWS respond poorly to treatment. The abolition of CSWS activity following benzodiazepines, ACTH or steroid have been reported. A common experience, however is that such effects are often self limited. We report a case of a child with LKS who responded to high dose levetiracetam i.v.

Method: 8 years old boy with normal developmental milestones until 6 years was evaluated for right tonic–clonic seizures during sleep. The EEG at the time showed left frontotemporal abnormalities, the MRI was normal and carbamazepine was tried initially whit seizures resolution. Few months later he presented the first language problems, at that time the sleep EEG showed CSWS whit a left predominance. The CBZ was immediately stopped and various AEDs were tried (valproic acid, ethosuccimide, benzodiazepines, ACTH) without seizures and behavior improvements. In the last follow-up intravenous levetiracetam therapy (2 gr) was attempt.

Results: The video monitoring during sleep after 2 weeks showed a dramatic improvement with few theta burst activity in the left temporal area.

Conclusion: Few report described the benefit of levetiracem in a child with continuous spike waves activity of sleep and only on recent study reported a good response of LEV in LKS This case confirm the possibility that LEV should be considered as therapy for LKS.

Bibliography: Landau-Kleffner syndrome responsive to Levetiracetam. Kossoff EH, Boatman D, Freeman JM. Epilepsy Behav. 2003 Oct;4 (5):571–5.

E685
OPTIMAL INITIAL MAINTENANCE DOSE OF TOPIRAMATE IN NEWLY DIAGNOSED CHILDREN WITH EPILEPSY

D. Kang, and H. Moon†*
**Changwon Fatima Hospital, Changwon, Korea; and*
†Yeungnam University College of Medicine, Daegu, Korea

Purpose: To investigate the appropriate initial maintenance dose of Topiramate (TPM) for children with new onset epilepsy.

Method: Fifty-five patients between age 2 and 16, who were newly diagnosed as epilepsy at Changwon Fatima Hospital between July 1, 2004 and Feb. 29, 2008, were given TPM at different maintenance dose over six months period. Seizure outcomes and adverse reactions were compared. Data were collected from patient charts and electronic medical records retrospectively.

Results: Out of fifty-five patients, mean maintenance dose of TPM was 2.8mg/kg (1.4~6.0 mg/kg) and 38 patients (69%) were diagnosed as partial seizures, 17 patients (31%) generalized seizures. 24 patients (44%)

experienced adverse reactions. Seizure free rate at 6 months was 75%, 12 months 78%, 18 months 78%, 24 months 79%, 30 months 74% and 36 months 70%. 26 children maintained TPM below 2.5mg/kg (mean 2.0 mg/kg). The other 29 children maintained above 2.5mg/kg (mean 3.5 mg/kg). (1) There were no significant difference statistically between two groups in respect to duration of medication, duration of titration and duration of elapsed time to start of medication from onset of seizure. (2) There were no statistically difference as to sex, family history of epilepsy, seizure classification and incidence of adverse reactions between two groups. (3) Higher maintenance dose was applied to patients with early onset age of epilepsy and symptomatic etiology. (4) Seizure outcomes at 12, 18, 24, 30 and 36 months were not significantly different between two groups.

Conclusion: TPM at maintenance dose below 2.5 mg/kg was effective as conventional dose in control of seizures in children with new onset epilepsy.

E686
BENIGN MYOCLONIC EPILEPSY IN INFANCY: NEW CASES AND PROSPECTS OF TREATMENT

V. Josef, and V. Oksana
City Center of Epilepsy, Children's City Clinical Hospital [1]3, Novosibirsk, Russia

Purpose: To present the clinical description of new cases of benign myoclonic epilepsy in infancy (BMEI) and to estimate success of medicament therapy of these patients.

Method: 8 patients (4 boys, 4 girls) aged between 15 months and 6 years with BMEI were observed and treated for 6 months – 3 years.

Results: The age of onset was between 9 months and 4.5 years. In all cases at onset we observed solitary jerks which within weeks – months achieved frequency of tens in a day. All patients have jerks which took place during wakefulness; 75% at drowsiness, 50% after awakening. All patients had jerks which involved muscles of the upper limbs, 7 – muscles of a neck, 5 – eyelids, 4 – muscles of a trunk, 3 – the lower limbs and in one case – myoclonic seizures (MS) were observed in chewing muscles. Motor development corresponded to age; 2 patients had the delay of speech development. In one case the familial anamnesis on epilepsy in two generations was revealed. Video-EEG-recordings demonstrated that MS were accompanied by a discharge of fast generalized spike-waves or polyspike-waves. We used VPA 30 – 50 mg /kg/d. by a first lain at 7 patients. Seizures-free were in 1 case. MS reductions > 75% were achieved by 4, and > 50% by 2. Add-on therapy we used ESM 25 – 30 mg /kg/d in 4 cases and LEV 27 and 50 mg /kg/d in 2 cases, that allowed to achieve 100% reduction of attacks. One patient undertakes monotherapy LEV 37 mg/kg/d, remission is achieved.

Conclusion: The submitted cases correspond to criteria of the BMEI diagnosis. The prognosis for seizure control is favorable, but frequently demands assignment of polytherapy. LEV may be perspective AED in therapy of BMEI.

E687
PARENTING STRESS IN MOTHERS OF CHILDREN WITH INTRACTABLE EPILEPSY

E. Wirrell, L. Wood†, L. Hamiwka‡, and E. Sherman‡*
**Mayo Clinic, Rochester, USA; †University of Alberta, Edmonton, Canada; and ‡University of Calgary, Canada*

Purpose: To determine the prevalence and characteristics of maternal stress in families of children with intractable epilepsy.

Method: Mothers of children aged 2–18 with intractable epilepsy were asked to complete a Parenting Stress Index Scale, Scales of Independent Behavior-Revised and Child Behavior Checklist, and were queried regarding family type, maternal education and family income. Neurology clinic charts were reviewed for seizure variables including age at onset, number of failed therapies and seizure frequency. The Parenting Stress Index measures stress in two broad domains [stress related to characteristics of the child (Child Domain) and stress related to characteristics of the parent (Parent Domain)] as well as a Total stress score.

Results: Fifty two of 80 (65%) eligible mothers returned completed questionnaires. Sixty three percent scored in the clinical range for Total Stress, 75% for the Child Domain but only 29% for the Parental Domain. Mothers scored more adversely on Isolation, Health, Role Restriction and Spouse subscales of the Parent Domain, but more favorably on the Attachment subscale. A moderate to high correlation was found between behavior problems in the child and higher Total Stress scores, but no significant correlations were found between other seizure or demographic variables.

Conclusion: Intractable childhood epilepsy is associated with markedly increased maternal parenting stress. Increased stress is predominantly due to child factors. Mothers would strongly benefit from added support to alleviate the constant caregiving demands.

E688
FOCAL SEIZURES IN PATIENT WITH SYNDROME OF INVERTED DUPLICATION OF PERICENTROMERIC CHROMOSOME 15

M. Ryzí, H. Osejsová, J. Sukalová, V. Vávrová, and M. Vilémová
Faculty Hospital Brno, Czech Republic

Purpose: The inverted duplication of pericentromeric chromosome 15 is the most common of extra structurally abnormal chromosome syndromes, accounting for about 50% of supernumerary marker chromosomes (Hook E et al., Am J Hum Genet. 1987 February; 40 (2): 83–101.). The severity of clinical presentation varies according to the presence of 15p or 15q tetrasomy. (Torrisi L et al., Am J Med Genet. 2001 Summer;106 (2):125–8.) We present a patient with minimal phenotype of this syndrome and focal seizures.

Method: Genetic examination included fluorescence in situ hybridisation (FISH), high resolution comparative genomic hybridisation (HR-CRH), multiplex ligation-dependent probe amplification (MLPA). Neurological examination with video EEG, MRI and PET was performed.

Results: We present a case report of one patient with mild mental retardation, learning disabilities (dyslexia, dysgraphia), short stature (bellow 10 percentile), relative macrocephaly and discrete craniofacial stigmatisation (full lips, bushy eyebrows, high-arched palate, prominent and lower position ears, lower hairline). The first seizures occurred at the age of 16, described as partial complex seizures with suspected beginning in the left frontal or parietal lobe, according to the video EEG findings. The treatment was repeatedly changed without any effect. The MRI and PET studies were performed with normal findings. The genetic investigations (FISH, HR-CGH, MLPA) proved the marker chromosome in area 15q11.1-q14.

Conclusion: The possibility of abnormal structural chromosome syndromes is needed to be taken into account in cases of untreatable focal nonlesional epilepsy even in cases with minimal phenotype.

E689
TELEVISION-INDUCED SEIZURES IN PRESCHOOL CHILDREN

M. Brinciotti, M. Matricardi, and A. Mittica
Sapienza Rome University, Italy

Purpose: To report clinical and EEG features of epileptic seizures induced by television in preschool children.

Method: We studied 45 children (20 males, 25 females) of preschool age (8 months – 6 years) with epileptic seizures induced by TV. Spontaneous seizures were reported in 34 cases (22 partial, 12 generalized); 11

patients had only reflex seizures. All patients underwent video-EEG recordings with standardized visual stimulations (ILS and Pattern) and during at least 30 minutes of TV watching; moreover, prolonged 24-h ambulatory EEG recording was used in some cases.

Results: Mean onset of spontaneous seizures was 3.5 years, while reflex seizures usually started later (mean 4.6 yrs). A positive family history of epilepsy occurred in 34 cases (76%). Epileptic abnormalities at rest EEG were recorded in 42 cases (temporooccipital 10, occipital 8, parieto-occipital 5, fronto-central 7, frontotemporal 2, centrotemporal 4, generalized 6). In all patients abnormalities were activated by visual stimuli: 32 (71%) by ILS+Pattern, 8 (18%) by ILS, and 5 (11%) by Pattern. Recorded seizures were characterized by visual signs and/or symptoms (26 hallucinations, 10 micro/macropsias, 9 eyelid myoclonias, 7 amaurosis), stare and impairment of consciousness (28), acute intraorbital pain (24), and dizziness (2).

Conclusion: Television induced seizures seem to be relatively common in preschool epileptic children, especially when EEG abnormalities involve the occipital areas. Even if generalized seizures may occur, partial seizures are the most common type of clinical manifestation induced by television in preschool age.

E690
AUTOIMMUNE INFLAMMATORY DISEASE AS A CAUSE OF SOME CATASTROPHIC EPILEPSIES IN CHILDREN?

J. Hadac, and K. Brozova
Thomayer Hospital, Prague, Czech Republic

Purpose: To demonstrate the effect of immunomodulatory therapy with corticosteroids in six cases of suspected 'autoimmune epilepsy.

Method: The effect of corticosteroid therapy has been evaluated in six children (two boys and four girls aged 4–16 years) suffering from refractory epilepsy. Their epilepsy started after an inconspicuous viral infection and had catastrophic course with cognitive deterioration in all. Four of six patients showed mild pleocytosis or elevated CSF protein, other two had nonspecific inflammatory changes on MRI. The therapeutic regimen with dexamethasone and/or methylprednisolone was individually conformed to the clinical course.

Results: A significant effect of corticosteroids (seizure-freedom with improvement of cognitive functions) could be observed in two of six patients. In other two children, the therapy had only partial or transient effect. Last two patients showed no amelioration during or after the therapy.

Conclusion: In absence of detectable epileptogenic lesion, cerebral vasculitis, metabolic or degenerative disease a possible atypical focal inflammation with autoantibodies e.g. against ion channels or receptors should be suspected. Unfortunately, available diagnostic procedures are of limited diagnostic value. That is why we recommend therapeutic trial with corticosteroids (or IVIG) in all patients with suspected autoimmune etiology of their epilepsy.

E691
STATUS EPILEPTICUS IN SLOW WAVE SLEEP IN SYMPTOMATIC EPILEPSIES

B. Jocic -Jakubi, M. Jovanovic*, D. Stankovic Jankovic†, and M. Mitic**
**Pediatric Clinic, Medical School of Nis, Serbia; and †Clinic of Mental Health, Medical School of Nis, Serbia*

Purpose: Electrical status epilepticus in slow sleep (ESES/CSWS) is originally defined as strong activation of epileptiform activity in the EEG during sleep with diffuse spike-waves during 85% of slow wave sleep. It is age-related encephalopathy which can arise from benign childhood epilepsy, but more than one third of patients have an abnormal brain pathology.

Method: We presented 6 children (5 girls, one boy) who were diagnosed as symptomatic ESES. All of them have different kind of underlaying brain pathology such as: cerebral palsy, leucoencephalopathy with temporal cysts, hydrocephalus, bilateral striatal necrosis and polymicrogiria, multicystic encephalomalatia and cortical atrophy.

Results: All examined children aged 6–11 years, fulfilled criteria of definition of ESES (Commission,1989). The different kind of seizures including focal motor, focal with secondary generalization, infantile spasms (in two of them) absences were observed. The seizures were started in first year of life in 2 patients (infantile spasms) and they were diagnosed as West syndrome. The ESES started from 2 to 6 years after the first seizure was occurred, at the age 4 to 9 years. All children are severe mentally retarded (total IQ 20–25) except one (IQ 62). Half of them have no more seizure and in all of them duration of ESES is from 1–3.5 years. The SWI was 75–100% in 4 patients, in two 50–75%.

Conclusion: Damage or disruptive injuries that occur during critical periods of brain development interfere with the process of neuron-to-neuron connection and with the structuring of the corresponding cortical functions. It can be explanation for appearance of ESES in patient with different underlying brain pathology.

E692
SCN1A MUTATION ANALYSIS AIDS EARLY DIAGNOSIS OF INFANTILE ONSET EPILEPSIES

A. Brunklaus, R. Birch†, S. Stenhouse†, and S. Zuberi**
**Fraser of Allander Neurosciences Unit, Royal Hospital for Sick Children, Yorkhill, Glasgow, UK; and †Duncan Guthrie Institute of Medical Genetics, Royal Hospital for Sick Children, Yorkhill, Glasgow, UK*

Purpose: Genetic analysis of the sodium ion channel subunit gene *SCN1A* has recently become available as a service in the UK. Our objective was to determine whether genetic studies of *SCN1A* aid early diagnosis of infantile onset epilepsies.

Method: Clinicians completed a standard referral form prior to DNA analysis. Coding exons of the *SCN1A* gene were sequenced. In negative cases, when the phenotype suggested *SCN1A* related epilepsy, multiplex-ligation-dependent-probe-amplification (MLPA) was performed to detect large scale rearrangements. Mutation positive cases were reviewed with particular reference to the age at genetic diagnosis and mutation type.

Results: 437 samples were sequenced in the first 27 months of the service. 139 mutations in *SCN1A* were detected by sequencing: 70 (50%) missense, 61 (44%) truncating, 7 (5%) gross rearrangements and 1 (1%) in-frame deletion. Of the seven gross rearrangements, four were whole gene deletions, one deletion exons 1–16, one deletion exons 17–26 and one deletion exon 1. 6 (4%) had mutations identified in the first year of life, 26 (19%) under the age of 2 years and 68 (49%) mutations were detected in children under the age of 5 years.

Conclusion: The syndromic diagnosis of *SCN1A* related infantile epileptic encephalopthies is frequently delayed for years until the whole syndrome evolves. Our findings suggest that referrers use the investigation when they suspect a *SCN1A* associated diagnosis and not simply to confirm classical cases. Earlier definitive diagnosis through genetic studies may clarify a treatment strategy, prevent costly and invasive investigations and provide information for genetic counselling.

E693
LEVETIRACETAM IN THERAPY FOCAL FORMS OF EPILEPSY IN CHILDREN EARLY AGE

S. Sivkova, and F. Zaykova
Children Neurology Hospital [1]8Kazan, Tatarstan Republic, Russia

Purpose: This is the prospective study of clinical efficacy, safety and tolerability of the new antiepileptic drug levetiracetam (LEV) for treatment different focal forms of epilepsy in children early age.

Method: Levetiracetam was used in 32 patients aged from 6 month to 4 years, mean age was 2.7 years (14 male and 18 female). All patients received medications for between 1 – 28 months, mean observation time was 13.5 months.

Results: Levetiracetam in combination with other antiepileptic medications was used in doses 125–750 mg/day and 20 – 60 mg/kg/day (average 45 mg/kg/day). Seizure freedom was achieved in 6/32 (18%) patients. Reduction in seizure frequency more than 75% was observed in 5/32 (15%) cases; > 50% seizure reduction was in 7/32 (22%). In 3/32 (9%) of patients seizures frequency gradually returning to a baseline 1–3 month after positive effect achievement. Side effects (SE) were detected in 8/32 (25%) of all cases. The main of them was sleep disorders and hyperactivity, but no one patient withdrawal therapy was necessary.

Conclusion: Our clinical results show that levetiracetam is highly effective, well tolerated new antiepileptic drug for treatment of different focal forms of epilepsy in children early age.

E694
CLINICAL-ELECTRO-NEUROVISUALIZATIONAL CHARACTERISTICS OF PARTIAL FORM OF EPILEPSY

M. Lepesova, G. Tairova, and A. Kazakenova
Almaty Post Graduate Institute for Physicians, Khazakhstan

Purpose: Khazakhstan children's partial epilepsy clinical-electro-neurovisualisational characteristics.

Method: 177 children with partial epilepsy observed, occipital – 25 (14.12%), temporal – 7 (3.95%), frontal -16 (9%), Rolando -18 (10.16%), secondary generalized seizures – 111 (62.71%).

Results: Rolando epilepsy revealed – 18 (4.8%). Debut at 4 years with high night frequency. EEG – interictal period revealed complex 'acute slow wave' in frontocentral (3), frontotemporal (2) abstraction, safe basic activity. Occipital epilepsy observed – 25 (14.1%). Debut: from 3–6 before 9–14 years. EEG – epileptic activity 'peak-wave' in occipital abstractions. MRI- brain structural changes – 4 (2.3%). Temporal epilepsy as symptomatic revealed – 7 (4%). In children with temporal epilepsy (7) observed aura as scream (2), smell sense (1), unexplained fear (3). Seizure developed often with disconsciousness, safe automatic motor activity presented as oral alimentary (5), gestures (4), ambulatory automatisms (3) with combination of tonic-distonic arrangement of extremities (2), tonic–clonic seizures (3). MRI – temporal lobe sizes decrease, hippocampus sclerosis – 3. Frontal epilepsy diagnosed – 16 (9%), including autosome – dominant night frontal epilepsy – 5 (2.8%) with debut before 10 years – 3, older than 10 years – 2. EEG – epileptic activity presented as 'acute slow wave' in frontal (2), frontotemporal abstractions (3). MRI – residual encephalopathy (3). Symptomatic frontal epilepsy revealed – 11 (6.2%). EEG – videomonitoring – regional deceleration (5), 'acute slow wave' (11) in frontal abstractions. MRI – atrophic process frontotemporal area (7), residual encephalopathy (9). Thus, study of the partial forms of the epilepsy showed prevalence over generalized, additional attention to epilepsy particular forms diagnosis.

E695
ETIOLOGY AND RESPONSE TO THERAPY AS PREDICTORS OF OUTCOME IN PATIENTS WITH WEST SYNDROME

D. Nikolic, N. Dimitrijevic*, D. Bogicevic*, M. Tomasevic†, and V. Mitic**
**University Children's Hospital Belgrade, Serbia and*
†Polyclinic Medikom, Serbia

Purpose of this study was to determine predictive value of etiology and response to therapy in outcome of patients with West Syndrome (WS).

Methodology: Study comprised 81 patients with West syndrome: 45,7% with simptomatic, 39,5% with criptogenic and 14,8% with idiopathic WS. All patients undergone the same diagnostic protocol, i.e. neurological examination at the onset of spasms, after 1, 3 and 12 months, EEG at the onset, after 3 and 12 months.

Results: In our study group there were 11,1% with normal neurological finding upon onset od spasms, mild delay had 14,8%, moderate delay 21%, severe psychomotor retardation 30,9% and 22,2% had very severe psychomotor retardation. Etiology of WS is significant outcome predictor with great majority of patients (91,7%) with idiopathic WS having seizure cesation after one month and good therapeutical response after one year. Most of children (66,2%) had statistically significant improvement in psychomotor development after 12 months of therapy. There is statistically significant difference in psychomotor development after one year in relation to the presence of seizures 3 months after initiation of therapy. There is no predicitive value of EEG after 3 months on neither psychomotor development nor response to therapy after 12 months, but there is significant correlation between EEG after 12 months and good therapeutical response as well as psychomotor development.

Conclusion: We have found idiopathic etiology, absence of seizures after 3 months and improved EEG after 12 months of therapy to be predictors of good outcome.

E696
PREVALENCE AND COMPLETE REMISSIONS OF EPILEPTIC SEIZURES IN PATIENTS WITH CEREBRAL PALSY AFTER ADOLESCENCE

J. Wendorff, and K. Polatynska
Mother Polish Memorial Hospital, Lodz, Poland

Purpose: Currently there is no data concerning prevalence of manifesting epilepsy among the patients with cerebral palsy (CP) after adolescence. Remission of seizures is achieved until this period in 40–60% of cases.

Aim: Evaluation of prevalence and course of epilepsy among the patients with CP during 2nd and 3rd decade, treated since childhood.

Method: The studied group consisted of 30 patients with CP and epilepsy I 3rd decade, who achieved full remission. The control group consisted of 24 patients who did not develop remission. The clinical characteristics of both groups were compared. The results were obtained with use of standardized inquire, neurological examination and EEG testing. Selected clinical parameters were evaluated. Statistical analysis was performed with chi square test.

Results: The 3 of patients developed epilepsy not until 20 years of age. Patients in studied group were mainly hemiplegic (44%, $p<0.05$) and of prenatal etiology. Patients in control group were tetraplegic in majority (52%, $p<0.05$) and of perinatal etiology. First seizures occurred before first year of age in control group ($p<0.01$). In studied group, occurrence of one type of seizures ($p<0.01$), short remissions and monoterapy (both $p<0.05$) were more frequent.

Conclusion: During adulthood occurrence of a first seizure in life is very unlikely. Complete remission is more likely achieved by patients with hemiplegic form of CP with prenatal etiology with late onset and in patients with short remissions treated with monoterapy.

E697
EPILEPSY IN SCHOOL AGE – LEARNING DIFFICULTIES: IS THERE ANY CORRELATION?

M. Tomasevic, N. Dimitrijevic†, D. Nikolic†, and S. Saric‡*
**Polyclinic Medikom, Belgrade, Serbia; †University Children's Hospital Belgrade, Serbia; and ‡School of Medicine, Belgrade University, Serbia*

Children with epilepsy could have signs of hyperactivity, depression, confusion, disorganized speech, inability to listen to and to comply with direction and lack of attention.

Aim of this research was to examine difficulties for listening, reading and learning, memory, and conversation problem which could be found in children suffering from epilepsy. It was measured with the Serbian version of the Qolie-AD-48, 9/48 questions which were exploring memory and concentration functions. Study comprised 61 child, 32 boys and 29 girls. 50 of them (81.96%) were on the monotherapy, 10 (16.39%) got two drugs. Most of the children had problem with finding the right word when explaining something (72,13%-29.5% very often-once a day at least, 18.03% sometimes, and 6.55% always). In the all other questions connected with concentration (for reading, understanding lectures and for the usual daily activities) more then a half children never had a problems. They better understand when they read then they had lectures and this has statistically important value ($p<0.01$). 42.62% of children had problems to remember what they learn for more than two days. Every second child found they have problems when thinking, some of them could connect this problem with taking drugs.

Conclusion: Epilepsy by itself could be reasons for problems with finding the right word when children speaking, what is correlated with literature data. They better understand when they read than lectures, also they forget often what they learn.

E698
CLINICAL OBSERVATION OF 3 CHILDREN WITH RASMUSSEN ENCEPHALITIS (RE) IN ONE TERTIARY MEDICAL CENTER

A. Nechai
Paediatric Hospital No1, Kiev, Ukraine

Purpose: The paper is based on clinical observation of 3 children diagnosed with RE and followed for 10 years. Clinical manifestation and efficacy of some drugs may contribute to understanding of pathophysiology of the disease.

Method: Case history review.

Results: Two patients were boys and one was a girl. The age of debut was 5 years in girl (patient 1), 8 years (patient 2), and 2,5 years (patient3). The disease debuted with partial and secondary generalized seizures. All had episodes of status epilepticus. MRI showed hemiatrophy, with basal ganglia involvement and unchanged picture during last 8 years in patient 1; and debuting in insular region in patient 2. Besides hemiparesis the girl also had mild dystonia and dysartria. Accompanying disturbances: the girl had precocious puberty, older boy was obese, and younger boy often developed allergic dermatitis. AED were of limited benefit but presumably prevented status epilepticus. Surgery was performed only in patient 2. The girl underwent a course of i.v. immunoglobulin without benefit. She demonstrated good but short duration response to topiramate. Periodic putting on short courses of acetazolamide keeps the girl seizure-free during this period.

Conclusion: Presence of accompanying medical conditions in all children supports the hypothesis of autoimmune nature of RE. The character of MRI changes in patient 1 allows presuming possible self limiting course of RE. There is a questioning regarding possible hormonal mechanism of the condition. Good temporary response to inhibitor of carbonic anhydrase in patient 1 is poor understood but may stimulate further research.

E699
SUCCESSFUL TREATMENT WITH PROLOGED USE OF HIGH DOSE DIAZEPAM MONOTHERAPY IN LANDAU-KLEFFER SYNDROME

L. Bello-Espinosa
Mayo Clinic, Rochester, USA

Landau-Kleffner syndrome (LKS) is disorder in which children, develop language regression associated with verbal auditory agnosia, significant sleep activation of continuous epileptiform activity, behavioral dysfunction, and occasional clinical seizures. There is no consistent effective treatment for LKS. Conventional antiepileptic drugs has yielded only partial beneficial treatment and the use of medications like valproic acid, carbamazepine, ethosuximide, clonazepam, carbamazepine, lamotrigine, felbamate, vigabatrin, levetiracetam, have been associated with significant side effects, including worsening of the symptoms. Corticosteroids use has also been associated with significant side effects. IVIG also has yielded partial success. We report two children who experienced complete resolution of LKS after they were treated with prolonged use of continuous high dose of diazepam (0.75 mgs/kg) orally, nightly as monotherapy over one and a half years, without any use of other antiepileptic, or immunosuppressive therapies. Both children experienced complete resolution of the clinical signs of LKS. The patients did not developed tolerance, or other serious side effects, despite the high dose of diazepam. The prolonged use of high dose of Diazepam monotherapy can be used safely and results in complete resolution of Landau-Kleffner syndrome. High dose diazepam monotherapy for Landau Kleffner syndrome can be both safe and efficacious, and should be consider as a potential initial monotherapy for patients with Landau-Kleffner syndrome.

E700
PHARMACOKINETICS OF OXCARBAZINE IN NEONATAL PERIOD AND DURING LACTATION

I. Öhman, and T. Tomson†*
**Solna, Clinical Pharmacology Unit, Karolinska Institutet, Stockholm, Sweden; and †Karolinska Institutet, Stockholm, Sweden*

Purpose: To investigate the excretion of 10-hydroxy-oxcarbazepine (MHD) to breast-milk in women treated with oxcarbazepine during pregnancy and the neonates' capacity to eliminate MHD.

Method: High-performance liquid chromatography (HPLC) was used to determine plasma and milk concentrations of the active metabolite MHD in three pregnant women with epilepsy treated with oxcarbazepine and in their offspring. Two of the patients were studied both at delivery and during lactation, and one patient was investigated during lactation only.

Results: The umbilical cord plasma/maternal plasma concentration ratios of MHD were close to one. Plasma levels in the newborns declined slowly and at 36 h postpartum MHD plasma levels in the infants were approximately 70% of the cord plasma levels. At sampling before dose intake three to four weeks after delivery the milk/plasma concentration ratio was mean 0.67 (range 0.65–068) for the three women. The breast-fed infants' plasma concentrations were 2.7 and 3.2 μmol/L, respectively, approximately 5% of the mothers' plasma levels.

Conclusion: Our limited observations suggest free transfer of active metabolite MHD over placenta and indicate a rather low capacity in the newborn to eliminate MHD. Transfer of MHD to breast milk is extensive, but plasma concentrations appear to be low in breast-fed infants. No adverse effects were observed in the infants.

E701
CLINICAL COURSE OF THE PATIENTS WITH IDIOPATHIC GENERALIZED EPILEPSIES

M. Jovanovic, B. Jocic Jakubi, D. Stankovic Jankovic, and M. Mitic
Clinic of Child Disease, Clinic Center Nis, Serbia

Purpose: To analyze clinical course of the patients who are diagnosed as idiopathic generalized epilepsies.

Method: All patients were following up at least one year. Antiepileptic drug withdrawal was made after established stable clinical and EEG remission at least three years.

Results: Twenty-five patients were diagnosed with juvenile myoclonic epilepsy. Thirteen patients had relapses of the seizures: 3 during the therapy, 5 during discontinuation and 5 after discontinuation of the therapy. Only one patient is seizure-free for the 3 years after discontinuation of the drug. One patient with grand mal seizure on awakening was on the monotherapy, and had relapse of the seizure during the discontinuation of the therapy. One patient was diagnosed as juvenile absence epilepsy (JAE) is seizure-free after discontinuation 1, 5 year. Group of other generalized idiopathic epilepsies included 23 patients. Six patients had relapses of the seizures: 3 patients during the therapy, 1 patient during the discontinuation of the drug, and 2 patients had relapses after discontinuation. Two patients are without seizures after discontinuation of the therapy more than one year. Twenty-nine patients were diagnosed as childhood absence epilepsy. There were no relapses during the therapy. Four patients had relapses of the seizure after discontinuation of the therapy.

Conclusion: We concluded that most of the patients with idiopathic generalized epilepsies are well controlled with properly choice of the drug, but there is quite number of the relapses among the patients with idiopathic generalized epilepsies during and after discontinuation of the therapy. The possible course of the relatively small number of the relapses in our patients is short time of the follow up period.

E702
OXCARBAZEPINE MONOTHERAPY IN CHILDREN: A SINGLE-CENTER CLINICAL EXPERIENCE

G. Dizdarer, M. Anil, A. Bal, and N. Aksu
Tepecik Research and Education Hospital, Izmir, Turkey

Purpose: Oxcarbazepine, a keto analog of carbamazepine, is indicated for use as monotherapy or adjunctive therapy in the treatment of adults and children with partial seizures. The purpose of this study was to examine the efficacy and tolerability of oxcarbazepine in children with partial seizures.

Method: A prospective, single-center six-month study was conducted at the department of pediatrics of Tepecik Training and Research Hospital in Turkey. We enrolled a series of 114 patients with partial epilepsy (61 male; mean age 7.8 ±2.8 years, ranged from 2 to 14 years) who received oxcarbazepine treatment (mean dose 35.5 ±10.4 mg/kg/day) as monotherapy.

Results: Thirty-eight (32.2%) developed adverse events including drowsiness, skin rash, insomnia, dizziness and headache. Six patients (5.2%) discontinued oxcarbazepine as a result of adverse events (drowsiness and skin rash) during the first month of treatment. In children who continued oxcarbamazepine theraphy, 81 children (75%) became seizure-free at the third month. At the end of the 6 months, 82 children were seizure-free. No abnormality was determined in laboratory parameters. Most of the parents (72.9%) reported significant reduction in the number of seizures.

Conclusion: These findings suggest that oxcarbazepine therapy without major adverse effects is effective in children with partial epilepsy.

E703
THE RELATIONSHIP OF NEONATAL SUBCLINICAL ELECTROGRAPHIC SEIZURES TO NEURODEVELOPMENTAL OUTCOME AT ONE YEAR OF AGE

S. Hiz Kurul, S. Sutcuoglu, U. Yis, N. Duman, A. Kumral, and H. Ozkan
Dokuz Eylul University School of Medicine, Turkey

Purpose: The objective of this prospective study was to evaluate the influence of only electroencephalographic and electroencephalographic plus clinical seizures during neonatal period on neurodevelopment of the infants at one year of age.

Method: The long-term digital-video-EEG tracings of the first three days of life of 30 neonates were assessed. The babies were subdivided into three groups: newborns in group 1 (n=10) had neither electroencephalographic nor clinical seizures. Group 2 babies (n=7) had electroencephalographic seizure activity but no clinical seizures. Group 3 newborns (n=13) experienced both electroencephalographic and clinical seizures. The presence of psychomotor retardation and epilepsy were evaluated at corrected age of one year.

Results: Of the newborns, 21/30 (70%) were male and 24/30 (80%) were preterm. The mean birthweight was 1952.50 ± 978.74 (685–4103)g. The mean gestational age was 32.53 ± 4.26 (24–40)weeks. There was no significant difference between the three groups in regard to sex, gestational age and birth weight. One baby (10%) in group1 and 7 babies (53.8%) in group 3 had psychomotor retardation at one year of age. No babies in group 2 experienced psychomotor retardation. The differences between the groups 1 and 3, and groups 2 and 3 were found statistically significant. But the difference between the groups 1 and 2 was not significant. Only one baby in group 3 had epilepsy at one year of age. In groups1 and 2, no babies had epilepsy. The differences between the groups were not statistically significant.

Conclusion: Our results suggest that, neonatal seizures, but not silent electroencephalographic seizures are in relationship with poor neurodevelopmental outcome evaluated at corrected age of one year in preterm and term newborns.

E704
POSTOPERATIVE OUTCOME AFTER EPILEPSY SURGERY IN CHILDREN WITH FOCAL CORTICAL DYSPLASIA

G. Gröppel,†, A. Dressler†, M. Freilinger†, E. Gelpi¶, H. Mayer†, G. Kasprian§, B. Plattner**, L. Urak†, T. Czech‡, D. Prayer§, and M. Feucht†*
**Abteilung Für Neurologie, SMZ Ost, Vienna, Aurtria; †Universitätsklinik Für Kinder Und Jugendheilkunde, Vienna, Austria; ‡Universitätsklinik Für Neurochirurgie, Vienna, Austria; §Universitätsklinik Für Radiologie, Vienna, Austria; ¶Klinisches Institut Für Neurologie, Vienna, Austria; and **Universitätsklinik Für Psychiatrie Des Kindes- Und Jugendalters, Vienna, Austria*

Purpose: To identify the prognostic value of presurgically collected data for postoperative outcome after epilepsy surgery in pediatric patients with focal cortical dysplasia (FCD).

Method: We examined the postoperative value of following parameters: (1) age at onset, (2) duration of epilepsy, (3) gender, (4) preoperative seizure-frequency, (5) history of epilepsy in the family, (6) trauma, (7) meningitis/encephalitis, (8) complication during pregnancy/birth, (9) febrile convulsions, (10) type of seizures, (11) localization of the FCD, (12) type of surgery, (13) results of the histological examination. Postoperative follow up was at least 12 months. For statistical reasons postoperative outcome was defined as follows: group I: seizure-free and auras (Wieser

1a+1) (2) group II: not seizure-free (Wieser 2–6). We used Fisher's exact test of independence for univariate analyses. For variables with a significant result in the univariate analysis, we performed standard stepwise multiple logistic regression to identify variables predicting outcome independently.

Results: We found a significant correlation between the location of the focal cortical dysplasia in the temporal lobe and an excellent postoperative outcome (p= 0.045).

Conclusion: To achieve an excellent outcome in children with FCD a complete resection of the lesion is necessary. It is proved that patients with a temporal lobe located dysplasia have a better outcome than patients with lesions in the neocortex. The reason might be that the amount of the resection in the neocortex is smaller to spare the eloquent areas. We were able to corroborate these results.

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E705
CHROMOSOMAL ABNORMALITIES: CLINICAL AND NEUROPHYSIOLOGIC PATTERNS IN CHILDREN

I. Carrilho, M. Santos, A. Ribeiro, R. Chorão, and C. Barbot
HM Queen Maria Pia, Porto, Portugal

Purpose: Our purpose is to report clinical and neurophysiologic patterns of pediatric patients with chromosomal disorders.

Method: We retrospectively reviewed clinical and EEG registries of children with chromosomopathy followed in our outpatient clinic. All patients had at least one EEG performed at our department. We considered the following variables: age, sex, mental retardation, type of seizures, EEG abnormalities.

Results: We report 66 patients (38 female, 28 male). The first EEG was performed between 1month and 16 years. Eighteen patients had Down syndrome, eleven had Angelman syndrome, two had deletion 1p36 syndrome, two Wolf-Hirschhorn syndrome, two deletion 22q.11.2 and two Trisomy 8. All others were isolated cases of Trisomy 6, Trisomy 13, Klinefelter syndrome, 49XXXXY, several balanced translocations and other more complex chromosomal abnormalities. Mental retardation was present in all patients. Seizures occurred in 71%. Five had only febrile seizures, two only neonatal seizures. Forty had epileptic syndromes – West syndrome in 7 patients (6 with Down syndrome), focal epilepsy in 5, Continuous Spike-Waves During Sleep 1 patient and different generalized syndromes in 27. In most of the patients EEG data were not specific, ranging from normal to slow activity, or patterns reflecting the epileptic syndrome. The characteristic pattern was found in patients with Angelman.

Conclusion: We found a wide spectrum of mental retardation, seizures severity and epileptic syndromes. The small number of most of the cases unable us to make any conclusions. Nevertheless we tried to contribute to a better knowledge of clinical and EEG phenotypes of these rare disorders.

E706
TREATMENT OF REFRACTORY STATUS EPILEPTICUS TO ANESTHETIC AGENTS WITH KETOGENIC DIET: CASE REPORT

M. Vaccarezza, M. Aberastury, W. Silva, C. Maxit, and G. Agosta
Hospital Italiano, Buenos Aires, Argentina

Purpose: Refractory status epilepticus (RSE) is a life-threatening condition defined as ongoing intermittent or continuous status epilepticus despite the administration of adequate doses of two standard intravenous anticonvulsant drugs. The ketogenic diet (KD) has been employed as a treatment for medically refractory epilepsy for more than 80 years however we found only one report with the use of KD in refractory status epilepticus.

Method: We describe two patients who aborted status epilepticus after 3 days of KD. Patient 1, a 17-month-old boy with developmental delay secondary to bifrontal cortical dysplasia who developed a refractory status epilepticus refractory to multiple medical therapies including thiopental coma with burst-suppression pattern for 48 hs. KD was introduced after 9 days of RSE. After 3 days, the EEG showed seizures but cessation of status epilepticus. Patient 2, a previously healthy 6-year-old girl presented a seizure following a mild febrile illness. Initial magnetic resonance imaging showed no abnormalities. CSF white cell count was 40, all virological studies and cultures remained negative. During this hospital stay, nonconvulsive status epilepticus developed and was refractory to multiple medical therapies including thiopental coma with burst-suppression pattern, gamaglobuline and steroids. KD was introduced after 50 days of RSE. After 3 days of KD the video-EEG showed a total cessation of seizures.

Conclusion: These results support the potential efficacy of KD for children with refractory SE. Larger prospective series are needed to confirm these results.

E707
REFLEX SEIZURES IN CHILDREN WITH NONIDIOPATHIC FOCAL EPILEPSY

A. Perez-Jimenez, M. García-Fernández*, J. Alvarez-Linera†, J. Rodriguez-Uranga*, and F. Villarejo**
**Niño Jesús Pediatric University Hospital, Madrid, Spain; and †Ruber Internacional Hospital, Madrid, Spain*

Purpose: To describe the electroclinical pictures of children with reflex seizures and symptomatic or probably symptomatic focal epilepsy.

Method: Twenty patients (aged 3–18 years, median 9 years) with reflex seizures recorded by video-EEG monitoring between 2000 and 2007 and focal/ hemispheric EEG/ MRI abnormalities were reviewed.

Results: Reflex seizures were refractory and very frequent in 16 patients. Spontaneous seizures were noted in most of the cases. According to precipitant stimuli, seizure patterns, and MRI findings, several pictures were distinguished. 1. Startle-induced tonic seizures (supplementary motor area seizures) were recorded in eight patients, associated with vascular congenital hemiplegia (3), hemispheric malformations of cortical development (3), or normal clinical and MRI findings (2). 2. Seizures induced by local somatosensory stimuli, mostly focal sensitivomotor seizures, were observed in six patients with perirolandic or parietal malformative (2) or destructive (4) lesions. 3. Eating-induced partial complex seizures were documented in one patient with asymmetric bilateral perisylvian polymicrogyria. 4. Music-induced right temporal partial complex seizures were observed in a girl with nonlesional MRI. 5. Visual-induced occipital seizures were recorded in two cases with posterior cortex destructive lesions. 6. Seizures induced by emotional stimuli (autonomic or tonic seizures) were recorded in two children with ill defined video-EEG/MRI findings.

Conclusion: Patients with nonidiopathic focal epilepsies and reflex seizures frequently show a good anatomo-clinical correlation among type of precipitant stimuli, regional cortical dysfunction, and MRI topography of the lesions. Startle and somatosensory-induced seizures associated with lesions involving central or postcentral cortex are the most common electroclinical pictures.

E708
ANTIEPILEPTIC DRUGS WITHDRAWAL IN PATIENTS WITH IDIOPATHIC GENERALIZED EPILEPSY

M. Pavlovic, N. Jovic†, and M. Knezevic Pogancv**
**Institute for Health Care of Children and Youth of Vojvodina, Novi Sad, Belgrade, Serbia; and †Clinic for Neurology and Psychiatry of Children and Adolescents, Belgrade, Serbia*

Purpose: To analyze the outcome of antiepileptic drugs (AED) withdrawal in patients with idiopathic generalized epilepsy (IGE) in pediatric population.

Method: Medical records of consecutive patients with IGE from two tertiary clinics were retrospectively evaluated between 2001 and 2006. Inclusion criteria were clinical and EEG diagnosis of IGE subtypes according to the ILAE classification and follow up of at least 2 years after AED withdrawal. The cohort consisted of 58 patients (37 females, 21 males, aged 19.1 ± 5.5 (11–36) years). Duration of follow up after AED withdrawal was 3.3 ± 2.02 years (1–10). Prognostic factors of importance to the outcome were analyzed by survival methods.

Results: There were 18 (31.04%) patients with childhood absence epilepsy (CAE), 10 (17.2%) with juvenile absence epilepsy (JAE), 13 (22.4%) with IGE with generalized tonic–clonic seizures (GTCS) and 17 (29.1%) with juvenile myoclonic epilepsy (JME). After AED withdrawal, seizures reappeared in 22 (37.9%) patients. In 15 (25.8%) patients EEG worsened during follow-up (epileptiform abnormalities reappeared) so the AED were reintroduced. These subgroup was excluded in further analysis. During the first 6 months after withdrawal 60% of patients relapsed (20% during withdrawal), 65% after one year and 95% after two years of follow up. According to syndrome classification, 50% patients with JAE relapsed, 80% with IGE with GTCS and no patient with CAE. In multivariate analysis, retained significant factors in predicting seizure relapse were: seizure types (GTC seizures alone and combined with absences), EEG worsening during and/or after AED withdrawal and presence of hereditary factors in family history.

Conclusion: Considering closely related and often overlapped IGE syndromes, AED withdrawal is a challenging task for clinician This study identified the following prognostic variables associated with the higher risk of seizure relapse: seizure pattern, EEG worsening during and/or after AED withdrawal and hereditary factors.

E709
GOURMAND SYNDROME IN A CHILD WITH PHARMACORESISTANT EPILEPSY

M. Kurian, T. Schmitt Mechelke†, C. Korff*, J. Delavelle*, T. Landis*, and M. Seeck**
**University Hospital, Geneva, Switzerland; and †Children's Hospital, Luzern, Switzerland*

We report the case of a 10-year-old boy with pharmacoresistant epilepsy, symptomatic of a right temporal-parietal hemorrhagic lesion, who displayed an eating passion as described in the Gourmand syndrome (GS) in adults and discuss the role of epilepsy in GS. This patient presented a significant change in his eating habits (abnormal preoccupation with the preparation and eating of fine quality food) concordant with the onset of his seizure disorder, without any previous history of eating disorders or psychiatric illness. This observation corroborates the important role of the right cerebral hemisphere in disturbed eating habits including the relatively benign GS, and may be rarely, in less benign eating disorders such as anorexia and obesity.

E710
EPILEPSY AND ELECTROENCEPHALOGRAPHIC CHANGES IN ANGELMAN SYNDROME

S. Rocha, C. Martins, P. Breia, A. Duarte, J. Monteiro, and M. Fonseca
Hospital Garcia de Orta, Almada, Portugal

Purpose: To evaluate the contribution of electroencephalogram (EEG) for diagnosing Angelman syndrome in patients with severe developmental delay; establish eventual relationship between electrophysiological patterns, genetic mutation and prognosis.

Method: Retrospective descriptive review of four cases of Angelman syndrome. Data about clinical presentation, genetic confirmation, evolution, electroencephalographic patterns and therapeutic response were collected.

Results: Two boys and two girls were included, with a follow-up time ranging from 4 to 10 years. Genetic investigation revealed an interstitial deletion at 15q11.2-q13 region in three patients and one paternal uniparental dissomy. Beginning of epilepsy preceded diagnosis in three patients. Seizures were mainly of myoclonic type (4/4) and began between 10 months and 4 years of age. Other seizure types occurred: partial and generalized tonic–clonic (1/4), atonic (1/4) and episodes of nonconvulsive status (NCS) (1/4). Clinical status epilepticus (SE), as a first epileptic manifestation, occurred in 2 children. EEGs showed patterns I (3/4), II (1/4), III (1/4), NCS (1/4). Distinct patterns coexisted in 3 patients (1-I and SE; 2-normal, I and SE; 3-I,II and NCS). EEG changes preceded epilepsy in 2 patients. Seizure control was achieved in 3 cases, by monotherapy with sodium valproate (2/3) and clonazepam (1/3). Refractory epilepsy was observed in one patient, despite therapy with sodium valproate, lamotrigin and clonazepam.

Conclusion: Typical EEG patterns, when present, should alert for the diagnosis of Angelman syndrome in children with severe developmental delay, even in the absence of clinic epilepsy. NCS, frequently unrecognized, is sometimes detected by caregivers and must be confirmed by an EEG recording.

E711
CROSSOVER STUDY ON DOOSE SYNDROME DOUBLE-BLINDED LEV VERSUS VPA

M. Carignani
Rosario National University, Sante Fe, Argentina

Purpose: Evaluation of efficacy, in monotheraphy, of both drugs in this particular, usually refractory syndrome, best knowing as MAE (myoclonic-astatic epilepsy).

Method: Determined baseline during 40 days, recruiting only patients with cotidiane Sz., total 12 patients, with more that one year of disease duration. Then initiated crossover theraphy, double-blinded, during a period of 60 days, crossing in two (2) weeks the formulation for each group, increasing the new drug until reaches desirable dose and them suppressing gradually the previous drug, so the final results were on VPA group receiving 600–800 mgs/ day, and LEV group receiving 3000–5000 mgs/ day.

Results: At the end, LEV group showed 43% Sz. free patients during the given period, and VPA group only 27% Sz. free patients in correspondent period. I'll provide statistical studies.

Conclusion: LEV in monotheraphy is far better drug at 3000–5000 mgrs./day than VPA, at least for the study period. Seems to be a serious candidate for first choice drug in treating this particular syndrome.

E712
TYPES OF THE POSTNATAL EPILEPSY IN CHILDREN AFTER NEONATAL SEIZURES

C. Cornelia, T. Constantin†, I. Ion*, G. Stanislav‡, and H. Svetlana**
**Hospital of Mother and Child Heath Care, Moldova; †National Psychiatric Hospital, Moldova; and ‡Emergency Hospital, Moldova*

Purpose: To determine types and the structure of the postnatal epilepsy (PNE) developed in children with neonatal seizures.

Method: The study included 130 children (52 females and 78 males), admitted to the Pediatric Neurology Department of the Research Institute of Mother and Child Health Care in the period 2004–2007, diagnosed clinically and EEG confirmed having neonatal seizures.

Results: Immediately after birth resuscitation was necessary in 40.7% (n=53) children. 36.9% (n=48) of which were premature, and 63.1% (n=82) were term infants. Neonatal seizures were caused the most frequent by metabolic disorders, perinatal asphyxia, hemorrhage, CNS infection, CNS dysgenesis and other. Antiepileptic drug therapy was administered to control seizures in 103 patients (79.2%). Thirteen children were lost for the follow-up because neonatal death (10%), thus the original sample reduced to 117 children and from this group 44 children (37.6%) developed PNE. Out of them 8 patients (18.1%) manifested infantile spasms, 15 children (34%) showed symptomatic focal epilepsy, 2 children (4.5%) with Lennox-Gastaut syndrome, 1 child with early epileptic encephalopathy or Ohtahara syndrome (2.2%) and other generalized symptomatic epilepsy – 18 children (40.9%). Postnatal epilepsy during the follow-up period was observed in 28% at 12 months, 34% at 24 months and 38% at 36 months.

Conclusion: The study shows that neonatal seizures are associated with high incidence of the postnatal epilepsy (37.6%), including severe forms of epilepsy in children (West and Lennox-Gastaut syndrome).

E713
EFFICACY OF ANTIEPILEPTIC DRUGS IN ABDOMINAL PEDIATRIC EPILEPSY

E. Barragán, M. Hernández, A. Huerta, and F. Capistro
Hospital Infantil de México Federico Gómez, Mexico

Purpose: Describe the efficacy drugs in pediatric patients with abdominal epilepsy.

Method: We analyze the clinical response of pediatric patients, both gender, between 5 to 10 years treated in the neurology department of the Hospital Infantil de México. Clinical and neurological examination, EEG characteristics and response to treatmnent were evaluated.

Results: 10 patients, 7 males and 3 females, were treated for abdominal epilepsy. The antiepileptic drugs used were 5 with valproate, 2 with oxcarbazepine and 3 with topiramate. Of these, only 3 patients (33%) respond to AEDs (1 with one of each AEDs). The other 7 patients were no responders, inclusive with higher doses and 4 of these patients with two AEDs. Interesting, more than 50% of the no responders have a good response to beta-blocker (propanolol).

Conclusion: Its important to reevaluated the clinical diagnosis of abdominal epilepsy and their treatment, because many can respond to treatment for abdominal migraine, that can be maybe try to reclassified these symptomatology. A double-blind crossover treatment had to be done.

E714
EFFICACY AND SAFETY OF LEVETIRACETAM IN EPILEPTIC CHILDREN

H. Shin, S. Eun, and B. Eun
Korea University College of Medicine, Korea

Purpose: There are limited reports about levetiracetam (LEV) to pediatric epilepsy. This study was performed to assess the efficacy and safety of LEV as add-on therapy in children with refractory epilepsy.

Method: The epileptic children, who visited the pediatric neurology Clinic of Korea University Guro Hospital from April 2007 to February 2008, were included. The retrospective study was performed for proving the effectiveness of add-on therapy of LEV in patients who were refractory to the other antiepileptic drugs. The data include previous medication history, LEV dosage titration schedule, clinical outcomes, and adverse effects.

Results: The study group consisted of thirty-one patients aged 4–17 (10.0¾4.8) years with refractory seizures. At all patients, add-on therapy of LEV was started with dose of 4.8–22.7 (14.0¾4.7) mg/kg, titrated for 3–8 (5.2 ¾1.8) weeks and maintained with dose of 28.6–66.7 (54.1 ¾11.1) mg/kg for at least 12 weeks. At 12 weeks after initiation of LEV, nine patients (29.0%) experienced seizure-free, and thirteen patients (41.9%) had a >50% reduction of seizure. Eight (36.4%) of twenty-two patients, who were evaluated at 24 weeks, had been seizure-free, and nine (40.1%) had a > 50% reduction of seizure. twelve (39%) patients experienced a clinically significant adverse event as like somnolence (16.1%), aggressive behavior (6.5%), and irritability (6.5%).

Conclusion: The efficacy and safety of LEV were excellent. The efficacy of add-on LEV was not related to doses of LEV nor other antiepileptic drugs, and not associated with significant adverse events nor laboratory abnormality.

E715
SEIZURES VERSUS DYSTONIA IN ENCEPHALOPATIC CRISIS OF GLUTARIC ACIDURIA TYPE I

C. Jaume, C. Alfredo, V. Maria Antonia, and S. Francisco
Hospital Universitari Sant Joan De Deu, Barcelona, Spain

Purpose: Glutaric aciduria type I (GAI) begins with an acute encephalopatic crisis with hypotonia and generalized rigidity, neurologic depression, irritability, seizures and dystonia. Many times, dystonic movements may be confused with seizures. To describe the clinical features and the initial electroencephalographic findings in GAI patients.

Method: Descriptive, retrospective study based on the review of clinical histories of GAI patients.

Results: We review 13 GAI patients, 9 males and 4 females, mean age 8.7 months (range 3–15 months). 4/13 had consanguineous parents; 7/13 had macrocephaly. 12/13 patients (92%) had seizures or pseudoseizures. In 8 of the 13 patients (62%) those episodes were the first neurologic symptom. In 11/13, the dystonia appeared after the second day. Other clinical features included irritability (12/13), neurologic depression (11/13) and hypotonia (7/13). 35 EEG were analyzed during the first year (25 EEGs in the first month). EEG paroxysms in 2 patients; 8/13 slow background activity and 4/13 asymmetries in background activity. In the follow-up of 11 patients, none of them had seizures later. Antiepileptic drugs were discontinued during the first year.

Conclusion: Even though seizures are part of the symptoms of the GAI onset, certain paroxysmal movements could be dystonic episodes and not genuine seizures. This hypothesis is supported by the fact that seizures do not continue to occur after dystonic tetraparesis is noticed, EEG paroxysms are infrequent in the acute stage, antiepileptic drugs are not needed on follow-up.

E716
A STUDY OF CLINICAL FEATURES, EEG, PATHOPHYSIOLOGY AND PROGNOSIS OF 18 PATIENTS WITH PANAYIOTOPOULOS SYNDROME

J. Liang
Children's Hospital, Chongqing Medical University, China

Purpose: To characterize the clinical, EEG, pathophysiology and prognosis of Panayiotopoulos syndrome (PS).

Method: According to the criteria of PS made by ILAE (2001), eighteen patients with PS were prospectively followed up in the clinical manifestation, interictal and ictal EEG as well as treatment for 5 yrs.

Results: The initial onset of seizures occurred in 2.2 to 8.6 yrs with an average of 4.5 yrs. Among them, 4 cases have family history of epilepsy, of which one had the idiopathic epilepsy, 3 have history of migraine, 5 have febrile seizures. PS have pronounced autonomic seizures (AS), including pallor, nausea, retching and ictal vomiting, abdominal discomfort et al; the next is eye and head deviation, and then the complex partial seizures (CPS) or secondary generalization (SG), and even status epilep-

ticus (SE) with a partial impairment of consciousness; 5 had sporadic attacks with seizure free intervals more than 6 m, 8 occurred one time within 1~5 m, another 5 have seizures every 1~5 m, two of whom had more than ten times daily. 8 had unilateral or bilateral occipital spikes,4 had temporal spikes, Rolandic spikes, and temporal-parietal-occipital spikes; 2 had frontal and frontal-occipital spikes or spike-wave discharges (SWD); one had generalized SWD. Epileptic foci were unsteady, easily migating and movable or absent. Ictal EEG shown the occipital or frontal predominant or generalized rhythmic SED associated with AS or SG. Neuroimagine is normal.

Prognosis: CBZ,VPA and TPM were comparatively more respond to PS. Seizures nearly disappeared in 9 cases, markedly compromised in 4, an worsen in 2. Developments were normal in all children but mild learning and behavioural problems were found in 11.

Conclusion: PS is an epileptic syndrome characterized by AS, and age-specific occurrence with or not CPS & SG or SE. Epileptic foci were occipital predominance, but might be multifoci or migrating. Careful study of clinical features, EEG, pathophysiology and evolution of PS is mandatory to elucidate the mechanism of autonomic and systematic epilepsy.

E717
CLINICAL ASPECTS OF EPILEPSY IN CHILDREN AND ADOLESCENTS WITH CEREBRAL PALSY

P. Ignjatovic
Clinic of Neurology and Psychiatry for Children and Youth, Belgrade, Serbia

Purpose: To analyze the age of seizure onset, seizure types and the efficacy of antiepileptileptic drugs in our patients with cerebral palsy (CP).

Method: The group of 36 children and adolescents with CP and epilepsy with a mean age of 11 years (range, 3 to 26 years) was studied retrospectively. There were 32 patients with spastic form (spastic hemiplegia – 12 patients, quadriplegia 10, diplegia 9, paraplegia 1) and 4 patients with mixed form. The follow-up period for at least 2 years was one of inclusion criteria.

Results: The mean age of seizure onset was 2.8 years (range, 1 month to 14 years). Seizure onset before the age of 2 years was noted in 53% of children. The majority of our patients (67%) experienced focal seizures with/without secondary generalization. Multiple seizure types occurred in 19% of patients. One child had startle epilepsy. Infantile spasms were observed in 3 of 10 children with spastic quadriplegia. CP was associated with mental retardation in 86% of patients. Fifty-eight percent of our patients were on AED monotherapy while 42% were treated with two or three AEDs. Twenty-eight patients (78%) became seizure-free. Complete seizure control was mainly achieved in children with spastic hemiplegia (10/12) and diplegia (7/9).

Conclusion: Early seizure onset was found in the majority of our patients. The most common seizure types were focal and secondary generalized seizures. Complete seizure freedom was mainly achieved in patients with spastic hemiplegia and diplegia.

E718
CLINICAL CHARACTERISTICS AND PROGNOSTIC EEG FACTORS OF EPILEPSIES WITH CONTINUOUS SPIKES AND WAVES DURING SLOW SLEEP

K. Katerina, C. Marina†, K. Olga*, S. Natalya*, K. Olga*, T. Elena*, and L. Elena**
**Children's Regional Hospital, Russia; and †Nizhny Novgorod State Medical Academy, Russia*

Purpose: To compare the clinical and neurophysiologic features of idiopathic and symptomatic cases of epilepsy with continuous spikes and wave during slow sleep (CSWS).

Method: Twelve patients were included (7 idiopathic and 5 symptomatic cases). The day and overnight video-EEG monitoring (VEEG) were performed each 4 months during four years. Clinical and EEG variables were evaluated. The patients were admitted for overnight VEEG to evaluated sleep architecture, quantity of sleep patterns, arousals during sleep and time of maximum of epileptiform activity.

Results: We suggest that clinical manifestations of idiopathic CSWS include a focal motor seizures, behavior and cognition deteriorations. In symptomatic cases the patients had serious perinatal pathology, optical atrophy (4 cases), hydrocephaly, and neurological deficit and MRI abnormalities. The child had focal motor seizures with tonic component in three cases. The dynamic VEEG during sleep revealed the distinctive features of EEG patterns of symptomatic CSWS in child, such us multifocal spikes and waves and different form amplitude of epileptiform activity. The patients with idiopathic CSWS had a short time of approach of dream, decreased of EEG arousal activity and movements and absent sleep spindles. The occurrence of sleep spindles and EEG arousal activity, increase of frequency of spikes and wave discharges during one second and reduction of this amplitude predicts the favorable outcome.

Conclusion: The dynamic VEEG revealed the differences of idiopathic and symptomatic CSWS in child. The prognostic factors of good outcome were offered.

E719
HIPPOCAMPAL VOLUMETRICS AND MEMORY PERFORMANCE IN CHILDREN WITH TEMPORAL LOBE EPILEPSY

P. Klaas, T. Wehner, B. Diehl, J. Haut, R. O'Dwyer, and A. Gupta
Cleveland Clinic Foundation, Cleveland, OH, USA

Purpose: A number of studies have utilized volumetric MRI measurements to examine hippocampal volumes in patients with temporal lobe epilepsy (TLE). Few studies have investigated this in children.

Method: We performed manual volumetry on both hippocampi in twenty five right handed children with right or left TLE and examined the possible relationship with memory for auditory and visual information. Volumetries were calculated for each hippocampus. These measures were correlated with memory scores obtained in the presurgical evaluation to determine the relationship between memory performance and volume.

Results: In children with left temporal seizure focus, the ipsilateral hippocampus was slightly smaller compared to the contralateral structure. Contralateral hippocampal volume was correlated with performance on immediate and delayed visual memory measures, immediate verbal memory and learning (all at $p<0.05$ or better). No significant relationships were found for patients with right TLE.

Conclusion: These findings support previous reports of smaller hippocampi ipsilateral to seizure origin. In addition, the relationship between right hippocampal size and both visual and verbal memory in children with left TLE may have implications for postsurgical outcome. Further examination using volumetric methods in a larger sample with a control group may help to reduce the variability seen between this and other studies and may help to answer questions regarding distribution of lateralized functions within the pediatric population with TLE.

E720
LEVETIRACETAM IN THE TREATMENT OF REFRACTORY EPILEPSY IN CHILDREN

G. Dýzdarer, O. Sývaslý, M. Anýl, A. Bal, and N. Aksu
Tepecik Research And Education Hospital, Izmir, Turkey

Levetiracetam (LEV) is a broad-spectrum antiepileptic drug that is effective against a variety of seizure types. It is a pyrridoline derivative drug. Controlled and open-label studies have shown its efficacy and safety as initial monotherapy and add-on treatment for partial-onset seizures in

children and adults. The purpose of this study was to assess the efficacy and safety of levetiracetam in pediatric chronic refractory epilepsies prospectively. We treated 30 patients with levetiracetam for 6 months. The data include patients with partial and generalized seizures, concomitant antiepileptic drug use. Seizure frequency, drug dosages, adverse events, and neurologic examinations were documented at baseline and routine follow-up visits. Ten patients were discontinued for lack of efficacy or adverse events. Three patients reported improvements in cognition or behavior. Levetiracetam was generally effective and well tolerated in this open-label study. Levetiracetam is a new antiepileptic drug that appears to be a useful add-on treatment in patients with refractory epilepsy. Large, well-controlled studies are needed to fully define levetiracetam's potential in children with refractory epilepsy.

E721
SEIZURE OUTCOME IN PATIENTS WITH SURGICALLY TREATED SYMPTOMATIC REFRACTORY FOCAL EPILEPSY AND COEXISTING BENIGN FOCAL EPILEPSY OF CHILDHOOD (BFEC)

T. Wehner, S. Haspolat, A. Gupta, P. Kotagal, I. Tuxhorn, E. Wyllie, D. Lachhwani, and W. Bingaman
Cleveland Clinic Epilepsy Center, Cleveland, OH, USA

Purpose: Epilepsy surgery is successful in treating refractory symptomatic focal epilepsy in patients with coexisting benign focal epileptiform discharges (BFEDs; Pan et al, Epilepsia 2004;45:284). Seizure outcome in patients with both pharmacoresistant symptomatic focal epilepsy and symptomatic BFEC has not been reported.

Method: We reviewed all pediatric epilepsy surgery patients since 1998 (n=501) who had BFEDs documented (n=7) during their epilepsy evaluation at Cleveland Clinic.

Results: We identified 3 patients with electrographic evidence of seizures due to BFEC in addition to pharmacoresistant lesional focal epilepsy. Patient 1: 6 year old male with left temporal epilepsy due to MCD, right BFEC. Postoperative follow-up 18 months. Patient 2: 6 year old female with left temporal epilepsy due to MCD, left BFEC. Postoperative follow-up 33 months. Patient 3: 2 months old male with left hemispheric epilepsy due to left hemimegalencephaly, right BFEC. Postoperative follow-up 36 months. All three patients became free from their habitual seizures following epilepsy surgery, but continued to experience rare rolandic seizures.

Conclusion: Lesional pharmacoresistant focal epilepsy can be successfully treated with resective epilepsy surgery even when coexisting with BFEC. Careful documentation of breakthrough seizures during post operative follow-up due to BFEC is important so that these patients are not labeled as surgical failures. Natural course of BFEC may include remission by 16 years of age, however this will be clear with longer follow-up.

E722
SUPPRESSION OF COMPLEX FEBRILE SEIZURES BY ELEVATING RESPIRATORY CO2 USING A REBREATHING TECHNIQUE – TWO CASE REPORTS

S. Schuchmann, D. Schmitz*, A. Grüters-Kieslich†, S. Vanhatalo‡, and K. Kaila§,¶*
**Neurowissenschaftliches Forschungszentrum, Charité, Berlin, Germany; †Centrum Für Kinder- Und Jugendmedizin, Charité, Berlin, Germany; ‡University Central Hospital, University of Helsinki, Finland; §University of Helsinki, Finland; and ¶Neuroscience Center, University of Helsinki, Finland*

Purpose: We have shown that experimental febrile seizures (FS) in infant rats are triggered by a respiratory alkalosis, and that the FS can be blocked within 20 s by elevating the ambient CO2 level to 5% (Schuchmann et al., Nat. Med. 2006, 12: 817–823). The present work was done to examine whether FS in children are also associated with and triggered by respiratory alkalosis.

Method: We measured blood pH and CO2, and treated recurrent FS using a re-breathing bag that permitted simultaneous measurement of its O2 and CO2 level.

Results: Here we report successful rebreathing treatment of a 3 2/12 year old girl and a 4 3/12 year old boy, with recurrent complex FS. Both suffered from a viral infection of the upper airways with fever up to 40°C, and were taken to the hospital after the occurrence of complex FS which were initially suppressed using diazepam. The blood gas analyses showed a respiratory alkalosis in both children (pH 7.47, 7.49; pCO2 29.4, 30.7 mmHg; values after recovery from fever pH 7.38, 7.40; pCO2 39.8, 44.2 mmHg). Even under antipyretic treatment both children showed repetitive increases in body temperature (39°C) and recurrent FS during the first days in the hospital. In five of five trials, the FS were completely blocked within minutes by rebreathing, with a maximum CO2 level of 3.0% and 3.2% in the bag.

Conclusion: Our data suggest that FS in humans are triggered by a respiratory alkalosis; and that rebreathing as well as other techniques that abolish the respiratory alkalosis may provide an effective treatment of FS.

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E723
CLINICAL CHARACTERISTICS AND ETIOLOGY OF EPILEPSY DURING FIRST YEAR

V. Mitic, D. Bogicevic, N. Dimitrijevic, D. Nikolic, and G. Cuturilo
University Children's Hospital, Belgrade, Serbia

Purpose: To evaluate the clinical characteristics and etiology of epilepsy in children during first year.

Method: We investigated 71 children (33 boys, 38 girls) 1–12 months old, admitted in hospital from 2006 – 2008 because of epileptic seizures. Their past medical history, neurologic finding, EEG and neuroimaging (MRI/ CT) were evaluated. In some case we made special investigations depending on clinical features. According to the results, in the first step we classified patients into 3 groups – symptomatic, cryptogenic, and probably idiopathic/ or unclassified, followed by the classification of particular cases into epileptic syndromes.

Results: The mean age at onset was 5, 6 months.26/71 infants (36, 6%) had normal neurologic finding.49 / 71 (69%) were in the symptomatic group, 14 /71 (19, 7%) had cryptogenic epilepsy, 8 /71 (11, 2%) had some form of idiopathic epilepsy or were unclassified during hospital stay. West syndrome had 30/ 71 (42, 2%). 26/30 were symptomatic. 11/26 had hypoxic-ischemic sequelae (HIS) −1/11 prenatal, 10/11 perinatal; 5/26 had Tuberous sclerosis; 4/26 brain malformations; 1/26 had probably metabolic disease; 5/26 children were with unknown etiology at onset of the condition. One child had Early myoclonic encephalopathy. In the other infants with symptomatic epilepsy (22/ 49) we found: 10 / 22 HIS – 8/10 perinatal, 2/10 postnatal; 7/22 brain malformations; 2/22 infections; 2/22 metabolic disease; 1/22 Sturge-Weber syndrome.

Conclusion: Neurologic deficits had 63% of patients, symptomatic or cryptogenic epilepsy had 88%. The most frequent cause of symptomatic epilepsy was HIS (42%). West syndrome had 42% of babies.

E724
QUALITY OF LIFE IN CHILDREN WITH EPILEPSY IN CROATIA

B. Muèiæ -Puciæ
Hospital for Choronically Sick Children Gornja Bistra, Zagreb, Croatia

Precise data about prevalency of childhood epilepsy are not available, it is estimated there are about 0.7% –0.8% children.

Purpose: Our study shows the current state, hoping to construct a model to help children and the family to lead a life free from medical and psychosocial complications of epilepsy, in which epilepsy does not play a central role, dictating their way of living.

Method: From 01. 01. 2000 to 01. 01. 2006. Our outpatient clinic registered 1.636 patients suffering from epilepsy. Using questionnaire QOLIE-AD-48. (J. Cramer et al. Epilepsia 1999, 40(8):1114–1121), 157 patients entered the study, 85 boys, 72 girls. The beginning of epilepsy was from 0 to 18 yrs. (median 8,29). The patients fulfilled the questionnaire in the doctor's waiting room (about 20 minutes), and discussed it during the check-up with the doctor. The questionnaire consists of 48 questions: epilepsy impact (12), memory/concentration (10), attitudes towards epilepsy (4), physical functioning (5), stigma (6), social support (4), school behavior (4), health perceptions (3). Answers provided were from: 1 bad, 2 somewhat better, 3 almost same, 4 much better, 5 almost excellent). Internal consistency reliability was estimated for each of the final factor-based scales as well as for overall summary score with Cronbach's alpha coefficient.

Results: Total amount was 74.89, epilepsy impact 79.57, memory/concentration 78.44, school attitude 93.34, physical functions 76.30, stigma 81.41, attitude towards epilepsy 26.06, social support 82.71.

Conclusion: Children scored least in their attitude towards epilepsy. Older children have lower overall score, then younger ones. So psychosocial help is most needed in that group to become happy adults.

E725
FIRST AFEBRILE SEIZURE – FEAR OF THE SECOND FIT

N. Dimitrijevic, D. Nikolic*, D. Bogicevic*, A. Dimitrijevic†, and V. Mitic**

**University Children's Hospital, Belgrade, Serbia; and †Gynecology and Obstetrics Clinics 'Narodni Front' Belgrade, Serbia*

Purpose: Retrospective identification of indications for antiepileptic drug treatment of children with first afebrile seizure.

Method: All patients were evaluated for the following parameters: age at onset of seizure, duration, type of seizure (generalized vs. partial), electroencephalographic finding, neurological status of the patient.

Results: 248 children with first afebrile seizure were observed. Follow-up period was 3 years. In a subgroup of 144 (58,1%) children with drug treatment, 52 (36,1%) had second or more seizures, and epilepsy diagnosis was established. In a subgroup of 104 (41,9%) children without treatment, second seizure occurred in 62 (59,6%).

Conclusion: There is no statistical significance in treatment efficacy between two observed subgroups regarding all followed parameters. Decision about initiation of treatment is made with parent's consent. Parent's fear of another fits was the 'strongest' reason for drug treatment. Pathological EEG finding and psychomotor retardation were next two reasons for initiation of therapy. Further parent's education and psychological support is needed since for most patients drug treatment was not indicated.

E726
ANALYSIS OF EEG AND SPEECH IN CHILDREN WITH DEVELOPMENTAL DYSPHASIA – EFFECT OF ANTIEPILEPTIC TREATMENT

L. Neuschlová, K. Štìrbová*, J. Žáèková*, V. Komárek*, J. Tuèková†, and P. Zetocha**

**2nd School of Medicine, Charles University, Motol Hospital, Prague, Czech Republic; and †Faculty of Electrical Engineering, Czech Technical University, Prague, Czech Republic*

Purpose: To determine incidence of epileptiform activity in our sample of children with developmental dysphasia. To evaluate the effect antiepileptic treatment on language development. To develop suitable computerized method for evaluation of speech disorder.

Method: Population: 37 children with developmental dysphasia, aged 39 – 112 months. Six-month open prospective study with oral Diazepam (dose 0.5–0.7 mg/kg per day) – 6 children with discharges on treatment, 6 controls without discharges and without medication. Overnight sleep video-EEG. Psychological evaluation: Standford-Binet Intelligence Scale-4th Revision, Gessel Developmental Schedules. Speech analysis using vowel classification and visualisation by a supervised Self-Organizing Maps (a type of artificial neural network based on Kohonen's map). Standardized speech protocols of 37 dysphatic children were compared to database trained on 72 healthy children aged 4–10 years.

Results: We found epileptiform discharges in 12 children. Comparing results of psychological assessments (verbal and performance IQ) of 12 children with discharges and 25 children without discharges did not show significant difference. In the prospective study of children on Diazepam treatment, we found progress, expressed as growth of verbal IQ, only in one case. Computerized speech analysis differentiated dysphatic and healthy children.

Conclusion: Our study confirmed higher incidence of epileptiform activity in dysphatic children. Our results do not support the hypothesis that antiepileptic treatment can improve language development in these children. Computerized speech analysis can be in future suitable tool for assessing degree of speech impairment and possible therapeutical effect.

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E727
MEASUREMENTS OF MANUAL FUNCTION IN CHILDREN WITH CP AND EPILEPSY USING GROSS MOTOR FUNCTION MEASURE SCALE AND LEVELS

E. Gajewska, E. Mojs, and W. Samborski

**Rheumatology And Rehabilitation, University of Medical Sciences Poznan, Poland*

Cerebral palsy (CP) was first described by William Little in 1940. It is characterized mainly by disturbances in motor function and posture, that result from a damage of the central nervous system. Classification of CP should be based not only on topography but also on objective measurement of function, for example based on Gross Motor Function Measure (GMFM) or manual function measured by Manual Ability Classification System. First of these scales was described in 90-ies and is widely used to assess the developmental status of a child with CP. It is possible to assess several motor functions as elements of the developmental status of a given child at any moment. The second mentioned scale is called MACS (Manual Ability Classification System) and is used as a tool to assess how children with CP use their hands to handle objects in everyday activities. MACS is based on spontaneous manual activities with special attention paid to usage of objects that are within grasp. Material consisted of 73 children in whom cerebral palsy and epilepsy was recognized. All children were assessed using GMFM. Collective assessment was also expressed as GMFM level and was compared to the level achieved in MACS.

Results: Very close correlation between MACS and five elements of the development based of GMFM was found, as well as between MACS and levels of GMFM and epilepsy – partial seizures.

E728
MANUAL FUNCTION AND FUNCTIONAL DEVELOPMENT DIAGNOSING IN CHILDREN WITH CP SHOWING MENTAL IMPAIRMENT

E. Gajewska, E. Mojs, M. Sobieska, and W. Samborski

Rheumatology and Rehabilitation University of Medical Sciences Poznan, Poland

Introduction: Manual Ability Classification System -MACS is designed for children with cerebral palsy, aged 4 to18 years. MACS provides a systematic method to classify how children with cerebral palsy use their hands when handling objects in daily activities. MACS is a subjective classification system and is based upon self-initiated manual abilities, with a particular emphasis on handling objects in a individual's personal space. Functional development was based on Gross Motor Function Measure (GMFM) consisting of four-points assessment system for every performed activity, where criteria and conditions are described in details. Points gained are summed, a percentage against desired age level is calculated and it shows the developmental status of the child. The aim of the study was measurement of manual function and functional development (using GMFM) in children with cerebral palsy showing mental impairment.

Material and Method: The study was conducted on 73 children in whom cerebral palsy was recognized, accompanied by mental retardation. Children were also divided according to mental retardation assessed by a physician and expressed in Wechsler's scale. All children were subjected to complex diagnosing of the functional fitness, based on Manual Ability Classification System (MACS) and GMFM.

Results: Close relationship was found between both MACS and GMFM result and degree of mental impairment, but the relationship to MACS was more significant. Thus manual function is more closely related to mental disturbances than general physical activity. It could be observed that only children with deep impairment showed disturbed activity on GMFM A level.

E729
EPILEPSY AS A RISK FACTOR OF THE OCCURENCE OF BEHAVIORAL PROBLEMS IN CHILDREN AGED 7–12 YRS OF AGE

E. Mojs, E. Gajewska, M. Glowacka, and W. Samborski
Poznan University of Medical Sciences, Poland

Epilepsy is a disease which can impair cognitive and emotional functioning. The changes could be connected to brain pathology what is a reason of epilepsy or with epileptic seizures. The aim of the study was to estimate behavioral problems of children with epilepsy. 40 of pts with newly diagnosed (20) and drug resistant (20) epilepsy participated in the study. The mean of age was 10.8 yrs, the time of reavealing of the disease was 5.3 yrs of age. Generalized and partial seizures there were diagnosed. The ASEBA questionnaire used in the stud. The results show that children with epilepsy has much more behavioral problems than children in general population. Somatic problem, aggressive behavior difficulties in control of emotions appeared statistically rebost. There is a correlation between kind of seizures and type of behavioral problems additionally.

E730
EPILEPSY IN CHILDREN WITH MITOCHONDRIAL DYSFUNCTION

O. Globa, N. Zhourkova, O. Kondakova, E. Tikchomirov, E. Basargina, E. Sorokina, E. Semikina, L. Kuzenkova, and V. Pinelis
Scientific Center of Children's Health, RAMS, Moscow, Russia

Mitochondrial diseases (MD) a heterogeneous group of multisystem disorders characterized by impaired energy production due to genetically based oxidative phosphorylation dysfunction. Epilepsy are common manifestations of many of these conditions. Thirty two patients (6 months – 16 years) were studied. All patients had full biochemical, hematological, immunological tests, neuroimaging studies, EEG, ECG. Lactate, ammonia, carnitine level were measured. A molecular analysis of mitochondrial DNA was also performed by sequence. In 23 of children the MD were confirmed, in other still not determined. Epilepsy (E) was observed in 11 patients, manifested mainly by myoclonic seizures, usually refractory to standard treatment, in combination with dilated cardiomyopathy in 3 children. In 10 patients without E the epileptiform EEG discharges were found. Different mtDNA mutations were revealed. In our study in 3 children with high-frequency MELAS mutation A3243G, A11084G had no stroke, but epilepsy. On the contrary in 5 stroke patients no MELAS mutation was found. In prospective study in 3 of tham epilepsy was developing. 16SrRNA mutation represent of hypoglycemia, epileptiform EEG discharges, seizures, stroke-like episodes. In patients with MD, even without seizures, the serum autoantibodies level to GluR1 and NR2A was significantly high vs control group (GluR1-180±15c.u., NR2A 171,4±14c.u.) ($P<0.05$). The high level of activation markers CD122+, low level of CD19+ in MD patients was revealed. The most adequate achievement in seizure control was in combination of new antiepileptic drugs with metabolic therapy. In conclusion, epilepsy may be the only manifestation or the initial manifestation of a mitochondrial disorders and the early diagnostic of MD need for providing adequate therapy options for these disorders.

E731
FRONTAL LOBE DYSFUNCTION IN CHILDREN WITH NONLESIONAL EPILEPSY

S. Kwon, and S. Hye-Eun
School of Medicine, Kyungpook National University and KNU Hospital, Daegu, Korea

Purpose: The neuropsychological assessment of 'nonlesional' epilepsies is crucial to better understanding the role of epilepsy for cognitive, attentional or executive functions. However, the knowledge is quite limited especially in children. The aim of this study was to investigate the presence and severity of frontal lobe dysfunctions in children with nonlesional epilepsy.

Method: Fourteen children with nonlesional epilepsies, with ages ranging from 6–14 years (10 males, 4 females) were assessed at the time of first visit using a comprehensive neuropsychologic battery which is specifically designed to assess cognitive, executive, attentional, language, visuospatial, and learning/memory functions. We used Wechsler Intelligence Scale for Children, Bender Gestalt Test,Verbal fluency, Stroop Test, Auditory Verbal Learning Test, Rey-CFT, Wisconsin Card Sorting Test and visual Attention Diagnostic System and so on.

Results: Out of 14 subjects, one had frontal lobe epilepsy (7%) and 2 had benign rolandic epilepsy (14%). Global cognitive function was considered within normal, but evidence of subnormal cognitive function is apparent in 4 of 14 subjects (29%). In addition, they scored significantly lower in verbal and categorial fluency (43%, 29%), visuospatial tasks (36%), learning (14–50%), memory (50%), executive (36%) and attentional functions (50%). The mean scores on these domains were >1.5 standard deviations below the normative mean. On the majority of subtests, 2 out of the subjects (14%) scored in the impaired range.

Conclusion: Despite the small sample size, the findings indicate the potential presence of frontal lobe dysfunction, risk to academic achievement in children with nonlesional epilepsy. We therefore think the routine neuropsychological assessment may be needed in children with nonlesional epilepsy.

E732
TEMPORAL LOBE EPILEPSY IN CHILDREN: SURGICAL AND NEUROPSICOLOGICAL OUTCOME IN 29 PATIENTS

L. De Palma, S. Bergamo*, M. Cendron*, S. Francione†, G. Lorusso†, H. Meencke‡, C. Makowski‡, C. Prager‡, C. Boniver*, and M. Vecchi**
**Clinical Neurophysiology Unit, Azienda Ospedaliera Padova, Italy; †C. Munari, Center for Epilepsy Surgery, Ospedale Niguarda, Milano, Italy; and ‡Epilepsy Centre Berlin-Brandenburg, Berlin, Germany*

Temporal lobe epilepsy (TLE) in children is a common type of partial epilepsy, even if it is less frequent than in adults. About 1/3 of these patients

has a drug resistant epilepsy. Presurgical investigations examine the anatomical and electroclinical correlations, and aim to localize the epileptogenic zone, i.e., the zone from where the seizures originate, in a selection of patients that can receive a surgical treatment. Epilepsy surgery is a well established therapeutic option in nonmedical tractable cases and show a seizure-free rate in more than 80% of patients and an increase in the Quality of Life. Only in the last years, the research focused also on the neuropsychological outcome of patients with TLE after surgery.

Purpose: (1) To retrospectively analyze the surgical outcome of a population of children with drug resistant TLE surgically treated and to identify factors that predict the outcome). (2) To observe the neuropsychological profile before and after surgery.

Method: With the collaboration of the Epilepsie-Zentrum Berlin-Brandenburg and the Paediatric Department of Padova, we identified 29 patients with TLE surgically treated from 2 to 18 years old. Successively clinical, surgical and neuropsychological data were retrospectively collected. We examined the following variables, in relation with the Engel classification for the outcome: lateralization of the epileptogenic zone, age at seizure onset, frequency of seizure, duration of epilepsy, clinical semiology, interictal EEG scalp, MRI findings, choose of invasive monitoring, extension of surgical resection, histology. We also considered these cognitive functions before and after surgery: intellectual functioning, language, verbal and nonverbal memory, attention, praxies.

Results: Our population showed an excellent outcome: 12 months after surgery, the seizure-free rate (Engel class 1A) was 88.5%, 24 months after surgery was 87.5% and 36 months after surgery was 95% (Engel class 1A+1C). The majority of our patients (59%) was treated with an anterior temporal lobectomy (ATL) associated with a partial resection of the mesial temporal structures. Histological findings showed tumoral lesions, malformative-dysplastic lesions and mesial temporal sclerosis in respectively 34%, 24% and 14% of patients; in 24% of patients was observed a 'dual pathology' that is an association between two of these three histological findings. We didn't find a significative difference in the distribution of patients in the Engel outcome-classes in relation with the clinical variables (lateralization of epileptogenic zone, age at seizure onset, epilepsy duration, frequency and semiology, interictal EEG, MRI and histological findings). It is interesting to note that patients that received an invasive diagnostic exploration showed a statistically worse outcome (p=0,041) than patients that didn't receive an invasive exploration. The presurgically neuropsychological profile is placed at the mean of the general population for the investigated functions; at 6 months after surgery we observed a worse trend for these functions, following at 12 and 24 months to an increased profile, particularly in the verbal memory that demonstrate a statistical improvement at 24 months (p=0,050). The study of single cases helped us to confirm this trend: we observed not only a nonnegative effect of the surgery but also an improvement of the neuropsychologic performance.

Discussion and Conclusion: This study confirmed that surgical treatment in pediatric patients with medically resistant TLE had a high success rate. Moreover, despite the high clinical variability, we found no prognostic factors for the outcome. This is due to an elevated proportion of seizure freedom, guaranteed by a correct methodology of presurgical investigation trough anatomical and electroclinical correlation and individualisation of the operable patients. This consideration is confirmed by the uselessness (and even negative effect, according to our results) of invasive investigation, that must be used only when noninvasive investigations fail to localize the epileptic zone. The long-term profile in verbal memory suggest that early epilepsy surgery can be the next step to guarantee a better general improvement also in the cognitive functions of children. This preliminary data must be integrated with a prospective study of a wider sample of children with TLE designated to the surgical treatment and observed with an homogeneous set of neuropsychological tests.

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E733
INVESTIGATION OF COGNITIVE FUNCTION IN EPILEPSY AND THE INDEPENDENT RISK FACTORS IN CHINA

Y. Zhao, C. Ding†, J. Li*, and H. Wu†*
**The Affiliated Hospital of Medical College of Chinese People Armed Police Forces, China; and †Tiantan Hospital, Attached to Shoudou Medical University, China*

Purpose: To observe the cognitive function of patients with epilepsy and to explore the factors that affects it.

Method: The cognitive function of 125 patients with epilepsy, who met the criteria of the study, were assessed with the Wechsler Children and Adult Intelligence Scale. Retrospect analysis was used for factors of the cognitive function of patients, such as age, epileptic seizure types, epilepsy syndromes, etiologies, seizure frequency, severity of seizure, EEG, taking AED and kindred history etc.

Results: Children and adult epileptic patients had lower Final Intelligence Quotient (FIQ), Performance Intelligence quotient (PIQ), Vocal Intelligence Quotient (VIQ), Verbal comprehension factor (VCF), Perceptual organization factor (POF) and Memory Factor (MF) than the healthy controls, with significant difference ($P<0.05$). Multiple linear regression analysis for the three loads of IQ revealed that VCF, POF and MF affect IQ of epilepsy patients. Many factors were the risk factors of affecting cognitive function of epilepsy patients including age, course of diseases, seizure type, frequency, severity of seizure, discharge of EEG at interval, the number of taking AED.

Conclusion: There were obvious cognitive dysfunction in patients with epilepsy. The number of taking AED, severity seizure and epileptic seizure type was the independent factors for affecting the cognitive function.

E734
KNOWLEDGE, ATTITUDES AND PERCEPTIONS OF EPILEPSY AMONG SECONDARY SCHOOL-TEACHERS IN NIGERIA: A COMMUNITY-BASED STUDY

A. Mustapha
CHS Ladoke Akintola University of Technology, Nigeria

Purpose: The attitudes towards people with epilepsy are influenced by the degree of knowledge of the condition. The social problems encountered by schoolchildren with epilepsy as a result of negative attitudes and beliefs are enormous. The study therefore looked at the knowledge, attitudes and perceptions of teachers, who see a lot of epileptics, relate to them on a daily basis and have influence on them.

Method: A cross-sectional survey, using a self-administered questionnaire obtained from the author of a similar study in the United States was carried out among 269 school teachers randomly selected from various secondary schools in Osogbo, the Osun state capital in South-West Nigeria. The questionnaire included the scale of attitudes towards persons with epilepsy (ATPE), a summated rating scale that measures both attitude towards persons with epilepsy and knowledge about epilepsy as well as demographic and teaching experience survey among others.

Results: Despite the high level of education of the teachers ranging from Masters Degree to National Certificate in Education, there were significant deficits in terms of general knowledge about epilepsy (70% of the respondents reported their general knowledge about epilepsy in the lower half of the scale) as well as the first aids measures in the classrooms. Some of them felt it was contagious and sufferers should not be kept in regular classes. However, their attitudes towards epilepsy were generally positive.

Conclusion: We conclude that teachers need to have health education courses on common disease conditions such as epilepsy that are prevalent

in school age; this might help to reduce the prejudice and increase the acceptance of epileptic individuals in the classrooms. Also generally public health campaigns should be encouraged in this field.

E735
RAVLT AS AN INSTRUMENT IN DIFFERENTIAL DIAGNOSIS BETWEEN TLE AND MCI

F. Andelman, Y. Zeidman†, A. Schweiger†, V. Vachapov*, R. Verhovsky*, I. Halperin*, M. Neufeld*, I. Fried*, and A. Korczyn**

**Sourasky Medical Center, Israel; and †Tel-Aviv College, Israel*

Purpose: Previous work suggests that memory is not a unitary construct and the nature of memory impairment may vary in neurological diseases as a function of different etiologies and brain regions involved (Dickerson et al, 2004). The objective of this study was to characterize the nature of recall and recognition memory errors in patients with temporal lobe epilepsy (TLE) versus minimal cognitive impairment (MCI).

Method: 97 TLE surgical candidates and 33 MCI patients whose MMSE scores were between 25 and 27 participated in the study. Measures of learning, recall and false alarm (FA) rate of recognition memory of the Rey Auditory Verbal Learning Test (RAVLT) were used to analyze memory performance in these two populations.

Results: MCI patients demonstrated significantly more FA errors than TLE patients ($p=0.02$). By contrast, TLE patients showed a significantly worse performance compared to the MCI patients on the learning and active recall measures ($p<0.001$) of RAVLT. In addition, a significant correlation between the number of FA errors and the degree of impairment on MMSE was found in the MCI ($p=0.04$). No significant relationship was found between the FA mistakes and measures of general cognitive function in the TLE group.

Conclusion: The findings of this study suggest that performance on learning and recall, but not on the recognition memory measures is reflective of hippocampal function often compromised in TLE. On the other hand, a high FA rate demonstrated by the patients with MCI may reflect sensitivity to interference associated with more diffuse temporal lobe dysfunction.

E736
MARITAL PROSPECTS OF PEOPLE WITH EPILEPSY IN KOREA

M. Kim, Y. Kim†, O. Kwon‡, Y. Cho§, S. Kim¶, S. Lee**, H. Kim††, K. Jung‡‡, and I. Lee§§*

**Chonnam National University Medical School, Korea; †Wonkwang University School of Medicine, Korea; ‡Gyeongsang National University School of Medicine, Korea; §Keimyung University School of Medicine, Korea; ¶Inje University College of Medicine, Korea; **Seoul National University College of Medicine, Korea; ††Chosun University College of Medicine, Korea; ‡‡Korea University College of Medicine, Korea; and §§Seoul Brain Neurology Clinic, Korea*

Purpose: To get basic data on marital status and to clarify the clinical factors affecting marital status of Korean people with epilepsy (PWE).

Method: A multicenter questionnaire survey was performed with a total of 583 patients at 9 epilepsy centers in Korea.

Results: The marriage rate among Korean PWE was about 80% of expected in general population and male gender was associated with low marriage rates. More than 30% of patients who were single at the time of the Korean survey replied that they were unmarried because of epilepsy. However, it seemed that seizure factors (seizure type or severity) did not influence the marital status of PWE. Occupational status of men with epilepsy also influenced their marital status. Patients with earlier onset of epilepsy were less likely to be married than those with later onset of epilepsy. In relation to spouses' awareness of the disease, only 34.6% of PWE had informed their spouses of the disease before marriage. The overall divorce rate in general population aged more than 20 years in Korea was 0.7% as compared with 6.3% of PWE in our survey.

Conclusion: Poor marital prospect and high divorce rate of PWE in Korea reflect the effects of social stigma and many other adverse factors that the PWE have to face. There should be greater attention of this important aspect of life of PWE from the professional and lay epilepsy societies.

E737
STATUS OF ATYPICAL ANTIPSYCHOTIC USE FOR EPILEPTIC PSYCHOSIS IN THE EPILEPSY WARD OF OUR HOSPITAL

K. Hino, S. Tanaka*, M. Miyajima*, K. Sakamoto*, K. Hara*, S. Takahashi†, M. Kato‡, T. Onuma‡, Y. Watanabe*, and M. Watanabe**

**National Centre of Neurology And Psychiatry, Tokyo, Japan; †Tukuba University Hospital, Tokyo, Japan; and ‡Musashino-Kokubunji Clinic, Tokyo, Japan*

Purpose: Although psychotic symptoms are known to be associated with epilepsy, treatments for these symptoms are not yet adequately reported. We investigated the efficacy and adverse reactions of atypical antipsychotics used for the treatment of psychotic symptoms accompanying epilepsy in the Epilepsy Ward of the National Center of Neurology and Psychiatry in Japan.

Method: Patients hospitalized between April 1, 2006 and July 31, 2007 were investigated. Among them, 24 patients who were hospitalized for the treatment of psychotic symptoms during the interictal phase were studied. A retrospective review of the clinical charts was performed. Diagnosis of psychotic symptoms was based on ICD-10.

Results: Symptoms: Diagnosis of psychotic symptoms and epilepsy. Drugs chosen for psychotic symptoms and their efficacy Efficacy of each drug: RIS was effective in 9 patients and ineffective in 3 patients, OLZ was effective in all 14 patients, QTP was effective in all 5 patients, and ARP was effective in both patients. Mean dose of each drug at discharge: Adverse reactions of each drug: Parkinson symptoms was observed for RIS, seizure exacerbation was for OLZ, none for QTP, and none for ARP.

Conclusion: (1) While OLZ and RIS were effective to a certain extent, two patients treated with OLZ showed exacerbation of epileptic seizures, and one patient treated with RIS developed extrapyramidal symptoms. (2) The efficacy of QTP and ARP is difficult to judge due to small numbers of patients.

E738
REFERRAL PATTERNS OF EPILEPTIC PATIENTS TO THE EPILEPSY CENTER IN ILSAN AREA

J. Lee, and G. Kim

National Health Insurance Corporation Ilsan Hospital, Goyang, Korea

Purpose: We investigated the referral patterns of epileptic patients in National Health Insurance Corporation Ilsan Hospital Clinic and their social variables, in order to formulate the optimal role of tertiary epilepsy program.

Method: From July 2002 to July 2006, 271 patients were serially registered to National Health Insurance Corporation Ilsan Hospital Epilepsy Clinic for the first time in their lives. The contents of epilepsy registry were reviewed and analyzed.

Results: (1) Referral route: self referral through mass media was 39.2% and physician referral was 60.8% (primary physician 32.7%, psychiatrist 13.4%, neurologist 10.6%, rose club 4.1%) (2) Majority of the patients (88.2%) was seeking for the better management of long-standing epilepsy, whereas 11.8% was for initial diagnostic issue. (3) Duration of illness before the referral was less than 1 year 8.2%, 1 to 5 years 28.7%, 5 to 10 years 20.4%, 10 to 20 years 30.2%, over 20 years 12.5% (4) Age at the registration was below 10 7.7%, 10 to 20 26.6%, 20 to 30 38%, 30 to 40 19.7% over 40 8.2% (5) Tentative variables such as seizure type, frequency, education, rural vs urban living and job occupancy were not correlated with referral patterns.

Conclusion: At the present time, a tertiary epilepsy center confronts a variety of heterogenous patient population, with wide clinical spectrums, which renders the formulation of specific task very difficult.

E739
SOCIAL COGNITION IN PATIENTS WITH LOCALIZATION RELATED EPILEPSY AND WITH EPILEPSY ONLY

B. Brunner, F. Arter, R. Winkler, R. Henzen, and H. Jokeit
Swiss Epilepsy Center, Zurich, Switzerland

Purpose: There is an ongoing controversy as to whether the difficulties people with epilepsy have in social adaptation are due to underlying lesions, seizures or the social burdens of the disease. We investigated whether the localization of epilepsy influences the ability to solve an advanced theory of mind task (recognition of faux-pas test).

Method: 168 subjects (age: 34.5 (SD=12.2), IQ: 105.7 (SD=16.8), female/male: 81/87) performed a faux-pas test: left-sided frontal lobe epilepsy (FLEl=6), right-sided FLE (FLEr=7), left-sided mesiotemporal lobe epilepsy (mTLEl=29), right-sided mTLE (mTLEr=22), left-sided epilepsy extramesiotemporal/frontal (xTFLEl=6), right-sided epilepsy extramesiotemporal/frontal (xTFLEr=6), patients with epilepsy only (EO=42), and healthy controls (CONTROL=50). Patients with an IQ<75 or with a systemic disease were excluded.

Results: The prevalence of those considered to show impaired ability (cut-off<6) was as follows: CONTROLs 8%, FLEl 50%, FLEr 29%, mTLEl 24%, mTLEr 36%, xFTLEl 33%, xFTLEr 0%, and EO 19%. When controlling for IQ, comparison of mean performance revealed that patients with FLEl and mTLE performed worse on average than CONTROLs ($p<.05$). Patients with FLEr, EO, and xTFLE were not significantly impaired.

Conclusion: Patients with left frontal and left and right temporal lobe epilepsies find it more difficult to recognize a faux-pas in a higher-order theory of mind task than other patients with epilepsy. Therefore, we assume that frontal and mesial temporal lobe lesions may interfere with social cognition in patients wirth epilepsy. The high prevalence and the specifity of these deficits highlight the need and the usefulness of neuropsychological diagnostics of social cognition in epileptology.

E740
PSYCHOPATHOLOGICAL SYMPTOMS AND PERSONALITY IN CHILDREN WITH CHRONIC SYMPTOMATIC TLE AND FLE – A PROSPECTIVE PILOT STUDY

B. Plattner, N. Planer, T. Czech, and M. Feucht
Medical University Vienna, Universitätsklinik Für Psychiatrie Des Kindes Und Jugendalters, Austria

Purpose: Behavioral/emotional dysfunction and psychopathology are frequently observed in children with epilepsy. For symptomatic epilepsies, neurosurgical interventions have been attributed a role in psychiatric outcome. Aim of this prospective study was to investigate personality and psychopathological symptoms in children with temporal lobe epilepsy (TLE) and frontal lobe epilepsy (FLE) before (pre) and after surgical intervention (post).

Method: The WAI was used to assess personality and the YSR was used to assess psychopathological symptoms in children treated for TLE and FLE at the MUW pediatric-epilepsy-centre.

Results: Out of 19 FLE (5 postoperative) patients, nine (4 postoperative) completed all surveys. Out of the 34 TLE (11 postoperative) patients, 19 (13 postoperative) complete all surveys. 33.3% of the pre-TLE and 38.5% of the postoperative TLE patients exhibited internalizing symptoms. 50% of the pre-TLE and 7.7% of the postoperative TLE patients showed externalizing symptoms. The mean attention deficit score in the pre-TLE group was significantly higher than in the postoperative TLE patients. We did not find a personality typology descriptive of TLE. We did not find psychopathological symptoms in the pre-FLE or postoperative FLE group. Interestingly we found that personality typologies characterized by low emotional reactivity to be descriptive for FLE patients (both pre- and postoperatively). We found significant positive correlations between suppression of aggression and consideration of others and time span post surgery in the postoperative FLE group.

Conclusion: Our results indicate that children with chronic symptomatic TLE and FLE exhibit different forms of psychiatric abnormalities. TLE seems to be associated with psychopathological symptoms. After epilepsy surgery, attention deficit seems to decrease, whereas internalizing symptoms seem to persist. FLE seems to impact personality, in that FLE patients present with a personality typology characterized by emotional numbing. Due to our results, epilepsy surgery might have a positive impact on personality development in FLE.

E741
ALCOHOL CONSUMPTION AND DEPENDENCY INCREASE THE RISK FOR DEVELOPING EPILEPSY

D. Hesdorffer, C. Mills‡, W. Hauser*, E. Olafsson†, P. Ludvigsson†, and O. Kjartansson†*
**Columbia University, New York, NY, USA; †Landspitalinn University Hospital, USA; and ‡New York City Department of Health and Human Hygiene, New York, NY, USA*

Background: Alcohol consumption and dependency are associated with prevalent epilepsy, possibly due to a decreased seizure threshold linked to toxic or chronic effects of consumption. No study has quantified the increased risk for developing epilepsy associated with alcohol consumption and dependency. We evaluated whether (1) cumulative alcohol consumption and (2) alcohol dependence were associated with an increased risk for first unprovoked idiopathic/cryptogenic seizure and incident epilepsy.

Method: In this Icelandic population-based case-control study of adults aged 16 years and older, cases (n = 167) with first unprovoked seizure or first diagnosis of epilepsy of unknown etiology and controls (n = 334) were selected from the population registry and matched 2:1 to cases by age and sex. A standardized interview collected information on alcohol consumption by decade and an Icelandic translation of the SCID was used to ascertain alcohol dependence according to DSM-IIIR criteria. Conditional logistic regression was used to evaluate associations.

Results: Compared with middle-level amounts of cumulative alcohol consumption, low consumption was associated with an increased risk for unprovoked seizure [odds ratio (OR)=1.5; 95% CI= 0.9–2.5]; high consumption was associated with a 1.9-fold increased risk (95% CI= 1.1–3.1). Former drinkers had a 3-fold increased risk for unprovoked seizure compared to never drinkers (95% CI= 1.3–7.3). Alcohol dependency was associated with a 2.2-fold increased risk for unprovoked seizure (95% CI= 1.1–4.6).

Conclusion: High cumulative alcohol consumption and alcohol dependence increase risk for developing unprovoked seizures of unknown etiology. Future work should focus upon potential mechanisms that may explain these associations.

E742
MEDICAL INTRACTABLE EPILEPSY: ANALYSIS OF CLINICAL PROFILE AND OUTCOME OF NONSURGICAL CANDIDATE

C. Lui, N. Cheung†, K. Man†, F. Cheung†, J. Chan†, P. Li†, and S. Leung†*

**Tseung Kwan O Hospital, Hong Kong; and †Queen Elizabeth Hospital, Hong Kong*

Purpose: Patients with medical intractable epilepsy will undergo presurgical evaluation for possibility of curative surgical resection. However, only some of them will have concordant results for isolated epileptic foci that proved to have good surgical result: For those patients that were not feasible for surgical intervention, less is known about their clinical profile and outcome. In this study we analyses the clinical profile and the ultimate outcome of a cohort of nonsurgical candidates.

Method: Retrospective review of hospital and clinic records was carried out in Queen Elizabeth Hospital of Hong Kong from 1996 through 2005. Those patients with refractory epilepsy who underwent long -term EEG monitoring for presurgical evaluation but finally being rejected were collected. A self rating questionnaire were completed for all patients and the proportion of significant seizure reduction was also measured.

Results: 30 subjects were available for analysis at an average of > 4 years after surgical evaluation. None of them had complete seizure freedom and 15 (50%) of them had significant seizure reduction. 6 (20%) of them reported satisfaction of their lives at time of follow up. There was no clinical parameters or investigation results that represent predictors of good seizure control.

Summary: A significant portion of patients with medical intractable epilepsy, yet not feasible for surgical intervention, has reasonable good seizure control within the first decade after the presurgical evaluation. The quality of life was, however, not satisfactory.

E743
PEPE, THE PSYCHO-EDUCATIVE PROGRAM FOR PEOPLE WITH EPILEPSY AND MILD INTELLECTUAL DISABILITY, A DUTCH LANGUAGE VERSION

A. Haenen, and B. Huber†*

**Epilepsy Centre Kempenhaeghe, Heeze, The Netherlands and †Bethel Epilepsy Centre, Bielefeld, Germany*

Purpose: The Psycho-Educative Program for people with Epilepsy (PEPE) is an established German educational program for people with epilepsy and intellectual disabilities, designed to enhance their understanding of epilepsy and related issues. PEPE is a multimedia program 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 a Dutch version tailored to the needs of people with epilepsy and mild intellectual disability in the Netherlands.

Method: Written materials were translated and video footage remade for the Dutch version. Involvement of clients with mild intellectual disabilities in remaking the video clips was an important component of the process. The Dutch version was made in close co-operation with the German originators.

Results: We now have a Dutch version of the PEPE program, which is accommodated to the Dutch circumstances and views. In general we followed the original PEPE program in terms of content, but because of differences in cultural aspects, protection against risks is less emphasized in the Dutch version. We have designed a training program for Dutch facilitators to deliver the PEPE course this autumn. By the end of the year we expect to evaluate the first courses.

Conclusion: The German version of PEPE is an important source of support to the target group. We expect that the Dutch version will have a similarly significant impact in the The Netherlands, as there are no equivalent tools to educate and empower people with epilepsy and mild intellectual disability.

E744
A PROPOSED ALGORITHM TO DETERMINE FITNESS TO DRIVE IN PATIENTS WITH EPILEPSY

E. Somerville,†, R. Granot*, J. Dunne‡, A. Black§, M. Cook¶, R. Beran**, J. Archer††, and A. Harvey‡‡*

**Prince of Wales Hospital, Sydney, Australia; †Chairman, Driving Committee, Epilepsy Society of Australia and Australian and New Zealand Association of Neurologists, Australia; ‡Royal Perth Hospital, Perth, Australia; §Queen Elizabeth Hospital, Adelaide, Australia; ¶St Vincent's Hospital, Melbourne, Australia; **Liverpool Hospital, Sydney, Australia; ††Austin Hospital, Melbourne, Australia; and ‡‡Royal Children's Hospital, Melbourne, Australia*

Background: Certification of fitness to drive by the treating doctor may create a conflict of interest which can result in damage to the doctor-patient relationship, inappropriate certification decisions and legal vulnerability for the doctor. The Epilepsy Society of Australia and Australian and New Zealand Association of Neurologists believe that certification is the role of the driver licensing authority (DLA) rather than the treating doctor.

Purpose: In order to facilitate certification by DLAs, a decision tree has been developed to allow determination of fitness according to the Australian national standards, using information provided by the treating doctor.

Method: The standards contained in Assessing Fitness to Drive 2003 were converted to a list of questions. The answers are then processed in a logical sequence to form an algorithm, yielding outputs including: 'Fit to drive'; 'Unfit until [date] and requires recertification at that time'; and 'Requires formal review'. The algorithm was converted to a computer program. To reduce the risk of accidental determination that a driver is fit, based on inconsistent or incomplete information on the form, or incorrect data entry, several safeguards and consistency checks have been included.

Results: The approach was accepted by the Registration and Licensing Taskforce, representing all driver licensing jurisdictions in Australia.

Conclusion: The Australian standards can be applied by a nonmedically trained clerk, using information supplied by treating doctors. However, an expert neurological review mechanism is essential to decide cases where fitness to drive is unclear, including cases where qualifying information is supplied by the treating doctor.

E745
SEIZURES CONNECTED TO RELIGIOUS CONCEPTS: NOTIONS IN FEATURE FILMS

F. Schmitt

Holy Spirit Hospital, Cologne, Germany

Purpose: In the meantime the term 'sacred disease' has become a widespread expression for epilepsy, not only in the historical medical literature. The depiction of seizures in feature films can be viewed as an expression of publicly accepted notions about epilepsy.

Method: Movie databases and scientific publication were reviewed to obtain a list of 216 feature films, in which a scene with an epileptic seizure was depicted, the term 'seizure' or 'epilepsy' was mentioned in the film itself or the original literature source. Films were analyzed regarding implicit or explicit connection of the seizures to religious concepts.

Results: Altogether 11 films fulfilled the criteria (5,1%), Films were produced between 1958 to 2006 and countries of production were USA (n=3), Great Britain, Mexico, Germany and France (all n=2). Connection was made to a biblical narration (n=5); to the process of exorcism (n=3) or ascension (n=3).

Conclusion: Connecting the occurrence of seizures to religious concepts remains a publicly accepted notion and may still be a source for stigmatizing epilepsy patients.

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E746
TWO DIFFERENT PATTERNS IN CLINICAL COURSE OF POSTICTAL PSYCHIATRIC SYMPTOM

M. Okazaki, M. Ito*,†, N. Adachi*,‡, M. Kato*,§, M. Watanabe*, Y. Watanabe*, and T. Oonuma*,§*
**National Center of Neurology and Psychiatry, Musashi Hospital, Tokyo, Japan; †Tenshi Hospital, Tokyo, Japan; ‡Adachi Mental Clinic, Tokyo, Japan; and §Musashino-Kokubunji Clinic, Tokyo, Japan*

Purpose: To evaluate the symptomatology of the clinical course of postictal psychiatric symptom (PPS).

Method: 70 PPS episodes in 40 epilepsy patients (23 men and 17 women; mean ?} SD, 36.6 ?} 11.9 years; TLE, n=31; FLE, n=8; SGE, n=1) were identified and recruited as subjects for this study. The episodes which met the criteria of acute schizophrenia-like psychotic disorder (F23.2 in ICD-10) were diagnosed as postictal psychosis (PIP) (n=55) and the remaining episodes were diagnosed as non-PIP (n=15). Symptoms related to psychosis, mood change, anxiety and social dysfunction were assessed every 1–7 days and the duration of each symptom was evaluated.

Results: The symptoms of PPS were divided into two groups in based on their duration: short acting symptoms (hallucination, delusion, exaggeration, psychomotor excitement, etc; mean 1–14 days) and long acting symptoms (hypochondria, irritability, dysphoria, social disturbed behavior, etc; mean 13–150 days). 36 episodes (PIP, n=30; non-PIP, n=6) showed biphasic pattern of clinical course in which an acute phase mainly consisting of short acting symptoms (5.0 ?} 3.87 days) was followed by a recovery phase mainly consisting of long acting symptoms (31.5 ?} 29.5 days). During the recovery phase, the patients suffered from social dysfunction due to the symptoms. The remaining 34 episodes showed a monophasic pattern in which they returned to the baseline level of mental state immediately after resolution of the acute phase.

E747
FRONTAL LOBE BRAIN DYSFUNCTION, COGNITIVE AND EPLEPTIC PERSONALITY DISORDERS IN DEVELOPMENT OF EPILEPTIC PSYCHOSES

S. Nosov
Dniepropetrovsk State Medical Academy, Ukraine

Purpose: The research is devoted to the peculiarities of epileptic psychoses development depending on frontal lobe brain dysfunction degree of manifestation (FLBD), cognitive disorders (CD) and epileptic personality disorders (EPD).

Method: 230 patients, aged 19–50 years, with acute, prolonged and chronic alternative (AP) (60 patients) and nonalternative (NAP) (170 patients) epileptic psychoses were researched). The clinical-psychopathological, catamnestic, psychometric (PI, FAB, MMSE scales) methods and statistics were used.

Results: FLBD (points): AP (acute – 2.29±0.22, prolonged – 2.17±0.31, chronic – 2.06±0.18); NAP (acute – 1.24±0.08, prolonged – 1.24±0.08, chronic – 0.99±0.08). CD (points): AP (acute – 27.1±0.9, prolonged – 26.7±1.3, chronic – 26.0±1.4); NAP (acute – 23.9±1.2, prolonged – 23.6±1.3, chronic – 18.2±1.5). EPD. AP: by grows of psychosis activities the EPD manifestation is increased and predominance of schizoepileptic or explosive type over dysthymoepileptic. NAP: by grows of psychosis duration the EPD manifestation is increased, the predominance of schizoepileptic, explosive type and dementia.

Conclusion: The FLBD increase results in psychosis course prolongation, typical AP replacement by atypical ones with incomplete seizures termination and partial ''forced normalization of EEG'' development, the increase of probability of spontaneous NAP progress of growing duration and AP origin termination. CD increase under intensification of pathogenetic connection of epileptic psychoses with durable chronic and epileptic brain dysfunction from AP to NAP. The increase of epileptic psychosis duration, rising incompleteness of alternation and NAP formation combine with increasing EPD marked, mostly presented in explosive, schizoepileptic variants in comparison with hysteroepileptic and dysthymoepileptic. FLBD initialize the epileptic psychoses development, CD and appointed EPD variant identify its clinical structure.

E748
CHILDREN WITH ADHD AND EPILEPTIFORM ABNORMALITIES: TREATMENT OPTIONS AND SEIZURE RISK

D. Socanski, A. Herigstad†, and D. Aarsland‡*
**Stavanger University Hospital HF, Division of Psychiatry, Department of Child and Adolescents Psychiatry, Stavanger, Norway; †Stavanger University Hospital HF, Division of Psychiatry, Norway; and ‡Stavanger University Hospital HF, Department of Clinical Neurophysiology, Stavanger, Norway*

Purpose: To investigate treatment options and seizure risk in ADHD children with epileptiform abnormalities (EAs) when diagnosed, and at 3 years follow-up.

Method: 41 children (71% males) aged between 5–14 years, mean 9.6+2.7, with ADHD and EAs were studied. At least two EEGs were performed on all patients. Treatment choices and epileptic seizure occurrence at inclusion and at follow-up 3 years later were analyzed.

Results: 14 children (79%males) had epilepsy comorbidity. Active epilepsy was diagnosed in 11 patients. 8 had idiopathic and 3 symptomatic epilepsies. 27 children (66%males) showed only EAs on EEGs. AEDs were used in 22 patients, 11 patients with epilepsy comorbidity and 11 patients with only EAs. During the observation period 36 patients (88%) were treated with methylphenidate (MPH) as a first-choice drug. In addition 3 patients were treated with dextroamphetamine and 3 with atomoxetine. ADHD symptoms for 4 children with EAs only improved slightly with AEDs. Of these, 2 children showed significant improvement of ADHD symptoms when MPH was added. No seizure exacerbation was observed in 14 patient with epilepsy. None of the 27 children with only EAs developed epileptic seizure. At follow-up 3 years later, pharmacological treatment was changed in the majority of patients. 12 children (7 patients with epilepsy) still used AEDs, 22 patients used MPH, and 2 used atomoxetine.

Conclusion: AEDs are often used in children with ADHD and EA, and can improve ADHD symptoms in some cases. Medical treatment of ADHD with MPH is safe and not associated with an increased seizure risk.

E749
INTERMITTENT EXPLOSIVE DISORDER: EPILEPTIC PATHOGENESIS?

D. Ulbricht, and M. Gleis
Centre Hospitalier Emile Mayrisch, Luxemburg

Introduction: Intermittent explosive disorder (IED, episodic dyscontrol) is characterized by episodes of failure to resist aggressive impulses that result in serious destructive acts, out of proportion to precipitating stressors, not better explained by another mental conditions.

Case report: An 18-year-old man brought up in a home came to our attention for chronic aggressive behabior due to a difficult familiar setting. He had aggressive outbursts easily explained by situative contexts, but others without evident reasons, observed by himself or others, too. Neuroleptic treatment failed to significantly reduce the spontaneous out bursts, while hospitalization reduced environmental triggered ones. Neurological and physical history were uneventful. Neurological exam showed soft signs suggestive of cerebral disintegration and intermittent facial cloni without any semiological resemblence to epileptic myocloni. Clinically, there were signs of emotional and cognitive dysexecutive syndrome. Technical workup included normal routine MRI, EEG with left frontal psychomotor variant. Holter-EEG failed to documentate an outburst of aggression, but displayed left frontal thetas of high voltage for up to 12 seconds. SPECT disclosed interictal left frontal and frontomesial relative hyperperfusion. A therapeutic trial of Carbamazepine (CBZ) led to marked improvement of the spontaneous attacks, but the patients mental state remained otherwise unchanged.

Discussion: The clinical picture seemed at first glance compatible with maladaptive behavior but extended to IED. The signs of dysexecutive syndrome and lateralized frontal brain dysfunction indicates epileptic genesis of spontaneous aggressive outbursts, and responded well to CBZ treatment. Whether this represents frontomesial or frontoorbital seizures or subclinical seizures facilitating IED remains unclear.

E750
NEUROPSYCHOLOGICAL COURSES IN PATIENTS WITH POSTENCEPHALITIC EPILEPSY

K. Hara,†,‡, R. Muramatsu*, S. Tanaka*, S. Watanabe*, Y. Watanabe*, A. Maki*, M. Kato*, Y. Nagafusa*, K. Sakamoto*, K. Hino*, M. Hara†, M. Matsuura‡, and M. Watanabe**
**National Center of Neurology and Psychiatry, Tokyo, Japan; †Hara Clinic, Tokyo, Japan; and ‡Tokyo Medical and Dental University, Tokyo, Japan*

Purpose: In addition to seizures, patients with postencephalitic epilepsy often have difficulties due to degradation of higher brain functions. We examined the course of changes in neuropsychological performance to obtain a better understanding of the factors for their outcomes.

Method: Adults with postencephalitic epilepsy were recruited from the Epilepsy Ward in the Department of Psychiatry at the National Center of Neurology and Psychiatry, Japan, between April 2006 and February 2008. Individuals were admitted to the hospital due to seizure, psychosis, difficult behavior or related problems. Data were examined longitudinally for individuals who were tested at least twice on a series of neuropsychological tests including subtests of the Wechsler Adult Intelligence Scale (WAIS, WAIS-R, WAIS-‡V).

Results: Five of a total of 14 patients with postencephalitic epilepsy met the criteria for this study. Patients were diagnosed with encephalitis between the ages of 26 and 49 years, and had a high school or higher education. On admission, they were 31 to 50 year-old and had daily, weekly or monthly seizures. Of the five patients, different patterns of results were observed. One patient showed progressive neuropsychological decline across four years. One patient remained stable across four years. The three remaining patients showed improvement in two months, three months, and eight years. Neuropsychological improvement was associated with seizure control, reduction in side effects of antiepileptic or antipsychotic drugs, emotional stability, environmental coordination, and occupational therapy.

Conclusion: Patients with postencephalitic epilepsy show a range of neuropsychological progression which may be benefited by comprehensive therapy.

E751
EPILEPTIC PAROXYSMAL SYMPTOMATOLOGY IN PATIENTS WITH ORGANIC DEPRESSED DISORDER IN DISTANT PERIOD OF CRANIOCEREBRAL TRAUMA (CCT)

V. Sergeev, O. Golubchikova, and P. Sergeeva
Ural State Academy of Post Diploma Medical Education, Russia

Purpose: The study of comorbidity depressed disorders, manifested at the period of delayed consequences of CCT and epileptic paroxysmal symptomatology.

Method: The two groups of inpatients comprising 53 men and 37 women with moderate and serious depression were examined by EEG and clinical examination. The main group consisted of 45 patients with organic depressed disorder in distant period of CCT. The control group was formed by 45 patients with endogenous depression.

Results: In 18 patients (40%) of main group were revealed epileptic paroxysms in anamnesis. The simple focal (motor, somatosensor, vegetovisceral, psychosensor, affective), complex paroxysms and their combination were found out more often, than generalized seizures. Epileptic paroxysms were registered more often among patients with more serious CCT – 53%, concussions and contusions of brain led to paroxysmal symptomatology more seldom – 31% ($p<0,05$). Only 2 patients (4,4%) of control group had isolated vegetative paroxysms ($p<0,001$). In 44 patients (98%) of the main group and in 19 ones (42%) of control group were revealed diffused and focal neurological symptomatology ($p<0,001$). EEG disturbances were registered in 100% patients of main group and in 39% patients of control group ($p<0,001$); paroxysms – in 24% and 7% cases correspondingly ($p<0,05$). In most cases paroxysmal symptomatology was fixed during this investigation for the first time, while it manifested long before that. The prescription of antiepileptic drugs (AEDs) to these patients assisted in reduction of paroxysms and in prevention of recurrences of depressed disorders.

Conclusion: Organic depressed disorder, manifested at the period of delayed consequences of CCT, revealed high comorbidity to epileptic paroxysmal symptomatology, which was the more expressed, the more serious CCT was. Information about the presence of paroxysms in anamnesis, analysis of neurological and EEG examination provides the reliability of diagnostic conclusions and correctness of the therapy, including AEDs.

E752
RISK FACTORS OF SELF-AGGRESSIVE BEHAVIOR IN EPILEPSY PATIENTS

Y. Shcheglova
Ukrainian Scientific Research Institute of Social, Forensic Psychiatry And Narcology, Ukraine

Purpose: To discover risk factors of self-aggressive behavior (suicidal ideations, threats, attempts) in epilepsy patients.

Method: Two patient groups – 150 adult epilepsy patients with history of self-aggressive behavior (basic group) and 80 adult epilepsy patients who never had self-aggression were assessed with clinical interview, Hamilton depression rating scale (HDRS), Hamilton anxiety rating scale (HARS), Buss-Durkey Inventory. Methods of statistical analysis were Fisher's test, Pearson's chi-square test and Kendall's correlation coefficient τ.

Results: Three groups of risk factors (clinical, personality-related and social) were revealed. Clinical predictors of self-aggressive behavior are: malignant course of disease, partial epilepsy, cognitive impairment, dysphoric disorders, moderate or severe depression and anxiety, acute or chronic psychoses, twilight states of consciousness, alcohol or drug abuse, treatment with two or more antiepileptic drugs, poor compliance. Group of personality-related factors includes impulsive and dependent personality traits as well as high level of aggressiveness and hostility. Group of social risk factors consists of erroneous upbringing in childhood, loneliness, poor work adaptation and stigmatization.

Conclusion: Risk factors of self-aggressive behavior in epilepsy patients should be considered in creation of treatment and prophylactic programs for epileptic patients, especially in psychiatric units. Some of these factors can be removed with correct treatment and monitoring, social and psychological assistance.

E753
SEIZURE-ASSOCIATED INTRACRANIAL CYSTIC LESIONS

O. Jimenez-Vazquez, and N. Nagore
Universidad Michoacana de San Nicolas de Hidalgo, Morelia, Michoacan, Mexico

Purpose: To present a series of cases with different types of seizure-associated intracranial cystic lesions, where precise diagnosis and early treatment is stressed.

Method: Patients with various types of intracranial cystic lesions associated with different forms of seizures were subject to early diagnosis, which included clinical evaluation and image studies with computed tomography (CT) and/or magnetic resonance (MR). According to each of the patient's results, different treatment options were selected and promptly executed.

Results: The patients included in the series are the following: Patient 1, a 70 year-old woman with generalized tonic–clonic seizures since infancy, had a right frontoparietal arachnoid cyst located in the brain convexity. After surgical drainage and standard a dose of lamotrigine, the patient has remained seizure-free. Patient 2, a 34-year-old man who suffered from generalized tonic–clonic seizures due to multiple intraparenchymal cysticerci, had seizure control after 600mg/day of carbamacepine and removal of the parasites. Patient 3 is a 20-year-old woman who presented temporal lobe-type seizures refractory to carbamacepine and levetiracetam. An MRI disclosed a cystic glioma which was resected, resulting in complete control of the seizures. Patient 4 is a 24-year-old woman with left facio-braquial motor seizures due to multiple frontal cysts. At surgery, several Virchow-Robin cysts were observed and drained. Subsequent antiepileptic treatment with carbamacepine has resulted in satisfactorily control of the seizures.

Conclusion: Precise diagnosis and prompt treatment with antiepileptic drugs and surgical interventions may yield successful results upon seizure control in patients with various types of intracranial cysts.

E754
EFFECT OF TEMPORAL LOBE SURGERY ON CARDIOVASCULAR AUTONOMIC RESPONSES IN EPILEPTIC PATIENTS

M. Tripathi, S. Chandra, K. Vani, S. Mukherjee, and K. Deepak
All India Institute of Medical Sciences, India

Purpose: Earlier surgical treatment of intractable Temporal lobe epilepsy has shown to modulate autonomic tone and BRS. It is not known whether such surgery influences autonomic reactivity or not.

Aim: The aim of the present study was to find out the effect of temporal lobe epileptic surgery on cardiovascular autonomic function.

Method: 15 patients (19 male and 6 female) of mean age (22.11±10.18) with intractable epilepsy over a year or more and selected for the surgery. Autonomic reactivity was assessed by a battery of tests and autonomic tone was assessed by a standard monitoring of ECG for 5 minutes in supine position.

Results: A nonsignificant decrease in parasympathetic reactivity markers like VR {[1.9 (1.3–2.9) 1.75 (1.31- 2.24)], 30:15 ratio in HUT [1.1 (1–1.36), 1.09 (1–1.33)]} and a change in heart rate [24 (2–33), 23 (5–35)] during DBT decrease after surgery. Similarly a post surgical nonsignificant decrease in sympathetic marker like delta change in diastolic BP in HGT and CPT {[12 (6–22) 8 (-4–32)] and 16 (6–34) 12 (-2– 40)]} was observed. The parameters of time domain analysis like SENN, SDNN, RMSSD, NN50 and pNN50 also showed a nonsignificant decrease after surgery and also in frequency domain measure a nonsignificant decrease in LF with increase in postsurgical sympathovagal balance (LF/HF ratios) was observed in the study.

Conclusion: The present study showed a trend toward decrease in sympathetic and parasympathetic reactivity and decrease in autonomic tone after surgery. A well planned prospective study should be planned to document the affect of surgery.

E755
EFFECT OF VAGAL NERVE STIMULATION (VNS) ON CARDIOVASCULAR AUTONOMIC FUNCTIONS IN REFRACTORY EPILEPTIC PATIENTS

S. Chandra, N. Chaudhary, K. Deepak, V. Padma, and M. Tripathi
All India Institute of Medical Sciences, India

Purpose: VNS is an accepted treatment for patients with refractory epilepsy in whom surgical approach is contraindicated. The cardiovascular autonomic functions were evaluated in 3 patients with refractory epilepsy who underwent VNS.

Method: Autonomic function tests were done in a three patients one male and two female with refractory epilepsy having 5–6 complex partial seizures per month due to encephalitis in one and due to Lennox Gastaut syndrome in another. After implanting the VNS device, autonomic tone (HRV) and reactivity (using 5 standard tests) were assessed periodically for 9 months. Relevant clinical details were noted results. The seizure frequency decreased by 30–50% at the time of last recording (9 month). Series of vagal nerve stimulations was associated with gradual decline in mean SBP, Valsalva ratio (VR), E:I and 30:15 ratio and gradual increase in autonomic tone (Table).

Results: The mean Cardiovascular autonomic functions after vagal nerve stimulation (average in three patients showed a decrease in the systolic blood pressure. The Expiratory inspiratory ratio changed from 1.17 to 1.42. The valsalva ratio from 2 to 1.33. The SDNN changed from 17.19 to 35. The low frequency spectrum changed from 14.71 to 24.017. The high frequency from 23.81 to 179.01.

Conclusion: This study on three patients shows that VNS therapy reduces seizure frequency along with changes in autonomic drive to the heart. The results indicate that a large study should be planned to document autonomic changes, which may serve as guide to VNS.

E756
CLINICAL FEATURES, EEG, PATHOPHYSIOLOGY AND PROGNOSIS OF 18 PATIENTS WITH PANAYIOTOPOULOS SYNDROME

J. Liang
Children's Hospital, Chongqing Medical University, China

Objective: To characterize the clinical, EEG, pathophysiology and prognosis of Panayiotopoulos syndrome (PS).

Method: According to the criteria of PS made by ILAE (2001), eighteen patients with PS were prospectively followed up in the clinical manifestation, interictal and ictal EEG as well as treatment for 5 yrs.

Results: The initial onset of seizures occurred in 2.2 to 8.6yrs with an average of 4.5 yrs. Among them, 4 cases have family history of epilepsy, of which one had the idiopathic epilepsy, 3 have history of migraine, 5 have febrile seizures. PS have pronounced autonomic seizures (AS), including pallor, nausea, retching and ictal vomiting, abdominal discomfort et al; the next is eye and head deviation,and then the complex partial seizures (CPS) or secondary generalization (SG), and even status epilepticus (SE) with a partial impairment of consciousness; 5 had sporadic attacks with seizure-free intervals more than 6 m, 8 occurred one time within 1~5 m, another 5 have seizures every 1~5 m, two of whom had more than ten times daily. 8 had unilateral or bilateral occipital spikes, 4 had temporal spikes, rolandic spikes, and temporal-parietal-occipital spikes;2 had frontal and frontal-occipital spikes or spike-wave discharges (SWD); one had generalized SWD. Epileptic foci were unsteady,easily migating and movable or absent. Ictal EEG shown the occipital or frontal predominant or generalized rhythmic SED associated with AS or SG. Neuroimagine is normal. Prognosis: CBZ, VPA and TPM were comparatively more respond to PS. Seizures nearly disappeared in 9 cases, markedly compromised in 4, an worse in 2. Developments were normal in all children but mild learning and behavoural problems were found in 11.

Conclusion: PS is an epileptic syndrome characterized by AS, and age-specific occurrence with or not CPS & SG or SE. Epileptic foci were occipital predominance, but might be multifoci or migrating. Careful study of clinical features, EEG, pathophysiology and evolution of PS is mandatory to elucidate the mechanism of autonomic and systematic epilepsy.

E757
SURGICAL TREATMENT OF DRUG-RESISTANT EPILEPSY WITH FOCAL CORTICAL DYSPLASIA

D. Kim, S. Lee†, K. Chu†, and S. Park‡*
**Konkuk University Hospital, Korea; †Seoul National University Hospital, Korea; and ‡Seoul National University Bondang Hospital, Korea*

Purpose: Although surgical resection has been an important alternative treatment for patients with intractable epilepsy related to focal cortical dysplasia (FCD), the prognostic relevance of the degree of pathological severity is controversial and there has been only limited information regarding the prognostic factors involved in the surgical treatment of refractory epilepsy in patients with FCD.

Method: We undertook the present study to assess whether the pathological subtypes of FCD affect surgical outcomes in patients with drug-resistant epilepsy. We also studied the prognostic roles of clinical factors and various diagnostic modalities in the surgical treatment.

Results: A total of 206 consecutive patients were included. By univariate analysis, incomplete resection of epileptogenic zone ($p < 0.001$), mild pathological features ($p = 0.001$), hippocampal sclerosis (HS) on presurgical MRI ($p = 0.01$), and the presence of secondary tonic–clonic seizures (2GTCS) ($p = 0.05$) were associated with poor surgical outcomes. There was a strong tendency for patients with severe pathological features to have MRI abnormalities ($p = 0.002$). Incomplete resection of epileptogenic zone ($p < 0.001$), Mild pathological features ($P = 0.001$) and HS on presurgical MRI ($p = 0.01$) were poor independent outcome predictors on multivariate analysis. The results of MRI, scalp EEG, fluorodeoxyglucose–PET, and ictal SPECT were not associated with surgical outcomes.

Conclusion: Our study shows that there is a strong tendency for patients with severe pathological features to have MRI abnormalities, and patients with incomplete resection, mild pathological features, HS on presurgical MRI, or the presence of 2GTCS, have a high chance of a poor surgical outcome.

E758
RESECTIVE SURGERY FOR INTRACTABLE EPILEPSY IN CHILDREN. SURGICAL PROGNOSIS

T. Otsuki, T. Kaido, A. Takahashi, Y. Kaneko, E. Nakagawa, K. Sugai, and M. Sasaki
National Center of Neurology and Psychiatry, Tokyo, Japan

Purpose: Neuroimaging studies such as MRI, PET, SPECT and MEG play an essential role when indicating resective surgery for intractable epilepsy in children, especially for younger age group. We investigated surgical prognosis of resective surgery based on multimodal neuroimaging studies in children.

Method: Ninety-one consecutive cases of children from the age of 1 month to 15 years (av. 7.2 y) at the time of surgery with follow-up from 1 to 14 years (av. 5.3 y) were analyzed. After presurgical evaluation including multimodal neuroimaging studies, resective surgery was indicated to 73 children (23 temporal resection, 17 frontal, 10 parietal, 5 occipital, 1 cerebellar, 8 multilobar resection/disconnnection, 9 hemispherotomy) with 29 intracranial electrode placements.

Results: As a whole, Engel's class I outcome was obtained in 75%, II in 1%, III in 18%, and IV in 5%. Seizure outcomes of infants (n=15) and younger children (n=16) were not different from elder ones (n=42) although they often required more extensive cortical resection. Regarding to etilology, class I was obtained in 100% of hippocampal sclerosis (n=3), 95% of dysplastic tumor/angioma (n=19), 74% of cortical dysplasia (n=31), 63% of hemimegalencephaly (n=8), 63% of ulegyria (n=8), and 25% of gliosis (n=4). Callosotomy indicated to the remaining 18 children resulted in class I-II in 11%, and III-IV in 89%.

Conclusion: Favorable surgical prognosis can be obtained for children with intractable epilepsy even in early age of life if resective surgery is carefully indicated based on multimodal neuroimaging studies.

E759
CARDIAC VAGAL TONE CHANGES BEFORE EPILEPTIC AND DISASSOCIATIVE SEIZURES

R. Delamont, F. Kazi*, S. Hansen†, L. Goldstein‡, and J. Mellers§*
**Regional Neurosciences Centre, King's College Hospital NHS, UK; †Clinical Physics, South Glasgow University Hospitals Division, Glasgow, UK; ‡King's College London, Institute of Psychiatry, London UK; and §South London & Maudsley NHS Foundation Trust London UK*

Purpose: To examine whether there are differences in cardiac vagal tone (CVT) between resting and preseizure epochs in patients with partial epilepsy (ES) and disassociative seizures (DS).

Method: Twenty-five adults with video-EEG telemetry confirmed ES and 17 adults with DS had a 30 second ECG data epoch analyzed from a 20 minute resting supine period between 0900 & 1200 (baseline) and compared to a 30 second data epoch collected immediately prior to a clinical seizure. ECG data was used to determine CVT (Delamont et al. Epilepsy research 1998; 8:87–94.). One seizure per patient was studied. Nonparametric statistical test (Wilcoxon) was used.

Results: The two groups did not differ in age, gender distribution or baseline CVT. The ES group had a nonsignificant difference in the median CVT between baseline and preseizure epochs (p = 0.054) with 73% showing a fall in CVT in the preseizure epoch. The DS group had no significant difference in CVT between baseline and preseizure epochs (p = 0.156). Comparing only those patients awake at the onset of their seizures, the ES group (18 patients) showed a significant median CVT difference between baseline and preseizure epochs (p=0.006). The DS group was unchanged (p=0.156).

Conclusion: Cardiac vagal tone changes significantly in the 30 seconds before the onset, from the awake state, in epileptic but not dissociative origin seizures. Further studies to profile the autonomic changes seen in different types of seizures from different states of arousal may reveal the mechanisms for periictal symptoms and death.

E760
LONG-TERM OUTCOME OF RESECTIVE SURGERY, AT LEAST 5 YEARS AFTER THE OPERATION IN EPILEPSY CENTRE BRNO

R. Kuba, M. Brázdil, Z. Novák, M. Pazourková, H. Oslejsková, J. Chrastina, I. Tyrlíková, and I. Rektor
St. Anne's University Hospital and Faculty of Medicine, Masaryk University, Brno, Czech Republic

Purpose: The purpose of this study was to analyze the postoperative results of resective surgery in all patients at least 5 years after surgery.

Method: We included 101 patients with refractory epilepsy who had undergone surgery between 1995 and 2003. Seventy-four of the patients had temporal lobe epilepsy (TLE) and 27 patients had extratemporal epilepsy (exTLE). Of the TLE patients, 39 had mesial temporal sclerosis (TLE-MTS) and 35 had another pathology (TLE-OTH). We evaluated the outcome according to the Engel classification.

Results: In the whole group, 5 years after the surgery, 70.3% of patients were evaluated as Engel I, 22.3% as Engel II+III, and 7% as Engel IV. In the TLE patients, 74.3% were evaluated as Engel I, 21.6% as Engel II+III, and 4.1% as Engel IV. Similarly, in the exTLE patients, 59.3% were classified as Engel I, 25.9% as Engel II+III, and 14.8% as Engel IV. In the whole group, 52.5% of the patients experienced neither epileptic seizure nor epileptic aura during the entire five postoperative years; i.e., they were always classified as Engel IA. A complete withdrawal of antiepileptic drugs (AED) was reached in 29.7% of the patients, and a reduction of at least one AED was reached in 47.5%. A significant complication occurred in 5.9% of the patients.

Conclusion: Our study showed that the long-term outcomes of resective surgery in refractory epileptic patients at the Brno Epilepsy Centre are favorable and comparable to literature data.

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E761
CESSATION OF REFRACTORY CONVULSIVE STATUS EPILEPTICUS AFTER INITIATION OF VAGUS NERVE STIMULATION (VNS)

A. Soto, F. Duran*, F. Scovino*, L. Castro*, P. Marín*, J. Garcia*, and A. Rivera†*
**Hospital Domingo Luciani, Caracas, Venezuela; and †Hospital Domingo Guzman Lander, Barcelona, Venezuela*

Purpose: We report the cessation of refractory convulsive status epilepticus (SE) after initiation of vagus nerve stimulation (VNS) in a girl, aged 15 years.

Method: The patient was diagnosed with bacterial meningitis and received intravenous antibiotics at age 9 days, and 3 days later she began having seizures, which ceased with phenobarbital. Her first episode of SE occurred at age 11 months. She continued to have several simple partial motor (SPM) and secondarily generalized tonic–clonic (GTC) seizures daily. She had additional episodes of SE at the ages of 18 months and 3 years. At age 30 months, she was diagnosed with global developmental delay and right hemiparesis. She was treated with carbamazepine, oxcarbazepine, valproic acid, lamotrigine, topiramate, diazepam, clonazepan, and the ketogenic diet but did not attain seizure control and experienced several episodes of SE. She was implanted with VNS at age 15 years during an episode of refractory SE. Initial settings were output current (OC) 1.0 mA, frequency 30 Hz, pulse width 500μs, 30 sec 'on', 5 min 'off'.

Results: Refractory SE ceased after implantation, with 100% reduction of GTC and 70% reduction of SPM. One month later, she presented with breakthrough SPM and infection of the surgical wound, which was successfully treated with antibiotics. OC was increased to 1.50 mA, and no seizures have been reported for more than 4 months except for one brief SPM.

Conclusion: VNS may be a valid alternative for the treatment of refractory convulsive SE.

E762
ATTITUDE TOWARD EPILEPSY SURGERY: A SURVEY AMONG SWEDISH NEUROLOGISTS

E. Kumlien, and P. Mattsson
Uppsala University, Sweden

Purpose: The utilization of surgery procedures to treat epilepsy is low in relation to number of estimated candidates. Moreover, the number of resective surgeries has declined during the last 10-years in Sweden. This study was conducted to investigate attitudes towards epilepsy surgery and selection criteria for surgical intervention referral among Swedish neurologists.

Method: A questionnaire was sent out to neurologist treating epilepsy working in 69 hospitals and 14 private practices. The hospitals were identified through an official medical register and private neurologists via yellow pages in the phone book. Neurologists working in university hospitals with epilepsy surgery facilities were not included. Totally there are about 400 neurologists in Sweden, which has 9 million inhabitants.

Results: In total there was 100 responders, 92 from neurologists working in hospital and eight in private practice. Eighty-one (81%) had experience from own referrals. A majority considered surgery to be beneficial regarding reduction of seizure frequency (60%) and improvement of life quality (90%). Ninety-two percent regarded surgery as a cost-effective treatment. Fear of complications was expressed by 39%. The most important indications for candidate selection were seizure frequency and severity (95%), quality of life (91%), and patients own wish (93%). MRI and EEG-findings were important to 82% and 77% of the responders. Fifty-five percent considered lack of mental retardation to be a requirement for surgery.

Conclusion: In general there was a positive attitude towards epilepsy surgery among Swedish neurologists. The reason for decreasing number of yearly-operated patient in Sweden has to be further explored.

E763
MULTIPLE SUBPIAL TRANSECTION IN LENNOX-GASTAUT SYNDROME: REPORT OF THREE CASES

P. Vrielynck, L. Danvoie, S. Ghariani, G. Vaz, K. van Rijckevorsel, and C. Raftopoulos
Reference Center for Refractory Epilepsy, Cliniques Universitaires St Luc, Brussels and Centre Neurologique William Lennox, Ottignies-LLN, Université Catholique de Louvain, Belgium

Purpose: Lennox-Gastaut syndrome (LGS) is a difficult-to-treat condition with disabling multiple seizure types. Common surgical treatments

are mainly palliative, including callosotomy or vagal nerve stimulation. Here we report three LGS patients who underwent multiple subpial transection (MST).

Method: Diagnosis criteria were (1) mental retardation and cognitive regression, (2) more than one seizures type with at least atypical absences and tonic seizures, (3) diffuse slow spike waves discharges and sleep fast activity on the EEG. The patients (all males; 3, 9 and 17 years old) were medically intractable. Presurgical evaluation included video-EEG, MRI, FDG PET, amobarbital test (patient 1) and invasive EEG (patients 2 and 3). MST was achieved under electrocorticographical control.

Results: MRI showed subtle abnormalities in two patients, PET was not contributive. EEG analysis demonstrated in all patients that a leading hemisphere was responsible for the generalized epileptic activity. MST alone (patient 2), MST plus frontal lobe disconnection (patient 1) and MST plus cortectomy (patient 3) were performed. Number of cortical incisions was between 51 and 75. There was no permanent neurological postoperative deficit. Outcome is favorable in all three patients, 11 months to 5 years after surgery: patient 1 is seizure-free and has a better cognitive status, two others have no more epileptic falls and only sleep related seizures.

Conclusion: MST was effective and well tolerated in these patients. It may be a valuable surgical technique in treating LGS, alone or combined with resective surgery.

E764
LONG-TERM WITHIN-GROUP CHANGES IN SEIZURE FREQUENCY AND ADAPTIVE BEHAVIOR OF CHILDREN WITH MEDICALLY REFRACTORY EPILEPSY TREATED WITH OR WITHOUT VAGUS NERVE STIMULATION

L. Corpaci, N. Zamponi*, T. Capriotti*, F. Costanzi*, C. Cardinali*, F. Rychlicki†, and M. Piccirilli‡*
**Children's Hospital, Ancona, Italy; †Ospedali Riuniti, Ancona, Italy; and ‡University of Perugia, Italy*

Purpose: Vagus Nerve Stimulation (VNS) is a treatment that bears consideration for children with medically refractory epilepsy. The aim of this study was to evaluate whether VNS leads to seizure reduction and improvements in children's adaptive behaviors.

Method: We compared within-group changes in seizure frequency and adaptive behavior with Vineland Adaptive Behavior Scales (VABS) from baseline through 18 months in 2 groups of children with medically refractory epilepsy and very compromised cognitive status: a non-VNS-treated group (n=28), who received best medical practice alone, and a VNS-treated group (n=30), who received best medical practice plus VNS.

Results: After 18 months of treatment, within-group changes in the non-VNS group showed mean increase of 11.6% in seizure frequency, and statistically significant decline in adaptive behavior scores. Within-group changes for VNS group showed statistically significant decrease of 56.0% in seizure frequency ($p<0.0001$ t-test), and no statistically significant changes in adaptive behavior scores.

Conclusion: VNS can help deter the effects of medically refractory seizures and may help lessen the deterioration of adaptive skills, even though VNS seems to spares the physiological decline of adaptive skills in children with very compromised development and refractory epilepsy. Besides, although the VABS is considered an appropriate assessment for patients with mental retardation, the results of this assessment must be viewed within the context that most of our patients had a high degree of mental retardation. Further research is needed to understand what kind of instruments could be used to assess improvements reached by severely compromised children after VNS treatment.

E765
ANTIEPILEPTIC DRUG WITHDRAWAL AFTER SUCCESSFUL EPILEPSY SURGERY: A PROSPECTIVE CONTROLLED STUDY

F. Kerling, E. Pauli, and H. Stefan
Epilepsy Center (ZEE), University Hospital of Erlangen, Germany

Purpose: Many patients ask for drug withdrawal after successful epilepsy surgery, but apart from retrospective studies little is known about the risk of seizure relapse. We introduce a prospective withdrawal study performed in our epilepsy center.

Method: Sixty completely seizure free patients were included between 1997 and 2002. One year after surgery patients decided whether medication was discontinued (withdrawal group, N = 34) or kept at the same dosage (control group, N = 26). Discontinuation was administered in small tapering steps over one year. When patients had more than one drug at the beginning of withdrawal, the second drug was discontinued in the next year and so forth. Withdrawal was stopped, when seizures relapsed or the patients disagreed with a further discontinuation. All patients were invited to follow up visits every year in the first five postsurgical years.

Results: 79% (27 of 34) in the withdrawal group and 62% (16 of 26) in the control group were seizure-free five years after surgery. There was no significant difference between these two groups with respect to seizure freedom ($p=0.128$).

Conclusion: In our 60 patients modified antiepileptic drug discontinuation starting one year after successful epilepsy surgery was not associated with a higher risk for seizure recurrence. This study will be continued to enrol more subjects and to gain insight into long-term outcome of drug withdrawal.

E766
VAGUS NERVE STIMULATION IN A POPULATION OF PHARMACORESISTANT EPILEPTIC PATIENTS: 1995–2008, A LONG-TERM FOLLOW-UP STUDY

S. Jensen, V. Pelliccia, C. Pizzanelli, C. Frittelli, M. Baldini, F. Giorgi, R. Galli, and A. Iudice
University of Pisa, Pisa, Italy

Purpose: Vagus nerve stimulation (VNS) is a well established nonpharmacological add-on treatment for patients with medically refractory epilepsy who are not eligible for epilepsy surgery. In this study we assessed the long-term efficacy and tolerability of VNS in a group of patients implanted at our Centre since 1995.

Method: We retrospectively assessed 22 patients (15M/7F) aged 23–68 years (mean 46.3±13.1), with refractory focal (N=11) and generalized epilepsy (N=11) of either symptomatic or cryptogenic origin. Subjects were considered pharmacoresistant, having tried at least 3 antiepileptic drugs (AEDs) unsuccessfully. The patients were implanted in the years 1995–2007; the follow-up period ranged from 1 to 13 years (mean 5.8±4.3).

Results: The mean number of AEDs before implantation was 3.5 (range 3–5). At maximum follow-up (range 1–13 years), mean stimulation output current was 1.68mA (range 0.50–3.00) and mean number of AEDs remained substantially unchanged. Mean reduction in monthly seizure frequency was 37.5±22.8%, with greater reduction in the patients with a longer follow-up period. Stimulation intervals were set to 30 seconds every 5 minutes (n=9), and every 3 minutes (n=13). All patients experienced a better quality of life in terms of improved vigilance and mood. Adverse effects of VNS therapy were transient and tolerable, including hoarseness and coughing.

Conclusion: In our retrospective study, VNS proved to be a safe and effective therapy. The response to VNS therapy appeared increased over

time and kept a long-term sustained effect in refractory epilepsy. Seizure frequency reduction was not the only variable that benefited from VNS in this epilepsy population.

E767
EARLY MENTAL OUTCOME IN BABIES AT RISK FOR DEVELOPING EPILEPSY

E. Porras- Kattz, J. Barrera-Reséndiz, T. Harmony, J. Ricardo-Garcell, and E. Rodríguez-De Paz
Unidad de Investigación en Neurodesarrollo 'Dr Augusto Fernández Guardiola' Instituto de Neurobiología UNAM, Campus Juriquilla, Querétaro, México

Purpose: To evaluate the early mental outcome in babies with perinatal risk factors for developing epilepsy.

Method: We studied 15 control babies and 77 babies with perinatal risk factors. Babies (preterm and term) younger than 4 months corrected aged (CA) with perinatal risk factors for neurodevelopmental deficits were included and clinical follow up was carried out until 24 months CA. All of them were evaluated by Bayley's scale. Mental Development Index (MDI) was analyzed with the nonparametric Kolmogorov-Smirnov test for comparing two samples.

Results: We observed a statistically significant difference in MDI between babies with perinatal risk factors and controls (p= 0.01) and significant difference between children who developed epilepsy and controls (p= 0.001). Also significant difference was observed between babies at risk for neurological damage without epilepsy and babies at risk for neurological damage with epilepsy (p= 0.0001) and between control babies and babies in risk but without epilepsy (p=0.033). When neonatal seizure background was analyzed, nonstatistically significant difference (p=0.196) was found in MDI between babies with neonatal seizures and without neonatal seizures. Significant difference was observed between control babies and children with perinatal risk without neonatal seizures (p=0.02) and also with babies with neonatal seizures (p=0.01).

Conclusion: Early epilepsy is an important factor for the early mental outcome, but not the neonatal seizures background. This condition it seems to be an ominous risk factor for early mental outcome only if other perinatal risk factors for neurodevelopmental deficits are present.

E768
COGNITIVE FUNCTIONS BEFORE AND TWO YEARS AFTER EPILEPSY SURGERY IN CHILDREN AND ADOLESCENTS

G. Viggedal, B. Rydenhag*, E. Svensson†, P. Uvebrant*, and I. Olsson**
**Sahlgrenska University Hospital, Sweden; and †Statistics Dept. Örebro University, Sweden*

Purpose: To evaluate the impact of epilepsy surgery on cognitive functions in children and adolescents operated at Sahlgrenska University in Gothenburg 1987–2004.

Method: Ninety-five children and adolescents <19 years underwent epilepsy surgery and two-year postoperative follow-up. Eighty-four were neuropsychologically assessed before and two years after surgery. Methods for cognitive assessment according to the child's level of functioning and age were used.

Results: The mean age of the 45 female and 39 male children was 10.8 (SD, 4.8) years at the preoperative assessment. The median Intelligence Quotient (IQ) was 73, range 6–127. Mental retardation (IQ<70) was found in 39 (46%), 24 of these had a moderate to profound mental retardation (IQ<50). Fifty percent of all children became seizure free and another 21% had >75% reduction of seizure frequency at the two-year follow-up. Irrespective of IQ-level before surgery no major change in cognitive level was found in those children who became seizure free or had a >75% seizure reduction, even though the latter group showed a larger variation in change of IQ. More children in the group with <75% reduction of seizure frequency showed a decrease of IQ-level, indicating that ongoing severe epilepsy may have a negative influence on cognitive functions and development.

Conclusion: The same pattern of change in IQ was seen in children irrespective of preoperative IQ level. These findings are important and show that learning disabled children and children with severe mental retardation may benefit from epilepsy surgery without a loss of cognitive function.

E769
PARENTS' PERCEPTIONS OF OUTCOME AFTER EPILEPSY SURGERY IN CHILDREN

B. Olovson, B. Rydenhag*, E. Svensson†, and I. Olsson**
**Sahlgrenska Universty Hospital, Sweden; and †Statistics Dept Örebro University Sweden*

Purpose: To study the parents' perception of change in epilepsy related daily life activities in their children two years after epilepsy surgery.

Method: Ninety-five children and adolescents <19 years were operated for epilepsy in Gothenburg 1987–2004 and followed two years after surgery. Eleven adolescents who filled in an quality of life questionnaire for adults were excluded, as were five reoperated within the period. Out of the remaining 79, the parents of 73 children (92%) participated in the evaluation. At the two-year follow-up a group of 33 parents assessed the perceived change in parental concern about the child's epilepsy, in the child's peer relationships and learning capacity. The same variables were assessed preoperatively and at the two-year follow-up by the 40 parents included 1995 and onwards. In addition, alertness and leisure time activities were assessed. Nonparametric statistical methods for analysis of change in ordinal data were used.

Results: A significant improvement in parental concern was found in 79% and in 75% in the two groups, respectively. Corresponding improvements were found in peer relationships (56% and 53%), learning ability and attention (56% and 68%). Improvements in perceived alertness and leisure time activities were found in 72% and 62%, respectively, of the group of 40 parents. The perceived improvement according to the parents mainly concerned children who had become completely seizure-free or had >75% reduction of seizure frequency.

Conclusion: Parents perceive improvements in daily life activities and learning capacity in their children after successful epilepsy surgery.

E770
ANTERIOR TEMPORAL LOBE RESECTION WITHOUT HIPPOCAMPECTOMY

C. Gyimesi,†, H. Pannek†, F. Woermann†, R. Schulz†, A. Elsharkawy†, S. Horstmann†, J. Aengenendt†, H. Steffen†, J. Janszky*,†, and A. Ebner†*
**University of Pecs, Hungary; and †Epilepsy Center Bethel, Clinic Mara GGmbH, Germany*

Purpose: We assessed the results of epilepsy surgery in patients who underwent anterior temporal lobe resection without hippocampectomy due to temporal epileptogenic lesions.

Method: Anterior temporal lobe resection without hippocampectomy was performed in sixty-two patients with temporal lobe epilepsy. Presurgical evaluation including video-EEG monitoring and high-resolution brain MRI was carried out in all patients.

Results: The 6-month seizure outcome was assessed in 62 patients. All patients had an improvement postoperatively: Of these 90.3% of them

became seizure-free (Engel 1), 6.5% of them became almost seizure-free (Engel 2) and 3.2% were non–seizure-free but had significantly improved seizure outcome (Engel 3). The 2-year seizure outcome was assessed in 42 patients. All of the patients had improvement postoperatively: Of these 78.6% of them became seizure-free (Engel 1), 14.3% of them became almost seizure-free (Engel 2) and 7.1% were non–seizure-free but had significantly improved seizure outcome (Engel 3). Histopathology showed tumors in 31 cases, malformations of cortical development in 11 cases and cavernomas in 9 cases.

Conclusion: More than 78% of patients became seizure-free postoperatively, which is comparable to standard surgical procedures in temporal lobe epilepsy. Anterior temporal lobe resection without hippocampectomy is an effective surgical therapy in some patients with temporal lobe epilepsy.

E771
PRE- AND POSTOPERATIVE EEG IN SURGICALLY TREATED SYMPTOMATIC PATIENTS WITH EPILEPSY WITH CONTINUOUS SPIKES AND WAVES (CSWS)

M. Peltola, E. Liukkonen†, M. Granström‡, R. Paetau†,‡, E. Kantola-Sorsa†, L. Valanne§, B. Falck*,**, G. Blomstedt¶, and E. Gaily†*

**Turku University Hospital, Finland; †Epilepsy Unit, Hospital for Children and Adolescents, Helsinki University Central Hospital, Finland; ‡Brain Research Unit, Helsinki University of Technology, Finland; §Helsinki Medical Imaging Centre, Helsinki University Central Hospital, Finland; ¶Helsinki University Central Hospital, Finland; and **University Hospital, Uppsala, Sweden*

Purpose: Published data on the effect of surgical treatment on clinical and EEG outcome in children with symptomatic CSWS epilepsy are scarce. Our aim was to look for EEG factors predictive for postoperative outcome.

Method: Thirteen children with drug resistant symptomatic epilepsy with CSWS and cognitive deterioration and/or daily frequent atypical absences underwent anterior or total callosotomy, hemispherotomy or focal resection. Seven children had unilateral and six had bilateral structural abnormalities on brain MRI. The CSWS propagation pattern, propagation to frontal, centro-temporal and parietooccipital areas and maximal strength in source montage were retrospectively analyzed from pre- and postoperative EEG-recordings. Clinical outcome was assessed at six months and at two years after surgery. Favorable outcome was defined as more than 90% reduction of the most disturbing seizure type and/or halted cognitive deterioration.

Results: Favorable clinical outcome was seen in ten of thirteen of patients. Preoperatively, bilateral synchronous or asynchronous CSWS with one-way interhemispheric propagation was more often associated with favorable outcome compared to bilateral asynchronous CSWS and two-way interhemispheric propagation (eight vs. two patients). All patients with a centro-temporal focus had favorable outcome. The CSWS source which was the most active preoperatively showed continuous spiking also after surgery in all patients. Reduction in either CSWS propagation area or in source strength was seen in all patients with favorable outcome compared to one of three patients with unfavourable outcome. Inhibited interhemispheric propagation had no independent effect on outcome.

Conclusion: The preoperative CSWS propagation pattern seems to have value in predicting outcome of epilepsy surgery in CSWS patients. Postoperatively, favorable outcome was reflected as diminished CSWS propagation area and source strength.

E772
FAMILY FUNCTIONING IN CHILDREN WITH EPILEPSY AND ANXIETY AND COPING SKILLS OF THEIR PARENTS

F. Sönmez, K. Fazlýoðlu, Ç. Hocaoðlu, and A. Cansu

Karadeniz Tecnical University Faculty of Medicine, Turkey

Purpose: In this study, we aimed to investigate the family functioning, anxiety of parents and coping strategies of parents in children with epilepsy according to sociodemographic and clinical characteristics.

Method: The study population included either mothers or fathers of 60 children at 6 to 16 years of age, who were diagnosed with epilepsy in KTU Medical School Pediatric Neurology Clinics between November 2006 and June 2007. Control group included either mothers or fathers [matched with patient group in terms of age, gender, level of education and place of residence (village, township, town center)] of 60 healthy children aged between 6 to 16 years. Sociodemographic Data Form, Family Assessment Device, STAI-1, and Cope Scale were applied to all participants, respectively.

Results: Parents of children with epilepsy were found to be dysfunctional in respect of family functions (roles, emotional reaction, showing required interest, general functions) when compared to parents of healthy children. Additionally, level of anxiety in parents of children with epilepsy was more than the level observed in parents of healthy children. In respect of coping strategies, mental coping strategies of parents having epileptic children were found to be significantly lower than parents of healthy children. No significant difference was detected between the parents of epileptic and parents of healthy children in terms of other subscales of Cope Scale.

Conclusion: Having a child with epilepsy effects family functioning negatively besides significantly increasing the level of anxiety in parents. On the other hand, coping strategies are not affected significantly.

E773
VAGAL NERVE STIMULATION FOR DRUG RESISTANT EPILEPSY IN ADULT, ADOLESCENT AND PEDIATRIC PATIENTS: IS THERE ANY DIFFERENCE?

G. Colicchio, E. Cesaroni†, M. Fuggetta*, M. Meglio*, F. Papacci*, D. Policicchio*, F. Rychlicki‡, M. Scerrati‡, and N. Zamponi†*

**Università Cattolica Del Sacro Cuore, Roma, Italy; †Children's Hospital G. Salesi, Ancona, Italy; and ‡University of Ancona School of Medicine, Italy*

Purpose: To compare the outcome with respect to: age of implant, aetiology and duration of epilepsy.

Method: 117 drug resistant epileptic patients, excluded from ablative surgery, were submitted to vagal nerve stimulation (1995– 2006). Etiology: 54 cryptogenic, 63 symptomatic; age of implant: (0–12y) 35; (13–18y) 26; 56 (more than 18y). Duration of epilepsy ranged from 3 months to 45 years. Clinical outcome was determined by comparing the seizure frequency after stimulation at 3-6-12-18-24-36 months with the previous 3 months. ''Responders'' were the patients experiencing a seizure frequency reduction of 50% or more. Statistical analysis: Wilcoxon test, MANOVA, Multivariable Regression Model, Logistic Multivariable Regression Model.

Results: The seizure frequency reduction was significant, in the group as a whole, between baseline and first follow-up (Wilcoxon test). The percentage of responders remained stable in time, showing only an incremental trend (McNemar test). Multivariate analysis showed a significant

effect of the age of implant on seizure frequency reduction: children and adolescents had better clinical outcome than adult patients (MANOVA test). The results were validated by a Multivariable Regression Model for percentage variation of seizure number at 36 months respect to baseline and by a Logistic Multivariable Regression Model to predict percentage of ''responder'' at 3 months. Duration of epilepsy was strictly connected to age of implant; etiology showed no influence on outcome.

Conclusion: this study confirms the well-known efficacy of vagal nerve stimulation as treatment for drug-resistant epilepsy. The significant positive outcome predictor being the younger age at the implant.

E774
OUTCOME OF RESECTIVE SURGERY IN LENNOX-GASTAUT SYNDROME

Y. Lee, S. Kim*, H. Kim*, and H. Moon†*
**Severance Children's Hospital, Korea; and †College of Medicine, Yeungnam University, Korea*

Purpose: Advances in imaging and electrodiagnostics studies enables to determine the primary epileptogenic region in some cases of Lennox-Gastaut syndrome (LGS). We reviewed the outcome of resective surgery in patients with LGS.

Method: Twenty-seven patients (16 boys, 11 girls) were treated with resective surgery from 2000 to 2007 at Sanggye Paik Hospital and Severance Children's Hospital. Clinical characteristics, findings from diagnostic studies (MRI, video-EEG monitoring, SPECT and PET), type of surgery, pathologic findings, seizure outcome for more than 6 months after surgery and developmental outcome, were reviewed.

Results: (1) Engel class I outcome was achieved in 16 cases (59.3%), class II in 5 cases (18.5%), class III in 1 case (3.7%) and class IV in 5 cases (18.5%). (2) Even using detailed application of high resolution MRI techniques, 7 cases (7/27, 25.9%) were nonlesional. (3) PET showed concordant findings in 19 cases (19/26, 73.1%), and interictal SPECT in 18 cases (18/22, 81.8%) from primary epileptogenic region. (4) Hemispherectomy was performed in 6 cases (22.3%), frontal lobectomy in 10 cases (37.0%), temporal lobectomy in 1 case (3.7%), and multilobar resection in 10 cases (37.0%). (5) Cortical dysplasia including microdysgenesis was the most common pathology seen in 19 cases (70.4%), gliosis in 4 cases (14.8%), but 3 cases did not show abnormal pathology. (6) In cases with Engel class I outcome, significant improvement was seen in cognitive development.

Conclusion: Resective surgery should be considered in intractable LGS in cases with suspected underlying focal cortical pathology.

E775
CORPUS CALLOSOTOMY IN LENNOX-GASTAUT SYNDROME

S. Kim, Y. Lee*, H. Kim*, E. Seo†, and H. Chung‡*
**Severance Children's Hospital, Korea; †College of Medicine, Soonchunhyang University, Korea; and ‡National Health Insurance Corporation Ilsan Hospital, Korea*

Purpose: Lennox-Gastaut syndrome (LGS) is one of the most devastating pediatric epileptic syndromes characterized by various disabling seizure types, generalized forms of abnormal epileptiform EEG features and progressive psychomotor retardation. Corpus callosotomy is one of treatment options in patients with intractable LGS without definitive focal cortical pathology. This study was designed to evaluate efficacy and safety of corpus callosotomy in patients with LGS.

Patients and Method: Thirty patients (21 boys, 9 girls) with LGS who had corpus callosotomy at Severance Children's Hospital from October 2003 to January 2007, were enrolled with mean follow-up of 34.6''b14.0 months. We retrospectively reviewed medical records, video-EEG monitoring, MRI, seizure outcome and postoperative complications.

Results: Mean age at the corpus callosotomy is 103.5 ± 60.5 months. Twenty-four patient (80.0%) of 30 were underwent total corpus callosotomy and 6 (20.0%) were done anterior 4/5 corpus callosotomy. Seizure outcomes were as follows: 5 patients (16.7%) in Engel class I, 10 (33.4%) in class II, 7 (23.3%) in class III and 8 (26.6%) in class IV. Satisfactory surgical outcomes (class I and II) were achieved in 50.1% of total patients. Postoperative complications were seen in 2 cases (6.7%), such as involuntary movement (1 case) and transient ataxia (1 case), but both were recovered completely. Subsequent resective surgery was performed in 5 cases, whose EEG features became lateralized without complete seizure control. All of these cases could achieve the complete seizure free outcome after resective surgery.

Conclusion: Corpus callosotomy is effective and safe treatment in medically intractable LGS without localized pathology.

E776
COST-EFFECTIVENESS OF SURGERY FOR INTRACTABLE TEMPORAL LOBE EPILEPSY

P. Putkonen,†, L. Jutila†, P. Aronen‡, A. Immonen†, J. Kinnunen§, H. Sintonen‡, and R. Kälviäinen†*
**Helsinki University of Technology. Espoo, Finland; †Kuopio University Hospital (KUH), Kuopio, Finland; ‡University of Helsinki, Helsinki, Finland; §University of Kuopio, Kuopio, Finland; and ¶National Research and Development Centre for Welfare and Health (STAKES), Helsinki, Finland*

Purpose: Surgery for temporal lobe epilepsy (TLE) is offered to intractable patients; however, there are few studies of its cost-effectiveness. The objective was to investigate whether TLE-surgery and drug treatment for adults with medically intractable epilepsy (MIE) is cost-effective in comparison to drug treatment only.

Method: 131 adult MIE patients operated for drug-resistant TLE in the KUH between 1988 and 1999 were invited to retrospective study during March-April 2004. 65 patients were included. In a mirror-image design, effectiveness was measured by the number of epileptic seizures and direct costs related to treatment of MIE in three years before and after TLE-surgery. The cost-effectiveness (CE) results are reported as an incremental CE-ratio, CE-plane and CE-acceptability curve with and without psychiatric treatment cost.

Results: The incremental cost of one avoided epileptic seizure by surgery in comparison to treatment without surgery was 85€ and including psychiatric costs 98€. Based on probabilistic sensitivity analysis the mean incremental effectiveness was 367 (CI 95%:234–548) avoided epileptic seizures. The mean incremental cost was 31354€ (range 26109€–36700€) and including psychiatric costs 36094€ (range 29410€–43598€). TLE-surgery reduced substantially the need for postoperative care. Average treatment cots for postsurgical period excluding surgery and psychiatric treatment costs were 9048€ in comparison to 17188€'s in presurgical period.

Conclusion: The combination of surgical and medical treatment was more effective but more costly than drug treatment alone. If TLE-surgery in successful cases retains its effectiveness, then after 6 years TLE-surgery would be cost saving and for all patients after 14.5 years.

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E777
COMPLICATIONS OF INVASIVE SUBDURAL AND DEPTH ELECTRODE IN MONITORING FOR EPILEPSY SURGERY IN CENTERS OF ARGENTINA

M. Galan, M. Aberastury, M. Garcia, C. Ciraolo, C. Maxit, G. Agosta, S. Kochen, and R. Rey
Hospital Italiano de Buenos Aires, Argentina

Purpose: Analize the type and frequency of complications associated with placement of subdural grid, strip and depth electrode for invasive VEEG monitoring during epilepsy surgery in children and adults with refractory localization-related epilepsy.

Method: We retrospectively reviewed the clinical records of 19 patients who underwent invasive VEEG monitoring in three centers of epilepsy, between march 2005 and september 2007.

Results: The average age at implantation was 8.4 years, (ranged from 1 to 39 years). The total number of electrodes ranged from 36 to 226 (mean 95) Subdural grids were placed in 17 patients. Subdural strips in 4 patients with a mean of 2.5 strips per patient and depth electrodes in 10 patients. Coverage was unilateral in 17 patients and bilateral in 2 patients. These different electrode types were used alone (10 p.) and in combination (9 p.) Duration of electroencephalographic monitoring ranged from 3 to 10 days (mean 5.8 days) with a follow-up period of 6 to 36 months (mean 14.8 months). The total rate of neurological complications related to electrode implantation was: 26.3% (5/19p.). They consisted in: cerebral abscess (n:1), subdural empiema (n:1), unexplained fever (n:1), and cerebral edema (n:1). One patient required reimplantation due to electrode displacement. We did not observe neurological deficit during invasive video EEG.

Conclusion: Even though Argentina is a developing country, our results show similar percentage of complications as in developed countries. Our observations suggest that Invasive monitoring for intractable epilepsy is generally safe and does not add neurological deficit.

E778
LONG-TERM EFFICACY OF MESIAL TEMPORAL LOBE EPILEPSY SURGERY: CURATIVE SURGERY OR PHARMACORESISTANCE CONTROL?

N. Canas, C. Romero, J. Correia, and P. Cabral
Hospital De Egas Moniz, Portugal

Purpose: The surgical efficacy for refractory mesial temporal lobe epilepsy (MTLE) is classically evaluated by the Engel classification. However, this doesn't consider the contribution of the postoperative antiepileptic treatment (AET) for the surgical results. We evaluated the long-term efficacy of MTLE surgery considering the postoperative AET.

Method: The postoperative seizures (Engel) and AET of MTLE patients with more than 1 year follow-up were analyzed (n=58; 58% woman; all hippocampal sclerosis); AET before surgery and at last observation were compared.

Results: At 10-years follow-up, 85% of the patients are in Engel Ia, 100% in the first year, 80% at 10th. An overall reduction in AET was achieved in 88% of the patients; although the AET reduction (dose/number of antiepileptics) started at the first year postsurgery, only after the second its suspension was possible. From that time (n=52), 29% of the patients are considered cured (Engel Ia, no AET), 54% controlled (Engel Ia, with AET) and 17% noncontrolled (maintaining seizures/AET; 33% with AET increased compared with baseline). The main factors associated with the nonsuspension of AET were a short-term follow-up and seizure recurrence during AET reduction (15% of the patients).

Conclusion: Although the excellent long-term surgical results for refractory MTLE may lead to the assumption that its a curative surgery, we demonstrate that, in fact, most of the patients need postoperative AET (even at low dosages) for seizure control. Our results suggest that MTLE surgery should mainly be considered as a pharmacoresistance control.

E779
THE IDENTIFICATION OF PROGNOSTIC FACTORS PRIOR TO INVASIVE VIDEO-EEG MONITORING

E. Carrette, K. Vonck*, V. De Herdt*, A. Van Dycke*, R. El Tahry*, I. Dewaele*, L. Goossens*, R. Raedt*, G. Van Maele†, A. Meurs*, D. Van Roost*, W. Wadman‡, and P. Boon**
**Reference Center For Refractory Epilepsy, Ghent University Hospital, Ghent, Belgium; †Ghent University Hospital, Ghent, Belgium; and ‡Swammerdam Institute of Life Sciences, Vrije Universiteit, Amsterdam, The Netherlands*

Purpose: Invasive video-EEG monitoring (IVEM) is performed in patients with refractory epilepsy in whom the noninvasive presurgical evaluation is insufficient to localize the ictal onset zone prior to resective surgery (RS). In order to optimize the patient flow towards invasive investigation, this retrospective study aims to identify positive or negative predictive factors for 1. IVEM outcome and 2. RS outcome.

Method: Patients characteristics in 68 patients who underwent IVEM between 1992 and 2007 at Ghent University Hospital were analyzed and correlated with 1. localizability of the ictal onset zone with IVEM; 2. suitability to undergo RS, defined as an unique focus without overlap with functional cortex and 3. Engel class I outcome following RS of a unique focus, using Fisher exact and Mann-Whitney exact statistical testing with $p<0.05$.

Results: IVEM was able to localize the ictal onset zone in 56/68 patients (82%). In this patient group a seizure free interval in the medical history occurred significantly less frequent ($p<0.05$). 20/56 patients with localized ictal onset (36%) were considered unsuitable candidates for RS. The surgical outcome of 22/28 patients that eventually had RS, can be classified Engel class I (79%). The identification of a structural abnormality on MRI was significantly more the case in these patients compared to the patients with class II-IV outcome ($p<0.05$).

Conclusion: Based on this retrospective statistical analysis a seizure free interval was identified as a negative predictive factor for IVEM outcome and the identification of a structural lesion as a positive predictive factor for RS outcome.

E780
STUDIES ON PREDICTORS OF THE POSTSURGICAL OUTCOME IN EPILEPSY

H. Zuchun, and W. Xiaoping†*
**Chongqing Medical And Pharmaceutical College, China; and †Sichuan Provincial People's Hospital, China*

Purpose: The goals of this study were to determine predictors of the postsurgical outcome in epilepsy.

Method: Epileptic patients as candidates for operation were undergone presurgical evaluation which including seizure semi logy, magnetic resonance imaging (MRI), video electroencephalography (VEEG)£¬ magnetoencephalography (MEG) and ECoG. By chi-square test, the accuracy and predictive value of noninvasive presurgical investigations are evaluated. Logistic regression analysis was applied to assess the relationships between presurgical predictors and postsurgical outcome.

Results: 134 patients had undergone operation. These were 72 mesial temporal lobe epilepsy, 18 neocortical temporal lobe epilepsy and 44 extratemporal epilepsy. 97 patients achieved postsurgical seizure-controlled effectively during 1 year's follow-up. Combined with the postsurgical outcome, anyone of these noninvasive presurgical investigations

alone does not has sufficient predictive value regard to postsurgical seizure free (P0.05). Only when the three investigations had concordant results, the postsurgical seizure free might be positively predicted. Logistic regression analyses revealed that three factors as followed: clinical manifestation, the position of epileptogenic zone, the number of spike focus in ECoG interoperation were related with seizure controlling after operation.

Conclusion: Only when MRI ¢MEG ¢VEEG investigations had concordant results, the postsurgical seizure free might be positively predicted. Clinical manifestation, the position of epileptogenic zone, the number of spike focus in ECoG interoperation were related with seizure controlling after operation.

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