Epilepsia, 51(Suppl. 4):1–189, 2010
doi: 10.1111/j.1528-1167.2010.02658.x

9TH ECE PROCEEDINGS

9th European Congress on Epileptology, Rhodes, Greece, 27 June–1 July 2010

Genetics
Monday 28th June 2010
11:30–13:00

001
INFANTILE ONSET FOCAL EPILEPSY AND EPILEPTIC ENCEPHALOPATHIES ASSOCIATED WITH PCDH19 GENE MUTATIONS: NEW DE NOVO AND FAMILIAL MUTATIONS

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Purpose: To explore the causative role of *PCDH19* gene, located at Xq22, in females with epilepsy.

Method: Clinical and genetic study of 116 females with a wide spectrum of epilepsies including febrile seizures (FS), generalized epilepsy with febrile seizures plus (17), focal epilepsy (25), generalized epilepsies (18), Dravet syndrome (DS) (19), other epileptic encephalopathies (25), myoclonic astatic epilepsy (6) and unclassified epilepsy (6).

Results: Mutational analysis revealed *PCDH19* mutations in 12/116 patients (10%). Mean age at seizure onset was 8.3 months; 8 patients (67%) presented with FS and 4 (33%) with a cluster of focal seizures. Overall, seizures, which were more frequent at onset, were precipitated by febrile illnesses in 6/12 patients (50%). Seven out of 12 patients (58%) had a presentation consistent with DS, 5/12 patients (42%) had focal epilepsy. Mental retardation was present in 10 patients, ranging from mild (5), to moderate (2), and severe (3). Two patients had normal cognitive functions, and 4 had autistic features, 3 of whom with mental retardation. Mutations were missense (6), truncating (2) and frameshift (4), 10 have never been reported. Mutations were inherited in 3 patients (25%): 2 from apparently unaffected fathers, and one from a mother who had had afebrile seizures.

Conclusion: In our cohort *PCDH19* mutation frequency was 10%. *PCDH19* plays a major role in infantile focal epilepsy and in epileptic encephalopathies with clinical features partially overlapping with DS. Clinical and molecular diagnosis is important for better understanding, prognostic implications and for genetic counseling.

002
PHENOTYPING OF IGE PATIENTS WITH A PHOTOPAROXYSMAL EEG RESPONSE (PPR) FOR EUROPEAN GENETIC STUDIES: TWO MAIN PHENOTYPES APPEAR TO BE SIMILAR IN NORTHERN AND SOUTHERN EUROPEAN COUNTRIES

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Purpose: PPRs may constitute an endophenotype for IGE, which could be useful to dissect their complexity. Two independent genome-wide linkage screens in multiplex PPR families identified the loci 7q31, 16p13 (Tauer et al. 2005) and 6p21, 13q31 (Pinto et al. 2007). These different loci might reflect the phenotypic difference of the two samples; the first having predominantly absences, and the other myoclonic seizures. We investigated the distribution of these types in single IGE-PPR cases and whether there are differences between northern and southern EU countries.

Method: 203 IGE patients with a PPR in at least one EEG (60% female, median range 8–18 years) and who gave consent for genetic studies were phenotyped in three major categories, based on clinical histories: myoclonic, absence type or GTCS only. The patients were recruited through the EU consortium ''Genetics of Photosensitivity and Visually Sensitive Epilepsies'' and the Dutch NIGO study. Simple parametric statistics was applied.

Results: About equal percentages (40%) had either myoclonic or absence seizures and 20% GTCS only. No difference was found between the Dutch sample (40% absences, N = 78) and the southern European sample (34% absences; N = 125) ($p = 0.13$).

Conclusion: Compared to the Dutch national IGE cohort (17%), PPR-IGE patients have more often a myoclonic type of epilepsy with equal distribution of the absence and myoclonic seizure types. No difference was found between Northern and Southern Europe, which probably means that there is no referral bias. It might thus be useful to subdivide the PPR-IGE patients in myoclonic and absence phenotypes.

003
A NONSENSE MUTATION OF *GABRG2* FOUND IN A SEVERE EPILEPSY PHENOTYPE AND WHICH LEADS TO A TRAFFICKING ABNORMALITY OF $GABA_A$ RECEPTORS

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Purpose: Mutations in *GABRG2*, encoding $\gamma 2$ subunits of $GABA_A$ receptors, can cause generalized epilepsy with febrile seizures plus(GEFS+) and Dravet syndrome. Most *GABRG2* truncating mutations associated with Dravet syndrome result in premature termination codons and are stably translated into mutant proteins with potential dominant-negative effects. We investigate cell-biological consequences of a nonsense mutation (c.118C>T, Q1X) in *GABRG2*, which was identified in Dravet syndrome.

Method: The genetic abnormality was explored within candidate genes of Dravet syndrome, such as *SCN1A, 2A, 1B, 2B, GABRA1, B2* and *G2*. The electrophysiological properties of the channels harboring the identified mutation were examined. Immunohistochemistry and immunostaining were employed to characterize the expression and intracellular localization of the mutant channel molecules.

Results: Electrophysiological studies with the reconstituted $GABA_A$ receptors of HEK cells show that GABA-induced current values for the receptors are reduced when mutated $\gamma 2$ DNA is cotransfected with those of $\alpha 1$ and $\beta 2$ subunits. The immuno-histochemistry of $GABA_A$ receptors with antibodies against $\alpha 1$ and $\gamma 2$ subunits shows granules in neuronal soma and neuropils. When mutated $\gamma 2$ cDNA is transfected, the intracellular trafficking of $GABA_A$ receptors monitoring $\alpha 1$ and $\beta 2$ subunits is inhibited and retained in the endoplasmic reticulum.

Conclusion: Our findings suggest that the pathomechanism of ''channel trafficking abnormality'' may provide a new channelopathy paradigm for the unsolved questions underlying epilepsy. These include the differences between GEFS+ and Dravet syndrome, which share causative genetic abnormalities in the same genes and hence, have so far been considered within the spectrum of one disease entity or allelic variant.

004
THE ASSOCIATION BETWEEN CARBAMAZEPINE-INDUCED CUTANEOUS ADVERSE DRUG REACTIONS WITH HLA-B*1502 ALLELE IN MAINLAND OF CHINA

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Purpose: To investigate the association between carbamazepine (CBZ) induced cutaneous adverse drug reactions (cADRs) and HLA-B*1502 allele in mainland of China.

Method: Twenty-eight subjects with cADRs, including 6 with SJS/TEN and 22 with mild maculopapular eruption (MPE), 45 CBZ-tolerant controls, and 69 healthy volunteers were recruited from five Hospitals of Sichuan province in China during March to November 2009. All subjects were genotyped by polymerase chain reaction (PCR)-sequence-based-typing (SBT) method.

Results: HLA-B*1502 allele frequency was 100% (6/6)in patients with CBZ-induced SJS/TEN, 13.6% (3/22) in patients with CBZ-induced MPE, frequency was 6.7% (3/45) in CBZ-tolerant subjects, and 7.25% (5/69) in the healthy volunteers. All the six patients with SJS/TEN were found positive with HLA-B*1502 allele (100%, OR = 168), and there was no difference in the frequency of patients with HLA-B*1502 allele between MPE and control group (13.6% vs. 6.7%; p = 0.629, OR = 2.2).

Conclusion: The patients with CBZ-induced SJS/TEN, but not the MPE, have the significant association with HLA-B*1502. The test of HLA-B*1502 allele is essential for the Chinese Han people before taking the CBZ treatment if it is possible.

005
IDENTIFICATION OF A 15Q13.3 MICRODELETION IN CLINICALLY AFFECTED AND UNAFFECTED MEMBERS IN A PEDIGREE WITH IDIOPATHIC GENERALIZED EPILEPSY

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Purpose: Idiopathic generalized epilepsies (IGE) account for up to one third of all epilepsies and, in the majority of affected individuals, have a complex genetic etiology. The underlying genes involved remain largely unknown. Recently, a 15q13.3 microdeletion has been identified in 1% of IGE cases compared to <0.02% of controls. Individuals have a broad range of phenotypes including epilepsy, mental retardation, schizophrenia, autism. The most common form of the deletion on 15q13.3 (2Mb) removes seven known genes, including *CHRNA7* encoding the $\alpha 7$ subunit of the nicotinergic acetylcholine receptor. This candidate gene for the epilepsy phenotype is linked to juvenile myoclonic epilepsy and benign rolandic epilepsy, as well as the P50 sensory gating deficit, an endophenotype of schizophrenia and bipolar disorder. Part of the gene is a copy number variant, due to a duplication of exons 5–10 and 3′ sequence of CHRNA7 in *CHRFAM7A* which is present in many individuals. We investigated the 15q13.3 microdeletion in a pedigree that includes six individuals with IGE, associated in some with learning difficulty.

Methods: The pedigree was clinically characterized. The microdeletion was initially identified by comparative genomic hybridization and confirmed in available family members by quantitative PCR.

Results: Of the six individuals with epilepsy, five living affected family members had the larger 15q13.3 microdeletion (4Mb), which additionally removes CHRFAM7A. One apparently clinically unaffected female also has the deletion, demonstrating incomplete penetrance.

Conclusion: This pedigree provides an excellent opportunity to investigate other genetic influences contributing to the phenotype, including copy number variants in *CHRNA7*.

Pediatric epileptology
Monday 28th June 2010
11:30–13:00

006
THE MANY FACES OF GLUT1 DEFICIENCY – WE ALWAYS HAVE TO RETHINK ON OUR ''OLD'' PATIENTS

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GLUT1 deficiency syndrome (GLUT1DS) is a treatable epileptic encephalopathy caused by impaired glucose transport through the blood brain barrier. It can be diagnosed by hypoglycorrhachia (CSF glucose <40 mg/dl), ratio of CSF to blood glucose of <0.45, and impaired uptake of glucose into erythrocytes.

It was lately related to heterozygote mutations in the SLC2A1 gene.

De Vivo who ''established'' this entity described infantile intractable epilepsy including hypsarrythmia followed by microcephaly,

developmental delay and complex movement disorder with immediate response to the ketogenic diet which provides alternative source of energy to the brain.

Recently this diagnosis was made (isolated case reports) in sporadic and familial cases with childhood generalized epilepsy, usually intractable, occasionally accompanied by ataxia, behavioral and cognitive deficits and in addition in few families with exercise induced dyskinesia.

We describe 5 patients with atypical generalized epilepsy beginning at their early childhood (first half decade), and one with exercise induced dyskinesia which were found to have hypoglycorrhachia, In 4/6 patients CSF glucose level was ≤40 mg/dl but CSF/blood ratio >0.45. 5/6 patients are normocephalic. Two had cerebellar ataxia, one of them had also paroxysmal movement disorder in addition to their epilepsy and developmental delay.

In 4/6 we could identify very similar sleep and awake EEG pattern which will be described.

SLC1A2 gene mutation was detected in all patients in one family it was inherited from the mother side, 4/6 mutations are newly described mutations.

Conclusion: Hypoglycorrhachia related to GLUT 1 DS and SLC2A1 gene mutations should be considered and looked for in children with early childhood onset of atypical generalized epilepsy especially with specific EEG features with or without additional neurological and cognitive deficits, in patients with immediate and good response to ketogenic diet and in ones with various paroxysmal movement disorders, in order to establish diagnosis that has great implication on treatment planning, prognosis and genetic counseling.

007

IMMUNE-MEDIATED AND INFLAMMATORY DISEASE IN ETIOLOGY OF EPILEPSIA PARIALIS CONTINUA IN CHILDREN

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Purpose: The aim of the study is to evaluate clinical characteristics, neurophysiologic features and response to the treatment in children with epilepsia partialis continua (EPC) caused by inflammatory or immune-mediated disorders of the brain, excluding Rasmussen encephalitis.

Method: The study included patients with EPC caused by inflammatory or immune-mediated disorders aged 1–18 years, in period from 1993 to 2009. Duration, phase of disease when EPC appeared, ictal scalp EEG and therapeutic response were analyzed.

Results: EPC was diagnosed in 19 children: acute (7) and subacute viral encephalitis (5), subacute sclerosing panencephalitis (2), limbic encephalitis (1), CNS tuberculosis (3), sclerosis multiplex (1). EPC appeared in the first (11), second (6) and in terminal (2) phase of disease. Mean EPC duration was 10.4 days. Ictal EEG showed focal in 10, generalized epileptic discharges in 5 and generalized abnormal background activity in 4. EPC was resistant to antiepileptic drugs and the best response was observed to midazolam in continuous intravenous infusion combined with high dosage of corticosteroids (11) and plasmapheresis in one case.

Conclusion: EPC is more frequent in subacute then in acute form of encephalitis and appears often in later phases of disease. It might suggest that not only inflammation but also immunological processes play the rule in its pathogenesis. Good response to corticosteroids and plasmapheresis even in acute disease support such mechanism. On the other hand, ictal scalp EEG in numerous cases showed generalized abnormalities implying that EPC is very focal manifestation of diffuse brain disorder.

008

INFANTILE EPILEPTIC ENCEPHALOPATHY WITH LATE ONSET-SPASMS: REPORT OF 19 PATIENTS

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Purpose: Late-onset Spasms (LOS) are epileptic spasms starting after the first year of life. Our aim was to assess the electroclinical features and the follow-up of the patients with this particular type of epileptic seizure.

Method: We retrospectively included all patients with LOS confirmed by electroencephalogram between 1989 and 2008. Clinical and electroencephalographic findings at diagnosis and during follow-up were collected. The Vineland scale was used to evaluate the neuropsychological outcome.

Results: We report 19 patients with LOS over 240 patients with recorded epileptic spasms. Eighteen patients had an epileptic encephalopathy with late-onset spasms. The ictal EEG showed a focal or generalized discharge of triphasic slow-waves, slow-spikes or slow spikes-waves with fast activities. The interictal EEG usually showed focal or generalized slow-waves or slow spikes- waves without hypsarythmia. LOS were controlled in only 6 patients. Three developed typical Lennox-Gastaut Syndrome and ten had a severe epileptic encephalopathy. Neuropsychological outcome was evaluated in 15 patients with the Vineland scale. Cognitive functions were normal in only one patient whereas severe cognitive delay was observed in 12/15.

Conclusion: Epileptic spasms may appear after the age of 1. They are more frequently observed in patients with epileptic encephalopathy. In few patients, this type of seizure was observed before the patients fulfill Lennox-Gastaut syndrome criteria. In one patient, we conclude to focal epilepsy with seizures occurring in cluster. When LOS are related to an epileptic encephalopathy, this epileptic syndrome seems to be linked to refractory epilepsy and severe cognitive outcome unrelated to the etiology.

009

EARLY PROGNOSTIC FACTORS IN PATIENTS WITH SEVERE MYOCLONIC EPILEPSY IN INFANCY (SMEI)

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Purpose: SCN1A is the most clinically relevant epilepsy gene, most mutations (70–80%) leading to severe myoclonic epilepsy of infancy (SMEI). The aim of the present study was to identify possible phenotype-genotype correlations with SCN1A alterations in a population of patients with definite clinical diagnosis of SMEI.

Method: This retrospective study comprized 20 patients with a diagnosis of SMEI (5 Male, 15 female; mean age:10,26; range: 2–30 years). We performed a clinical and genetic study focusing on SCN1A, using dHPLC, gene sequencing and MPLA to detect genomic deletions/duplications on SMEI patients. Data from neuropsychological assessment were available for a group of 8 patients.

Results: SCN1A analysis by dHPLC/ sequencing revealed 14 mutations (case group) comprising missense and truncating mutations. MLPA showed genomic deletions/duplications in only one of 6 patients (control group) in whom no mutation of SCN1A had been identified previously by direct DNA sequencing. The phenotype of patients with SCN1A mutation was characterized by a number of seizures ≥5 before one year of age ($p = 0.02$) and the presence of epileptic status ($p = 0.03$) with a

worse prognosis. Other clinical features (gender, seizure type, family history, mean age seizure onset) were not associated with the gene mutation.

Conclusion: These findings suggest that the seizure number and the presence of epilepticus status are associated to SCN1A gene mutation and represent negative prognostic factors in the natural history of patients with early complex febrile seizures. This phenotype-genotype correlation confirms the high sensitivity of genetic approach in the diagnosis of SMEI.

010
RISK FACTORS FOR SEIZURE PROGNOSIS IN MYOCLONIC-ASTATIC EPILEPSY

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Purpose: MAE is characterized by onset in early childhood, multiple seizure types and variable prognosis. Time course of remission and risk factors for prognosis are debated in literature, but until now concordant data is missing. Aim of study was evaluation of long term prognosis of syndrome, identifying risk factors predicting outcome.

Method: Sixteen patients with MAE were evaluated and followed for 4 years. In all cases detailed video EEG (including sleep and awake EEG) and MRI was performed. Follow up included evaluation once per year.

Results: Age at onset of MAE varied from 9 months to 3 years. Female/male ratio was 7/9. Myoclonic and/or myoclonic-astatic seizures were observed in all patients. Fourteen patients had more then 2 seizure types. Rare GTCS in12 patients, absences in 6, brief tonic seizures during sleep in 9, stupor like state or nonconvulsive status in 7, photosensitivity in 11. Stormy like onset was in 9 patients. Six patients evolved to MAE from West syndrome. After 1 year from onset remission of all seizure types was observed in 56%, after 4 years in 44%. Decline in IQ appeared in 31%. Stormy onset, initial resistance to treatment, number of seizure types, photosensitivity did not influence prognosis ($p < 0.01$). Predictors of unfavorable outcome (1) for seizures, evolution from West syndrome ($p < 0.05$), sleep tonic seizures ($p < 0.01$), early onset off syndrome, (2) for cognition, existence of nonconvulsive status

Conclusion: Evolution from West syndrome, tonic seizures in sleep are predictors of resistant seizures, nonconvulsive status leads to decline of IQ.

011
EPILEPTIC ENCEPHALOPATHY – SEIZURE AND DEVELOPMENTAL OUTCOME AFTER FUNCTIONAL HEMISPHEROTOMY

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Purpose: To evaluate prospectively the postoperative seizure and developmental outcome of children and adolescents with epileptic encephalopathies after functional hemispherotomy.

Method: Pre-/postoperative clinical, neurophysiological and neuropsychological data from pediatric patients with epileptic encephalopathies were collected prospectively. Patients were seen 6 months after surgery and then once per year. Seizure outcome was scored according to the criteria published by Wieser et al. (Epilepsia, 2001). Control visits included MRI, 48-hour video-EEG, clinical neurological and neuroopthalmological investigations and neuropsychological testing.

Results: Data from 28 children (11 girls; age at surgery: median: 6.0 years, range: 1 year–17 years) were analyzed for this report. Fourteen patients had perinatal strokes, 12 had cortical dysplasias, one patient had a hypothalamic harmartoma and one patient suffered from Rasmussen encephalitis. Postoperative follow-up was up to 11 years (median 2.0, range: 6 months–11.0 years). Twenty-three children were long time seizure-free after surgery. Thirteen patients showed a significant EEG improvement (especially with respect to continuous spike and wave during sleep). All these children were free of seizures, none of the children with continuous seizures showed an improvement in the EEG. Seizure freedom after surgery and improvement in the postoperative EEG were correlated with a neuropsychological progress. Results were best, but not statistically significant, in young children with perinatal stroke.

Conclusion: Functional hemispherotomy should be performed early in the course of drug-resistant epileptic encephalopathies to improve the neuropsychological development in children.

Epilepsy Surgery
Monday 28th June 2010
11:30–13:00

012
RADIOFREQUENCY THERMOCOAGULATION (RFTC) OF ICTAL ONSET ZONE BE MEANS OF STEREOELECTROENCEPHALOGRAPHIC (SEEG) ELECTRODES

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Purpose: To assess the outcome in refractory focal epilepsy patients treated by RFTC as a therapeutic option following SEEG evaluation for epilepsy surgery.

Method: The medical charts and video-SEEG-records of 13 patients (10 cryptogenic, 3 focal cortical dysplasia) treated by SEEG-guided RFTC were retrospectively reviewed. Two to 13 RFTC per patient were produced by applying 40–50 Volt, 75–110 mA current for 10–60 seconds on depth electrodes contacts within the ictal onset zone (IOZ) as established by SEEG. Follow-up ranged from 3 months to 9 years.

Results: Seven patients had left-sided, and 6 had right-sided focal epilepsy. In 8 cases the IOZ was located close to an eloquent area. A very restricted IOZ as established by SEEG was the main indication for proposing RTFC to 8 patients, in whom all seizures started on 2–4 electrode contacts. Only one patient became long-term seizure-free after RFTC of the left-sided ventral premotor cortex. An improvement was achieved in 3 additional patients, 2 of whom were seizure-free for 3 months after RTFC. Four patients were subsequently operated on, yet without significant benefit; 3 are awaiting surgery; 2 died from SUDEP and suicide, respectively.

Conclusion: Although small, our study confirms that RFTC remains less effective than the standard surgical procedures in refractory focal epilepsies. It should be an option for patients not eligible for resective surgery and whose IOZ is very restricted in space, yet further, especially

prospective studies are needed to better define RFTC indications and to optimize its methodology

013

THE TIMETOSTOP STUDY II. THE RELATION BETWEEN TIMING OF ANTIEPILEPTIC DRUG WITHDRAWAL AND SEIZURE RECURRENCE AFTER CHILDHOOD EPILEPSY SURGERY

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Purpose: Risks and benefits of early discontinuation of antiepileptic drugs (AEDs) after childhood epilepsy surgery are unknown. We investigated the relation between seizure outcome and timing of AED withdrawal, and identified independent preoperative or surgical predictors of unfavorable AED discontinuation.

Method: TimeToStop is an international multicenter retrospective cohort study of 759 children, operated between 2000 and 2008 in fifteen participating centers from eight countries, who reached postoperative seizure freedom and in whom AED reduction was started. Time intervals from surgery to start of AED withdrawal (I_start) and to complete discontinuation (I_stop) were related to seizure recurrences during or after withdrawal, and to eventual seizure outcome (Engel I), using Cox regression analysis. To this model we added previously published predictors for postoperative seizure outcome.

Results: Four hundred thirty-nine of 759 children completely stopped medication, 93 had seizure recurrences during or after AED withdrawal. At latest follow up, only 25 patients were not seizure-free. Shorter I_stop, but not I_start, was independently related to seizure recurrences after withdrawal, as were bilateral MRI abnormalities, and incomplete resection of the anatomical lesion ($p < 0.05$). I_start and I_stop did not affect eventual seizure freedom. The number of preoperative AEDs, left sided surgery, and incomplete resection of the structural lesion predicted seizure outcome.

Conclusion: Early start of AED withdrawal does not independently increase the risk of seizure recurrences. Early complete AED discontinuation predicts seizure recurrences but not eventual seizure outcome. Early AED withdrawal may unmask surgical failure, but not at the cost of permanent loss of seizure freedom.

014

EFFECTIVENESS OF NEUROSURGICAL TREATMENT FOR SEIZURE CONTROL IN PATIENTS WITH CEREBRAL ARTERIOVENOUS MALFORMATION

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Purpose: Assess the efficiency of different treatment options: microsurgical resection, endovascular embolization and Gamma knife surgery in controlling epileptic seizures in patients with cerebral AVM.

Method: Forty-four patients from 23 to 54 years old with symptomatic epilepsy caused by cerebral AVM were divided on 3 groups according to the applied type of neurosurgical treatment: 18 – underwent microsurgical resection, 12 – endovascular embolization and 14- Gamma knife irradiation. In all groups distribution of patients according to the age, duration of epilepsy, AVM's localization was almost similar. Postoperative follow up was from 1 to 6 years.

Results: Complete microsurgical excision of AVM performed in all 18 cases. Seizure-free observed in 4 patients, rare seizures had 5 patients. Worthwhile decrease was in 5, insignificant reduction – in 4 cases. Total endovascular embolization achieved in 2 cases. Epileptic fits stopped in 1 case, in 3 cases seizure's frequency reduced significantly, in 7 cases no changes was observed and 1 patient had seizures worsening. After Gamma knife treatment complete AVM obliteration achieved in 9 patients, two refused from control angiography. Seizure-free observed in 4 patients. In 5 cases seizure frequency reduced significantly, in 3 patients seizures worthwhile decreased and in 2 cases seizure frequency did not change.

Conclusion: Best seizure control in patients with cerebral AVM was achieved after open microsurgical excision or Gamma knife irradiation when malformation was completely eliminated. Management needs to be individualized to each patient and requires careful assessment of surgical risks and expectation of the positive results.

015

HYPERMOTOR SEIZURES IN PATIENTS WITH TEMPORAL LOBE EPILEPSY: A RETROSPECTIVE ANALYSIS OF CLINICAL FEATURES AND OUTCOME AFTER TEMPORAL LOBE RESECTION

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Purpose: Temporal lobe epilepsy (TLE) is usually associated with dialeptic seizure semiology. Hypermotor seizures are supposed to be unusual. Since we witnessed several patients with TLE and ictal hypermotor symptoms we retrospectively assessed the number, clinical findings and the seizure outcome in such patients who had undergone temporal lobe resection.

Methods: We reviewed medical history, video-EEG recording and neuroimaging of adult patients who underwent epilepsy surgery for temporal lobe epilepsy in the Kork Epilepsy Center over the last 20 years with a minimum postoperative follow-up of 12 month.

Results: Among 293 patients who were resected exclusively in the temporal region we identified 16 (5.5%) who presented with hypermotor semiology such as violent vocalization, complex movements of the proximal segments of the limbs, rotation of the trunk, pelvic thrusting, early tonic or dystonic posturing. Most of the patients had a preceding aura. Ictal EEG activity was located in the corresponding temporal region, usually with a wide distribution over anterior or posterior temporal electrodes with fast propagation to unilateral frontal electrodes and to the other side. Neuroimaging revealed extended lesions in the temporal lobe involving mesial and neocortical structures. Most of the patients underwent classical 2/3 temporal lobe resection plus amygdalo-hippocampectomy leading to seizure freedom. Histology showed mainly focal cortical dysplasia plus hippocampal sclerosis.

Conclusion: Hypermotor seizure semiology is no contradiction to the hypothesis of temporal lobe epilepsy when scalp EEG patterns and neuroimaging are corresponding. The seizure outcome is favorable.

016

THE POSTERIOR FACE OF HYPERMOTOR SEIZURES

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Introduction: Hypermotor seizures (HS) typically suggest a frontal lobe origin, but may be associated with a seizure onset zone (SOZ) involving

the temporal lobe or the insula. A single patient was reported to have HS of temporoparietal origin.

Method: We investigated four patients with drug-resistant cryptogenic HS whose stereoelectroencephalography (SEEG) investigation demonstrated a SOZ primarily involving the right (n = 2) or left (n = 2) posterior cortex (PC: posterior cingulate in 2, posterior perisylvian in 2). They all benefited from a videoEEG monitoring, a MRI, a FDG-PET. SEEG was repeated twice in two patients.

Result: While MRI was normal, FDG-PET showed a clear-cut focal hypometabolism over the PC in all patients. SEEG showed at seizure onset a low voltage fast activity originating within the PC hypometabolism area, and which was either asymptomatic or picted as an undefinable feeling. Hypermotor behavior was delayed by 10–25 seconds. Right perisylvian resection rendered one patient seizure-free (follow-up 7 months). In another case, seizures recurred afetr left cingulate surgery, maybe related to the occurrence of infectious complication and insufficient surgery in this right-handed patient. The two remaining patients are awaiting surgery. Pathological examination demonstrated typical features of focal cortical dysplasia in the two patients operated.

Conclusion: Identifying the SOZ in patients with cryptogenic HS is particularly difficult, due to the multiplicity of potential ictal generators. The delayed occurrence of hypermotor behavior seems to represent one reliable indicator of an extrafrontal SOZ, while FDG-PET coregistrated on MRI proved instrumental in all cases to suggest a PC origin.

017

LONG-TERM DEVELOPMENTS IN PRESURGICAL EVALUATION AND SURGICAL TREATMENT OF EPILEPSY AT ONE TERTIARY CENTER – PART II: SURGICAL OUTCOME

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Purpose: To assess changes over the period 1988–2008 in surgically treated epilepsy patients and their outcomes at a major epilepsy center.

Method: We analyzed all patients who underwent resective surgery after presurgical evaluation. Patients were classified by underlying pathology (histopathology/MRI). Data were analyzed by linear regressions to determine increases/decreases over the observation period in a year-wise fashion and were tested for significance ($p < 0.05$) with indication of the correlation coefficients (R).

Results: Resections were performed in 1703 patients. Most frequent diagnoses were: mediotemporal lobe epilepsy with ammon's horn sclerosis (MTLE-AHS), N = 593, i.e. 34.8% of all resected patients (+1.1%/year; R = 0.57); benign tumor, N = 369/21.7% (−1.0%/year; R = −0.70); nonlesional, N = 164/9.6% (change over time not significant [n.s.]); focal cortical dysplasia (FCD), N = 163/9.6% (+0.5%; R = 0.66). 74.7% of the presurgically evaluated MTLE-AHS patients finally underwent resective surgery (−1.5%/year; R = −0.76); benign tumors: 84.6% (−1.2%/year; R = −0.61); nonlesional 29.0% (−1.4%/year; R = −0.57); FCD 72.4% (n.s.). One thousand one hundred seventy-four patients were followed for ≥2 years (mean 5.6 ± 3.5 years); 563 were continuously and completely seizure-free since surgery, i.e. 48.0% (n.s); another 35 had auras only (3.1%); 143 patients were completely seizure-free during the last year of follow-up (12.6%). Rates of patients continuously and completely seizure-free: MTLE-AHS 48.2% (n.s.); benign tumors 60.2% (n.s.); nonlesional 23.4% (n.s.); FCD 55.3% (n.s).

Conclusion: Long-term seizure freedom rates have been stable over the last two decades, even though the proportion of patients with AHS and benign tumors proceeding to surgery is declining. This is an indicator of the growing number of ''difficult'' presurgical cases, even within these seemingly ''easy'' subgroups.

Neuroimaging I: Imaging progress in TLE and beyond
Monday 28th June 2010
11:30–13:00

018

BRAIN-WIDE SURVEY OF ANATOMICAL STRUCTURES AS CLASSIFIERS IN TEMPORAL LOBE EPILEPSY USING AUTOMATIC SEGMENTATION AND STRUCTURE SELECTION

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Purpose: To define the structures that can most effectively distinguish different groups of patients with temporal lobe epilepsy (TLE) from healthy controls.

Method: An automatic atlas-based segmentation method was performed to obtain volume measurements of 83 brain structures in 80 patients with TLE and 28 controls. An automatic structure selection method using a divergence measure based on the Kolmogorov distance was used to identify structures that distinguish patients from controls. Visual expert analysis showed hippocampal atrophy in 60 patients (pTLE) and normal MRIs in the remaining 20 (nTLE).

Results: Automatically identified distinguishing structure volumes were all significant at $p < 0.05$. In the pTLE group, mainly ipsilateral structures were identified, predominantly in the temporal lobe: hippocampus (23–25% volume loss); anterior temporal lobe (10–14%), parahippocampal gyri (4–7%); amygdala in pTLE_L (7%). Frontal lobe structures were medial orbital gyrus in pTLE_R (5%); anterior orbital gyrus in pTLE_L (12%); middle frontal gyrus in pTLE_R (5%). Other distinguishing structures were ipsilateral thalamus (5–8%) and cerebellum bilaterally (4–5%).In contrast, in the nTLE group, distinguishing structures were distributed throughout the brain with some predilection for the frontal lobes within the top ten, but no clear lateralization was evident. They included the substantia nigra (R & L) in nTLE_L (20–25%), the anterior TL (R) in nTLE_R (16%) and the amygdala (L) in nTLE_L (10%).

Conclusion: Using automated and reliable whole-brain segmentation and structure selection reveals and quantifies known structural abnormalities in pTLE. In addition, it detects previously unknown structural differences at the group level in pTLE and nTLE.

019

POLYMICROGYRIA: AN UNDERRECOGNIZED CAUSE OF EPILEPSY IN PATIENTS WITH HEREDITARY HEMORRHAGIC TELANGIECTASIA (RENDU-OSLER DISEASE)?

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Purpose: Experimental data suppport the hypothesis that impaired angiogenesis may lead to disorders of cortical development. Impaired angiogenesis is a hallmark of hereditary hemorrhagic telangiectasia (HHT). We observed focal areas of polymicrogyria at magnetic resonance imaging (MRI) in a patient with HHT. Polymicrogyria has been reported previously in the setting of other vascular dysplasias. We prospectively tested the hypothesis that HHT could be associated with malformations of the cerebral cortex.

Method: Patients with a definite diagnosis of HHT were prospectively included over a 8-year period. Patients underwent systematic MRI screening for intracranial vascular malformations. Screening for any disorder of cortical development was also performed using high-resolution MRI. Clinical and genetic evaluation was also obtained.

Results: One hundred fifty HHT patients were included. Ten had MRI evidence of polymicrogyria. Most HHT patients with epilepsy had areas of polymicrogyria at MRI. Areas of polymicrogyria were either focal or multifocal, uni or bilateral, and did not match with any previously recognized imaging pattern of heritable polymicrogyria. Polymicrogyria was associated with a high rate of intracranial vascular abnormalities, and with uncommon variants or dysplastic patterns of the cerebral arteries. Polymicrogyria was associated with epilepsy. Polymicrogyria was observed in both HHT types 1 and 2.

Conclusion: HHT was associated with a high rate of polymicrogyria.

020

ABNORMALITY OF THALAMIC SUBSTRUCTURE IN MESIAL TEMPORAL LOBE EPILEPSY ASSESSED USING NOVEL IMAGING METHODS

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Purpose: Although seizure onset in mesial temporal lobe epilepsy (mTLE) is in mesial temporal structures, evidence points to a widespread network of abnormalities. Volume loss and signal change in thalamus have been detected with MRI. Most methods previously have been unable to determine which thalamic nuclei may be predominantly affected. Here we implement recently developed imaging methods to undertake a ''virtual dissection'' of thalamus.

Methods: Eighteen normal subjects and 12 patients with mTLE were studied. All subjects underwent MRI acquisitions at 3T, including high-resolution T_1 and T_2 mapping and DTI. Firstly, each subject's thalamus was segmented into nuclear groups using a genetic algorithm to find clusters of relatively homogenous T_1 and T_2 signal corresponding to specific nulcear groups. Secondly, each subject's thalamus was segmented into nuclear groups using probablistic tractography, with each seed thalamic voxel being assigned to a cortical target region to which it was most likely to be connected. Thirdly, Canny filtering was applied to T_1 maps to detect boundaries between nuclear regions. Finally, SPM5 was used to compare T_1 and T_2 maps between normal subjects and mTLE.

Results: All methods successfully defined thalamic substructure reliably and reproducibly. Volume loss in the mTLE patients was most pronounced in mediodorsal and anterior nuclear goups, which were shown to be connected to temporal lobe. Increased T_2 signal was seen in these same regions and in ventral lateral region.

Conclusion: These new methods reliably define thalamic nuclear substructure, allowing differences between patients and normals to be ascribed to specific thalamic nuclei.

021

REORGANIZATION OF LANGUAGE IN TEMPORAL LOBE EPILEPSY AND PREDICTION OF EFFECTS OF TEMPORAL LOBE RESECTION

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Purpose: Anterior temporal lobe resection (ATLR) controls seizures in 70% of patients with intractable temporal lobe epilepsy (TLE) but, in the language dominant hemisphere, may impair language function, particularly naming. Functional reorganization can occur within the unaffected ipsilateral or contralateral hemisphere. We aimed to investigate whether preoperative functional MRI (fMRI) may predict naming decline following ATLR, and whether there was reorganization of language before and after ATLR.

Method: We scanned 25 healthy controls and 53 patients with unilateral mesial TLE (29 left) on a 3T GE-MRI scanner. All subjects performed language fMRI preoperatively. All patients underwent standard neuropsychological testing and repeat fMRI pre- and 4 months postoperatively.

Results: In controls and right TLE, better preoperative naming correlated with greater left frontal and left hippocampal fMRI activation with verbal fluency. In left TLE, naming correlated with greater right than left frontal activation and no such correlation was seen in the left hippocampus.

Greater preoperative fMRI activation in the dominant frontal lobe (FL) correlated with greater naming decline after ATLR. Postoperatively, greater fMRI activation in the nondominant FL correlated with higher postoperative naming scores.

Conclusion: Controls and right TLE patients show similar patterns of activation of left FL and hippocampus on verbal fluency. In left TLE, there was evidence for reorganization of naming function to the nondominant FL, in compensation for the diseased left fronto-temporal system preoperatively, and after dominant ATLR.

Preoperative language fMRI may be a useful predictor of postoperative naming deficits in patients undergoing ATLR in the dominant hemisphere.

022

RELIABILITY OF MRI FINDINGS IN TEMPORAL LOBE EPILEPSY ASSOCIATED WITH FOCAL CORTICAL DYSPLASIA

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Purpose: Focal cortical dysplasia (FCD) may be difficult to identify preoperatively. In temporal lobe epilepsy (TLE), some MRI characteristics of FCD cannot be unequivocally distinguished from other pathological changes or normal variations. Moreover, conclusion may vary among readers. Our aim was to test interrater variability in assessment of MRI findings in TLE associated with FCD.

Method: Three experienced epileptologists independently assessed MRI of 162 TLE patients (127 pts with histologically verified FCD or dual pathology, 35 pts with isolated hippocampal sclerosis). Investigators were aware of presence of pathology, but were not informed about the type and side. MRI scans were assessed in coronal FLAIR, T_1 and T_2, and axial T_1 and T_2. Following characteristics were evaluated extrahippocampally in both temporal lobes and labelled as present, absent or questionable: Abnormal gyral/sulcal pattern, Increased cortical thickness, Atrophy -regional reduction of white matter (WM) volume, WM T_2 signal increase. The presence of, and interrater agreement on each characteristic was assessed.

Results: There was relatively low agreement when assessing WM T_2 signal increase and atrophy, with full agreement in 67% and 57% respectively. However, these were the most frequently identified characteristics – 54% and 26% respectively. There was relatively higher agreement in assessment of abnormal gyral/sulcal pattern and increased cortical thickness. However, investigators fully agreed mostly on the absence of this finding.

Conclusion: This study indicates high interrater variability in assessment of subtle MRI characteristics in TLE patients with FCD. White matter T_2 signal increase was the most frequent and consistently identified MRI finding.

023

TEMPORAL LOBE FUNCTION IN FRONTAL LOBE EPILEPSY: AN FMRI STUDY OF LONG-TERM MEMORY IN FRONTAL LOBE EPILEPSY

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Background: A high degree of overlapping has been documented between the cognitive profiles of FLE and TLE patients. Cognitive and neuroimage studies have showed that TLE patients associate functional and structural abnormalities in their frontal lobes suggesting speeded damage to cortical areas beyond the epileptic focus. To our knowledge, no studies assessing the extension functional damage has been carried out on FLE population.

Purpose: To study the function of midtemporal lobe structures in FLE population using functional MRI and to evaluate long term memory function on our FLE population.

Method: We studied 33 FLE patients (18 with left and 15 with right epileptic foci) and 17 healthy volunteers using a memory encoding fMRI paradigm followed by a recognition test out of the scanner. Activation maps for the blocks of different stimuli and for the events successfully remembered where created with SPM5 software and compared between groups. Analysis of performance and neuropsychological evaluation was carried out.

Results: Maps of activation showed no differences on the activation of medial temporal structures between controls and FLE patients.FLE patients recruited wider areas of activation including bilateral mid frontal gyrus, perisylvian cortices and SMA during the presentation of to memorize items.

Conclusions: Activation of mid temporal structures during a memory tasks in a group of FLE is comparable to controls. A frontal epileptic focus seems not to disrupt activation of the inner temporal structures.

FLE patients recruit wider areas during the task suggesting a possible compensatory mechanism of the frontal lobe dysfunction.

Drug therapy: Pregnancy and AED adverse effects
Monday 28th June 2010
11:30–13:00

024

ADVERSE ANTIEPILEPTIC DRUG EFFECTS IN NEWLY-DIAGNOSED EPILEPSY: A CASE-CONTROL STUDY

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Purpose: Adverse effects (AEs) are a major concern for people starting antiepileptic drug (AED) treatment. We quantified the extent to which AE reporting in individuals with new-onset seizures started on AEDs is attributable to the medication *per se*, and evaluated which variables contribute to AE reporting.

Method: We conducted a pooled analysis, combining data from two large prospective studies: the Northern Manhattan study of incident unprovoked seizures and the Multicenter Study of Early Epilepsy and Single Seizures (MESS). Selection criteria included: age ≥16 years; history of ≥1 unprovoked seizures; and available Adverse Event Profile (AEP) data within 2 months of enrollment. Multivariate regression analyses compared AEP total and factor scores (modified from Perucca P et al., Neurology 2009;72:1223–1229) between subjects started on AEDs at enrollment (cases) and those in whom AEDs were withheld (controls), controlling for study, gender, age at seizure onset, seizure type, etiology, number of seizures, history of febrile seizures, and depression.

Results: We identified 223 cases and 203 controls. Most cases (95%) were taking a low AED dose. AEP scores did not differ significantly between the two groups. Depression was the strongest predictor of AEP total scores. The strongest predictors of AEP factor scores were: depression for Cognition/Coordination, Sleep and Tegument/Mucosa; symptomatic etiology for Mood/Emotion; history of febrile seizures for Cephalgia; and study for Weight.

Conclusion: When AED treatment is started at a low dose following new-onset seizures, AE reporting does not differ from untreated individuals. These findings will aid clinicians in better counseling regarding AED tolerability.

025

THE IMPACT OF ANTIEPILEPTIC POLYTHERAPY ON MOOD AND COGNITIVE FUNCTION

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Purpose: This retrospective study was performed to reevaluate the effect of polytherapy on mood and cognitive function and to separate it from the effect of a long refractory course of the disease by a multiple regression analysis.

Method: One hundred thirty-nine patients with refractory epilepsy were screened with a neuropsychological test battery and a depression score the day after admission to a specialized neuropsychiatric ward. The number or antiepileptic drugs taken on admission was recorded. Associations between several independent variables that best predict values of neuropsychological parameters were examined using multiple linear regression analysis.

Results: Our regression model with age at admission, duration of the disease and number of antiepileptic drugs as independent variables had a significant influence on 10 out of 11 neuropsychological parameters but not on depression. Looking at the significance of each predictor variable the number of antiepileptic drugs had a significant effect only on the estimation of the fluid intelligence. The standard error of regression coefficient was well above 50% of the regression coefficient itself for the other neuropsychological parameters. A significant effect on five neuropsychological parameters was found for the predictor variable duration of the disease.

Conclusion: So our data do not support the commonly reported hypothesis that antiepileptic polytherapy itself is a substantial risk factor for cognitive deficits or depression in patients with refractory epilepsy. But an accumulation of sedating drugs as part of a polytherapy may cause substantial cognitive problems.

026

DEVELOPMENTAL ABILITIES OF CHILDREN EXPOSED IN UTERO TO ANTIEPILEPTIC DRUGS: A COMPARISON BETWEEN SODIUM VALPROATE AND LEVETIRACETAM

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Purpose: The aim of the study was to compare the developmental outcome of children exposed in utero to sodium valproate (VPA) and levetiracetam (LVT).

Method: Children exposed to LVT (n = 49), VPA (n = 42) and control children (n = 46) were assessed for development by the Liverpool and Manchester Neurodevelopment group between 2003 and 2006. The children were all under the age of <24 months and completed the Griffiths Mental Development scale (1996), a standardized assessment of child development.

Results: On overall developmental ability children exposed to VPA differed significantly from both LVT ($p < 0.001$) exposed children and the control group ($p = 0.001$). LVT did not differ significantly from controls ($p = 1.0$).

Maternal IQ, social economic status, maternal epilepsy type, gestational age and age of child at assessment were all controlled for using a linear regression analysis. When compared with controls LVT exposure was not associated with overall developmental outcome ($p = 0.88$). When compared with LVT exposure, VPA exposure was negatively associated with overall developmental outcome ($p = 0.02$).

Conclusion: Children under the age of 2 years, exposed to LVT in utero did not differ from control children on developmental scores. When compared to LVT, VPA exposure is negatively associated with developmental outcome. The results support the notion that LVT may be a preferable alternative drug choice for WWE of childbearing age, in regards to cognitive developmental outcomes in the child. Caution is needed interpreting the preliminary results of this study due to the young age of the children.

027

PRESCHOOL BEHAVIORAL PROBLEMS AFTER PRENATAL EXPOSURE TO ANTIEPILEPTIC DRUGS: A FOLLOW-UP STUDY

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Purpose: To study the association between maternal epilepsy with or without antiepileptic drug (AED) treatment and behavioral problems in preschool children.

Method: A population-based cohort study based on the Danish National Birth Cohort, which stores information on mother's health, diseases, drug use during pregnancy, and potential confounders. We identified children (aged 4–5 years) prenatally exposed to their mothers' epilepsy, with (n = 133) or without (n = 304) AED treatment during pregnancy, and randomly selected peer children of mothers without epilepsy (n = 1,193). Children's behavioral development was assessed by use of the Strengths and Difficulties Questionnaire (SDQ), a five area questionnaire filled out by the parents. Questions on emotional, conduct, hyperactivity, peer, and prosocial behavior were scored as low (normal), middle or high, and combined to a total SDQ score.

Results: Questionnaires were returned by the parents of 828 (72%) unexposed children, 81 (64%) epilepsy and AED-exposed children, and 208 (70%) AED-unexposed children born to mothers with epilepsy. High total SDQ score was increased in AED-exposed children of mothers with epilepsy compared with unexposed children of women without epilepsy (odds ratio (OR) 4.8 (95% CI: 1.9–12.1)), and compared with AED-unexposed children of women with epilepsy (OR 4.0 (95% CI: 1.3–12.8)). OR of subarea high conduct score was increased in AED-exposed children compared with unexposed (OR 2.9 (95% CI: 1.4–5.9)), and compared with AED-unexposed children of women with epilepsy (OR 3.6 (95% CI: 1.5–8.7)).

Conclusion: AED exposure in prenatal life may increase the risk of behavioral problems in preschool children.

028

MALFORMATION RISKS AFTER MONOTHERAPY EXPOSURE TO ANTIEPILEPTIC DRUGS: FIRST REPORT FROM EURAP

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Purpose: The primary objective of EURAP is to evaluate the comparative risk of major congenital malformations (MCM) following intake of antiepileptic drugs (AEDs) during pregnancy.

Method: We analyzed pregnancy outcomes in the first 5,750 prospective pregnancies. The primary teratogenic end point was occurrence of MCM (EUROCAT criteria) at 12 months after birth. Chromosomal or genetic abnormalities (n = 43) were excluded from the present analysis, which focuses primarily on monotherapy exposures (n = 4,475).

Results: Of 5,707 pregnancies, 39 ended in induced abortions for fetal abnormalities, 43 perinatal deaths, 88 stillbirths, and 5,537 in live births. The MCM rate (95% CI) associated with monotherapy with lamotrigine was 2.9% (2.1–4.1), carbamazepine 5.7% (4.6–7.1), valproate 9.3% (7.6–11.3), phenobarbital 7.5% (4.6–12.0), other monotherapies combined 3.4% (2.2–5.3). A multivariate analysis, including 12 covariates in addition to type of treatment in the entire population, revealed that the risk of MCM was significantly associated with family history of MCM ($p < 0.0001$), family history of epilepsy ($p = 0.017$), folic acid use (higher with "appropriate use," $p = 0.040$), and with gender of offspring (higher in males, $p = 0.006$). Compared with lamotrigine monotherapy, MCM risks were significantly higher with: valproate, Odds Ratio (95%CI) 3.4 (2.1–5.7); phenobarbital, 2.7 (1.3–5.5); and carbamazepine, 2.1 (1.3–3.5).

Conclusion: Our results indicate that risk of MCM is influenced not only by type of AED, but also by other variables. Findings with individual AEDs should be interpreted cautiously because dose-effect relationships have not yet been analyzed.

029

MALFORMATION RISKS OF ANTIEPILEPTIC DRUGS (AEDS) IN PREGNANCY: AN UPDATE FROM THE UK EPILEPSY AND PREGNANCY REGISTER

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Purpose: To assess the relative risk of major congenital malformations (MCM) from exposure to AEDs during pregnancy.

Method: Fifteen year prospective observational registration and follow up study. Full outcome data were analyzed for exposures from 1996 through January 2009. The major outcome measure is the major congenital malformation (MCM) rate.

Results: Full outcome data was available for 6,225 cases. The risk of MCM was significantly higher in those women on AEDs during pregnancy (n = 5475) in comparison to those on no treatment (n = 445), RR:1.74 (95% CI 1.43–2.21), and significantly higher in those on polytherapy (n = 1199) than on montherapy (n = 4276), RR:1.72 (95% CI 1.30–2.27). The risk to those on valproate monotherapy was more than double that for those on either carbamazepine (RR:2.46,95% CI 1.64–3.69) or lamotrigene (RR:2.59,95% CI 1.72–3.91). Two hundred forty-one and 362 informative outcomes were obtained for topiramate and levetiracetam respectively,with corresponding MCM rates of 7.1%(95% C.I. 4.5–11.0%) and 2.5%(95% C.I. 1.3–4.7%). There were 3/79 (3.8%,95% CI 1.3–10.6%) cases of MCM in topiramate monotherapy and 14/162 (8.6%,95% CI 5.2–14.0%) cases in topiramate polytherapy. Four of the MCMs in the topiramate group were noted to be oral clefts. There were no cases of MCMs in levetiracetam monotherapy and 9/229 (3.9%,95% CI 2.1–7.3%) cases in levetiracetam polytherapy.

Conclusion: AED exposure during pregnancy increases the risk of MCM in the babies of women with epilepsy (RR 1.74,95% CI 1.43–2.12). Polytherapy exposure has a higher risk than that of monotherapy. Valproate exposure in mono- or polytherapy carries higher MCM risk than any other AED. Lowest risk is associated with carbamazepine or lamotrigene monotherapy. Results for levetiracetam, although numbers are small, look promising.

Epilepsy syndromes in adults
Tuesday 29th June 2010
11:30–13:00

030

REFLEX TRAITS IN JUVENILE MYOCLONIC EPILEPSY

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Purpose: Myoclonia is the hallmark of juvenile myoclonic epilepsy (JME) and may be sensitive to precipitant factors (PFs) such as sleep deprivation. Also higher mental activities as praxis, reading and calculating have been demonstrated as PFs of myoclonia in JME. Physiophatogenic mechanisms by which some of these factors induce seizures would be activation of specific cortical areas.

Method: To examine the effects of eye closure, hyperventilation, photic stimulation and higher mental activity as PFs of myoclonia in patients with JME, as demonstrated by a video-EEG neuropsychological protocol (VNPP). We included as reflex traits EEG discharges and/or seizures activation. A discharge index was defined as the number of discharges per recording time (number/minute) in each task divided by the number of discharges per recording time in awake EEG. Discharge indexes >2.0 were considered as activation.

Results: Eighty-six JME patients, treated and nontreated, with or without sleep deprivation, underwent VNPP. Forty two were females and 49 patients expressed reflex traits (57%). Praxis was the most effective activating factor seen in 28/86 patients (32.5%) followed by language tasks (reading and speaking) in 22 patients (25.5%), photosensitivity in 21 (24.4%), eye closure sensitivity in 17 (19.7%) and sensitivity to calculation in 5 (5.8%). Among sensitive patients, myoclonic seizures could be precipitated in 21/49 (42.8%) and more than one reflex trait was present in 32/49 (65.3%)

Conclusion: Reflex traits were found in a high proportion of JME patients. The association of more than one reflex trait in the same patient was frequent.

031

DIAGNOSIS OF EPILEPSY SYNDROME FOLLOWING A FIRST SEIZURE AND ITS CORRELATION WITH LONG-TERM FOLLOW-UP: LONGITUDINAL STUDY OF 132 PATIENTS FROM THE EMERGENCY ROOM

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Purpose: Evaluate the correlation between the diagnosis of epilepsy syndrome conducted in the emergency room (ER), supported by cranial CT and early EEG, and its correlation after long-term follow-up.

Method: Prospective study that included 132 adults who consulted consecutively for a fist seizure to the ER during 26 months. There was 55% of males, medium age 52.42 (±21.5)[16–98] years. Patients were included if a stereotyped paroxysmal event highly suggestive of an epileptic etiology was referred, without history of previous seizures. During the first 24 hours, patients performed cranial CT and EEG, being included into an epilepsy syndrome (ILAE 1989) if it was possible. They were referred to the Epilepsy Unit, reconsidering the diagnosis.

Results: Up to 57% of patients could be classified within an epilepsy syndrome (symptomatic focal epilepsy, 49 patients, cryptogenic focal epilepsy, 19 patients, and idiopathic generalized epilepsy, 6 patients). CT scanning detected abnormalities in 40% of cases (the most frequent pathology was cerebrovascular disease, followed by tumors). The PPV to identify patients with epilepsy was 78% and NPP was 47%. Early EEG showed epileptiform abnormalities in 41% of cases. PPV for EEG was 88% and NPP was 58%. During follow-up, diagnosis of epilepsy syndrome was confirmed in 94% of patients.

Conclusion: In a high percentage of patients it is possible to diagnose an epilepsy syndrome from the ER. Both cranial CT and early EEG demonstrated its usefulness evaluating the risk of recurrence; however, they should not be used to exclude the diagnosis of epilepsy.

032

ADULT-ONSET RASMUSSEN'S ENCEPHALITIS: THE CRUCIAL ROLE OF THE MESIOTEMPORAL-OPERCULAR-INSULAR NETWORK IN DETERMINING A COMMON ELECTROCLINICAL PATTERN

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Purpose: Rasmussen's Encephalitis is a rare immunomediate disorder characterized by unilateral hemispheric atrophy, drug-resistant epilepsy and progressive neurological deficits. Its onset is typically described during childhood but a wide spectrum of atypical features and variant forms including adult-onset RE (A-RE) have been reported. The aim of this study was to describe the electroclinical features in a group of seven A-RE patients.

Method: Our study included seven women aged 22–51 years (mean 32.5 years), with diagnosis of RE proposed according to commonly accepted diagnostic criteria (European Consensus Statement, 2005). All patients underwent prolonged Video-EEG monitoring, laboratory investigations and high resolution MRI follow-up. We analyzed electroclinical and neuroimaging findings and we revised the therapeutical options to better define this peculiar entity when occurring in adult life.

Results: The natural history of the disease in our population was characterized at onset by focal seizures at low frequency and symptoms of progressive hemispheric dysfunction. Patients progressively developed a drug-resistant focal epilepsy (simple or complex partial seizures, often recurring as status epilepticus). The ictal electroclinical semiology showed a typical evolution over the time in a monomorphic core characterized by vegetative/motor/somatosensitive signs reflecting, in all the cases, the involvement of perysilvian areas. Patients were treated with a combination of AEDs and immunotherapy (high-dose steroids and IVIg); epilepsy surgery was performed in 3 cases.

Conclusion: In our patients, A-RE showed a typical electroclinical pattern that reflects, especially in the "status phase," the progressive involvement of a specific network including mesiotemporal, opercular and insular structures.

033

THE GRENAT DATABASE: A NEW TOOL TO RECRUIT EPILEPTIC PATIENTS FOR MULTICENTRE CLINICAL TRIALS

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Always more studies concerning epilepsy are needed, requiring multicenter cooperation. However, establishment of large cohorts faces difficulties recruiting homogeneous groups of patients. Human networks exist but use homemade databases not compatible with one another.

We have developed a national french database of epileptic patients: the GRENAT database. Our strength is to offer, via a secured internet access (www.grenat.org), both an individual and a national database giving french physicians access to some selected datas issued from each individual database. We here report a descriptive analysis of the national data collected from GRENAT between December 2007 and December 2009: 4507 patients were included by 70 physicians in 27 centres evenly distributed through the country; 57.2% were children. Most epileptic syndromes are represented: symptomatic or probably symptomatic focal epilepsies (41.1%), idiopathic generalized epilepsies (15.5%), encephalopathies (12.7%), idiopathic partial epilepsy (7.3%), and unknown syndromes (17%). Etiologies of the nonidiopathic epilepsies are vascular origin (7.5%), cortical malformation (7.4%), acquired nonvascular (4.6%), inherited diseases (4.4%), tumor (3.2%) and neurocutaneous syndromes (2.1%). The distribution of syndromes and etiologies in our population is close to the epidemiological data from the literature. Therefore our database seems to be representative of the epileptic population. It allows us to perform longitudinal follow-up studies of epileptic patients. Moreover, the diversity of patients included in the database will facilitate the recruitment of patients for specific studies, especially for studies focusing on rare syndromes. GRENAT is therefore an original and powerful tool to promote clinical research in various fields concerning epilepsy.

034

DOES IT EXIST A SUBGROUP OF JUVENILE MYOCLONIC EPILEPSY PATIENTS WITH A SELF-LIMITED COURSE? SUPPORTING EVIDENCE FROM A LONG-TERM CLINICO-EEG STUDY

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Purpose: Juvenile myoclonic epilepsy (JME) is considered as an IGE syndrome with life-long duration. We aimed to explore the variability in the syndrome course and identify patients who can achieve long-term remission despite treatment discontinuation.

Method: We conducted a prospective study of all JME patients attending our epilepsy clinic. Included patients had a definite diagnosis of JME based on myoclonic jerks mainly on awakening (±GTCS and absences), EEG/Video-EEG recordings showing generalized 3–6Hz s-w discharges, normal intelligence and neuroimaging.

Results: There were 151 (98 women; 53 men) consecutive patients meeting the inclusion criteria for JME. Their mean ± SD age is 31.3 ± 9.8 (range: 15–72) years. Mean ± SD follow-up has been 6.6 ± 4.6 (range: 0.2–21) years, with 93 and 46 patients being followed for at least 10- and 5-years, respectively. The majority (137 patients) showed the typical course: good response to treatment (mainly valproate), and frequent seizure relapses due either to poor compliance or abnormal life-style. Six patients showed true drug-resistance (inadequate control despite AED combinations). Eight patients (5.3%) showed complete and prolonged seizure remission (of mean duration 12.8; range: 9–25 years), despite treatment discontinuation (after an average of 4.4 years from seizure freedom onset). Their mean age at seizure-

doi: 10.1111/j.1528-1167.2010.02658.x

cessation onset was 21.0 years. The characteristics of that group did not differ from those of the whole JME population.

Conclusion: A short, self-limited course may be seen in some JME patients, probably indicating a milder phenotypic expression. Some patients in this category probably remain undetectable because of the tendency to put JME patients under long-term treatment.

035
DEFINING THE AUTISM-EPILEPSY PHENOTYPE

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Purpose: Autism and epilepsy are common complex disorders which conservatively coexist in ~25–30% of cases. This study proposed to define an autism-epilepsy (AE) phenotype using unbiased empirical methods.

Method: Our overall dataset (N = 577) consisted of all cases of autism between the ages of 5–21 years; two subsets were identified from the overall dataset: (1) individuals >10 years of age (N = 280) and (2) individuals with autism and co-occurring seizures/epilepsy (N = 64). Latent Class Cluster Analysis (LCCA) was performed using 10 variables from the Autism Diagnostic Interview-Revised (ADI-R), Vineland Adaptive Behavior Scale (VABS), Aberrant Behavior Checklist-Community (ABC-C), and Repetitive Behavior Scales-Revised (RBS-R).

Results: LCCA of the overall dataset resulted in five distinct classes. One class showed a higher rate of seizures/epilepsy (~26%), earlier age of recognition of developmental problems, and higher frequencies of repetitive object use and unusual sensory interests. The age-restricted subset yielded four distinct classes. Again, one class showed a higher rate of seizures/epilepsy (44%), early recognition of developmental problems, and repetitive object use and unusual sensory interests. Finally, three distinct classes emerged from autism with co-occurring seizure/epilepsy dataset. The largest class (N = 47) was characterized by low developmental level and a higher rate of language impairment.

Conclusion: LCCA in an autism dataset revealed small but distinct classes characterized by seizures/epilepsy, early recognition of developmental problems, and both repetitive and sensory behaviors. Within an autism-epilepsy subset, developmental level and language impairment were salient features. Our results suggest potential new directions to consider in defining an autism epilepsy phenotype.

Clinical epileptology
Tuesday 29th June 2010
11:30–13:00

036
FREQUENCY OF CARDIAC SYMPTOMS IN A SWEDISH PATIENT POPULATION WITH EPILEPSY

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Purpose: Sudden unexpected death in epilepsy (SUDEP) is an uncommon but feared complication. Several theories have been proposed to explain this phenomenon which mostly affects young patients with refractory epilepsy. Ictal central apnea and cardioarrhythmia are the most believed theories. Our interest in SUDEP generated the following study.

Material: Medical records were collected using a list of outpatients admitted to the clinic of Neurology, Linköping University Hospital before the end of October 2005. Two hundred medical records were analyzed according to frequency of cardiac symptoms and ECG abnormalities.

Method: A quantitative retrospective epidemiological analysis of medical records was done. Medical files were screened for cardiac and ECG abnormalities and symptoms.

Results: The evaluation showed that cardiac symptoms and ECG abnormalities were registered for 3 out of 10 patients. In the group of patients over 60 years of age, 60% had cardiac symptoms/ECG abnormalities. In this category, most heart symptoms were thought not to be epilepsy related. In the cohort between 40 and 60 years of age, 23% had heart symptoms whereas among patients below 40 years of age, 12% had symptoms.

Conclusion: In this study we made an inventory of cardiac symptoms and ECG abnormalities among epileptics of different ages. This inventory study describes the situation locally and provides a starting point for further studies. We plan to stratify the material according to risk factors like polytherapy, high seizure frequency, and early onset of epilepsy. Further knowledge of cardiac manifestations in epilepsy is needed and may help in the prevention of SUDEP.

037
EEG PATTERNS IN NONCONVULSIVE STATUS EPILEPTICUS ON THE INTENSIVE CARE UNIT

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Purpose: To analyze EEG characteristics in patients with nonconvulsive status epilepticus (NCSE) admitted to intensive care unit (ICU) and to evaluate the etiology, the history of epilepsy, the clinical presentation, the therapy and the hospital outcome.

Method: We reviewed retrospectively the EEGs performed on 37 adult patients in the ICU with NCSE, of 3001 patients admitted from January 2003 to December 2008.

Results: Thirty-seven patients (1.2%) were found to have NCSE. EEG demonstrated focal or lateralized epileptiform discharges in 24 patients (64.9%): in 14 rhythmic sharp-waves, in 2 repetitive spikes, in 8 PLEDs. In 13 patients (35.%) EEG showed generalized or bilateral epileptiform discharges: in 7 rhythmic sharp-waves, in 1 repetitive spikes, in 5 rhythmic delta with intermittent spikes. Encephalitis was the most frequent etiology of NCSE in our population (21.6%). The largest group of patients (81.1%) had no previous diagnosis of epilepsy. The majority of the patients (56.8%) had isolated seizures or convulsive status epilepticus prior to the onset of NCSE. Twenty-six (70.3%) of the patients were comatose, while 11(29.7%) of the patients were obtunded or confused. All patients were treated with intravenous anticonvulsants, mostly PHT and MDZ. Four patients (10.8%) died of their underlying illness, and 33 (89.2%) patients survived to discharge. Hospital outcome was not related to specific EEG patterns.

Conclusion: On the basis of EEG, NCSE in patients on the ICU may be classified as generalized or lateralized. Prognosis of NCSE appears to be more related to underlying conditions rather than to EEG patterns.

038
EPILEPSY IN ANCIENT GREECE: FROM A SUPERSTITION TO A DISEASE

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Introduction: In ancient Greece people considered diseases and sickness including epilepsy, as acts or invasions by the gods, demons, or evil spirits. These were treated by the invocation of supposedly supernatural powers which witch doctors, faith healers, charlatans and quacks claimed they had. Hippocrates, who was born in Dodecanese in 460 BC, began a ''war'' against these ''magicians'' and revealed in his book, *The Sacred Disease,* that epilepsy is a medical illness which is caused by a disorder of the brain.

Aim: The main aim of this study is to collect all the information and historical sources in which epilepsy had passed from a considerate superstition to a well-explained disease in ancient Greece.

Methods: A critical literature appraisal was undertaken. Key words included: epilepsy, ancient Greece, and a thorough PubMed search revealed 28 papers. Only 22 were included for analysis as 2 were ahead offprint and 4 could not be located.

Results: Through close perusal of books by Hippocrates and his scholars, it is clear that he was the first doctor who claimed that epilepsy is an actual disease rather some supernatural condition. He also explained accurately the signs and symptoms, nature of and appropriate therapies of the time for the ''sacred disease'' as it was called.

Conclusions: Epilepsy from the very beginning connotes the constant struggle ongoing by the scientific-thinking people against superstition, foolishness and shameless quackery.

039
A NURSE-LED CLINIC FOR ADULTS WITH EPILEPSY AND LEARNING DISABILITY EXPERIENCING PROLONGED AND/OR REPEATED TONIC–CLONIC SEIZURES IN THE COMMUNITY TO REDUCE RISK OF STATUS EPILEPTICUS AND THE RISK OF SUDDEN UNEXPECTED DEATH IN EPILEPSY (SUDEP)

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Purpose: The National Sentinel Clinical Audit of Epilepsy-Related Deaths (2002) found 54% of adults with epilepsy received inadequate care premortem in the United Kingdom. Deficiencies include poor risk assessment, care planning and information provision. A nurse-led clinic for adults with epilepsy and learning disability supported by Community Learning Disability Nurses was established to address these deficiencies. A rescue drug and treatment care plan was given to patients who had experienced a prolonged (>5 minutes) tonic–clonic seizure and/or a cluster of 3 tonic–clonic seizures within one hour as recommended by NICE (2004).

Method: Questionnaire was given to the patient and their family/carers attending the clinic to evaluate effectiveness of the service and the use of the rescue treatment care plans over the previous six months.

Results: 70 (100%) completed the questionnaire. Forty-seven had a Buccal Midazolam Care Plan and 7 had Rectal Diazepam Care Plan to prevent Status Epilepticus. Fifty-one experienced tonic–clonic seizures. Twenty-five experienced tonic–clonic seizure lasting >5 minutes, 12 had 3 tonic–clonic seizure within 1 hour. Eight said that the rescue drug did not stop the seizure within ten minutes and called emergency services.

Conclusion: The risk of status epilepticus is reduced by rescue treatment care plans the community.

References: Hanna et al. (2002) National Sentinel Clinical Audit of Epilepsy-related Death: Epilepsy Death in the Shadows. The Stationary Office, London National Institute for Clinical excellence (2004) The Epilepsies Diagnosis and Management of the Epilepsies in adults and Children in Primary care. Clinical Guideline 20, NICE London.

040
LATE-ONSET TEMPORAL LOBE EPILEPSY WITH POSITIVE ANTITHYROID ANTIBODIES: IS IT AN AUTOIMMUNE EPILEPSY?

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Purpose: In a third of late-onset temporal lobe epileptic (LTE) patients, the etiology remains unknown. Many antibodies have been associated to focal epilepsy like antibodies to voltage-gated potassium channels(VGKC) in limbic encephalitis or anti decarboxilase of glutamic acid antibodies (antiGAD). One study conducted in LTE with mesial sclerosis (HS) also suggest that up to 50% of these patients can have an immune etiology. Some patients with LTE together with memory decline and obscure etiology have elevated antithyroid antibodies(AntiT+). Our purpose is to describe the clinical phenotype of LTE-AntiT+, as well as corticotherapy response in the pharmacoresistant group.

Method: Immunological basic study was done to LTE patients with unknown etiology (n = 36). Late onset was considered up to thirty years. Among them, patients with AntiT+ were selected: antithyroglobulin antibodies(antiTr) and antiiodur peroxidase antibodies(antiTPO) values >80 UI/ml regarded as positive. Neuropsychological tests were realized in all patients.

Results: Eight patients with LTE-AntiT+ were included: 6 women (75%), 2 men. AntiTPO:median 493 (101–1871) and antiTr:median 214'5 (83–3338). Age at epilepsy onset 43–75 years (SD64'25), mean evolution time 9.38 years (3–20). Three (37%) were seizure-free. HS was observed in 2 (25%), subclinical hypothyroidism in 4 (50%) and other autoimmune diseases in 3 (37%). Important memory deficits in 4 (50%). Corticoid treatment (60 mg/day 1 month, 30 mg/day maintenance) has begun in 3 of 4 pharmacoresistant patients', with seizure frequency decrease and memory improvement after 6 months.

Conclusion: (1) The clinical phenotype of LTE-AntiT+ is a middle aged woman, with a nonpharmacoresistant epilepsy with cognitive decline and associated autoimmune diseases. (2) Corticotherapy has to be considered in the pharmacoresistant subgroup.

041
LATE-ONSET EPILEPSY, MILD COGNITIVE IMPAIRMENT AND ANTI–VOLTAGE-GATED POTASSIUM (VGKC) ANTIBODIES: AN OBSERVATIONAL STUDY ON THE EFFECTS OF AN ORAL PREDNISOLONE COURSE

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Purpose: Voltage-gated potassium (VGKC) autoimmunity may present with late-onset epilepsy and cognitive impairment. Immunotherapy seems effective in patients with a (sub)acute VGKC encephalopathy.[1] In this study we evaluated the effects of oral prednisolone in patients with a chronic presentation.

Methods: We identified four cases with late-onset focal epilepsy (range: 58–72 years; temporal lobe n = 3; frontal lobe n = 1), mild cognitive impairment (MMSE 24–28), high values of VGKC-antibodies (576–3246 pmol/L) and a chronic symptom onset (>6 months). All patients remained seizure-free on one AED. None of the cases had evidence for neoplasia or neuromyotonia. Hyponatremia was documented in 2 patients. Two patients had evidence for bilateral hippocampal atrophy and signal change.

Results: Spontaneous clinical remission in parallel with a fall in VGKC-antibodies was noted in one patient 11 months after symptom onset. The remaining 3 patients with persisting symptoms 12–32 months after disease onset were treated with oral prednisolone (starting dosage 60 mg/day for 1 month, followed by dose tapering for 3 months). Two patients showed a marked clinical improvement together with a 65–95% reduction of VGKC-antibody levels following immunosuppressive therapy. In one patient a moderate but transient improvement was seen. The lack of a sustained response in this patient might be explained by the shortening of the prednisolone course due to delirium.

Conclusion: Oral prednisolone seems an effective treatment for VGKC encephalopathy even when started >1 year after disease onset. However, further controlled trials are needed to confirm these findings.

1. Vincent A, et al. Brain. 2004;127:701–12.

Clinical Trials
Tuesday 29th June 2010
11:30–13:00

042
RETIGABINE PROVIDES EFFECTIVE ADJUNCTIVE THERAPY IN ADULTS WITH REFRACTORY EPILEPSY WITH PARTIAL-ONSET SEIZURES, IRRESPECTIVE OF AGE, GENDER AND RACE

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Purpose: To assess the efficacy of retigabine, a first-in-class antiepileptic drug (AED) that enhances the activity of KCNQ (Kv7) potassium channels, by age, gender and race.

Method: RESTORE 1/2 (NCT00232596/NCT00235755) were multicenter, randomized, double-blind, placebo-controlled, parallel-group Phase III trials in adults with refractory epilepsy, ≥4 partial-onset seizures/28 days, receiving 1–3 AEDs, with/without vagus nerve stimulator. Patients underwent forced-titration to retigabine or placebo (t.i.d.), to 600 or 900 mg/day (RESTORE 2), or 1200 mg/day (RESTORE 1), followed by 12 weeks' maintenance. Responder rate (≥50% reduction in baseline seizure frequency) in maintenance phase and change in total partial-seizure frequency/28-days from baseline to double-blind period were analyzed by age group/gender/race (RESTORE 1) and age group/gender (RESTORE 2: >95% white/Caucasian).

Results: Patient disposition: RESTORE 1 placebo = 152, 1200 mg/day = 153; RESTORE 2 placebo = 179; 600 mg/day = 181; 900 mg/day = 178. Age, gender and race distribution were similar across treatments. Responder rates by age group (≤44, >44 years) RESTORE 1: placebo 25%, 16%; 1200 mg/day 52% ($p < 0.001$), 64% ($p < 0.001$); RESTORE 2: placebo 19%, 20%; 600 mg/day 41% ($p < 0.001$), 33% ($p = 0.149$); 900 mg/day 46% ($p < 0.001$), 50% ($p = 0.002$); gender (male, female) RESTORE 1: placebo 21%, 24%; 1200 mg/day 50% ($p < 0.001$), 60% ($p < 0.001$); RESTORE 2: placebo 19%, 19%; 600 mg/day 39% ($p = 0.007$), 38% ($p = 0.007$); 900 mg/day 38% ($p = 0.005$), 57% ($p < 0.001$); and race (white/Caucasian, Hispanic, other) in RESTORE 1: placebo 22%, 30%, 9%; 1200 mg/day 50% ($p < 0.001$), 73% ($p < 0.001$), 44% ($p = 0.021$). Similarly, retigabine reduced total partial-seizure frequency/28-days in all subgroups. There was no significant treatment interaction by age, gender or race at the retigabine doses tested.

Conclusion: Retigabine was more effective than placebo in all age, gender and race subgroups.

043
EFFICACY, SAFETY, AND TOLERABILITY OF CARISBAMATE 800 AND 1200 MG/DAY AS ADJUNCTIVE THERAPY IN PATIENTS WITH PARTIAL ONSET SEIZURES; RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Purpose: The efficacy and tolerability of 400 mg/day of carisbamate as adjunctive treatment of partial onset seizures (POS) is supported by results from randomized placebo-controlled studies. In this randomized, double-blind, placebo-controlled, multicenter study (October 2008–November 2009), we assess efficacy, safety, and tolerability of carisbamate 800 mg/day and 1200 mg/day in patients with POS.

Methods: Patients 16 years of age or older with an established diagnosis of POS for 1 year or more and uncontrolled on 1–3 antiepileptic drugs were enrolled. Eligible patients remained on stable doses of prescribed antiepileptic drugs (≤3) for an 8-week pretreatment phase, then were randomized (1:1:1) to receive carisbamate (800 mg/day or 1200 mg/day) or placebo, for a 14-week double-blind phase (including a 2-week titration period). Safety assessments included adverse events, laboratory tests, and ECGs.

Results: Patients (N = 547) were: 37 (12.2) (mean [SD]) years; 53% white and 43% Asian. The combined carisbamate dose groups did not separate from placebo for either the median percent reduction of POS seizure frequency from baseline ($p = 0.20$; primary measure) or responder rates (proportion of patients with ≥50% reduction in POS frequency)($p = 0.18$). Median percent reductions were 20.6 (placebo), 29.9 (800 mg/day), and 36.3 (1200 mg/day). Dizziness was the most common (≥5% difference) treatment-emergent AE in the total carisbamate group (31%) versus placebo (9%).

Conclusion: Carisbamate used as adjunctive therapy for patients with partial onset seizure did not demonstrate efficacy in this study compared with placebo. No new safety findings were observed.

Funding: Study funded by Johnson & Johnson Pharmaceutical Research & Development, LLC.

Acknowledgments: RWJ-333369 (S-2-O-carbamoyl-1-*o*-chlorophenyl-ethanol; carisbamate) is a novel neurotherapeutic agent, initially developed by SK Biopharmaceuticals. Wendy P. Battisti, PhD provided

(of Johnson & Johnson Pharmaceutical Research & Development, L.L.C) writing and editorial assistance.

044

LEVETIRACETAM MONOTHERAPY: OUTCOMES FROM AN EPILEPSY CLINIC

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Purpose: This retrospective audit explores outcomes in patients commenced on levetiracetam (LEV) monotherapy at the Western Infirmary, Glasgow, Scotland.

Method: LEV monotherapy was started in 228 patients (89 men, 139 women, aged 12–81 years [median 28 years]). LEV was prescribed as first AED in 149 (65.4%); 79 (34.6%) were switched to the drug from another AED because of lack of efficacy or side effects.

Results: In total, 112 (49.1%) patients have been seizure-free for ≥1 year on a median LEV dose of 1000 mg/day (range 500–3000 mg/day). Seizure freedom was more likely with LEV as a first monotherapy (81 of 149 [54.4%]), as opposed to switching from another AED (31 of 79 [39.2%]; p = 0.03). More patients became seizure-free with LEV after failing their 1st or 2nd AED (n = 39 of 64 [60.9%]), compared to later in the treatment schedule (n = 2 of 15 [13.3%]; p = 0.029). Patients with <5 seizures were more likely to become seizure-free than those with ≥5 seizures (p = 0.008). LEV was withdrawn in 37 (16.2%) patients (30 side effects, 7 lack of efficacy) at a median dose of 1000 mg/day (range 250 mg/day–3000 mg/day). The most common reasons for poor tolerability (n = 18, 7.9%) were neuropsychiactric side effects (7 aggression, 5 irritability, 4 mood swings, 2 depression). Other problems leading to LEV withdrawal were sedation (n = 7), nausea (n = 3), dizziness and headache (1 each).

Conclusion: Seizure freedom was achieved in around half the patients on a median LEV dose of 1000 mg/day. Over 50% of patients who stopped LEV due to side effects reported neuropsychiatric symptoms.

045

LONG-TERM EFFICACY OF LACOSAMIDE FOR PARTIAL-ONSET SEIZURES: AN INTERIM EVALUATION OF COMPLETER COHORTS EXPOSED TO LACOSAMIDE FOR UP TO 5 YEARS

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Purpose: Evaluation of sustained efficacy in long-term trials of antiepileptic drugs is confounded by patient dropout, often resulting in the appearance of progressive improvement over time as nonresponders drop-out of the trial. This analysis examined long-term efficacy of lacosamide in patient cohorts completing successively longer durations of lacosamide exposure in Phase II-III double-blind and/or open-label extension trials.

Method: Pooled data for lacosamide-treated patients in completed double-blind trials and/or corresponding open-label trials were used. For each cohort completing successively longer durations (1–5 years), data from the first day of lacosamide exposure to the cutoff date for the interim analysis (07-April-2008) were included. Efficacy end points included percent change in seizure frequency per 28 days and 50% responder rates from baseline to the cohort time interval of interest.

Results: A total of 1,327 patients were exposed to lacosamide in double-blind and/or OL trials. Median percent reduction in seizure frequency for the first 3 months of treatment was 45.5%, 50.0%, and 48.2% for the 1(n = 853), 3(n = 384), and 5-year (n = 67) cohorts, respectively. These results appeared to be sustained as the corresponding median percent reduction for the last 3 months of treatment was 52.4%, 72.7%, and 71.8%. Similarly, the proportion of ≥50% responders compared to baseline was sustained over subsequent time points in each cohort, ranging from 45.0–50.3% across cohorts for the first 3 months of treatment compared with 51.8–70.6% for the last 3 months.

Conclusion: Lacosamide produced long-term, sustained efficacy in cohorts of patients with partial-onset seizures who completed 1–5 years of treatment.

046

TOLERABILITY OF ESLICARBAZEPINE ACETATE BY TREATMENT PHASE IN ADULTS WITH REFRACTORY PARTIAL SEIZURES: A COMBINED ANALYSIS OF THREE RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIALS

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Purpose: To assess the tolerability of adjunctive eslicarbazepine acetate (ESL) in adults with refractory partial seizures, by treatment phase (titration, maintenance, tapering off).

Method: A combined analysis of three Phase III trials of adjunctive ESL therapy in adults with refractory partial seizures was conducted. Patients were randomized to 14 weeks' double-blind treatment (2 weeks' titration, 12 weeks' maintenance) with placebo (n = 290) or ESL 400 (n = 196), 800 (n = 284) and 1200 (n = 280) mg/day, followed by a 4-week tapering-off period (two studies only). Tolerability during titration, maintenance and tapering off was assessed by evaluating discontinuation rates and treatment-emergent adverse events (TEAEs).

Results: Discontinuation rates (any reason) for placebo and ESL 400, 800 and 1200 mg/day were 1.4%, 1.0%, 4.9% and 6.1% during titration, 7.3%, 7.1%, 8.1% and 18.6% during maintenance, and 2.1%, 1.5%, 1.1% and 0.4% during tapering off, respectively. Discontinuation rates due to TEAEs were 0.3%, 0.5%, 4.2% and 3.2% during titration, and 1.0%, 4.6%, 4.2% and 11.4% during maintenance, respectively; no patients withdrew due to TEAEs during tapering off. Overall rates of serious TEAEs were 1.4%, 4.6%, 3.5% and 3.2%, respectively. During each treatment phase, the most frequently reported TEAEs (ESL and placebo) were dizziness, somnolence, headache and nausea. Most TEAEs occurred early on during treatment.

Conclusion: Adjunctive ESL was well tolerated throughout all treatment phases. Discontinuation rates were dose-related, but rates of serious TEAEs were low and not dose-related. Discontinuation due to TEAEs during titration was low, despite a relatively short titration period.

These studies were supported by BIAL and the abstract by Eisai.

047

REPORTING OF ADVERSE EVENTS IS POOR IN EPILEPSY TRIALS AND HAS NOT IMPROVED FOLLOWING CONSORT GUIDANCE

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Purpose: To evaluate the quality of reporting adverse events (AE) in relation to antiepileptic drugs (AEDs) using the CONSORT guidelines 2004. To determine if reporting has improved since 2004.

Method: We searched MEDLINE for terms: ''epilepsy,'' ''antiepileptic drug,'' and ''seizure'' for trials published between 1999 and 2008. Data collected included: Journal, year of publication, funding source and data for 24 criteria from the CONSORT recommendations. Data were extracted independently by two reviewers. Results for industry versus non–industry sponsored trails were compared.

Results: One hundred fifty RCTs met our inclusion criteria. Ninety four were industry sponsored and 56 were non–industry sponsored. None met all 24 criteria. The median number of criteria met was 12 (range 0–23). Industry sponsored trials fared better than non–industry sponsored studies (Mean 12.5 vs. 9.0 $p \leq 0.001$). Analysis showed heterogeneity in adherence with poor adherence in: use of a validated dictionary (297% industry sponsored studies vs. 9% nonindustry studies); use of a validated instrument for recording adverse events (18% industry vs. 14% nonindustry) and recording of recurrent adverse events (7% industry vs. 4% nonindustry).

Reporting has not changed post publication of the guidelines (Mean 11.5 prepublication vs. 11 postpublication). Studies recruiting adults fared better than studies recruiting children (Mean 14 vs. 10.0 $p = < 0.001$).

Conclusion: Overall adverse event reporting remains poor with there being no change its quality since 2004. Industry sponsored trials report AE better possibly owing to access to better funds. Trials recruiting children report AE poorly compared with adults.

Neuroimaging II
Tuesday 29th June 2010
11:30–13:00

048
MEMORY DEFICITS ARE RELATED TO DISTURBANCE OF PREFRONTAL NETWORKS RATHER THAN HIPPOCAMPAL DYSFUNCTION IN CRYPTOGENIC LOCALIZATION-RELATED EPILEPSY

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Purpose: Memory impairment is frequently reported in patients with epilepsy. For memory deficits many studies have focused on the mesiotemporal lobe, but recent investigations have suggested that prefrontal networks are important for cognitive functioning too. To investigate the neuronal correlates of memory dysfunction in patients without structural lesions, we studied neurocognitive assessment, hippocampal volumetry and functional MRI of memory networks.

Method: Thirty-six patients with cryptogenic localization-related epilepsy and 21 healthy controls underwent IQ and memory assessment. Hippocampal volumetry and fMRI (at 3T) with picture-encoding and Sternberg-paradigms were performed. Functional connectivity analysis consisted of cross-correlation of signal time-series of the prefrontal and temporal regions.

Results: Patients performed worse than controls on all neurocognitive tests: IQ, digit-symbol substitution test (DSST), digit span, word and figure recognition ($p \leq 0.02$). This could not be related to differences of hippocampal volume or in functional activation. Decreased memory performance in patients was reflected in reduced strength of four prefrontal connections involving anterior cingulate, middle frontal and inferior frontal gyri, which correlated with DSST ($p \leq 0.04$) and word recognition ($p < 0.04$).

Conclusion: We hypothesize that memory deficits in localization-related epilepsy of both temporal and extratemporal origin cannot be attributed to hippocampal atrophy or function only, but are related to prefrontal network connectivity. As patients with symptomatic lesions or mesiotemporal sclerosis were excluded, the memory deficits cannot be attributed to detectable structural lesions. Therefore, these findings highlight the influence of epilepsy per se on the prefrontal network integrity, which may be an important factor for memory impairment in these patients.

049
HIPPOCAMPAL DEEP BRAIN STIMULATION REVEALS DECREASED rCBF IN THE HIPPOCAMPUS OF THE RAT: A μSPECT study

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Purpose: Deep Brain Stimulation (DBS) is a promising experimental approach to treat various neurological disorders. Neuro-imaging by means of Single Photon Emission Computed Tomography (SPECT) is a noninvasive manner of evaluating regional cerebral blood flow (rCBF) changes, which are assumed to reflect changes in neural activity. In this study, rCBF changes induced by different stimulation paradigms and amplitudes of hippocampal DBS were evaluated by means of subtraction analysis following small animal SPECT in the rat brain.

Method: Rats (n = 13) were implanted with a multicontact DBS electrode in the right hippocampus. Rats received 10mCi HMPAO-$Tc99^m$ during sham stimulation and during application of several hippocampal DBS paradigms and amplitudes. Consequently, μSPECT scans of the brain were manually coregistered with 3T-MRI images of the same rat. Coregistered images were evaluated by means of subtraction analysis between sham stimulation and during application of DBS.

Results: Hippocampal DBS caused a signficant decrease in relative rCBF, both in the ipsi- and contralateral hippocampus. A clear distinction in spatial extent and intensity of hypoperfusion could be observed between the different stimulation paradigms and amplitudes.

Conclusion: Small animal SPECT allows us to draw conclusions on the location, the spatial extent and the intensity of the rCBF changes induced by hippocampal DBS. Depending on the stimulation paradigm and amplitude, significant hypoperfusion was observed in the ipsi- and contralateral hippocampus. Our study demonstrates a new and innovative approach to visualize the effects of DBS and can be a useful tool in evaluating different stimulation paradigms and target areas.

050
THE EFFECT OF METHYLPHENIDATE ON N-BACK TASK PERFORMANCE IN BOYS WITH EPILEPSY / AND OR ADHD: A BEHAVIORAL AND FUNCTIONAL MRI STUDY

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Purpose: Approximately 1/3 of children with epilepsy also suffer from attention deficit/hyperactivity disorder (ADHD), which often includes deficits in working memory. Methylphenidate (MPH) can improve the behavioral difficulties in children with ADHD. However, it is not yet clear whether there are specific neurobehavioral differences between children with combined epilepsy/ADHD and children with developmental

ADHD and whether MPH shows comparable neurofunctional effects in working memory task-induced brain activation in both patient groups.

Method: Eleven boys with diagnosed epilepsy/ADHD, 14 boys with behavioral ADHD and 12 healthy controls (aged 9–14 years) were investigated using fMRI; once with medication and once without. In order to measure working memory performance, the popular N-back paradigm was used and scans were recorded on a 3T human head scanner.

Results: Healthy controls performed significantly better than both patient groups without medication, whereas patients' performance improved to normal after the intake of MPH. On the functional level healthy controls showed more activation in frontal, parietal and cerebellar regions than both patient groups. Within the patient groups there was no enhanced activation detectable due to medication.

Conclusion: These data indicate a clear effect of MPH on a behavioral level. However, this effect is not reflected by changes in functional brain organization. In contrast to healthy controls, patients showed decreased activation during N-back tasks in both conditions. Due to the behavioral and functional similarities of the two patient groups, data indicate that the neurobehavioral dysfunctions of working memory are comparable in children with epilepsy and/or ADHD.

051

CHANGES IN RESTING-STATE CONNECTIVITY AFTER EXPERIMENTAL HEMISPHERECTOMY REFLECT FUNCTIONAL REORGANIZATION AND NETWORK ALTERATIONS

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Purpose: Hemispherectomy is a last resort treatment for catastrophic hemispheric epilepsy. The remarkable motor recovery after hemispherectomy reflects the plastic capacities of the brain. Graph theoretical analysis of brain networks improves our understanding of higher cerebral functioning, and the impact of focal lesions on global network configuration.

Method: We studied the remaining hemisphere in hemispherectomized rats (n = 8), and age-matched controls (n = 13), 7, 35 and 49 days post surgery using resting-state fMRI, weighed graph and interregional connectivity analysis (ROIs were selected within the sensorimotor network; connectivity was measured using voxel-wise correlation coefficients). We quantified the local and global graph structures via the clustering coefficient C and the characteristic shortest path L. Synchronizability was estimated from the eigensystem decomposition of the Laplacian network matrix. Sensorimotor function was measured longitudinally by scoring neurological deficiency (NDS).

Results: After significant acute neurological deficits, NDS largely normalized in all animals within 2 weeks. Removal of the right hemisphere resulted in significant enhanced functional connectivity in the left hemisphere between cortical and subcortical regions, particular at acute time points, as compared to controls. Graph analysis revealed that C and L did not differ significantly between groups. Network synchronization was lowered in hemispherectomized rats ($p = 0.035$).

Conclusion: We have shown that rs-fMRI, connectivity analyses and specific network measures can provide unique insights into functional reorganization in the remaining brain after experimental hemispherectomy. The rapid motor recovery correlates in time with enhanced contralesional functional connectivity. Graph analysis synchronization results suggests a shift toward a more regular topology.

052

CONCOMITANT RECORDINGS OF INTRACRANIAL EEG AND FMRI: MRI SAFETY STUDY ON RF-INDUCED ELECTRODE HEATING IN A PHANTOM MODEL AND ANIMALS

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Purpose: Structural MRI is used in patients with implanted electrodes to obtain information about electrode location for intracerebral EEG (icEEG). Functional MRI (fMRI) has been considered unsafe, as it can induce heat in the electrodes due to interaction with the pulsed radiofrequency fields. We have determined the potential temperature change at the tip of the electrodes in a phantom and in animals.

Method: Human-shaped torso-phantom, filled with polyacrylic-acid gel with human tissue properties in conductivity, and a typical electrode implant was used to imitate a patient with 4 intracranial electrodes (one implanted parasagittally and 3 coronally). Female New Zealand white rabbits were used, with one single electrode implanted in each animal. The measurements were performed in a Siemens Sonata 1.5T MRI T/R head coil. Several MRI sequences were used, with different experimental settings: disconnected and connected electrode wires from the cable unit with and without loops, moving the electrode end anterior/posterior within the magnetic bore.

Results: The temperature increase in the phantom at the tip of the electrode was at maximum 1.1°C during EPI sequence for perpendicular electrode and 0.6°C on the coronal electrode. The highest increase for DTI sequence was 1°C. Correspondingly, the mean increase in the animal model was 1.2°C (electrode not connected), 0.5°C (electrode connected for EPI) and 1.9°C (for DTI sequence).

Conclusion: Variation of the temperature depends on the electrode wire position as well as connection to the cable unit. This indicates that further MR safety studies for using electrodes in simultaneous icEEG/fMRI are advisable prior to translating into human use.

053

SIMULTANEOUS INTRACRANIAL EEG-fMRI IN PATIENTS WITH EPILEPSY

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Purpose: Intracranial EEG (icEEG) has much greater sensitivity and spatial resolution than scalp EEG but coverage is limited. We aimed to simultaneously record intracranial EEG and fMRI to study the hemodynamic correlates of localized epileptic icEEG activity over the whole brain.

Method: Two patients undergoing presurgical evaluation with icEEG (#1 76 subdural contacts, #2 66 subdural contacts and 2 × 6 contact depth electrodes) were scanned with a 1.5T scanner. We used a head RF-coil, low-SAR sequences (≤0.1 W/Kg head-average), exact external electrode cable configuration; 64-channels of invasive EEG was recorded with MR compatible equipment (as specifically safety tested). We acquired 2 × 10 min EPI acquisitions (TE/TR40/3000 ms 38 × 2.5 mm slices, 0.5 mm gap, 3 × 3 mm in-plane resolution) during rest. Standard artefact correction methods were applied to EEG and then general linear models containing visually identified interictal epileptiform discharges (IEDs) were applied to fMRI data.

Results: Direct visual inspection of the cortex upon electrode explantation showed no evidence of adverse effects. The corrected icEEG was of good quality and fMRI image quality was sufficient (artefact was dependant on electrode type/location). Significant activations to IEDs were obtained ($p < 0.001$ uncorrected) both local to the IED-contacts and remote from any implanted electrodes.

Conclusion: Under specific tested circumstances, simultaneously icEEG and fMRI can be acquired safely in epilepsy patients. Data quality was sufficient to produce both activations local to electrode contacts with IEDs and remote from any electrode. The simultaneous acquisition of intracranial EEG and fMRI allows the investigation of epileptic activity over a greater range of spatial and temporal scales.

Neurobiology of epilepsy I
Tuesday 29th June 2010
11:30–13:00

054
EXPRESSION OF IL-1 BETA INDUCED BY EPILEPTIFORM ACTIVITY IN THE ISOLATED GUINEA PIG BRAIN IN VITRO

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Purpose: Brain inflammation has been recently considered in the pathogenesis of focal epilepsy. Increasing evidence strongly suggests that an inflammatory reaction occurs in the brain during the establishment of an epileptic condition. Synthesis of the proinflammatory cytokine IL-1beta can be triggered in the central nervous system by seizures contributing to neuronal injury and to the development of epilepsy. Moreover, IL-1 beta synthesis and expression could cause transient changes in the functional and structural features of the BBB, that lead to an impairment of its integrity. In the present study the expression of IL-1beta into the brain parenchyma was verified after pharmacological induction of seizure-like activity in the in vitro isolated guinea pig brain preparation, in the absence of extracerebral influences.

Method: In this preparation, brief application of the GABAa receptor-antagonist, bicuculline, consistently induced focal ictal discharge in the limbic region, as verified by simultaneous electrophysiological recordings of extracellular activity in CA1 of both hemispheres.

Results: Immunohistochemical analysis of isolated brains in which seizure-like activity was induced revealed the expression of IL-1beta exclusively in those areas mainly involved in ictal activity (limbic cortices). In control brains maintained in vitro for comparable time without induction of epileptiform activity, no immunoreactivity for IL-1beta was observed, suggesting a trigger role played by seizures for IL-1 beta expression.

Conclusion: In conclusion, seizure-like activity-induced IL-1beta synthesis supports the hypothesis that inflammation plays an active role in pathophysiology of seizures. Further studies will clarify the role of IL-1beta in neuronal cell loss, astrogliosis and BBB damage.

055
PERIRHINAL CORTICAL KINDLING IN GENETIC ABSENCE EPILEPSY RAT STRAINS

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Purpose: The genetic models of absence epilepsy, GAERS and WAG/Rij rat strains, are resistant to progression of partial seizures induced by amygdaloid and hippocampal kindling. Perirhinal cortex is a crucial area for the secondary generalization of partial seizures. Kindling epileptogeniticy is propagated from perirhinal cortex to other areas that are responsible for generalized seizures. Therefore we focused on perirhinal cortical kindling in both epileptic rat strains and compared them with Wistar rats.

Method: Adult, male GAERS, WAG/Rij and Wistar rats were implanted with stimulation/recording electrodes into the perirhinal cortex and recording electrodes over the cortex. After recovery period, the animals were stimulated twice daily at their afterdischarges threshold. Stimulations were repeated on the following days until the animals reached three stage 5 seizures or the maximum number of stimulations (30) had been delivered.

Results: The mean AD threshold was significantly higher in WAG/Rij and GAERS compared to Wistar group (406.3 ± 34.6 mA, 383.3 ± 16.6 mA and 287.5 ± 24.5 mA, respectively). Analysis of the rate of perirhinal cortical kindling for the 3 strains indicated highly significant differences ($p < 0.01$, $p < 0.001$). The mean number of stimulations for the development of the first stage 2, 3, 4 and 5 seizures was significantly higher in WAG/Rij and GAERS groups compared with Wistar rats.

Conclusion: This results show that the resistance to secondary generalization of partial seizures is not restricted to amygdala and hippocampus, limbic cortical areas such perirhinal cortex also playing an important role in underlying mechanisms of this kindling resistance.

056
CORTICAL HYPERSYNCHRONICITY AND EPILEPTOGENESIS FOLLOWING PHOTOTHROMBOTIC STROKE: POTENTIAL PREVENTION USING SPG STIMULATION-INDUCED VASODILATATION

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Purpose: Recent studies demonstrated that electrical stimulation of the Spheno-Palatine Ganglion (SPG) elevates regional cerebral blood flow (rCBF) and may improve outcome following experimental stroke. Since stroke is the most common cause for new onset focal epilepsy in adults, we studied the effect of SPG stimulation on cortical activity, synchronicity and epileptogenesis in a stroke model in rats.

Method: Craniotomy was performed over the sensory-motor cortex in anesthetized rats (n = 29). Stroke was induced by photothrombosis following injection of Rose Bengal and direct illumination of the exposed cortex. Continuous cortical activity was recorded over the treated region using implanted EEG epidural electrodes (Data Science Instruments Ltd). In some animals (n = 8) SPG was stimulated for 3 h per day, 4 consecutive days. Sham-operated rats were used as controls.

Results: Photothrombosis induced a focal ischemic lesion surrounded by a wide cortical region with blood-brain barrier breakdown. EEG analysis showed increased fast activity with enhanced cortical synchronicity and appearance of short duration seizure-like activity within 2–7 days after the induction of ischemia. Stimulation of the SPG induced vasodilation and partial reperfusion of the ischemic lesion. Injury-related EEG changes were not observed in the SPG-stimulated group.

Conclusion: We demonstrate a new approach to follow postischemic cortical response and epileptogenesis. We suggest that increased rCBF by stimulation of the SPG results in EEG normalization. We propose that continuous EEG recordings in behaving animals may serve as an objective approach to assess cortical damage and repair.

057
TWO DISTINCT PATTERNS OF HIPPOCAMPAL NEUROGENESIS IN VIVO AND IN VITRO CAN BE IDENTIFIED IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY AND CORRELATE WITH EACH PATIENT'S ABILITY TO STORE AND RECALL MEMORY

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Purpose: The brain maintains its capacity to generate new neurons throughout life. Animal data identify neurogenesis in the hippocampus as a cellular substrate for learning. Similar mechanisms may operate also in humans, but experimental evidence is difficult to obtain. We compared the propensity of adult human stem cells to differentiate into neurons when obtained from MTLE-patients with or without learning impairment prior to hippocampectomy.

Method: Adult neural stem cells were isolated from 23 human hippocampi obtained from epilepsy surgery. After pharmacological induction of neuronal differentiation, quantitative immunocytological analysis were performed and compared with each patient's memory capacity tested prior to surgery as well as with patterns of integration of newly born neurons and neuronal cell loss in the resected hippocampus.

Results: Induction of neuronal differentiation was achieved in up to 71% of the total cell population, when cell progenies were obtained from patients with normal memory acquisition (n = 11). Hippocampal progenitors failed to differentiate into neurons in vitro (1–3%) when obtained from epilepsy patients with severe learning impairment (n = 12). In the latter patient group, granule cell loss and lower numbers of doublecortin-immunoreactive presumably immature neurons in the hippocampus were encountered in vivo.

Conclusion: Our experimental protocol allows a reliable characterization of the regenerative capacity in the human hippocampus in vivo and in vitro. The results also reveal deteriorated neurogenesis in a subgroup of patients suffering from severe cognitive impairment, suggesting that the generation and anatomical integration of new neurons play a pivotal role in human memory formation.

058
DOES PERINATAL CORTICAL PHOTOTHROMBIC ISCHEMIC STROKE INDUCE EPILEPTOGENESIS IN RATS?

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Purpose: Perinatal stroke results in long-term neurological defects, experienced by more than half of affected infants. Neonatal seizure is the most common clinical finding triggering assessment. Perinatal stroke is otherwise recognized retrospectively with emerging hemiparesis or seizures after early months of life. We aim to elucidate whether induced photothrombic stroke in periods before initial jump in EEG development can induce epileptogenesis.

Method: Immature rats P7, 9, 12, 15 were implanted with epidural EEG electrodes. EMG bipolar electrodes were placed in nuchal muscles to assess behavioral state and 2 h later connected to VideoEEG and EMG for 30 min. After energy and entropy analysis of EEG P7 was selected. Intravenous BengalRose (2 mg/ml) injection was followed by laser illumination over motor cortex for 5 min. Motor deficits were assessed 2 months later. EEG cortical and hippocampal electrode implantation followed a week of recovery then continuous Video EEG monitoring. Animals were transcardially perfused and brains cut for histological staining.

Results: EEG activity during development revealed biphasic rhytmogenesis. Entropy and signal energy rose with age, highest in intervals P7–9, P12–15 respectively. Lesions penetrated motor cortex reaching external capsule; volume ration analysis (ischemic/contralateral hemisphere) revealed significant reduction in volume of ischemic hemisphere. Unlike Rotarod and Barholding, inclined grid test revealed change in latency; rotarod revealed changes in forepaw and shoulder blade posture during stance and swing phase contralaterally. Video-EEG monitoring preliminary results show partial hippocampal seizures with secondary generalization.

Conclusion: Albeit perinatal cortical ischemic lesions lead to immense reduction in tissue volume and epileptogenesis, minimal functional deficits were observed.

P*roject support: GACR P303/10/0999.*

059
NEURONAL HEPARANASE MAY FACILITATE THE MIGRATION OF INFILTRATING MONOCYTES IN THE RAT HIPPOCAMPUS FOLLOWING *STATUS EPILEPTICUS*

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Purpose: Heparan sulphate chains (HSC) may impede extravasated monocyte progression within brain tissue parenchyma. Heparanase, an enzyme which specifically cleaves extracellular and cell surface HSC, is expressed by both monocytes and neurons. We tested the hypothesis that its upregulation in hippocampal neurons following status epilepticus (SE) coincides with degradation of HSC present at the surface of infiltrating monocytes.

Method: SE was induced at weaning or at the adult stage in male Sprague-Dawley rats after lithium-pilocarpine (Li/Pilo) or pilocarpine (Pilo) administration, respectively. HSC were visualized using a peptide corresponding to HS binding domains of the rat heparanase protein. Levels of heparanase transcript and protein were determined at different times following SE, using RT-qPCR, western-blotting and immunohistochemistry.

Results: Numerous infiltrating monocytes were detected in the hippocampus of both immature and adult rats within the 24 h post-SE. At that time, HSC were expressed at high levels at the surface of infiltrating monocytes, but could not be detected later. Disappearance of HSC in rats subjected to SE was preceded by and concomitant with an increase in both heparanase transcript level and active/zymogen heparanase ratio. In addition, immunofluorescent labeling of both forms of heparanase was detected in numerous monocytes 24 h post-SE and was stronger 8 and 24 h post-SE in hippocampal neurons.

Conclusion: Both monocyte and neuronal heparanase may contribute to HSC degradation at the surface of infiltrating monocytes following SE.

Ongoing studies are determining whether such processes may occur in patients with intractable epilepsy, by analyzing surgically resected hippocampus.

QOL and psychosocial impact of epilepsy
Tuesday 29th June 2010
11:30–13:00

060
THE IMPACT OF ANTIEPILEPTIC DRUG TREATMENT ON ATTENTION AND EXECUTIVE FUNCTIONS

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Purpose: To evaluate the effects of various antiepileptic agents and the overall drug load of antiepileptic regimens on attention and executive functions.

Method: This retrospective analysis included 1430 epilepsy patients who were assessed by the EpiTrack – a screening tool focusing on attention and executive functions. Twenty-eight percent of the patients were on monotherapy, 65% on polytherapy, and 6% were untreated. Stepwise multiple regression analysis was conducted to identify determinants of EpiTrack performance. Pharmacological treatment (antiepileptic agents, number of antiepileptic drugs [AEDs]), demographic (age, sex, education), and clinical variables (age at onset and duration of epilepsy, seizure types and frequency) were entered into the regression analysis.

Results: Stepwise regression analysis sequently identified the following predictors of a better EpiTrack performance: a higher education, a lower number of AEDs, absence of topiramate (TPM), treatment with levetiracetam (LEV) or lamotrigine (LTG), male sex, and a later onset of epilepsy. This regression equation explains 29% of the observed variance.

Conclusion: EpiTrack performance linearly decreases with an increasing number of AEDs. This effect cannot solely be attributed to the overall drug load. A higher number of AEDs may also implicate a more severe epilepsy. However, in this analysis seizure related variables except the onset of epilepsy did not predict cognitive performance. Treatment with LEV or LTG is associated with a better cognitive performance, whereas a treatment with TPM goes along with worse performance. Education seems to be a marker for reserve capacities in regard to negative cognitive AED effects.

061
SOCIAL COGNITION IN MESIAL TEMPORAL LOBE EPILEPSY

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Purpose: Mesial temporal lobe epilepsy (MTLE) may serve as a model for neuropathological changes in limbic structures, offering insight in neuroanatomical aspects of Social Cognition. One of the key features, Theory of Mind (ToM) refers to the ability to infer other people's mental states, thoughts and feelings. Another aspect of Social Cognition is Empathy, which implicates affective experience and understanding of another person's emotional state.

Method: We investigated 43 MTLE patients (26 left, 17 right) and 27 healthy controls using three ToM -Tests (Faux Pas Recognition Test - FPRT (Stone et al., 1998), Strange Stories Test -SST (Happé, 1994), Eyes-Test (Baron-Cohen et al., 2004) and one self-report questionnaire of Empathy (Interpersonal Reactivity Index-IRI (Davis, 1983).

Results: MTLE patients were impaired on all ToM-Tests ($p < 0.001$). In particular left MTLE patients achieved significant lower results than right MTLE patients. In contrast the MTLE patients showed no significant differences in their self-reported Empathy abilities measured by the IRI compared to the healthy controls, though they scored significantly lower than controls on the ''empathy question'' of the FPRT with the left MTLE patients scoring lowest.

Conclusion: Our results suggest that lesions in the limbic system may play a major role in the impairment on ToM-Tasks, whereas laterality matters. Particularly left MTLE is associated with ToM deficits. The fact, that MTLE patients did not differ from controls in their self-reported Empathy, though being impaired in answering the ''empathy question,'' needs further consideration. Tendencies to socially desirable answers need to be clarified.

062
THE BURDEN AMONG CAREGIVERS OF PATIENTS WITH EPILEPSY: IMPACT AND PREDICTORS

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Purpose: The objective of this study is to assess the burden among caregivers of patients with epilepsy and identify associations of this burden with sociodemographic and clinical characteristics.

Methods: A multicenter, international, observational, cross-sectional study is currently being conducted in three tertiary-care University Centers evaluating predictors affecting the quality-of-life of epileptic patients and their caregivers. We assessed 15 patients using Beck's Depression Inventory, Beck's Anxiety Inventory, Montreal Cognitive Assessment Test and Quality-of-Life in Epilepsy Inventory 31. Their caregivers were also assessed by administration of Zarit Burden Interview and the health survey SF36v2. Statistical analyses were performed using Pearson's correlation coefficient.

Results: All caregivers indicated some degree of burden being imposed to their personal lives by their relatives' disease (range 14–47). That degree of burden showed an association trend with their quality-of-life ($r = -0.85$ for the Physical Component Scale and -0.84 for Mental Component Scale) but not with the patient's quality-of-life ($r = 0.087$). Time spent for the care of the patient showed a strong association to burden for the caregiver ($r = 0.8$) and there was a moderate association trend with the duration of the disease ($r = 0.43$) and a weak association trend with seizure frequency ($r = 0.2$).

Conclusions: There is substantial burden of Epilepsy to the caregivers. That appears to have direct impact to the caregivers' quality-of-life. Time spent with the patient and duration of the disease appear to be the most significant predictive factors of caregiver's quality-of-life. Further enrollment is ongoing and will hopefully elucidate which pairs of patients-caregivers may benefit from social services assistance.

063
A SURVEY OF KNOWLEDGE AND ATTITUDES TOWARDS EPILEPSY IN RESIDENTS OF THE WESTERN DISTRICT IN TOTTORI PREFECTURE, JAPAN

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Purpose: Attitudes towards people with epilepsy (PWE) are influenced by the degree of familiarity as well as knowledge of the condition. This

study was aimed at assessing understanding and attitudes towards epilepsy in the western district in Tottori Prefecture.

Method: A 14-item questionnaire on knowledge of epilepsy and attitudes towards PWE was distributed to residents in the western district in Tottori Prefecture in 2008, and a total of 1313 copies were collected. The relationship between attitudes towards PWE and personal acquaintance with PWE was examined using chi-square test.

Results: Of the respondents, 56.2% had read/heard/seen something in the epilepsy, 45.9% knew someone with epilepsy, and 43.3% had witnessed a seizure. About 21% knew the treatment for seizure attack. PWE were in the employ at 3.7% of the workplace of the respondents. One third of respondents (33.4%) correctly identified epilepsy as a nervous system disorder, while 28.4 % did not know what epilepsy is. Of the respondents, 17.4% would not allow their children to marry someone with epilepsy and only 5.6% objected to having their children play with PWE. While 38.4% would offer PWE equal employment, 3.2% were against it. Personal acquaintance with PWE significantly influenced attitudes towards playing with, employment of PWE, individual association with PWE, and disclosure of epilepsy, but did not influence attitudes towards marriage to PWE.

Conclusion: Although understanding of epilepsy and attitudes towards PWE were favorable, the results indicate that personal acquaintance influenced attitudes towards PWE, and there is a need to implement public education campaigns.

064
FAMILY FUNCTIONING AND QUALITY OF LIFE IN ADULT PATIENTS WITH EPILEPSY AND THEIR FAMILY MEMBERS: A DESCRIPTIVE STUDY

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Purpose: The impact of epilepsy on family functioning and well being has been shown to be tremendous in children with epilepsy. Whether the impact remains in adult patients and their families, is less known. Therefore, we investigated family functioning, support in activities of daily living (ADL) and quality of life in adult patients with epilepsy and their families.

Method: A cross-sectional descriptive study was conducted in the Swiss Epilepsy Centre Zurich. Health related data, family functioning, support in ADL, as well as quality of life were assessed in all subjects and analyzed.

Results: Patients (n = 137, M = 37.5 years) and family members (n = 137; M = 49.8 years) were enrolled. The majority of patients (83.9%) were hospitalized due to symptomatic epilepsy. Family members were parents (42.3%), spouses (29.2%) or siblings (16.1%). Family cohesion was normal in 45% (n = 62) of patients and 51.8% (n = 7) of family members. Family adaptability was normal in 40.4% (n = 55) of patients and 54.8% (n = 71) family members, but chaotic in 50 % of patients and 38% of family members respectively. Patients perceived significantly lower support needs in ADL than family members ($p = 0.00$; $t = -4.699$, $df = 102$).

Family cohesion and adaptability were significantly correlated with self reported quality of life in patient ($r = 0.194$, $p = 0.02$) and family members ($r = 0.222$; $p = 0.00$).

Conclusion: Family functioning and support needs have to be addressed in adult patients and their families to ameliorate possible conflicts within family. Patient education by health care professionals should focus more on mutual topics of patient and family.

065
SEIZURE-FREE INTERVAL: IS IT A RELIABLE LIMITATION FOR DRIVERS WITH EPILEPSY?

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Purpose: In a previous paper we have shown that patients with epilepsy (PWE) in Greece do not comply with driving restrictions, mainly for employment-related reasons [Polychronopoulos P et al Neurology 2006 12; 67 (5): 869–71.]. In this study we try to identify clinical risk factors for seizure-related traffic accidents (TA) which would be considered when counseling PWE on driving.

Method: In a prospective case-control study, we compared 35 PWE who had seizure-related TA with 35 matched-control PWE who drove but hadn't TA. Both "case" and "control" patients were from the same clinic. Seizures etiologies and types were defined according to ILAE classifications schemes. Patient's data, epilepsy variables, driving practices and TA variables were collected from the patients' and relatives' reports and cross-checked with the medical files of our epilepsy monitoring clinic.

Results: Seizure type was the single factor that was significantly different between the two groups (χ^2 test, $p = 0.05$). Especially seizures like grand mal, which occur without warning or complex partial (CPS) with prolonged disturbance of consciousness, significantly increased the odds of crashing (χ^2 test, $p = 0.001$). Long seizure-free intervals (SFI), having reliable auras, drug compliance, driving hours per week and years of driving experience didn't differ between the groups.

Conclusion: Our results suggested that not the SFI, which is widely supported by the literature, but the seizure type, especially grand mal seizures and CPS, was significantly contributed to the TA. Detecting such risk factors might help grading the risk for accidents in PWE who drive.

Epilepsy syndromes in children
Wednesday 30th June 2010
11:30–13:00

066
LONG-TERM OUTCOME OF BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES: DUTCH STUDY OF EPILEPSY IN CHILDHOOD

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Purpose: Determine long-term outcome in a cohort of children with newly diagnosed benign childhood epilepsy with centrotemporal spikes (BECTS).

Method: Thirty children with BECTS were included in the Dutch Study of Epilepsy in Childhood. All children were followed for 12–17 years. Twenty children had typical BECTS, ten had atypical BECTS (age at onset <4 years, developmental delay or learning difficulties at inclusion, other seizures, atypical EEG abnormalities).

Results: Mean age at onset of epilepsy was 7.8 years with slight male preponderance. Most common seizure-types at onset were generalized tonic–clonic seizures (GTCS) and simple partial seizures; in 87% of the children seizures occurred during sleep. After 12–17 years, most patients (96.3%) had a terminal remission (TR_F) of >5 years and 89% of >10 years. Mean duration of epilepsy from onset to TR_F was 2.7 years; mean age at reaching TR_F was 10.6 years. Many children (63%) had experienced one or more (secondary) GTCS. Eighty percent had used antiepileptic drugs (mean duration 3.0 years). As far as we know, none of the children had developed learning problems or had shown any arrest of cognitive development during follow-up. No significant differences were observed in patient characteristics or outcome between children with typical BECTS and children with atypical BECTS.

Conclusion: All children in our cohort, both with typical and atypical BECTS, had a very good prognosis with high remission rates after 12–17 years. None of the predictive factors for disease course and outcome as described in earlier studies was prognostic in our cohort.

067

MORTALITY FOLLOWING CHILDHOOD CONVULSIVE STATUS EPILEPTICUS: RESULTS FROM STEPSOUT

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Purpose: Childhood convulsive status epilepticus (CSE) is associated with substantial morbidity and mortality, but its natural long-term outcome remains uncertain as available data are from inherently biased hospital-based studies. Having carried out the first pediatric population-based study on childhood CSE (NLSTEPSS), we are now conducting the childhood STatus EPilepticuS OUTcomes study (STEPSOUT), a follow-up of the 219 initial cohort survivors of the acute episode, 5–10 years after their initial episode to determine neurological, neuropsychological and neuroimaging outcomes. In this paper we present preliminary mortality data.

Method: Detailed contemporaneous clinical and demographic data are available on cohort members. Children are being identified and recruited for this study from 21 north London hospitals through local collaborators utilising the linked-anonymized identification system from the initial study. Survival status of children is determined through hospital and national databases. Details about cause of death are obtained from clinical records in deceased and survivors are being invited for detailed neurological, psychological assessments and neuroimaging.

Results: 129 survivors have been identified. Median age at initial CSE = 3.6 (range 0.17–16) years, median follow-up = 6.5 (0.3–7.4) years. Eight children died (0.06, 95% CI 0.03–0.12), median age at death = 8.8 (1.1–16.33) years. Seven had remote symptomatic and one had cryptogenic CSE. Mortality rate overall = 0.95 (95% CI 0.49–1.8)/100 person-years, and 2.3 (95% CI 1.14–4.26)/100 person-years for remote symptomatic CSE. Most deaths were result of complications of underlying etiology.

Conclusion: A substantial proportion of children will die within 5–10 years following CSE and etiology seems to be the major determinant.

068

CHARACTERIZATION OF EYELID MYOCLONIA IN A SERIES OF PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY

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Purpose: Description of clinical characteristics of eyelid myoclonia (EM) in a series of 76 juvenile myoclonic epilepsy (JME) patients submitted to video-EEG recording.

Method: Video-EEG monitoring of JME patients applying activation methods as eye closure, photic stimulation, hyperventilation and neuropsychological tasks.

Results: EM were recorded in nine JME patients (11.8%). Age of EM onset was 14.3 ± 2.9 and limb myoclonia, 13.4 ± 5.2 years. Five patients did not realize EM were seizures or even noted its occurrence. None presented auto-induction or mental retardation. Their EEGs showed generalized polyspike-wave discharges 3–6 Hz, sometimes with posterior predominance, appearing until two seconds after eye closure. Photosensitivity was found in six and photoparoxysmal response grade 4 in two. Five of 9 patients also had absences. Perioral reflex myoclonia (PORM) during talking or reading separated from EM were present in two, while EM were precipitated by talking, eye closure, intermittent photic stimulation, praxis tasks, eating or self manipulations of their faces. All patients had good school performance and six had control of the other seizure types under valproate or topiramate, although EM persisted in all. Interesting although EM was troublesome in one patient and was avoided trough sun glasses use in another, the other patients were not bothered or even perceived this phenomenon.

Conclusion: We propose EM is a different variant of reflex seizures in JME and the term reflex eyelid myoclonia (REM) can be used to designate it. Finally, although rarely recognized by the patient, EM was a persistent reflex trait in JME.

069

EPILEPSY IN CHILDHOOD AND ADOLESCENCE: ETIOLOGY AND ASPECTS OF TREATMENT IN AN UNUSUAL POPULATION

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Purpose: Assess the etiology of epilepsy and aspects of treatment in children and adolescents under the age of 16 years living in a high deprivation community. This community was considered particularly interesting because it is located in a rich neighborhood of São Paulo, the richest city of Brazil and receive medical assistance from an advanced hospital named Albert Einstein.

Methods: This study was conducted in two phases: in the first a questionnaire was applied to identifying the occurrence of seizures; in the second subjects in whom seizures were identified underwent neurological examination, followed by electroencephalogram and neuroimage exams.

Results: From 10,405 children and adolescents, 353 were included in the second phase. Epilepsy was confirmed in 101. Forty three subjects (42.6%) had symptomatic epilepsy, 16 (15.8%) idiopathic, and 40 (42%) cryptogenic. Thirty one (32%) had pre- and perinatal insults (19 hypoxic-ischemic encephalopathy, 10 malformations of the central nervous system, two cerebrovascular disease); eight (7.9%) had brain infection (four meningitis, two neurocysticercosis and two congenital cytomegalovirus infection); four (4%) presented genetic or progressive neurological conditions. 83% of subjects were treated: 53% were on monotherapy and 30% were on politherapy. Phenobarbital (18%) and carbamazepine (18%) were the most frequently prescribed drugs.

Conclusion: The most common etiology was hypoxic-ischemic encephalopathy and phenobarbital one of the most common drug. Although the possibility of adequate assistance, these results reflects the socioeconomic conditions of the population and indicates that education and prevention could be better than face the consequences.

070

CLINICAL AND NEUROPHYSIOLOGICAL FEATURES OF PROGRESSIVE MYOCLONUS EPILEPSY (PME) ASSOCIATED WITH SCARB2 MUTATIONS WITHOUT RENAL FAILURE

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Purpose: To outline the clinico-neurophysiological features of five patients with a severe PME associated with SCARB2 mutations, devoid of renal impairment (Dibbens et al., 2009).

Method: In these five patients (2 male, 3 females), before being tested for SCARB2 mutations (homozygous mutations in 4, heterozygous in 1), common causes of PME were previously excluded. Over the years, the patients underwent repeated neurophysiological investigations, that included wakefulness/sleep EEG, polygraphic recordings, multimodal evoked potentials, electromyography. All cases underwent brain MRI.

Results: Clinical onset occurred at a mean age of 19 years (range 14–26 years), with tonic–clonic seizures and action myoclonus and ataxia, rapidly worsening in few years, leading to a bedridden state (4 patients); in two patients prolonged myoclonic/clonic seizures evolving in convulsive status required repeated admissions to ICU. In 4 patients, death occurred after about 10 years from onset, without evidence of renal impairment. The only living patient (heterozygous), 5 years from onset presents with moderate/severe action myoclonus, marked ataxia, photosensitivity and mild proteinuria. Neurophysiologic investigations showed: 1) progressive deterioration of the EEG background activity with diffuse and posterior epileptiform abnormalities; sleep EEG demonstrated fast epileptic spikes over the vertex; 2) polygraphic evidence of action myoclonus and photic reflex myoclonus; 3) multimodal evoked potentials consistent with cortical hyperexcitability; 4) unremarkable EMG findings.

Conclusions: Our findings may expand the phenotypic expression of PME associated with SCARB2 mutations and suggest that SCARB2 gene mutations might account for unsolved cases of PME in Italy.

071

FOCAL INTERICTAL AND ICTAL EEG ABNORMALITIES IN CHILDHOOD ABSENCE EPILEPSY

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Purpose: The occurrence of nonlocalizing focal spike-wave discharges (FSWD) and asymmetrical generalized spike-wave discharges (GSWD) has been documented in some adults with idiopathic generalized epilepsy (IGE), particularly juvenile myoclonic epilepsy. To assess whether FSWD are age-related, or an inherent feature of IGE, we investigated the phenomenon in the archetypal IGE syndrome, childhood absence epilepsy (CAE).

Method: We analyzed 16 digital EEGs from 11 children with CAE, and noted the effects of overbreathing (OB) and sleep (three EEGs recorded after partial sleep deprivation). Fast ''paper speed'' was employed to identify possible areas of leading spike at GSW onset.

Results: There were 263 GSWD including 62 absences, captured on video. Of those, 130 (50%) had lateralized onset that was frontal-central in 112, occipital-parietal in 14 and left temporal in four. FSWD occurred in all but one child. Of the 171 FSWD in total, 156 were frontal-central (91%), 12 occipital-parietal (7%) and three left temporal 2%). Both GSWD and FSWD were activated by OB (average densities increased from 0.13 and 0.19 to 0.92 and 0.6 respectively) and sleep. Most of the GSWD and FSWD occurred within cyclic alternating pattern phase A (CAP-A), but they behaved differently in CAP-B: GSWD occurred at the transition of CAP-B to CAP-A while FSWD well inside CAP-B ($p = 0.028$; $p = 0.000$; $p = 0.000$). Lateralized ictal automatisms were noted on video in 8 children, at least once.

Conclusion: ''Focal'' interictal and ictal EEG and clinical manifestations are frequent in CAE, indicating an inherent to IGE variable cortical instability rather than maturational process.

Clinical neurophysiology
Wednesday 30th June 2010
11:30–13:00

072

A PROMINENT SENSORY ROLE OF HUMAN INSULA: A STEREO-EEG STUDY

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Purpose: To investigate the role of the human insula by studying the clinical manifestations induced by insular cortex intracerebral electrical stimulations (IES).

Method: Study population: 103 subjects with SEEG electrodes implanted into the insular cortex affected by drug-resistant epilepsy during the presurgical workout. In order to localize electrodes position within the insular cortex a postoperative 3D CT-scan or a 3D MRI was acquired. Images were then fused with the preoperative MRI in the same stereotactic referenced system. IES parameters: electrical bipolar stimulations were carried out at low (LF, 1 Hz, pulse width 3 msec, 30'') and high frequencies (HF, 50 Hz, pulse width 1 msec, 5''). Amperage ranging from 0.2 to 5 mA. The videos of IES procedures were reviewed and objective as well as subjective manifestations were analyzed.

Results: 424 IES (181 LF and 243 HF) were performed obtaining 240 clinical responses (57%). The most frequent induced symptom was a somato-sensory manifestation (73%) with a variable localization and lateralization (mainly paresthesic sensation involving the contralateral face and arm). Motor manifestations represented only 8% of the total amount, auditory modifications were present in 6%, language was involved in only 2%; autonomic and gustatory responses were found respectively in 1%.

Conclusions: Our data provide evidence of a prominent somato-sensory role of the human insular cortex. The fusion imaging methodology we

doi: 10.1111/j.1528-1167.2010.02658.x

used, allowing the precise localization of the stimulated contacts into the insular cortex, probably explains the higher amount of sensory manifestations to respect to previous articles.

073

MODULATION OF THE PAROXYSTIC ACTIVITY IN A PREMOTOR DYSPLASIA BY STIMULATIONS OF THE IPSILATERAL CENTROMEDIAN THALAMIC NUCLEUS DURING A PRESURGICAL STEREO-ELECTROENCEPHALOGRAPHIC EXPLORATION FOR PARTIAL DRUG-RESISTANT EPILEPSY

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Purpose: There is a growing interest in deep brain stimulation (DBS) as an alternative therapy for drug-resistant non surgical epilepsies. For a better understanding and use of DBS in epilepsy we studied the effects of stimulations of the centromedian (CM) thalamic nucleus on the cortical activity during a stereo-electroencephalographic (SEEG) exploration in a patient with partial drug-resistant epilepsy.

Method: This observation was performed in the preliminaries of a French multicentric clinical research project. Our patient had a SEEG for partial drug-resistant epilepsy related to a large left premotor dysplasia. One of the depth electrodes targeted the left CM. The electrodes positions were checked by merging the preoperative MRI and the postimplantation cranial scanner. We performed the recordings and the electrical stimulations according to the presurgical objectives. We also performed electrical stimulations of the CM and we analyzed its effects on the interictal activity of all explored areas. One per ictal stimulation of the CM was performed.

Results: The SEEG recordings confirmed the existence of a left premotor Taylor type dysplasia and proved its role in the epilepsy. The boundaries of a curative cortectomy were determined. The dysplasia interictal paroxysms diminished dramatically during the stimulations of the left CM by chocks and by high frequency trains demonstrating a reproducible functional modulation of the abnormal activity by the CM.

Conclusion: This observation encourages following the DBS studies in drug-resistant non surgical epilepsies. The CM seems to be an interesting target.

074

SCALP EEG SOURCE ANALYSIS IN EXTRATEMPORAL LOBE SEIZURES: COMPARISON WITH INTRACRANIAL FINDINGS

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Purpose: 1. To assess the utility of different scalp EEG source localization (ESL) tools for analysing non lateralizable/localizable seizure patterns in extratemporal lobe epilepsy (ETL).

2. To investigate the impact of analysing different time periods on ESL results.

Method: Five patients with ETL (four frontal, one parietal lobe epilepsy) with non lateralizable/localizable scalp ictal EEG (10–20 electrodes) were included. Spectral phase mapping, dipole source (DS) and CLARA (iteratively applied LORETA) analyses using BESA software were performed blinded to clinical data. Ictal onset and early propagation were estimated at three time points:

1. 0–5 s after EEG onset,
2. 5–10 s and
3. after EEG evolution was noted. The results were compared to the ictal onset zone determined during invasive recordings.

Results: Spectral phase maps localized correctly in four patients (80%) during the early (a, b), and in three (60%) during the late phase (c). DS and CLARA analyses were correctly localizing in three (60%) lateralizing in one additional and nonlateralizing in one patient in all seizure phases (a–c). One early pattern showed false lateralization using CLARA only. The pattern with false lateralization and non lateralizing patterns were characterized by polymorphic delta.

Conclusion: This pilot study shows that in ETL epilepsies, ESL can often lateralize or even localize difficult ictal scalp EEG patterns and is concordant with intracranial findings. Polymorphic delta frequencies compromized ESL analysis. Limited inferior electrode coverage may have an impact on our findings, and such studies need to be prospectively validated in a larger cohort.

075

MAGNETOENCEPHALOGRAPHY (MEG), SINGLE PULSE ELECTRICAL STIMULATION (SPES) AND THEIR CONCORDANCE WITH THE SEIZURE ONSET ZONE (SOZ) IN THE ELECTROCORTICOGRAM (ECOG)

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MEG is a noninvasive source localization method and SPES an invasive method for localization of epileptogenic cortex. SOZ in chronic ECoG can be seen as gold standard. We have assessed to what extent interictal MEG sources and SPES epileptogenic cortex are reflected in ECoG SOZ.

Methods: MEG data was collected using 275 channel system. Data time was 1 h. MEG data were coregistered with full volume anatomical MRI and subjected to an automated spatial filtering and spike-detection algorithm defining abnormal transient MEG activity in terms of increased kurtosis (SAMg2). SAMg2 identifies brain regions reaching statistical significance for presence of increased kurtosis and calculates synthetic depth electrodes. SPES was performed between adjacent subdural electrodes with a constant-current neurostimulator. A single constant current pulse was delivered every 5 sec. Intracranial EEG responses to each pulse were recorded. The locations of the abnormal responses to SPES were considered for this study.

Each MEG and SPES result was associated to the brain anatomical region from which SOZ arose in ECoG. The association was classified as concordant; results were allocated to the same anatomical region, and discordant, different anatomical lobes.

Result: 11 patients were included. MEG and SPES were concordant in 9, discordant in 1 and not applicable in 1. MEG and SOZ were concordant in 8, discordant in 2 and not applicable in 1. SPES and SOZ were concordant in 8, discordant in 1 and not applicable in 2.

Conclusion: MEG, noninvasive method, and SPES, invasive method, have correspondence with ECoG SOZ.

076

ABSENCE OF INTERICTAL SCALP EEG FINDINGS IN CENTRAL LOBE EPILEPSY: A RETROSPECTIVE COHORT STUDY

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Purpose: To determine the prevalence of the absence of interictal epileptiform discharges on scalp EEG (sIIEDs) and to investigate reasons for its occurrence in patients with central lobe (CL) epilepsy.

Method: In 45 patients (23 male; 19.5 ± 14 years, 1–54) with CL epilepsy evaluated at the Cleveland Clinic Epilepsy Center from 2003–2009, demographic data, interictal/ictal EEG, and MRI were extracted from the medical charts. Data of the patients that underwent invasive evaluations with subdural grids (number of grids/electrodes, number of spike populations (SP), number of grid electrodes with synchronous interictal discharges (Ge-syncIIED), and resection) were further analyzed.

Results: 33% of patients had no sIIEDs during prolonged surface-EEG evaluations. Majority (71%) of patients had an MRI-identifiable lesion. 14 patients (7 w/osIIEDs; 10 male) underwent invasive evaluation (1–6 plates; mean 123 electrodes). There wasn't significant difference in age (27 ± 16.5 vs.13.5 ± 6 years), age of onset (14 vs.7 years), and epilepsy duration (13 vs.6.5 years) between the group with and w/osIIEDs. There was significant difference ($p = 0.045$) in number of Ge-syncIIED between group w/osIIED (median 3; 2–12) and with sIIEDs (median 9; 7–10) but not in the number of SP (median 1 vs. 3). In the 12/14 patients who underwent surgery, the resection margins were more frequently confined to the borders of CL in the group w/osIIEDs ($p = 0.021$).

Conclusion: Absence of sIIEDs is commonly observed in patients with CL epilepsy. The extent of the epileptogenic zone determines the appearance or lack of sIIEDs in the special setting of epilepsy restricted to the CL and the depths of the central sulcus.

077

COMPUTER ASSISTED IDENTIFICATION OF THE EPILEPTIC ZONE BASED ON CHARACTERIZATION OF THE ICTAL PATTERNS BY QUANTITATIVE FREQUENCY ANALYSIS OF INTRACRANIAL EEG RECORDING

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Purpose: Approximately half of the patients with a diagnosis of pharmacoresistant epilepsy are potential candidates for epilepsy surgery. In 30–40% of cases the epileptic zone can only be defined by intracranial recordings. The correct presurgical identification of the epileptogenic area has a direct impact on postsurgical outcome. Evaluation of the SEEG is currently based on a traditional visual inspection. In this study we propose to assist this approach with a tool to faster elaborate large SEEG data and focus on the quantified seizure profiles with a clear results representation.

Method: Our method is based on the presurgical diagnostic SEEG recordings from the epileptic patients evaluated for surgical treatment at Niguarda Hospital. Evaluation algorithms were based on the time, frequency and spatial domain analysis. Target frequencies for every patient were identified by Fourier transformation with further integral calculation. Computer-assisted evaluation of the different patterns of the seizures was performed for reproducible ictal events in more then 10 recordings per patient. Seizure events were scanned in frequency range from DC to 250 Hz and compared among all recorded ictal events per patient.

Results: Using this approach we were able to reliably identify epileptic zone based on the reproducible profiles precisely selected and quantified for every patient.

Conclusion: Proposed algorithms to characterize and identify different patterns of seizure may help to improve stereo EEG evaluation and extend it to the new level of studies that may provide a new setting for innovative therapeutic strategies to cure resistant forms of epilepsy.

Drug therapy: Miscellaneous
Wednesday 30th June 2010
11:30–13:00

078

LIGHT AND SHADE OF THERAPEUTIC DRUG MONITORING OF ANTIEPILEPTIC DRUGS

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Purpose: Therapeutic drug monitoring (TDM) of antiepileptic drugs is a valuable tool in the medical treatment of epilepsies. During the last decade our Institute has processed about 20.000 antiepileptic drug (AED) samples. In view of the great potential of pharmacological interactions of this class of drugs, we decided to review our TDM data.

Method: Carbamazepine (CBZ), phenobarbital (PB), phenitoin (PHT), valproate (VA) and lamotrigine (LTG) plasma concentrations were studied in relation to the clinical information provided for each patient (AED's posology, coadministered drugs, renal and liver function).

Results: The following were the most interesting results: the coadministration of PB or PHT with CBZ decreases CBZ concentration; the cotreatment with a dihydropyridine calcium antagonist increases CBZ concentration but the association of amlodipine with PB or PHT doesn't result in any modification of the plasma levels of these drugs; VA coadministered with PB increases PB concentrations; the association of CBZ or PHT to a preexisting regimen with PB, doesn't modify PB concentration; tacrolimus or proton pump inhibitor associated with PB lead to an elevation of PB concentration; stimulation of VA metabolism by enzyme inducing AEDs decreases VA plasma concentration and when VA and LTG are coadministered, LTG plasma concentration increases.

Conclusion: The focus on AEDs management in a decade of TDM activity has allowed to depict a scenario on which pharmacological interactions effectively occur in clinical practice: some unexpected results could be explained by recent achievements in transport pharmacology (P-gp) or could rely on not well investigated variables (e.g. plasma protein binding).

079

ANTIEPILEPTIC DRUG-INDUCED OSTEOPATHY

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Purpose: Epilepsy patients can be regarded as a group of risk for the development of bone damage. Beside the increased fracture risk during an epileptic seizure a continuous antiepileptic drug (AED)-therapy seem to have an unfavorable effect on bone health as well. Due to the heterogeneous data situation concerning the influence of AEDs on bone metabolism there are no general guidelines for prevention and treatment of AED-induced osteopathy.

Method: The most valuable clinical parameter for the evaluation of the bone is the determination of the bone mineral density (BMD). We examined the effect of a long-term AED therapy on BMD of 100 epilepsy patients treated for more than 5 years with an AED mono- or polytherapy. We used the dual energy x-ray absorptiometry (DEXA) recommended as the standard method for determination of BMD. Further causes of secondary osteopathy were detected by using a standardized questionnaire. The results were compared with BMD values of a control group.

Results: More than half of the examined epilepsy patients showed pathological BMD with osteopenic or osteoporotic T-values. Among these patients only a few individuals had additional causes for secondary osteopathy. There was a significant difference of BMD values in epileptic patients compared to the control group.

Conclusion: We could demonstrate that long-term treatment with AEDs clearly affects BMD. These results underline the need of a careful monitoring of bone health in epileptic patients in order to identify and treat an AED-associated osteopathy in time.

080

ABCB1 GENE VARIANT INFLUENCES THE MAINTENANCE DOSE OF CARBAMAZEPINE IN PATIENTS WITH EPILEPSY

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Drug resistance in epilepsy can be due to a peculiar molecular subtype of the disease or to specific genetic variants involved in pharmacodynamics and pharmacokinetics of the drug response. P-glycoprotein (P-gp/MDR1) is one of the most clinically important transmembrane transporters in humans since it influences both absorption and excretion of a variety of drugs, including antiepileptic drugs. Numerous reports have indicated that a single-nucleotide polymorphism (SNP) at position 3435 of the ABCB1 gene (rs 1045642) is associated with multidrug resistance of different drugs. For elusidation the influence of this polymorphism on susceptibility to epilepsy and to efficacy of carbamazepine therapy, we analyzed the allelic frequency and genotype distributions of specific variant in 50 patients treated with different doses of carbamazepine and 88 normal controls from the Republic of Macedonia. The ABCB1 3435C → T polymorphism (rs 1045642) was analyzed by allelic discrimination TaqMan assay. No statistically significant difference in the allelic frequency (0.51 and 0.55 for C allele, p = 0.54) and genotype distribution (0.23, 0.57, and 0.20, and 0.32, 0.46 and 0.22 for CC, CT and TT genotypes, p = 0.53) was determined between controls and patients, respectively. Correlation analysis between genotype and therapeutic doses showed that patients with CC genotype need a lower maintenance dose of carbamazepine (473.3 mg) in comparison with patients with CT and TT genotype (634.8 mg and 636, 4 mg, respectively). Our data indicate that the ABCB1 3435 C-T variant is an important determinat of the maintenance dose of carbamazepine in patients with epilepsy from the Republic of Macedonia.

081

AN EVALUATION OF THE EFFECT OF ESLICARBAZEPINE ACETATE ON METABOLIC PARAMETERS: A POOLED ANALYSIS OF THREE DOUBLE-BLIND PHASE III CLINICAL STUDIES

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Purpose: Gain an understanding of the nature and risks of increases in serum lipids in association with the use of eslicarbazepine acetate (ESL) as adjunct therapy to 1–3 concomitant AEDs (oxcarbazepine was not allowed) in the pooled data of 3 Phase III studies.

Method: The Safety population (N = 1049) was defined as all patients who received at least 1 dose of study medication (ESL 400, 800 or 1200 mg or placebo). The incidence of sponsor-defined potentially clinically significant values was analyzed by treatment group. Mean changes from baseline following 14 weeks of treatment and serum lipid level related adverse events (AEs) were calculated for each treatment group.

Results: Mean change from baseline to end of the double-blind period in total cholesterol values were −0.12, 1.12, 0.63, and 3.296; mean changes in low-density lipoprotein were 0.34, −2.70, −0.97, 1.095; mean changes in high-density lipoprotein were −0.06, 1.64, 2.61, and 3.48; and mean changes in serum triglycerides were −7.82, 7.51, −5.81, and −25.16, for the placebo, ESL 400, 800, and 1200 mg groups, respectively. The incidence of serum lipid level related AEs in the ESL treatment groups was similar to placebo.

Conclusion: In this pooled analysis of 3 Phase III studies, no clinically significant mean changes from baseline were observed. The incidence of AEs related to serum lipids was similar between the ESL and placebo treatment groups.

Supported by BIAL- Portela & Co, SA.

082

CHANGES IN LAMOTRIGINE PHARMACOKINETICS INDUCED BY ANTITUBERCULAR DRUGS

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Purpose: Antitubercular drugs have pharmacokinetic interactions with drugs metabolized by the cytochrome P450 system. Interactions with drugs, such as lamotrigine that are mainly glucuronidated, are less predictable. We report the changes in lamotrigine pharmacokinetics induced by antitubercular treatment in a single case.

Method: Trough lamotrigine plasma levels were measured employing a dried bloodspot method.

Results Case: CB, a 45 year old female patient with a drug refractory idiopathic generalized epilepsy was treated with lamotrigine monotherapy. She had infrequent generalized tonic–clonic seizures or absences. During a stay in Indonesia an asymptomatic tuberculosis was discovered at routine checkup. The infection was initially treated with a combination of isoniazid, rifampicine, pyrazinamide and ethambutol. Pyrazinamide and isoniazid were replaced by moxifloxacine due to severe adverse reactions. The dose of lamotrigine was increased from 400 mg/day to 1000 mg/day, but had to be reduced due to side effects (dizziness, slurred speech). Seizure frequency remained high during antitubercular treatment. Lamotrigine plasma levels ranged between 4.5 μg/ml at baseline, to 14.3 μg/ml during antitubercular treatment.and the apparent clearance ranged between 50–170 L/24 h. Lamotrigine clearance decreased with approximately 15% with isoniazid and increased with 40% with rifampicine. However, the addition of ethambutol with moxifloxacine increased clearance threefold.

Conclusion: During treatment with antitubercular polytherapy with rifampicin, moxifloxacine and ethambutol lamotrigine clearance may increase more than threefold, with a potentially risk of reduced seizure control.

083

THE EFFECTS OF TOPIRAMATE AND SODIUM VALPROATE THERAPIES ON INSULIN, C-PEPTIDE, LEPTIN, NEUROPEPTIDE Y, ADIPONECTIN, VISFATIN, RESISTIN LEVELS IN CHILDREN WITH IDIOPATHIC PARTIAL AND GENERALIZED EPILEPSY

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Purpose: The aim of this study was to determine the effects of topiramate and valproate therapy on insulin, c-peptide, leptin, neuropeptide Y, adiponectin, visfatin and resistin levels with their relationship to weight and BMI in preadolescants with idiopathic partial and generalized epilepsy.

Method: Forty one epileptic children aged 6–12 years were included. The patients were divided into two groups (VPA; n = 21, TPM; n = 20). Weight, height. BMI and HOMA-IR were recorded and insulin, c-peptide, leptin, NPY, adiponectin, visfatin ve resistin levels were determined at the 0, 6 and 12th months.

Results: In the VPA group, weight and height increased significantly. Seven of them became overweight at the end of 1 year. Leptin was higher in the overweight subgroup (p = 0.03). Although insulin levels and HOMA-IR increased (p = 0.038 and 0.036), nobody showed hyperinsulinism or insulin resistance. Resistin decreased at the 6 and 12 months (p = 0.001). There was no significant difference in c-peptide, visfatin and NPY during the follow-up in both groups. In the TPM group, resistin increased at 6 months and decreased at 12 months, leptin showed a decrease and adiponectin showed an increase at 6 and 12 months but the results were not statistically significant.

Conclusion: VPA and TPM affect the weight, BMI, insülin and leptin levels in prepubertal children. We suggest that further studies including more patients and long follow up period are necessary to draw a conclusion regarding an association between the treatment of both antiepileptic drugs and the levels of leptin, insulin, adiponectin, visfatin, NPY and resistin.

This study was supported by the Scientific Research Comittee of Karadeniz Technical University.

Neurobiology of epilepsy II
Wednesday 30th June 2010
11:30 – 13:15

084

HIGH-FREQUENCY NETWORK ACTIVITY IN A MODEL OF NONLESIONAL TEMPORAL LOBE EPILEPSY

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Purpose: Recent observations on high-frequency activity (HFA: >100 Hz) suggest it plays an important role in epilepsy pathophysiology. The neuronal loss associated with hippocampal sclerosis has been implicated in the genesis of HFA in frequency band 250–500 Hz (fast ripples). In the current study we determined whether HFA occurred in a chronic model of nonlesional temporal lobe epilepsy to test whether neuronal loss is a necessary requirement.

Method: Ten adult Sprague-Dawley rats were injected with 4–5 ng tetanus toxin into right CA3. Bipolar electrodes were implanted into CA1, CA3 and DG bilaterally. Recording started 3–6 days postoperatively.

Results: All animals developed epileptic foci with: spontaneous seizures, interictal discharges, and HFA. Interictal discharges were present bilaterally in all animals. HFA was present both during interictal discharges and at seizure onsets. Interictal HFA was present in ipsilateral hippocampus in all animals (mean frequency 331 ± 4 Hz). In 50% animals HFA was observed also in contralateral hippocampus (mean frequency 235 ± 6 Hz). Ictal-onset HFA had mean frequencies in ipsi- and contralateral hippocampus of 339 ± 76 Hz and 220 ± 9 Hz respectively.

Conclusion: This study has demonstrated the presence of HFA in a nonlesional model of temporal lobe epilepsy. The absence of the hippocampal sclerosis in this model argues against the theory that HFA over 250 Hz (fast ripples) depends on cell loss. This epileptic HFA proved to be more a specific marker of the primary epileptic focus than interictal discharges.

085

PRENATAL ADMINISTRATION OF LEVETIRACETAM IMPEDES LATER EXPRESSION OF SEIZURES AND MOSSY FIBER SPROUTING IN A RODENT MODEL OF CORTICAL DYSPLASIA

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Purpose: In addition to seizure-suppressing effects, levetiracetam (LEV) has been shown to possess potential antiepileptogenic properties in some animal models. We sought to explore the hypothesis that LEV may alter the course of seizure development in the well-characterized model of in utero radiation-induced cortical dysplasia (CD), which demonstrates propensity for seizures following a second-hit.

Method: 59 Sprague-Dawley rats were divided into 4 groups. From E12 to birth pregnant mothers received s.c. q8h 54 mg/kg of either LEV or LO60 (inactive LEV entantiomer). Half of the mothers were irradiated with 145 cGy on E17. On PND 60 all offspring were given a subconvulsive dose (s.c. 50 mg/kg) of pentylenetetrazol (PTZ; "second hit"). Before sacrificing the animals we monitored their behavior and EEG for a subsequent 8 h. Immunocytochemistry for SV2A (LEV binding site), Cresyl-violet and Timm staining were performed.

Results: Rats receiving LEV in utero displayed significantly less severe seizures than those who did not. CV staining confirmed CD in irradiated rats. The hippocampal hilus and CA3 regions of LEV-pretreated irradiated rats were significantly more enriched with SV2A compared to rats that did not receive LEV. Mossy fiber Timm staining was increased only in irradiated rats that had not received LEV in utero.

Conclusion: In utero pretreatment with LEV impedes the expression of acute seizures induced by a "second-hit" in adult CD rats. Pretreatment with LEV during granule cell development appears to inhibit mossy fiber sprouting despite irradiation and seizure provocation. These findings suggest a disease-modifying effect of LEV in this animal model.

086

INCREASED PROMOTER METHYLATION AND SUSTAINED DOWN-REGULATION OF HIPPOCAMPAL MGLUR2 EXPRESSION AFTER STATUS EPILEPTICUS IN RAT EXPERIMENTAL TEMPORAL LOBE EPILEPSY

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Purpose: Epigenetic chromatin modifications have been previously identified in human temporal lobe epilepsies (Kobow et al., 2009), suggesting that promoter methylation and altered gene expression is triggered by seizure activity. Indeed, long-term regulation of gene expression has been confirmed in animal models of temporal lobe epilepsy (TLE), and is likely to contribute to enhanced epileptogenesis when associated with synaptic neurotransmission. Here we studied the metabotropic glutamate receptor 2 (mGluR2), which is located at the presynaptic membrane and mediates feedback inhibition of glutamate exocytosis. Down-regulation of mGluR2 has been detected in mossy fibers and perforant path projections in experimental TLE, suggesting a pathogenic role in the development of chronic hyperexcitability and enhanced hippocampal seizure susceptibility.

Methods/Results: Sustained down-regulation of mGluR2 was detected in the rat hippocampus already 24 h up to 3 month following Pilocarpine induced Status epilepticus. Bisulfite sequencing revealed a significant increase in hippocampal mGluR2 promoter methylation after 4 weeks. Neither down-regulation of mGluR2 gene expression nor changes in promoter methylation were observed in the cerebellum, when obtained from same animals.

Conclusion: Our data support the hypothesis, that DNA promoter methylation is an important mechanism for region-specific and sustained down-regulation of genes involved in the pathogenesis of chronic temporal lobe epilepsies. Targeting the epigenetic regulation machinery may open new pharmacological strategies for the treatment of drug resistant epilepsies.

087

TARGETING THE ENDOCANNABINOID SYSTEM IN THE AMYGDALA KINDLING MODEL OF TEMPORAL LOBE EPILEPSY

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Purpose: Because of its impact on neuronal excitability, the endocannabinoid system has been suggested to play a role in epileptogenesis and ictogenesis. In this study, we evaluated the impact of the cannabinoid (CB)-1-receptor-agonist WIN 55.212-2 on the development and progression of amygdala kindled seizures. In addition, we analyzed the effects of the fatty acid amide hydrolase–inhibitor URB 597 which catalyzes the intracellular hydrolysis of the endocannabinoid anandamide.

Methods: Thirty-eight male NMRI mice were stimulated once daily via an implanted depth electrode on 11 consecutive days. Thirty minutes before each kindling stimulation, they were treated with WIN 55.212-2 (2.5 mg/kg i.p.), URB 597 (1 mg/kg i.p.), or vehicle. Following a seven day lasting washout phase animals were restimulated without further administration of compounds.

Results: WIN 55.212-2 attenuated the progression of kindling in comparison to the control group. The number of animals exhibiting a generalized seizure during the 17-day kindling paradigm was significantly reduced to 17 % in the group receiving the CB1-receptor agonist. Considering data from the first 11 stimulation days and the re-stimulation phase, the number of stimulations required for induction of a generalized seizure was significantly increased in WIN 55.212-2 treated animals. In contrast, URB597 did not affect kindling acquisition.

Conclusion: We provide evidence that CB1 receptor agonism attenuates the development of a hyperexcitable network in the amygdala kindling model. Future studies are necessary to further evaluate whether these effects indicate a preventive potential of CB1 receptor modulators.

088

EXPERIMENTAL OCCIPITAL LOBE SEIZURE STATUS IN CATS: THE ROLE OF LATERAL GENICULATE BODY UPON SECONDARY GENERALIZATION

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Purpose: The complexity of epileptic network in the occipital lobe epilepsy is considered to be the cause of various clinical symptomatologies. Using kainic acid-induced focal occipital lobe epilepsy model, we investigated the role of the lateral geniculate body (LGB) using electroencephalographic and behavioral observation including intermittent photic stimulation.

Method: Stereotaxic surgery was carried out and depth electrodes were implanted to bilateral visual cortex (VC), bilateral LGB and mesencephalic reticular formation. A cannula for kainic acid (KA) injection was placed to the right occipital visual cortex. Electrodes were connected to the head socket. Eight days after the surgery, KA solution was injected via implanted cannula in the freely moving condition and occipital seizure status was induced. Intermittent light stimulation (ILS) was applied periodically under video-EEG monitoring.

Results: About 1 h after the injection, focal multiple spikes started at the injected site of the VC. The seizures recurred in every 5 min and progressively propagated to the LGB and MRF. The seizures developed and became secondarily generalized seizure status 3–12 h after the injection. During interictal period, ILS were tested. Although photosensitivity was not constant, some ILS session provoked photoconvulsive response in LGB and VC, which resulted in secondarily generalized seizures.

Conclusion: The present result demonstrated a facilitatory partcipation of LGB in the seizure development by the ILS. This focal seizure model of VC is not only applicable to study the mechanism of seizure development of occipital lobe seizure but also to understand the photosensitivie mechanism of LGB.

089

THE CELLULAR BASIS OF THE INFLAMMATORY RESPONSE FOLLOWING STATUS EPILEPTICUS

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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. Recent evidence indicates that inflammation following CSE may play a key role in subsequent outcome. However, the cellular aspect of inflammation following CSE has yet to be elucidated. This study investigates the time course of the inflammatory cells together with BBB and vascular response in the hippocampus following CSE in the lithium-pilocarpine rat model.

Method: Pilocarpine (n = 40) was administered to adult Sprague-Dawley rats. Animals were sacrificed at days 0, 1, 2, 3, 4, 5, 6, 7, and 14 following CSE. Immunohistochemistry was used to identify activated monocytes/microglia (ED-1), neutrophils (MBS), BBB breakdown (IgG), and vascular cell adhesion molecules (VCAM). Cell counts or intensity scores were then performed.

Results: In the hippocampus, no MBS staining was observed. ED-1 indicated that there was a gradual increase in activated microglia in CA1 that continued up to Day 14, whereas in CA3 peak numbers were found on Day 3 and none were found on Day 14. BBB breakdown was found only on Days 3 and 4. Peak VCAM staining was observed on Day 2 following CSE.

Conclusion: These data indicate that following CSE there is a lack of neutrophil infiltration in the hippocampus. VCAM expression peaked around Day 2, and by Day 3 high levels of activated microglia and monocytes can be found which coincides with BBB breakdown.

090
BYPRODUCTS OF PROTEIN, LIPID AND DNA OXIDATIVE DAMAGE IN EPILEPTIC SEIZURE

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Purpose: To get more insight into molecular mechanisms underlying oxidative stress and its role in different types of epileptic seizure, in this study, oxidative byproducts of proteins, lipids and DNA, as well as, antioxidant enzyme activities were studied in adult epileptic patients.

Method: Study was performed in 60 epileptic patients and in 25 controls. Plasma protein reactive carbonyl derivatives (RCD) and protein thiol groups (P-SH), byproducts of oxidative protein damage, as well as antioxidant enzyme activities, superoxide dismutase (SOD) and glutathione peroxidase (GPX) were studied spectrophotometrically. Urinary 8-epi-prostaglandin $F_{2\alpha}$ (8-epi-$PGF_{2\alpha}$) and 8-hydroxy-2'-deoxyguanosine (8-OHdG), representative byproducts of lipid and DNA oxidative damage, respectively, were determined by enzyme immunoassay.

Results: RCD levels were significantly increased ($p < 0.001$), while P-SH content was decreased in patients with first seizure ($p = 0.052$) compared to controls, independently of the seizure type. Urinary 8-epi-$PGF_{2\alpha}$ and 8-OHdG were significantly increased in epileptic patients ($p = 0.001$). Rise in 8-epi-$PGF_{2\alpha}$ was more pronounced in patients with generalized tonic–clonic (GTCS) compared to those with partial seizure (PS). Both SOD and GPX activity were significantly increased in epileptic patients compared to controls ($p = 0.001$), but only SOD activity was significantly higher in patients with GTCS than in those with PS.

Conclusion: Data on enhanced protein, lipid and DNA oxidation, together with upregulated antioxidant enzyme activities, confirm the existance of systemic oxidative stress in epileptic patients. It might be speculated that posttranslational modification to existing functional proteins, particularly alterations to ion chanels, might be at least partialy responsible for acute early changes in neuronal networks.

Mortality and neurobehavioral in epilepsy
Wednesday 30th June 2010
11:30–13:00

091
EVALUATION OF PSYCHIATRIC SYMPTOMS IN EPILEPSY PSYCHOSIS USING BRIEF PSYCHIATRIC RATING SCALE

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Purpose: Some patients with epilepsy exhibit schizophrenia-like psychosis (epilepsy psychosis). They are deemed to have milder symptoms than do schizophrenic patients and rarely have schizophrenic negative symptoms. To quantify the psychiatric symptoms in patients with epilepsy psychosis, we evaluated various symptoms in patients with or without psychosis and in schizophrenia patients using Brief Psychiatric Rating Scale (BPRS).

Method: Patients consisted of 76 patients with epilepsy psychosis (P), 184 patients with schizophrenia (S) and 117 epilepsy patients without psychosis (E). Psychosis-related items reviewed included age of onset, duration and dose of antipsychotics, while epilepsy-related items included age of onset, duration, epilepsy type, seizure frequency, and antiepileptic drugs taken. Psychiatric symptoms in all patients were evaluated using BPRS with factor analysis performed on 16 BPRS-item scores and the extracted-factor scores compared among the three groups.

Results: Age at onset of psychosis was older in P (27 years) than in S (24 years), whereas dosage of antipsychotic drugs did not differ between the two groups. Total BPRS was significantly higher in P (33.9) and S (36.4) than in E (21.0). Factor analysis extracted three factors: positive symptoms, negative symptoms, and anxiety-depressive symptoms. These three factors were significantly lower in E than in both P and S.

Conclusion: The finding that there were no psychopathological differences between epilepsy psychosis and schizophrenia, suggests a difficulty in differentiation of the two disorders using psychiatric symptomatology. In contrast, psychiatric symptoms in epilepsy patients without psychosis differed from those in epileptic psychosis patients or those in schizophrenia patients.

092
ANTIEPILEPTIC DRUGS IN THE TREATMENT OF PSYCHIATRIC DISORDERS

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Purpose: The pharmacologic interface between psychiatry and neurology is AEDs as they are utilized to treat both epilepsy and psychiatric disorders. Further, AEDs are commonly utilized in treatment of pain disorders. AEDs are primarily prescribed for treatment of psychiatric and pain disorders, not for treatment of epilepsy. The choice of which AEDs neurologists will utilize in treatment of epilepsy is most often premised on the classic benefits/risks/alternatives equation; however, consideration should be given to psychiatric comorbidities and which AEDs might best serve patients in both maximizing seizure control and minimizing psychiatric symptoms as patients with epilepsy (PWE) have a 50–80% lifetime prevalence of psychiatric disorders with a three-to-five-fold

increased risk of suicide compared to the general population. This overview of AED treatment of psychiatric disorders with inclusion of labeled and off-labeled uses can serve as a guide for neurologists and psychiatrists in better treating psychiatric comorbidities in PWE.

Method: Literature review.

Results: Of 16 AEDs reviewed, clinical studies have addressed >30 possible uses; however only 5 AEDs (benzodiazepines, carbamazepine, valproate, lamotrigine, and pregabalin) have received FDA/EMEA psychiatric indications. Most studies are uncontrolled case reports, open-label case series, and underpowered randomized controlled trials with methodological flaws. Regardless of the limited approved indications and in some instances negative pivotal trials, AEDs continue to be utilized adjunctively or in monotherapy treatment for a plethora of psychiatric diagnoses.

Conclusion: AEDs are pivotal in treating psychiatric comorbidities in PWE. Further placebo-controlled (augmentation and monotherapy) parallel-arm research with active-comparators is required in this complex field.

093
SUICIDE ATTEMPT IN EPILEPSY: INCIDENCE AND RISK FACTORS

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Purpose: Suicide attempt (SA) is associated with an increased risk for developing epilepsy; completed suicide is increased after epilepsy. We assessed whether SA has a bidirectional relationship with epilepsy and whether risk for recurrent SA is increased after epilepsy versus controls when SA precedes epilepsy.

Method: A matched, longitudinal cohort study using the General Practice Research Database (GPRD) compared the incidence of SA before and after incident epilepsy in 3,217 cases aged 10–60 years versus 12,020 matched controls. The effects of previous SA and depression were examined with respect to: SA recurrence before and after epilepsy onset; and to SA incidence after epilepsy.

Results: The incidence of SA was significantly increased for all 3 years before and for the first year after epilepsy onset. In cases and controls without a history of SA or depression, SA occurred in 1.2% versus 0.5% respectively ($p < 0.05$). In cases and controls with a history of depression, risk for a first SA after epilepsy onset was 2.5% (cases) versus 1.7% (controls) (n.s.). For cases and controls with only a history of SA, recurrence risk was 7.6% and 2.9% respectively ($p < 0.05$). Risk for recurrent SA in cases and controls with a history of both SA and depression was 17% in cases versus 6.1% in controls ($p < 0.05$).

Conclusion: Practitioners need to be aware that the risk for SA is greatest in people with epilepsy who have a history of psychiatric disorders or SA. Screening is needed to identify and counsel patients at greatest risk.

094
EFFICACY AND SAFETY OF PREGABALIN IN PATIENTS WITH REFRACTORY FOCAL EPILEPSY AND ANXIETY DISORDER

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Purpose: According to recent own data, 19.6% of patients with refractory focal epilepsy have also a diagnosis of an anxiety disorder. The purpose of the study reported here was to evaluate the efficacy and safety of pregabalin (PGB) in patients with the comorbidity of epilepsy and anxiety disorder.

Method: In an open, uncontrolled study, 45 patients with intractable partial-onset epilepsy were treated with PGB at daily doses up to 600 mg for 12 weeks (including titration) additionally to their existing medication. Two groups of patients were examined: one with an additional anxiety disorder and one without this comorbidity. In addition to changes in seizure situation, changes of psychological parameters were assessed. We used a disorder-specific questionnaire with subquestionnaires concerning body-related fears (BSQ), cognitions (ACQ), avoidance (MI), the Beck Depression Inventory (BDI), the questionnaire on life satisfaction (FLZ), PESOS, the Symptom Checklist (SCL-90-R), the Social Interaction Anxiety Scale (SIAS), the Social Phobias Scale (SPS) and the State-Trait Anxiety Inventory (STAI).

Results: Data are available for 33 patients. Patients with epilepsy plus anxiety disorder (n = 12) showed significant improvements in the anxiety and interpersonal sensitivity subscales of the SCL-90-R and a positive trend in the phobia subscale. In addition, there was an improvement in the ''Trait'' subscale of the STAI.

Conclusion: Our results indicate favorable effects of PGB on a comorbid anxiety disorder in patients with focal intractable epilepsy. Verification of the data obtained in this study in a large, randomized survey is desirable and necessary.

The study was supported by Pfizer.

095
COMPARISON OF MORTALITY RISK IN NEWLY-DIAGNOSED AND CHRONIC EPILEPSY IN ADULTS: 13 YEARS OF FOLLOW-UP IN AN ESTONIAN POPULATION

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Purpose: There are no population-based studies comparing the mortality risk for patients with newly diagnosed and chronic epilepsy drawn from the same population, over the same time. The aim of our study was to compare mortality risk in adult patients with newly diagnosed and chronic epilepsy over a 13-year period.

Method: 81 patients aged ≥20 years with newly diagnosed and 309 adult patients with chronic epilepsy were originally identified from population-based incidence and prevalence studies conducted in Tartu between 1994 and 1996. Patients were followed until the date of death or the end of 2007. The SMR was analyzed for both cohorts. The influence on the SMR of age at diagnosis, sex, epilepsy syndrome, seizure type and treatment compliance was also investigated.

Results: The SMR was significantly increased in both cohorts, but was higher in patients with chronic (SMR, 3.1; 95% confidence interval [CI], 2.5–3.8) as compared to newly-diagnosed epilepsy (SMR, 2.6; 95% CI, 1.8–3.5). In newly diagnosed epilepsy cohort the increased mortality risk was most pronounced in people with complex partial seizures (SMR, 5.6; 95% CI 2.4–11.0), whereas by chronic epilepsy mortality was higher in people with secondary generalized tonic–clonic seizures (SMR, 3.4; 95% CI 2.5–4.5). Non compliant patients had two times higher mortality risk (SMR, 4.2; CI 95% 2.7–6.2) as compared to those who were on anticonvulsant treatment.

Conclusion: Epilepsy mortality issues are more relevant to patients with chronic epilepsy. Mortality risks should be discussed with patients with epilepsy, especially if treatment is refused despite recurrent seizures.

096
HEALTH OUTCOMES IN PATIENTS WITH EPILEPSY: MORTALITY, LIFE EXPECTANCY AND SUDDEN UNEXPLAINED DEATH IN EPILEPSY: A COHORT STUDY IN TYROL

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Purpose: The aim of this study is to detect risk factors for premature death in a well defined epilepsy population in Tyrol, Austria.

Methods: All patients with epilepsy (n = 3334) treated at our outpatient clinic (1970–2000) were included. Diagnosis was based on ILAE-classification. Living or dead status was obtained from the Institut für Klinische Epidemiologie using a probabilistic record linkage. Patients were followed until death or end of 2005. A total of 48,595 patient-years were analyzed. SMRs were calculated by comparisons with those living in the same geographic area in Tyrol. We used the Cox proportional hazard model to calculate the hazard ratio (HR) of risk factors with 95% CIs. We used STATA 10 for windows.

Results: We observed 648 deaths compared to expected 297 (SMR 2.2 [2.0–2.4]). SUDEP (n = 34) accounted for 1.8% of all deaths (0.2/1 = 00PY). Patients not seizure-free at last follow up had a significantly increased risk to die (HR 2.18 [1.18–2.63]) compared to the seizure-free ones. Male gender (1.52 [95% CI 1.29–1.78]), generalized tonic–clinic seizures (1.39 [1.18–1.63]), and symptomatic etiology (2.34 [2–2.74]) were associated ($p < 0.001$) with an increased risk of death. Patients with cryptogenic epilepsy had a higher risk of death compared to idiopathic epilepsy (1.78 [1.22–1.59]).

Conclusion: Our data confirm previous studies showing a substantially increased mortality in epilepsy patients. Further calculations of our cohort will provide detailed information on potential risk factors and their translation into a reduced life expectancy.

Bursary Award Symposium
Wednesday 30th June 2010
14:30–16:00

097
SURGICAL STRATEGIES IN TUBEROUS SCLEROSIS PATIENTS: EFFECTIVENESS OF EXTENDED TUBERECTOMIAS

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Purpose: Epilepsy surgery is an important therapeutic option in patients with Tuberous Sclerosis Complex (TSC) and intractable epilepsy. Surgical planning in TSC is however highly complex due to the presence of multiple tubers and frequently multifocal scalp EEG epileptiform activity. The aim of the study was to analyze surgical strategies in our series and to assess patient's chance to obtain seizure-free outcome.

Method: Surgical series of 6 pediatric and 5 adult patients was retrospectively studied. Clinical, EEG, MRI, surgical and seizure outcome data were evaluated. Predictors of favorable and unfavorable postsurgical outcomes were analyzed.

Results: Mean age at seizure onset was 3.5 years. Four cases suffered from West syndrome. According to seizure semiology and EEG findings, four cases were regarded as multifocal. Epilepsy syndromes included temporal lobe epilepsy in five, fontal-frontocentral in five and temporo-parieto-occipital in one patient. Mean age at surgery was 18 years. Invasive monitoring was indicated in six cases; other patients had intraoperative electrocorticography. All patients underwent extended tuberectomias guided by intracranial EEG results. Eight of ten patients with 2 years of postsurgical follow-up are seizure-free. Two surgical failures were caused by multifocality and overlap of epileptogenic and eloquent cortical regions.

Conclusion: Indicated patients with TSC may significantly profit from epilepsy surgery. Not tuberectomias, but tailored resections guided by intracranial EEG data are successfully used in our centre. We thus supported the hypothesis that brain tissue surrounding tubers rather than the tuber itself is the source of seizures in TSC.

Supported by Grants MZOFNM2005 and Kontakt Programme ME09042.

098
COMPREHENSIVE INFORMATION IMPARTED TO PATIENTS WITH EPILEPSY AND COMORBIDITY AND DECREASED PREVALENCE OF ADVERSE TREATMENT EFFECTS: THE EDU-COM STUDY

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Purpose: Epilepsy requires long-term drug treatment and is frequently associated with other clinical conditions. Adverse drug reactions and drug interactions are expected and may affect compliance The primary objective of this study is to verify if a comprehensive and standardized educational plan is followed by a reduction of adverse treatment effects and an improvement of quality of life.

Method: The study is a multicenter, randomized, controlled, open-label, pragmatic trial. 220 consecutive adult epilepsy outpatients with at least one concurrent clinical condition on chronic treatment and at least one drug-related adverse event and/or clinically relevant drug interaction are being recruited from 9 epilepsy centers nationwide. Eligible patients are randomized to receive a comprehensive and standardized educational plan or usual care. The experimental plan consists in a counselling session about the cause of adverse event/drug interaction, the tolerability of each drug, contraindications of interfering drugs, indications and benefits of suggested treatment changes, and withdrawal of ineffective drugs. All patients will be seen at one, three and 6 months after admission.

Results: The primary outcome is defined by the number of patients free from clinically relevant adverse treatment events and/or the number of drug interactions. Secondary outcomes include health-related quality of life score changes using the QOLIE-31 questionnaire and the monetary costs of medical contacts, hospital admissions, and drugs.

Conclusion: The EDU-COM study will provide novel and evidence-based data on the impact of educational strategies in the clinical management of epilepsy patients with comorbidities.

099

IS BLOOD-BRAIN BARRIER DISRUPTION RELATED TO CHRONIC EPILEPSY?

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Purpose: In a previous study, we studied blood-brain barrier (BBB) disruption in the lithium-pilocarpine model of chronic epilepsy. We measured the expression of angiogenic factors and their receptors and checked tight junction integrity by staining zonula occludens 1 protein (ZO-1). We showed that angiogenesis was associated with a permanent BBB disruption, which is known to contribute to epileptogenesis.

Method: To assess that chronic epilepsy is related to BBB disruption, we investigated vascular changes in the chemical kindling model, which induces a progressive hyperexcitability without spontaneous seizures. This model was obtained by repetitive injections (every 48 h) of a subconvulsive dose of pentylenetetrazol (PTZ, i.p.). The progressive aggravation of seizures was measured by EEG recording and behavioral observation according to Racine scale. Rats were sacrificed at different time-points, and vascularization, tight junction integrity and angiogenic factors were evaluated.

Results: At first, we showed that seizures started synchronously in different structures (hippocampus, thalamus and cortex). At score1 we observed: 1) a peak of VEGF expression, 2) a significant neovascularization, 3) a decrease of ZO-1 staining along microvessels. At later scores, we noticed: 1) a return of VEGF expression back to basal level, 2) no more increase in vessel density, 3) a regular staining of ZO-1 indicating that BBB rebuilt.

Conclusion: In this model, we showed that BBB is transiently disrupted and resist to long-lasting seizures at later stages, suggesting a vascular tolerance. These surprising results strengthen the hypothesis of a correlation between BBB permeability and spontaneous seizures.

100

GENETIC VARIABILITY IN DRUG METABOLISING ENZYMES AS DETERMINANT OF CARBAMAZEPINE DOSE REQUIREMENT IN NEWLY DIAGNOSED EPILEPSY

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Purpose: The dose of carbamazepine (CBZ) required to achieve optimal seizure control varies considerably between patients. A number of drug metabolising enzymes (DMEs) contribute to the inactivation of CBZ. Common variants in genes encoding these DMEs may affect serum concentrations of CBZ and thereby influence dose requirement. We have assessed whether variation in genes encoding DMEs are associated with maintenance dose of CBZ when successfully employed as monotherapy in people with newly-diagnosed epilepsy.

Methods: A total of 161 individuals with newly diagnosed epilepsy (50% male, median age 37 years, range 6–78 years) who had been seizure-free over a period of at least 12 months on unchanged CBZ dose were included in the analysis. A total of 91 single nucleotide polymorphisms (SNPs) across 6 DMES (*CYP1A2, CYP2C8, CYP3A4, CYP3A5, EPHX1, UGT2B7*) were genotyped using a Sequenom MALDI-TOF-based platform. Associations between SNP genotypes/haplotypes and CBZ dose were identified by univariate analysis.

Results: A total of nine genetic variants showed a significant association with the maintenance dose of CBZ. Five of these SNPs were in the gene *UGT2B7* (rs3924194; $p = 0.007$, rs4356975; $p = 0.014$, rs7439366; $p = 0.030$, rs7375178; $p = 0.034$, rs4292394; $p = 0.034$). Haplotype analysis employing all genotyped variants in *UGT2B7* also showed association with CBZ dosing.

Conclusions: These initial findings suggest that genetic variants in the *UGT2B7* gene may influence the dose requirement of CBZ when used as monotherapy in newly-diagnosed epilepsy. This study represents the first step in pharmacogenetic efforts to individualize the dose of antiepileptic drugs required for successful seizure control.

101

ASSESSMENT OF THALAMIC PATHOLOGY IN PATIENTS WITH UNILATERAL MESIAL TEMPORAL LOBE EPILEPSY AND HIPPOCAMPAL SCLEROSIS (MTLE-HS) BY MEANS OF VOXEL-BASED MORPHOMETRY (VBM), T2-RELAXOMETRY AND ADC MAPPING

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Purpose: To assess thalamic pathology in patients with unilateral MTLE-HS.

Method: Thirteen patients with right MTLE-HS (RTLE), 11 patients with left MTLE-HS (LTLE) and 33 age and sex-matched healthy controls were studied. VBM was applied with a modulation step for the determination of grey-matter volume (GMV) changes. Whole-brain comparisons between controls and patient subgroups were performed using t-test statistics with FDR ($p < 0.05$). Local thalamic GMV changes were assessed using an anatomical mask. Mean/standard-deviation and left-right asymmetries of multislice T2-relaxometry (four consecutive TE = 45, 90, 135 and 180 ms) and ADC values (b = 0, 1000 s/mm^2) were computed using a 0.5 cm^2 ROI placed over the thalamus and were compared using two-sample t-test.

Results: Both subgroups showed GMV reduction in the ipsilateral hippocampus, and for the LTLE subgroup also in the ipsilateral parahippocampus gyrus, Heschl's gyrus, the insula and the claustrum. Local GMV analysis showed reduction in the ipsilateral pulvinar and lateral dorsal nucleus of the thalamus only in the LTLE subgroup. T2 and ADC analysis showed left-right asymmetries in 2 patients (1 RTLE patient with elevated ipsilateral ADC values and 1 LTLE patient with T2 and ADC changes).

Conclusion: Thalamic GMV reduction was exclusively observed in patients with LTLE. Differences in T2 and ADC were detected at the individual level in ~10% of the patients. These findings indicate that thalamic lesions are present in a subset of patients with MTLE-HS.

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SUBTRACTION ICTAL SPECT COREGISTERED TO MRI (SISCOM) IN EVALUATING CHILDREN WITH NORMAL MRI FOR EPILEPSY SURGERY: CLINICAL USE AND SURGICAL OUTCOME

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Purpose: To determine whether SISCOM is useful in localizing seizure onset and predicting postsurgical outcome in children with intractable epilepsy and normal MRI scans.

Method: A retrospective review was performed in all children with intractable epilepsy and normal MRI, who underwent SISCOM prior to epilepsy surgery at the Mayo Clinic Rochester between 1996–2008.

Results: Eighteen subjects were identified (mean age at surgery 14.1 years, male 66%). Scalp EEG monitoring showed focal ictal onset in 6 (33%) and lateralized onset with a dominant focus in 5 (28%). SISCOM revealed a focal hyperperfusion abnormality in 12 (76%) patients, rendering further localization in 4 of 7 (57%) patients whose scalp EEG showed no dominant ictal focus. Ten patients with focal SISCOM abnormality underwent intracranial EEG monitoring. The SISCOM abnormality lateralized to the site of intracranial ictal onset in all patients, being concordant with the intracranial ictal onset in 6. Seizure freedom was achieved in 7 (39%) patients at last follow-up. Favorable outcomes were present in 66% of patients with focal scalp EEG ictal onset, 50% of patients with localizing SISCOM abnormality, and 75% of patients with concordant scalp EEG and SISCOM findings. In patients with available postoperative MRI scans, favorable outcomes were present 2 of 3 (67%) patients with partially resected compared to none of 3 patients with non-resected SISCOM abnormality.

Conclusion: SISCOM is useful in the planning of resective surgery in children with intractable epilepsy and normal MRI. Resection of focal SISCOM abnormality may be a predictor of favorable surgical outcome.

Poster Session: Neurobiology and basic sciences I
Monday 28th June 2010
13:30–14:30

p103
ALTERATIONS IN GENE EXPRESSION IN THE DENTATE GYRUS IN EPILEPSY AND EPILEPTOGENESIS IN THE AMYGDALA STIMULATION MODEL OF THE TEMPORAL LOBE EPILEPSY

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Purpose: The purpose of the study was to evaluate alterations of the transcriptome in the Dentate Gyrus during epileptogenesis and epilepsy in the rat model of temporal lobe epilepsy.

Method: Epilepsy in rat was evoked by status epilepticus induced by electrical stimulation of the amygdala. To detect spontaneous seizures, continuous video-EEG monitoring was performed. Animals were sacrificed 14 or 30 days after stimulation. On the basis of video-EEG monitoring animals were assigned to epileptogenesis (no spontaneous seizures) or epilepsy (did have spontaneous seizures) groups. Dentate Gyrus was dissected, RNA was isolated and processed for hybridization to Affymetrix microarrays. Genes which expression differed between control versus epilepsy, control versus epileptogenesis, and epilepsy versus epileptogenesis by 1.2 log fold with $p < 0.01$ were selected. For 10 genes qRT-PCR reaction was performed to confirm data obtained from microarrays.

Results: Forty one genes fulfilled required criteria. For 9 out of 10 genes selected for qRT-PCR, data were confirmed. Some genes of these genes have been previously implicated in epilepsy (Npy, NpyR, TIMP1, Trh), others have not been studied in this context or are unknown genes. The functions of detected genes are related to synaptic function, cell death and inflammatory response.

Conclusion: There are differences in gene expression between control and epilepsy or epileptogenesis. There are also genes which expression differs in the dentate gyrus of epileptic rats when compared to epileptogenesis. Interestingly, these genes represent various biological and molecular functions.

Supported by Polish Ministry of Science and Education Grant 3/0-PBZ-MNiI-2/1/2005.

p104
UP-REGULATION OF POLYSIALYLATED NCAM AND CADHERIN IN THE HIPPOCAMPUS OF THE EPILEPTIC MUTANT EL MOUSE DURING DEVELOPMENT

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Purpose: The neural cell adhesion molecule (NCAM) and its posttranslational modification by polysialic acid (PSA) are involved in the formation, establishment, and plasticity of neural circuits in the central nervous system. The classic cadherins (calcium-dependent cell adhesion molecules) are also involved in synaptic organization and stabilization during development. These determinants of cellular interactions may be associated with the pathophysiology of epilepsy. The purpose of the present study is to examine whether the PSA-NCAM system is associated with the epileptogenesis by using the epileptic mutant EL mouse.

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 NCAM, PSA-NCAM, and cadherin were investigated by Western blotting in the seizure generalization site, hippocampus.

Results: In EL mice, levels of NCAM and cadherin significantly increased during early developmental stages (3–5 weeks) and then, decreased at 10 weeks, and remained very low thereafter. A sharp withdrawal was observed before experiencing frequent seizures. In contrast, expressions of PSA-NCAM remained upregulated.

Conclusion: In the brain of EL mice, PSA-NCAM and cadherin are upregulated before experiencing repetitive seizures. Highly polysialylated NCAM and overexpressed cadherins may lead to abnormal synaptic reorganization or abnormal plasticity, which can underlie the ictogenesis and epileptogenesis.

p105
GLUTAMINE SYNTHETASE (GS) IN A TEMPORAL LOBE EPILEPSY (TLE) MODEL EXHIBITS MODIFIED SUBCELLULAR EXPRESSION PATTERN

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Purpose: Glutamine synthetase (GS) is an enzyme that catalyzes the biosynthesis of glutamine from glutamate. GS is localized in the astroglia compartment, where it recycles glutamate in the ''glutamine-glutamate cycle.'' In epilepsy, astroglia undergo numeric expansion and excessive ramification, as demonstrated with glial fibrillary acidic protein (GFAP) staining (reactive astrogliosis). However, GS expression may be reduced in the epileptic hippocampus of both rodent models and human TLE patients, according to immunohistochemistry and Western blot studies.

We hypothesize that GS expressing cells are do not always coincide with GFAP astroglia. Instead, they consist distinct cell populations.

Method: The pilocarpine-induced chronic epilepsy model in Wistar rats was used additionally to human epileptic tissue from pharmacoresistant medial temporal lobe epilepsy (MTLE) patients. Immunohistochemistry for GS and GFAP was performed, using a monoclonal and polyclonal rabbit antibody, correspondingly. Brightfield microscopy was used for quantification and cell tracing with stereology and camera lucida setups. Confocal microscopy was applied for GS-GFAP colocalization imaging.

Results:
Our results indicate

No significant numeric alteration of GS-expressing cells in the rat model.

Reduced GS expression in thin ramifications of GS positive cells and enhanced expression in soma and proximal processes.

Only partial overlap of GS and GFAP epitopes under normal conditions.

No overlap of GS and GFAP in human epileptic tissue.

Appearance of strongly ramified GS expressing cellular elements.

Conclusion: GS and GFAP are distinct cell populations whose role in epileptogenesis is to be defined.

Supported by EXC NeuroCure, Epicure and SFB TR3.

p106

HUMAN ASTROCYTES IN CULTURE RESPOND TO ALBUMIN WITH AN INCREASE IN CYTOSOLIC CALCIUM AND DNA SYNTHESIS

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Purpose: A little is known about transition from normal to focal epileptic brain, although disruption in blood-brain barrier and albumin had recently involved. The main object of this work is to characterize the response of cultured human astrocytes to plasma albumin, assessing also the induction of DNA synthesis.

Method: Cortical tissue, functionally identified by electrocorticography, was obtained from 11 patients operated from temporal lobe epilepsy. Astrocytes were cultured for 3–4 weeks and cytosolic calcium concentration ($[Ca^{2+}]_c$) was measured. DNA synthesis was also assessed in response to albumin. Bovine (BPA) and Human Plasma Albumin (HPA) were used.

Results: We have observed: 1) A low concentration of albumin decreased $[Ca^{2+}]_c$, while higher concentration increased $[Ca^{2+}]_c$, mediated by inositol 1,4,5-trisphosphate and released from internal stores. 2) Heparin inhibited, in a competitive way, the effect of albumin in calcium response. 3) Increase in $[Ca^{2+}]_c$ was reduced a 4.4% by blocking the transforming growth factor-beta (TGF-β) receptor. 4) The increase in $[Ca^{2+}]_c$ by albumin was a 23.3% lower in astrocytes obtained from epileptogenic cortex. 5) Albumin induced DNA synthesis in a dose-response manner. 6) Induction of DNA synthesis was partially blocked by heparin and block of TGF-β; however, the combination of both doesn't inhibit completely DNA synthesis.

Conclusion: Plasma albumin activates human astrocytes mobilizing Ca^{2+} and also through the TGF-β receptor. Calcium increases are different in spiking and no-spiking cortices. Aforementioned both mechanisms are able to induce DNA synthesis. Perhaps, these mechanisms could be involved in the transition from normal to focal epileptic brain.

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CHARACTERIZATION OF CD4+ T CELLS SPECIFIC FOR GLUTAMIC ACID DECARBOXYLASE (GAD65) AND PROINSULIN IN A PATIENT WITH EPILEPSY AND STIFF-PERSON SYNDROME, BUT WITHOUT TYPE 1 DIABETES

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Purpose: Characterization of T-cell responses to GAD epitopes in a patient with stiff-person-syndrome and pharmaco-resistant epilepsy but without type-1 diabetes.

Method: T-cell clones were isolated from the patient and responses to GAD65 and proinsulin were determined. Production of IL-3, IL5 and IL-4 were determined.

Results: Fluctuating but persistent T cell reactivity to GAD65 was identified, as well as T cell reactivity to proinsulin at one time point. The majority of the T cell clones isolated from the SPS patient produced high levels of Th2 cytokines (IL-13, IL-5 and IL-4). We also examined levels of GADA, insulin and IA-2, and epitope specificity of GADA. High levels of GADA in both serum and cerebrospinal fluid persisted throughout the follow-up, but despite T cell reactivity to both GAD65 and proinsulin, no autoantibodies to other islet autoantigens were detected. The patient remained diabetes-free for the 44 month follow up.

Conclusion: T cells predominantly of Th2 type may be protective from progression to T1D in patients with epilepsy who have high levels of GADA.

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EFFECTS OF EXPERIMENTAL NOISE POLLUTION ON HYPERTHERMIC-INDUCED SEIZURES IN WISTAR RAT INFANTS

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Purpose: Febrile seizures which are often caused by high fevers are the most prevalent type of seizures that may be affected by Stress-inducing factors during prenatal and postnatal periods. Noise stress also seems to have influences on hyperthermic-induced seizures. In this study we examined the effects of fetal and infantile exposure to noise pollution on triggering febrile seizures.

Method: Pregnant female rats were divided into two groups. The first group rats (I) were exposed to the noise of 103 dB (2 h/day), including 5 min noise patterns with different frequencies followed by a one- minute silence period in a randomized manner. The second group rats (II) were kept in normal conditions. After birth, infants of the first group mothers (I) were also divided into 2 groups, one was exposed to a 2 h noise/day exactly after birth ($n = 9$) and the other was put into normal conditions ($n = 9$). Infants of the second group mothers (II) were also allocated in the normal ($n = 9$) and experimental ($n = 9$) categories with noise exposure and non exposure periods respectively. Eight days after birth all of the infants ($n = 36$) were examined for hypothermic-induced seizures.

Results: The results indicate a statistically significant difference ($p < 0.05$) in the mean time to the onset of febrile seizure between experimental (prenatally noise exposure/prenatally and postnatally noise exposure) and control groups.

Conclusion: This study confirms that, exposure to noise may reduce the time interval between initiation of hyperthermia and convulsions.

Keywords: Hyperthermic seizures, Noise pollution, Stress

p109

CORTICO-THALAMO-CORTICAL INTERACTIONS DURING ABSENCE SEIZURES

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Purpose: Generalized absence seizures are known to be generated within the cortico-thalamo-cortical system. However the exact interactions between the cortex and the different thalamic nuclei, which are needed for the generation and maintenance of spike-wave discharges (SWD) are still to be elucidated. This study aims to shed more light on

these interactions via multisite local field potentials recordings in freely moving, genetic epileptic rats.

Method: WAG/Rij rats were equipped with multiple electrodes targeting layer 4, 5 and 6 of the somatosensory cortex, the rostral and caudal RTN, the VPM, the anterior and posterior nucleus of the thalamus. The degree of dependence between signals and their maximal association was calculated during seizures and in control periods using the nonlinear association analysis.

Results: A significant increase in the degree of dependence and maximal association was found for SWDs as compared to control periods. This was predominantly seen for cortico-thalamic electrode pairs and to a lesser extend for intrathalamic pairs. Interestingly, the degree of dependence and the maximal association showed a stronger increase for indirect pathways (somatosensory-cortex – anterior thalamus) than for ''in-loop'' connections (somatosensory cortex -caudal RTN – VPM).

Conclusion: The increase of the maximal association as well as the increase in degree of dependence are in good agreement with the idea that network interactions and interdependencies within the cortico-thalamo-cortical loop are reinforced. The involvement of the anterior thalamus is striking since it was not previously included in seizure genesis or propagation.

p110

VALUE OF SPECTRAL ANALYSIS IN DIFFERENTIATING ATYPICAL PROLONGED BENIGN EPILEPTIFORM VARIANT FROM A SEIZURE: A CASE REPORT

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Purpose: To report an unusually prolonged benign epileptiform variant in a boy mimicking a seizure and to highlight the value of spectral analysis in differentiating it from electrographic seizure.

Methodology and results: 13 years old boy was referred for routine scalp electroencephalogram (EEG) as a part of evaluation for single episode of post traumatic amnesia of 10 h duration. He never had seizures. His magnetic resonance imaging of the brain was normal. The EEG revealed a rhythmic activity with varying frequencies, amplitudes and distribution, lasting for nearly an hour. It had uni or bitemporal onset with spread to become diffuse, during both awake and stage 1 sleep. Hyperventilation, photic stimulation, mental arithmetic, eye closure etc did not affect the rhythm. It subsided as soon as he entered stage 2 sleep and reappeared when woke up. He completed the detailed cognitive testing normally when EEG showed this rhythm. The spectral analysis revealed mixture of harmonic (6 Hz) and supra harmonic (12 and 18 Hz) frequencies.

Conclusion: The above benign epileptiform variant has features of both psychomotor variant and subclinical rhythmic EEG discharge of adults (SREDA). The unique feature of this rhythm is that it was unusually prolonged lasting an hour and occurred in pediatric age. The spectral analysis and cognitive testing helped us to differentiate it from a seizure.

p111

CORRELATION ANALYSIS OF CONTINUOUS EEG RECORDINGS OF WAG/RIJ RATS WITH GENETICALLY DETERMINED ABSENCE EPILEPSY FOR THE PURPOSE OF DEVELOPING A PREDICTION OR AN EARLY SEIZURE REGISTRATION TECHNIQUE

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Purpose: Develop an EEG-dependent method and software to identify predictors of absence seizures or early register them by means of correlation dimension analyses.

Method: The work was performed on inbred WAG/Rij rats (n = 12) with spike-wave signals which systematically appeared on cortical electrogram (7–11 Hz). Three dipped electrodes were used simultaneously at reticular thalamic nucleus, sensorimotor cortex and frontal cortex to register electrical activity. EEG was classified by: wakeful state, dormancy, seizure, artifacts of recording. Then series of surrogate data were prepared by consequent jointing data intervals of the same functional state. A software complex for the analysis of correlation dimensions of EEG data was also developed.

Results: Typical values of correlation dimensions of EEG for WAG/Rij rats in various functional states of brain were identified. Behavior of correlation dimension function before and after a seizure showed that a definite conclusion about the reduction of dimension can only be made after a seizure kick-off point. The software was tested on EEG data of a patient with absence epilepsy and it was shown that it could potentially be a decision-making mechanism for responsive stimulation to cut the seizure.

Conclusion: An observable difference between correlation dimensions for various functional states of a rat's brain as well as behavior of time-dependent correlation dimension starting from seizure kick-off allows us to determine the moment of seizure's onset using corresponding technique.

p112

POSTNATAL MALNUTRITION IN RATS INCREASE THE SUSCEPTIBILITY TO EXPERIMENTAL MODEL OF EPILEPSY INDUCED BY PILOCARPINE

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Purpose: The aim of this research is to study the susceptibility to epileptogenesis of adult rats submitted to malnutrition during early postnatal period. Using the pilocarpine model was evaluated acute, silent and chronic phases.

Method: Wistar rat pups were maintained on a starvation regimen from D1 to D21. Age-matched well-nourished rats were used as control. At the D60 the animals were divided in 3 groups: *Nourished plus Seizures (N+SE)* – pilocarpine (350 mg/kg Intraperitoneal) for induction of epilepsy model (n = 8 animals); *Malnourished plus Seizures (M+SE)* pilocarpine (200 mg/kg Intraperitoneal) to induce the epilepsy model (n = 8 animals) and *Malnourished Control (MC)* animals malnurished that received saline solution 0.9% (n = 8 animals). Surviving animals were placed in a video room during 9 weeks in order to determine the frequency of seizures.

Results: The results show that the minimum dose required to induce epileptogenesis in the malnourished animals was 200 mg/kg, while the already established dose used in normally nourished rats is 350 mg/kg. The silent phase in the *M+SE* group (6.38 ± 2.13 days) was 13 days shorter than in the *N+SE* group (18.88 ± 3.23 days) ($p < 0.05$). The frequency of seizures in chronic phase was great in the *M+SE* group (22.18 seizures/week) than in the *N+SE* group (3.0 seizures/week) ($p < 0.0001$).

Conclusion: Our findings suggest that malnutrition reduce the threshold to epilepsy seizures and promote alterations in brain development that remain in adult life. These findings indicate that the protein caloric malnutrition is pro epileptogenic.

Financial Support: CAPES.

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ALTERATIONS OF PHASIC AND TONIC $GABA_A$ RECEPTORS-MEDIATED INHIBITION IN HUMAN PYRAMIDAL NEURONS FROM PERITUMORAL TISSUE ADJACENT TO BRAIN GLIOMAS

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Purpose: About 30% of patients with brain gliomas develop epilepsy (tumor associated epilepsy – TAE). It is unclear why some tumors cause seizures and others do not. One of the very important findings is a lower number of GABAergic synapses terminating on pyramidal neurons located in peritumoral tissue where epileptiform discharges were recorded peroperatively compared with tissue without such activity. We tested a hypothesis that $GABA_A$Rs-mediated phasic and tonic inhibitions in pyramidal neurons are different in tumors, which initially presented with epileptic seizures as compared to gliomas in which seizures were not the first symptom.

Method: Tissue specimens were studied from patients with various histological types of gliomas as well as from patients after brain resection from different reasons. The $GABA_A$Rs inhibitory postsynaptic currents (IPSCs) were recorded and their parameters analyzed. The tonic current was revealed as an outward shift of holding current after a $GABA_A$Rs antagonist bicuculline was applied. The recorded neurons were labeled with biocytin for morphological assessment.

Results: We examined specimens from low-grade gliomas (n = 2), high-grade gliomas (n = 4) and nontumor tissue (n = 1). Although the number of cells was low, a trend for lower IPSCs frequency and amplitude was found in patients with TAE. The tonic current was lower in neurons recorded from the TAE patients.

Conclusion: Our preliminary data suggest that impaired GABAergic inhibition of pyramidal neurons in peritumoral tissue may account for higher propensity to develop seizures in patients with certain types of brain gliomas. Additional cells will be examined to reach more conclusive results.

p114

MOLECULAR CHARACTERIZATION OF DYSLAMINATION IN FOCAL CORTICAL DYSPLASIA WITHOUT BALLOON CELLS

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Purpose: In the present study we focussed on focal cortical dysplasia (FCD) without Balloon cells, malformations which are very controversially discussed concerning their development and whether they are ''true dysplasias.'' The aim of this study was to gain new insights in the development of dyslamination in FCD without Balloon cells.

Method: In this study we used layer-specific markers (ER81, RORß), interneuron stainings (reelin, calbindin, calretinin, parvalbumin) and maturation markers (doublecortin, vimentin) on the level of in situ hybridization and immunohistochemistry for a thorough molecular characterization of dyslamination of human FCD without Balloon cells (n = 35) and to correlate these findings with clinical parameters.

Results: The main results were:

1. The sequence of cortical layers from top to bottom was in principle preserved. Even in highly disturbed areas, vertical malpositioning of neurons was limited to certain compartments surrounding the normal position.
2. Most disturbances comprized more than one neuronal subtype or one layer.
3. Several brain region- and syndrome-related patterns of dyslamination were observed.
4. In many young patients a delay of maturation could be detected.
5. A significant correlation between numeric abnormalities in pyramidal cells and duration of epilepsy was not seen.

Conclusion: FCD without Balloon cells is a very complex disturbance of the cortical formation. Early defects in cell proliferation or late disturbances in ''fine tuning'' of cortical organization including apoptosis and delayed maturation seem to be more probable than profound migratory defects.

Poster Session: Neurobiology and basic sciences II
Monday 28th June 2010
13:30–14:30

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DYNAMIC CHARACTERIZATION OF NEURONAL SPIKING DURING ICTAL ACTIVITY IN THE MEDIAL ENTORHINAL CORTEX OF THE ISOLATED GUINEA PIG BRAIN

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Purpose: Main objective of the study is to characterize different firing patterns generated by entorhinal cortex (EC) neurons during epileptic seizures, to understand the mechanisms that lead to the transition from the initial phase into irregular tonic firing and bursting.

Methods: Intracellular recordings were performed with sharp electrodes from layer II–III and layer V–VI EC neurons in the in vitro isolated guinea pig brain. Extracellular potassium concentration was recorded with ion-sensitive electrodes. Seizures were induced by arterial perfusion of bicuculline (50 μM; *Gnatkovsky et al. 2008 Ann Neurol 64:674*). To characterize neuronal spikes we applied ''kinking'' analysis based on phase plot (dV/dt vs. V) represented as a loop. This method highlights the differences in resting membrane potential, threshold and rising/falling slopes of action potentials.

Results: Intracellular EC recordings during seizures, showed an initial fast activity followed by irregular tonic firing and a late bursting. Kinking analysis identified different populations of spikes and also a peculiar type of doublet spikes, probably of ectopic origin, generated in the transition from the initial phase of seizure and the irregular firing. No difference was observed between superficial and deep layer principal neurons. Putative interneurons showed different spike features compared to principal cells.

Conclusion: Reproducible changes in spike morphology were consistently observed during the 3 phases of a seizure in principal neurons of the EC. The correlation between spike features and extracellular potassium concentration demonstrate the generation of ectopic spikes during rises in extracellular potassium.

p116
NEUROFEEDBACK TRAINING IN ABSENCE EPILEPSY

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Purpose: Beneficial effects of Neurofeedback (NF) training on seizure occurrence have been described in epileptic patients. Little research has been done about differentiating NF effectiveness by type of epilepsy, particularly, whether idiopathic generalized seizures are susceptible to NF. Here we investigated the effects of NF training in a genetic model for absence epilepsy.

Method: Male adult absence epileptic (WAG/Rij) rats (n = 6) chronically equipped with subdural EEG electrodes were exposed to base-line measurement, followed by ten training sessions in which the occurrence of spike-wave discharges (SWDs) was reinforced by the presentation of a reward (food-pallet), and several post–training sessions. Number of SWDs in the EEG was analyzed.

Results: Operant conditioning by positive reinforcement of SWDs let to decreased SWD occurrences during training; however, the changes during training were not persistent in the post–training sessions.

Conclusion: Considering that the behavioral state is the major controlling factor in the occurrence of SWDs, it is proposed that the reinforcement situation increased arousal resulted in fewer SWDs. Additional tests supported this hypothesis. The outcomes have implications for the possibility to train SWDs with operant learning techniques.

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DO GLIAL NETWORK PLAY A ROLE IN EPILEPTOGENESIS? A STUDY IN A GENETIC MODEL OF ABSENCE EPILEPSY: THE GAERS (GENETIC ABSENCE EPILEPSY RATS FROM STRASBOURG)

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Recent studies have shown, in two rodent models of absence epilepsy that discharges start in a region of the somatosensory cortex, *the focus*, and then generalize. Moreover, recent works have suggested that glial cells are implicated in the synchronization of cortical neurons during the onset of epileptic seizures.

The general objective of this work is to address these new concepts by investigating the role of the cortical glial network within the "*cortical focus*" of absence seizures in a genetic model of absence epilepsy: the GAERS. We hypothesized that maturation of the cortical glial network is different in GAERS, as compared to controls, in the area of the cortical focus, during the first 4–5 postnatal weeks: the period of epileptogenesis.

First, the EEG investigation in rat pups during this period showed that the first spike-and-wave discharges occurred at 23–25 postnatal days in the somatosensory cortex. Second, using immunohistochemical labeling of the expression of GFAP (glial fibrillary acidic protein), we observed in the somatosensory cortex that radial glia-like cells were still present at P7 in GAERS, whereas they had almost disappeared in controls. Furthermore, a greater number of GFAP-positive cells were observed at P14 in GAERS, as compared to control animals. This difference persisted in adulthood when absence seizures are well-established. These data support our hypothesis that an anomaly in the maturation of the somatosensory cortex of GAERS could participate in the epileptogenesis of absence epilepsy.

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THE AUTOANTIBODIES TO GLUTAMATE RECEPTORS INVESTIGATION IN NEUROLOGICAL DISEASES IN CHILDREN

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Purpose: To estimate the autoantibodies (aAB) to glutamate receptors (GluRs) in children. Glutamate is the major excitatory neurotransmitter in CNS may triggering neurodegeneration as a result of excessive stimulation of postsynaptic receptors by l-glutamate in epilepsy, CNStrauma and brain ischemia. This process leads to the appearance of aAB to fragments of GluRs in blood.

Method: Serum level of GluRs-aAB was estimated in 152 pediatric patients with epilepsy (Epi), syncope (S), mild brain trauma (BT), mitochondrial diseases (MD) and in 20 children of control group (CG) by ELISA, synthetic peptides-analogues of GluR1 (AMPA) and NR2A (NMDA) subunits were used as antigens. GluRs-aAB level in CG was 100 ± 20 c.u.

Results: In Epi (n = 60) GluRs-aAB level was significantly higher versus CG (GluR1179 ± 15.3 c.u., NR2A161.4 ± 14 c.u.).In S (n = 15) the NR2AaAB was 173 ± 20.4 c.u. ($p < 0.05$), GluR1aAB elevated NS. In acute period of BT (n = 60) the GluRs-aAB were significantly increased, but the elevation of NR2AaAB was higher than GluR1. In follow-up studies GluR1aAB level was decreased in E remission, NR2A was still elevated. The decreasing of GluRs-aAB level was observed in children with BT and S. GluR1aAB level was elevated in children with repeated BT. The EEG examination revealed the paroxysmal discharges and epileptic activity in 25% of children in this group. In patients with MD (n = 17), even without seizures, the GluRs-aAB were extremely high. Epileptic seizures are a common occurrence in MD.

Conclusions: In E, S, BT and MD glutamate receptors are damaged as a result of excititoxicity. NMDARs dysfunction observed in all diseases mentioned above. AMPARs damage more specific for E and the elevation of GluR1aAB level is a risk for E develop in BT and MD.

p119
DOES STATUS EPILEPTICUS IN 12-DAY-OLD RATS LEAD TO IMPAIRMENT OF COGNITIVE FUNCTIONS LATER IN THE LIFE?

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Purpose: To investigate whether LiCl/pilocarpine-induced status epilepticus (SE) in P12 rats may induce long-lasting changes in spontaneous behavior and cognitive functions related to habituation and attention.

Method: SE was induced by pilocarpine (40 mg/kg) in P12 rats pretreated with LiCl. Animals were exposed to the open field at P18, 25 and 32 four times (5 min each) with 60 min intervals between sessions. Reaction of animals to a novel object was tested at P80. The thigmotactic scanning, centre walking, rearing, self-grooming, and immobility were evaluated. Habituation was assessed by comparing behavior between sessions 1 and 4, the investigation of new object was evaluated. After the end of testing, epilepsy was diagnosed using video/EEG monitoring.

Results: There were no differences in habituation between animals with SE and controls. In contrast, the duration of rearing was lower in SE

animals at P32, suggesting a nonselective attention deficit. Animals with SE spent less time in the center of arena in the last session suggesting a fear-related behavior in these animals. In adult rats no difference in habituation potency was found however, in animals with SE a marked decrease of investigatory response to a stimulus object was detected. Seizures were detected in subpopulation of animals.

Conclusion: Early SE leads to attention deficits detectable in both adolescent and adult rats. Whether these changes are related to epilepsy or brain impairment has to be further analyzed.

Supported by Grant P302/10/0971 of the Grant Agency and project LC554 and grant ME08045 of the Ministry of Education.

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INFLAMMATION IN HUMAN MESIAL TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS: PRELIMINARY EVALUATION

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Purpose: Experimental studies suggest that factors involved in inflammation participate in neuronal excitability and/or glial scar formation in epilepsy. Studies in human mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) suggest activation of hippocampal microglia with concomitant over-expression of HLA-DR (Human Leukocyte Antigen DR). This inflammatory process has been implicated in secondary epileptogenesis. However, its relevance as a primary event in human MTLE-HS remains to be elucidated.

Aim: To characterize the inflammatory status in hippocampus and temporal cortex of MTLE-HS patients.

Patients & methods: Ten patients with refractory MTLE-HS submitted to surgery were compared to 2 autopsy controls without neurological disease. HLA-DR expression in the hippocampal structure (lesion and perilesional cortical area) was characterized by immunohistochemistry.

Results: As expected we observed HLA-DR over-expression in hippocampal structures from MTLE-HS patients. The temporal cortex of these patients also showed increased expression of this antigen and gliosis.

Conclusion: This study demonstrates persistent inflammation in the hippocampus of MTLE-HS patients exceeding the lesional limits – extending as far as the adjoining temporal cortex, a region considered normal by morphological criteria. These results suggest that the epileptogenic process is more diffuse than initially expected. The inflammatory process may be secondary to recurrent seizures or may be associated with persistent neuronal loss and/or reactive gliosis in this brain region. Further characterization of this inflammatory process is underway.

Acknowledgements: Supported by a BICE-Tecnifar Grant.

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HIPPOCAMPAL NEUROTRANSMISSION IN THE PENTYLENETETRAZOLE KINDLING MODEL: ROLE OF EXTRASYNAPTIC $GABA_A$ RECEPTORS

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Purpose: Plastic changes in hippocampal extrasynaptic $GABA_A$ receptors have been shown in the kainate- and pilocarpine-induced animal models of temporal lobe epilepsy (Scimemi A et al. J Neurosci. 2005; 25: 10016–24; Zhang N et al. J Neurosci. 2007; 27: 7520–31). To identify possible hippocampal extrasynaptic $GABA_A$ receptor plasticity in the murine pentylenetetrazole (PTZ) kindling model we are investigating possible alterations in hippocampal synaptic transmission and tonic GABAergic inhibition.

Method: Extracellular and whole-cell patch-clamp recordings were performed on hippocampal brain slices from PTZ kindled and saline-treated mice. In extracellular recordings, a field excitatory postsynaptic potential (fEPSP) was evoked in the dentritic area of either dentate gyrus (DG) or CA1. Tonic inhibitory current was measured from whole-cell recordings in granule cells in the DG.

Results: We found no difference in synaptic input/output relationship of the fEPSP slope in either the DG or CA1 area from saline-treated and PTZ kindled mice 24–108 h after the last injection suggesting no change in overall synaptic transmission. Results from whole-cell recordings reveal that tonic current mediated by bath application of 5 μM GABA was similar in granule cells from PTZ kindled and saline-treated mice.

Conclusion: Results so far suggest no alteration in tonic GABAergic inhibition in DG granule cells in PTZ kindled mice, but further patch-clamp experiments with subunit-selective $GABA_A$ agonists/modulators and Western Blot analysis may reveal whether plastic changes in extrasynaptic $GABA_A$ receptors has occurred in the PTZ kindling model.

p122
ASTROGLIAL LOSS AND EDEMA FORMATION IN THE RAT PIRIFORM CORTEX AND HIPPOCAMPUS FOLLOWING PILOCARPINE-INDUCED STATUS EPILEPTICUS

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Purpose: In the present study, we analyzed aquaporin-4 (AQP4) immunoreactivity in the piriform cortex (PC) and the hippocampus of pilocarpine-induced rat epilepsy model to elucidate the roles of AQP4 in brain edema following status epilepticus (SE).

Method: We performed immunohistochemical study for AQP4 and double immunofluorescent staining for AQP4/glial fibrillary acidic protein (GFAP) in the rat PC and hippocampus of pilocarpine-induced epilepsy model hippocampus.

Results: In control animals, AQP4 immunoreactivity was diffusely detected in the PC and the hippocampus. AQP4 immunoreactivity was mainly observed in the end-feet of astrocytes. 12 h – 1 week after SE, AQP4-deleted area was clearly detected in the PC. In addition, AQP4 immunoreactivity was gradually decreased in the dentate gyrus, not in the CA1–3 regions. These reductions in AQP4 immunoreactivity were correlated to astroglial loss in these regions. Four weeks after SE, AQP4-deleted area was reduced and AQP4 immunoreactivity was enhanced in the PC as compared to controls. Similarly, AQP4 immunoreactivity in the hippocampus was increased as compared to control levels. These enhancements of AQP4 immunoreactivity were dependent to reactive astrogliosis.

Conclusion: Therefore, these findings indicate that reduced AQP4 immunoreactivity may result in regional specific edema formation in the PC and the hippocampus following SE.

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THE EFFECT OF HYPERCAPNIA ON THE DEVELOPMENT OF SEVERE TONIC–CLONIC SEIZURES

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Purpose: The initiation and inhibition of seizures is possibly controlled by blood and brain tissue pO_2, pCO_2 and pH levels. Hypercapnia is known to have pronounced anticonvulsive effect which mechanisms are still not completely revealed. The purpose of our research was to study the effect of hypercapnia on the development of severe convulsive seizures.

Method: The evaluation of anticonvulsive effect of hypercapnia was performed using a rat model of pentylenetetrazole (PTZ) induced seizures. The drug was administered 3 times (25 mg/kg i.p.) with 15 min intervals to avoid overdose and death of the animals. Animals were put into controlled atmosphere chamber. The first group of animals underwent 30 min exposure to the gas mixture containing 10% CO_2. Then seizure activity was initiated and seizures were observed and scored. The second group was extracted from the chamber after being exposed to 10% CO_2 during 5 min and then seizure activity was observed. EEG recordings were held during the experiment.

Results: Administration of PTZ induced severe tonic–clonic seizures in all animals at normocapnic conditions while only 80% of animals developed such seizures during hypercapnia. The latency of severe tonic–clonic seizures development increased in the atmosphere containing 10% CO_2. However animals extracted from the chamber after 5 min hypercapnia did not exhibited any decrease of seizure activity.

Conclusion: We conclude that respiratory acidosis decreases the rate of severe tonic–clonic seizures development but preapplication of 10% CO_2 gas mixture do not exhibit anticonvulsive effect.

p124

RO-25-6981, A SELECTIVE ACTIVITY-DEPENDENT BLOCKER OF NMDA RECEPTORS CONTAINING NR2B SUBUINT IN A MODEL OF CORTICAL EPILEPTIC AFTERDISCHARGES IN DEVELOPING RATS

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Purpose: During early postnatal development, glutamatergic transmission is controlled by NMDA receptors (NMDARs) containing predominant NR2B subunit and their overactivation is responsible for pathophysiology of epileptic seizures and excitotoxity. Due to the fact that blockade of NMDARs can prevent seizures, we were investigating effects of administration of Ro-25-6981,(aR, bS)-a-(4-Hydroxyphenyl)-b-methyl-4-(phenylmethyl)-1-piperidinepropanol maleate, a selective antagonist of NMDARs containing NR2B subunit on duration of cortical epileptic afterdischarges (ADs) in developing rats.

Methods: Experiments were performed in three age groups of male Wistar rats: 12-, 18-, and 25-day old. ADs were elicited by six subsequent series of biphasic rectangular pulses of 1 ms duration and 8 Hz frequency. Ro-25-6981 was injected 20 min after first ADs in a dose of 1- and 3 mg/kg. Changes in total duration of ADs were evaluated. Statistical analyses were performed by mean of ONE WAY ANOVA followed by Holm-Sidac post hoc test (overall significance = 0.05).

Results: Total duration of ADs in 12-day-old animals group was markedly influenced by 1 mg/kg dose of Ro-25-6981 and ADs were prolonged within 5th stimulation in comparison to 1st ADs. On the other hand 3 mg/kg dose resulted in a tendency to shorten subsequent ADs. In older, 18- and 25-days-old rats, ADs were not significantly affected by Ro-25-6981.

Conclusion: Ro-25-6981 exhibits protective effects against prolongation of ADs elicited in the youngest, 12-day-old group of rats but do not have any marked influence on ADs duration in case of 18- and 25-days-old rats.

This study was supported by a grant No: 200107 of the Grant Agency of Charles University.

p125

PHARMACOLOGICAL BLOCKADE OF OLFACTORY SYSTEM CHANGES OF SPIKE-WAVE DISCHARGES REGULATION IN WAG/RIJ RATS

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Purpose: To evaluate the possible role of olfactory system in the generation of spike-wave discharges (SWDs).

Method: Six adult WAG/Rij rats were used as experimental subjects. WAG/Rij rats were equipped with monopolar cortical electrodes in the frontal region of the cortex with coordinates AP +2.0; L 3.0 (Paxinos & Watson; 1998) under anesthesia (Nembutal 60 mg/kg i.p.). Reference and ground electrodes were inserted in the cerebellum. All animals were allowed to recover from surgery for at least 7 days before the ECoG recording. Experiments were performed in free moving animals in Plexiglas recording cages. Animals were adapted to the experimental and recording conditions for 2 h. The ECoG was recorded 1 h before treatment (this recording was considered as baseline). Then the ECoG was recorded for 1 h. Software program ''CONAN' was used for EEG recording and SWDs analysis.The deafferentation of perioral region of experimental rats induced by i.p. injection of the olfactory epithelial toxin 3-methyl indole (3 MI) in doses 200 mg/kg.

Results: The significant increases number of SWDs ($p = 0.005 < 0.01$ criteria of Wilcoxon matched pairs test) was found after pharmacological blockade. Analysis of duration of SWDs showed no significant effects.

Conclusion: The study 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.

p126

THE ROLE OF T- AND B-CELLS IN SEIZURES AND EPILEPSY

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Purpose: Innate immunity/inflammation in the brain plays a crucial role in acute and chronic seizure precipitation and recurrence in experimental models. Induction of proinflammatory pathways in glia and neurons occurs in human epileptogenic tissue. Alterations of both humoral and cell-mediated immunity have been detected in human epilepsy, although the presence of peripheral immune cell in brain parenchyma is scarse except for Rasmussen encephalitis. Innate immunity plays a major role in the activation and recruitment of peripheral inflammatory cells into injured tissue. We investigated the role of T- and B-cells in acute seizures and epilepsy development using immunodeficient mice.

Method: Seizures were induced by intrahippocampal injection of 7 ng Kainic Acid (KA) or intracerebroventricular injection of 0.1 μg KA, in SCID and NUDE mice, respectively lacking T- and B-cells or T-cells

only, and their respective (BALB/c and CD-1) wild-type. Seizures and the development of epilepsy were evaluated using quantitative EEG analysis. Histology was done to assess neuropathology.

Results: Onset and duration of seizures did not differ in SCID or NUDE mice versus their control strains. NUDE mice developed epilepsy as their wild-type controls. SCID mice injected with KA developed more neuronal cell loss and inflammation as compared to wild-type mice.

Conclusion: Lymphocytes are not significantly involved in the onset and maintenance of seizures, or the development of epilepsy. The lack of lymphocytes in SCID mice is associated with more severe seizure-induced neuropathology, highlighting a possible neuroprotective role of these cells.

Poster session: Cerebral dysplasias and epilepsy
Monday 28th June 2010
13:30 – 14:30

p127
DRUG RESISTANT EPILEPSY IN A CHILD WITH TUBEROUS SCLEROSIS COMPLEX TREATED WITH KETOGENIC DIET: A CASE REPORT

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Purpose: Case reports of children with tuberous sclerosis complex (TSC) and with drug resistant epilepsy treated with ketogenic diet are rare in the literature. We present case of such patient with long observation period.

Method: Girl with TSC, mild mental retardation and refractory epilepsy (complex partial seizures) aged 6 years and 9 months at the beginning of classic ketogenic diet (4:1 at start and 4, 25:1 after 1 year of treatment). Long period of observation – 5 years.

Results: We observed more than 50% reduction of seizures (seizures less frequent and less disabling), marked EEG improvement, no progression of mental retardation, no complications of ketogenic diet, cholesterol level in normal range.

Conclusion: Treatment of children with TSC and drug resistant epilepsy is possible with the ketogenic diet. However more cases are required to establish a place for such therapy.

p128
DIFFERENT CLINICAL EXPRESSIONS OF SUBCORTICAL BAND HETEROTOPIA IN MALES

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Purpose: To describe the peculiarities of subcortical band heterotopia syndrome in males.

Method and results: We present three cases of subcortical band heterotopia (SBH) in males, with different phenotypes. The first is a 3-year-old boy, who presented three epidodes of afebrile seizures, with a patological EEG and SBH on cerebral MRI. He did not suffered any crisis after treatment with valproic acid and he had a normal neurocognitive development. The second one, is a 4-month-old baby, who sufferd numerous episodes of infantile spasms and hypsarrhythmia on EEG. MRI revealed pachygyria and SBH in posterior regions. He developed a refractory epilepsy and associated encephalopaty. The last case is a 7-year-old boy diagnosed with lissencephaly and occipital SBH, who developed epilepsy controlled with treatment, and severe mental retardation.

Discussion: SBH syndrome is a neuronal migration disorder, which occurs rarely in males. Two genes have been involved in the etiology of SBH: doublecourtin gen located on chromosome Xq and LIS1 on 17p13.3. Affected individuals tipically present epilepsy and variable degrees of mental retardation. Classical diffuse SBH and diffuse bands with anterior predominance in MRI are more frecuent in females. Conversely, partial and intermediate posterior, pachygyria-SBH and diffuse bands with posterior predominace are more frecuently or exclusively present in males.

Conclusion: Our data support the variability in the phenotypic expression of SBH in males, concerning the degree of mental retardation involvement and response to antiepileptic treatment. Furthermore, our cases show that SBH in males is more frecuently presented as posterior bands associated with pachygyria.

p129
INFANTILE SPASMS AND PIGMENTARY MOSAICISM

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Purpose: We stress, that beyond well known neurocutaneous syndromes, the dermatologist could be helpful in establishing diagnoses of a much rarer occurrence in the child with infantile spasms.

Method: In this child with infantile spasms no cutaneous anomalies were found at repeat dermatologic evaluations in the first 2 years of life. After being suntanned his mother noticed some differences in skin pigmentation. Unilateral hypopigmented streaks could be seen with a Wood's lamp. Two skin biopsies were taken from contiguous normal and hypopigmented areas on his right thigh.

Results: Two skin biopsies were taken from contiguous normal and hypopigmented areas. Standard chromosome analyses of the cultured skin-fibroblasts showed trisomy 7 mosaicism with a percentage of 23% and 4% of the cells, respectively. Two independent chromosome analyses on cultured lymphocytes showed normal male karyotype in 15 and 100 metaphases.

Conclusion: The low percentage mosaicism possibly may not be so extremely rare, as could be suggested from the scarce amount of case reports in the literature, but difficult to get in mind as differential diagnose and technically difficult to diagnose. Our case points at the need for scrupulous attention to the skin in a child with IS and no etiologic diagnosis. The value of a specific diagnosis should not be underestimated in terms of parent knowledge, prognosis, and specific genetic advising.

p130
DOES REMOVAL OF THE SUBEPENDIMAL GIANT CELL ASTROCYTOMA IN PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX IMPROVE THEIR SEIZURE CONTROL?

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Purpose: Tuberous Sclerosis Complex (TSC) is an inherited multisystemic disorder of cellular differentiation, proliferation and neuronal

migration, resulting in hamartomas and often associated with epilepsy. Subependimal giant cell astrocytoma (SEGA) is the low-grade tumor occurring in 2–14% of TSC patients, mainly in first two decades of life.

Method: Out of 92 patients with TSC, 16 children and adolescents (6 male, 10 female), aged from 2.5 to 18 years (mean 15.2) had SEGA. Mean follow-up was 9.4 years. Tumor was disclosed in 7 pts on the regular CT/MRI follow-up. Increased intracranial pressure in three, neurological deficits in two and seizure aggravation in 4 patients revealed the lesion. Pre- and postoperative control of seizures was analyzed.

Results: Seizure onset ranged from 1.5 to 15.8 years. History of infantile spasms was noted in four cases. Focal seizures and mental insufficiency occurred in all but one patient with SEGA. At least one episode of status epilepticus occurred in 37.5%. Favorable, presurgical, pharmacological seizure control was achieved in five patients. SEGA removal with histological confirmation was total in 12 and partial in 4 patients. Surgical approach was transcallosal in 7, transcortical in 5 and by pellucidotomy in three patients. One patient died. During postoperative period of at least 12 months, seizure control was complete in 3, favorable in additional 4 and poor in 8 patients.

Conclusion: Seizures, mainly focal, intractable and with later onset occurred in all patients with SEGA. Surgical removal of SEGA did not appear to significantly improve epilepsy course.

p131
FOCAL EPILEPSY – FROM INFANTILE SPASMS AT BIRTH TO FUNCTIONAL RIGHT HEMIPARESIS

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Purpose: To present and discuss a clinical case with an unusual evolution of probable symptomatic epilepsy who started at birth.

Clinical case: We present a 7-year-old boy that began with infantile spasms in the first week of life, easily controlled with vigabatrin. Investigations to metabolic diseases and MRI were normal. No seizures till 3 years old when rare febrile induced seizures presented and clinical evolution with right hemiparesis (without pyramidal signs) and a bright cognitive profile.

At 5 years old he started having daily episodes of involuntary right limb ballistic movements, without conscience impairment, mainly precipitated by swimming and at night when falling asleep. This episodes where started by an odd sensation in the arm and he could control them partially.

A routine EEG was done during an episode that showed no epileptic discharges and a film of the episode was interpreted has involuntary paroxysmal choreic/ballistic movements (video).

However more complete EEG monitoring showed more than 40 seizures from the left interhemispheric fronto-parietal cortex. Subsequent 3 Tesla MRI failed to show a dysplastic lesion, but the EEG/fMRI produced an ictal BOLD activation near the EEG focus.

He was proposed to epilepsy surgery but was not accepted due to the risk of aggravating his right hemiparesis.

Comments: We discuss clinical evolution, highly atypical seizures, and treatment options in this unusual case.

p132
TYPING OF FOCAL CORTICAL DYPLASIA (FCD): THE VIENNA EXPERIENCE

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Purpose: Focal cortical dysplasia (FCD) is a widely recognized cause of drug-resistant epilepsies in children. Surgical removal of the epileptogenic zone is the ultimate treatment option in patients who do not respond to medical treatment with antiepileptic drugs. Resected brain tissue specimens of these patients show a spectrum of changes. Currently, there is however only limited international consensus concerning the histological classification of FCDs (3).

In this study we analyzed our series of pediatric FCD using the concepts of FCD classification as defined by Palmini et al (1) and Lerner et al. (2), assessing advantages and disadvantages of the two systems.

Methods: We analyzed resected specimens from all pediatric patients with the clinical and histopathological diagnosis of FCD who had epilepsy surgery at our center between 1996 and 2008 (n = 28, 17 male, 11 female).

Applying both classification systems on all cases we critically considered advantages and disadvantages of the two systems.

Results: We found the following advantage of the Palmini et al classification (1): well-structured classification scheme with distinct entities. In contrast, the system provided little flexibility. The Lerner et al (2) classification system allowed an overall more individualized FCD typing. However, this scheme included per definition FCD cases combined with other separate pathologies (e.g. hippocampal sclerosis). Over and above, reproducibility of the criteria used remain to be tested.

Conclusion: In our opinion, both systems for typing of FCDs were associated with advantages and disadvantages. More reliable criteria for FCD typing remain to be identified and defined.

p133
SURGICAL PATHOLOGIES AND MRI BETWEEN EPILEPTIC SPASMS AND PARTIAL SEIZURES IN CHILDREN

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Purpose: Epileptic spasms in older children have increasingly been recognized as a distinct seizure type and these patients are considered for surgical resection. This study compares histopathology, especially focusing the difference between gray and white matter, locations of surgical resections, MRI and seizure outcome from patients with and without epileptic spasms.

Method: We examined the neuropathology of patients with intractable epilepsy with partial seizures without epileptic spasms (11 patients) and epileptic spasms (11patients).

Results: Multilobar resetion was performed in 9 (82%) patients with epileptic spasmsm compared with 2 (18%) patients with partial seizures ($p = 0.0089$). FCD was most common MRI findings (6 in partial seizures vs. 5 in epileptic spasms). Normal MRI were seen (3 vs. 3). Histopathologgy showed abnormal cortical organizations as focal cortical dysplasia (5 vs. 3), microdysgenesis (4 vs. 4). Normal pathology was found in 1 versus 4. Cortical specimen showed subpial gliosis in all patients. Two patients with epileptic spasms showed hyaline proteoplasmic astrocytopathy. Subcortical white matter showed gliosis in all patients. Heterotopic neurons in the subcortical white matter were seen in 10 versus 10.

Conclusion: While epileptic spasm patients required multilobar resections, there were no morphological differences in cortex and subcortical white matter between patients with epileptic spasms and partial seizures. There was no specific histopathological findings in epileptic spasms with the exception of two patients with hyaline proteoplasmic astrocytopathy. This is a pilot study of the histopathology of resected specimen to elucidate the pathophysiology of intractable epileptic spasms in children.

p134
SEPTO-OPTIC DYSPLASIA AND EPILEPSY

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Purpose: Septo-optic dysplasia (SOD) is an uncommon developmental disorder involving variable midline brain structures, characterized by optic nerve hypoplasia, dysgenesis of septum pellucidum, and pituitary-hypothalamic dysfunction.

Method: We analyzed our findings in set of patients with septooptic dysplasia. We assessed presence of MRI abnormalities other than midline structures, motor and mental development and endocrinologic findings in time of diagnosis and compare this in subgroups with and without epilepsy.

Results: We assessed 10 children aged 1–13 years, 5 boys, 5 girls. Associated abnormality in MRI was found in 8 cases, psychomotor retardation in 8 cases, endocrinologic deficit in 8 cases (selective deficit, deficit in two axis 3, panhypopituitarism 1). 5 patient suffered from epilepsy. All of patients with epilepsy were hardly psychomotor retarded (under 9 month of normal development) and had larger structural abnormalities. No diferencies was found in endocrinologic deficits in children with and without epilepsy.

Conclusion: Septo-optic dysplasia is phenotypically variable disorder asociated with many types of malformations of cortical development and epilepsy without any significant diferencies in endocrinologic abnormalities in cases with or without epilepsy.

p135
RARE AND ATYPICAL OCCIPITAL EPILEPSY SECONDARY TOCORTICAL DYSPLASIA: 2 CASE REPORT

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Purpose: Identical genetic mutation in twins presents with different clinical course and atypical-rare occipital seizures.

Clinical case: We present the case of monochorial and bi-amniotic twins that presented with atypical occipital seizures.

Patient 1: At 16 months old, patient starts with sudden falls. Neurological examination shows hypotonia and ataxic gait. At 25 months of age, worse contact due to confusional status, confirmed by video-EEG, is added. MRI, CSF, metabolic studies and peripheral neurophysiological exams were normal. At age 6, the patient is admitted in our Epilepsy Unit because of poor seizure control. Atypical atonic-absence seizures starting at the right occipital region were observed. DT-MRI fiber tractography showed alterations in right posterior quadrant. Cerebral PET evidenced hipometabolism in that area.

Patient 2: At 23 months old, patient starts with similar electroclinical pattern as her sister. DT-MRI fiber tractography and cerebral PET were normal. Genetic study showed mutation in the LIS1 gene for both patients.

Conclusions:

1. The same genetic disorder may produce a different degree of cortical dysplasia in monochorial twins. In patient 1 morphological and functional test were positive but in patient 2 all these test were normal.
2. Electroclinical presentation is exceptional (early onset) and atypical for occipital lobe epilepsy (atonic-absences) being similar in both patients. Patient 1 had earlier onset and worse seizure control with more cognitive and behavioral problems.
3. We want to emphasize that even with the same genetic mutation, morphological, functional and clinical course is worse in patient 1 with more evident (greater) cortical dysplasia.

p136
RESECTIVE SURGERY FOR INTRACTABLE EPILEPSY IN THE FIRST 5 YEARS OF LIFE: THE MAYO CLINIC EXPERIENCE

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Purpose: To evaluate outcome of resective surgery for intractable epilepsy in children under 5 years.

Method: Charts of all children undergoing resective surgery at the Mayo Clinic under 60 months of age between 01/02 and 06/09 were reviewed to determine details of presurgical investigations and outcome.

Results: Twenty-eight children (54% male) were identified. Mean age at seizure onset was 9.6 months (SD 12.7) and at surgery 28.8 months (SD 17.7). Nearly 40% had moderate to severe cognitive delay preoperatively, and neurological examination was abnormal in 64%. Fifty seven percent had partial-onset seizures, 29% partial-onset seizures and spasms and 14% spasms alone. Children failed a mean of 4.6 AEDs and 14% also failed the ketogenic diet. Six underwent hemispherectomy, and 3, 7 and 12 underwent multilobar, temporal and extratemporal resection, respectively. Only 9/23 (39%) with recorded seizures preoperatively had a well-localized, single ictal focus. MRI was abnormal in 27 cases, showing focal pathology in 20. SISCOM showed focal abnormalities in 15/17 cases where it was performed (2-hemispheric, 12 single lobe, 1–2 lobes). One child died postoperatively. Of survivors, 16 (59.3%) were free of disabling seizures (Engel class I) and 2 (7.4%) more had only rare disabling seizures (Engel II) after mean follow-up of 30.7 months.

Conclusion: EEG frequently failed to show a single ictal focus in young children undergoing surgery for intractable epilepsy. MRI and SISCOM were more helpful, showing focal abnormalities in 71% and 88% respectively. Surgical outcome was favorable, with 67% being free, or nearly free, of disabling seizures.

Poster session: Surgical treatment I
Monday 28th June 2010
13:30–14:30

p137
THE TIMETOSTOP STUDY I. ANTIEPILEPTIC DRUG WITHDRAWAL POLICIES AFTER CHILDHOOD EPILEPSY SURGERY IN EUROPE

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Purpose: Little is known about the optimal timing of antiepileptic drug (AED) withdrawal after epilepsy surgery in children in relation to seizure and cognitive outcome. We studied current AED withdrawal policies in Europe, and identified possible predictors for early start and completion of AED discontinuation. The relation between timing of withdrawal and seizure outcome is presented in a parallel abstract.

Method: TimeToStop is an international multicenter retrospective cohort study of 759 children, operated between 2000 and 2008 in fifteen participating centers from eight countries, who reached postoperative seizure freedom and in whom AED reduction was started. Possible determinants for timing of postoperative withdrawal were related to the intervals from surgery to start of AED reduction (I_start) and to complete AED discontinuation (I_stop).

Results: Mean I_start was 16.8 months (SD ± 13.8, range 0–82 months) and mean I_stop (n = 439) 30.4 months (SD ± 18.0, range 0–105 months). There were large differences in time intervals between participating centers. Higher (for I_start) or lower (for I_stop) number of AEDs used before surgery, vascular pathology, hemispherectomy, parietal resections, complete resection of anatomical lesions, unifocal MRI lesions, and no preoperative intracranial recordings or postoperative EEGs performed, each were independent predictors for shorter intervals of medication withdrawal (multivariable linear regression, $p < 0.05$).

Conclusion: Current AED policy after epilepsy surgery in children is highly variable. Time intervals to start of withdrawal and to complete discontinuation of AEDs are strongly associated with preoperative and surgical variables, probably reflecting the anticipated chance of surgical success.

p138
OUTCOME OF VAGAL NERVE STIMULATION IN DRUG-RESISTANT EPILEPSY: EFFICACY AND TOLERABILITY

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Purpose: Vagal nerve stimulation (VNS) is an alternative therapeutic option for patients with refractory epilepsy, unsuitable for conventional resective surgery. The outcome of patients with drug-resistant epilepsies treated with VNS therapy at the Presurgical Evaluation Epilepsy Department (DDEP) of Milan (Italy) was discussed, trying to find out some clinical predictors.

Method: Thirty-four patients (18 males, 16 females) underwent VNS implantation between January 2005 and December 2008 (mean follow-up 25 months; range 12–55). Mean age at implantation was 30.4 ± 12.0 years (range 6–52), and epilepsy duration was meanly 23.6 ± 10.7 years (range 4–45). Clinical and neurophysiological data were collected before VNS implantation for each patient. Then, at each follow-up visit, information about seizure type and frequency, adverse events and other effects of VNS were registered.

Results: Despite none of the patients was rendered seizure-free, the majority presented a clear improvement in seizure frequency, and 73% of patients were responders (reduction of seizure rate ≥50%). A seizure frequency reduction ≥75% was found in 44% of patients; a seizure frequency reduction ≥50% was found in 29%; no significant improvement in seizure frequency (<50%) was found in 27% of patients. Moreover, 20 patients (59%) reported an improvement in quality of life, due to major alertness, attention and concentration and 17 patients (50%) reported mood improvement. More common side effects were hoarseness (45%) and coughing (85%) during the ''on'' stimulation period.

Conclusion: In our series VNS was effective as add-on treatment in drug-resistant patients, and generally well tolerated.

p139
OUTCOME AFTER CORTICO-AMYGDALO-HIPPOCAMPECTOMY IN PATIENTS WITH TEMPORAL LOBE EPILEPSY AND NORMAL MRI

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Purpose: We describe seizure and neuropsychological outcome obtained after CAH in patients with TLE and normal MRI evaluated in the modern imaging era.

Methods: Forty-five adult consecutive patients with TLE and normal MRI were studied. All patients had neuropsychological testing, interictal and ictal EEG recordings and MRI. They were divided into two groups: Group 1 (n = 18), included patients in whom noninvasive neurophysiological evaluation was lateralizing; Group 2 (n = 27) included patients with nonlateralizing neurophysiological data who were submitted to invasive recordings.

Results: Seventy-seven percent of the Group 1 patients were rated as Engel I; 11% were rated as Engel II and 11% as Engel III. In Group 2, there were 57% of patients seizure-free, 26% in Engel II and 14% in Engel III. Preoperatively, mean general IQ was 82 and 78 in Group 1 and 2, respectively; postoperatively, mean general IQ was respectively 86 and 71. Some degree of verbal memory decline was noted in all patients submitted to dominant temporal lobe resection in both Group 1 and 2. At last follow-up visit, 22% of Group 1 and 11% of Group 2 patients were receiving no antiepileptic drugs (AED).

Conclusions: Our data showed that patients with TLE and normal MRI could get good surgical results after CAH although 60% of them would need invasive recordings and their results regarding seizure control and cognition were worse than those obtained in patients with MRI defined temporal lobe lesions. Caution should be taken in offering dominant temporal lobe resection to this subset of patients.

p140
DEEP BRAIN STIMULATION (DBS) FOR REFRACTORY EPILEPSY: UNIQUE TARGETING IN DIFFERENT EPILEPTIC SYNDROMES

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Purpose: We studied the seizure outcome after DBS in patients with secondary generalized (SG), extratemporal (ExT) or bitemporal epilepsy (BiT).

Methods: Seven patients with SG, 6 with ExT and 6 with BiT were studied. All patients were implanted bilaterally using Kinetra electrodes. Patients with SG were implanted in the centro-median thalamic nuclei (CM); those with ExT were implanted in the anterior nuclei of the thalamus (AN); and patients with BiT received bilateral hippocampal leads (HIP). MRI was normal or showed diffuse atrophy in SG and AN patients. Three BiT patients had normal MRI and 3 had bilateral mesial temporal sclerosis.

Results: Mean follow-up time was 18, 13 and 7 months for SG, ExT and BiT patients, respectively. All patients received continuous stimulation at 130 Hz and 300 μsec. Intensity ranged from 4–6 V in both CM and AN patients. In BiT patients, intensity ranged from 3–7 V. CM and AN received bilateral stimulation. BiT patients were implanted bilaterally, but stimulation was started unilaterally; all these patients received only unilateral chronic stimulation so far. Short-term (2 weeks) bilateral

hippocampal stimulation led to no additional memory deficits in BiT patients. Mean seizure frequency reduction in the SG group was 77% (30–95%), 65% in the AN group (32–100%) and 85% in the BiT patients (70–100%).

Conclusions: DBS seems to be a promising technique to treat people with refractory epilepsy regarding seizure control and attention level increase, who would be otherwise not suitable for conventional resective treatment. Distinct epileptic syndromes need different targeting for best results.

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PROSPECTIVE LONGITUDINAL 10-YEAR EMPLOYMENT AND SEIZURE OUTCOME OF RESECTIVE EPILEPSY SURGERY IN SWEDEN

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Purpose: Reports on long-term employment outcome following epilepsy surgery are scarce. The aim of this study was to look at employment status related to seizure outcome two and 10 years after epilepsy surgery.

Method: The Swedish National Epilepsy Register provides population-based data on all patients operated in Sweden since 1990 including extensive preoperative data and two-year follow-up. Long-term prospective and longitudinal follow-up of all patients 10 years after surgery was initiated in 2005. This study cohort consists of all patients who underwent resective epilepsy surgery 1995–97.

Results: 124 adult patients were followed two and 10 years after resective epilepsy surgery, 97 had temporal lobe resections and 27 had various extratemporal resections. Before surgery 60% were employed, 7% were studying and 32% were neither employed nor studying. At the two-year follow-up after surgery, 57% were seizure-free, and of those 61% were employed full or part-time, 14% studying, 23% neither studying nor employed. Of those not seizure-free, 49% were employed at 2 years and 45% were neither studying nor employed. At the ten-year follow-up 65% were seizure-free and of those 62% were employed full or part-time, 26% were neither studying nor employed. Of the 35% who were not seizure-free, 37% were employed, 57% were not working, studying or old-age pensioners.

Conclusion: In this study of employment related to seizure outcome two and 10 years after resective epilepsy surgery the employment rates are stable for seizure-free patients, but decline over time in those who continue to have seizures.

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EXTRATEMPORAL MEDICALLY REFRACTORY EPILEPSY DUE TO FOCAL CORTICAL DYSPLASIA: PROGNOSTIC FACTORS OF SURGICAL OUTCOME

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Purpose: Focal Cortical Dysplasia (FCD) constitutes the commonest malformation of cortical development. In our current communication we present a series of patients surgically treated for epilepsy secondary to FCD of extratemporal origin.

Method: In our retrospective analysis 34 patients (19 M and 15 F) with FCD were included. Their mean age was 24.8 years. The mean duration of epilepsy was 5.8 years. All patients underwent routine preoperative work up. Lesionectomies of anatomically and/or electrophysiologically abnormal epileptogenic areas were performed. Engel's classification system was utilized for outcome evaluation. The mean follow-up time was 3.3 years.

Results: Preoperative MRI revealed abnormalities in 23 patients (67.6%), while in 11 (32.4%) no abnormalities were seen. The anatomic location of the resected epileptogenic foci was frontal in 14 patients, fronto-parietal in 7, parietal in 4, and occipital in 8 patients and parietal-occipital in 1. Outcome data showed that 56.7% had class I, 23.3% class II, and 20% class III, at the completion of the first year. The outcome for the second year were: 44.4% class I, 22.2% class II, and 33.4% class III. Surprisingly, patients with normal preoperative MRI had better outcome (7/11 class I) compared with those with abnormal MRI (10/23 class I). Patients with FCD of frontal origin had the worst outcome (5/14 class I).

Conclusion: Seizure-free outcome was achieved in 56.7% of our patients. However, the number of patients with class I outcome progressively decreased. In our cohort, preoperative MRI and location of epileptogenic focus were the only factors affecting outcome.

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EXTRATEMPORAL SURFACE EEG FEATURES DO NOT PRECLUDE SUCCESSFUL SURGICAL OUTCOMES IN DRUG-RESISTANT EPILEPSY PATIENTS WITH UNILATERAL TEMPORAL MRI LESIONS

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Purpose: To assess the impact of extratemporal surface EEG features on surgical outcome, for drug-resistant temporal lobe epilepsy patients with unilateral temporal MRI lesions treated with standard procedures.

Method: Among 53 patients with unilateral temporal lobe MRI lesions (25 Medial Temporal Sclerosis, 24 Low-growth Tumors and 4 Focal Cortical Dysplasia) operated-on with standard procedures (Anteromedial Temporal Resection and/or Lesionectomy), 7 patients (13.5% of the total cohort – 2 Medial Temporal Sclerosis, 3 Low-growth Tumors, 2 Focal Cortical Dysplasia) with extratemporal surface EEG features were prospectively identified and followed-up for evaluation of surgical outcome.

Results: Extratemporal surface EEG features pointed to ipsilateral frontopolar (2 patients with Medial temporal Sclerosis), ipsilateral frontocentral (2 patients with Low-growth Tumors and 1 with Focal Cortical Dysplasia), ipsilateral parietotemporal (1 patient with Low-growth Tumor) and ipsilateral frontopolar and temporooccipital (1 patient with Focal Cortical Dysplasia) regions. Patients were followed-up for at least 6 months (mean postoperative time 3.4 years). 6/7 enjoy Engel class I outcome, and 1/7 is greatly improved (Engel class II).

Conclusion: Extratemporal surface EEG features in patients with unilateral temporal lobe MRI lesions and concordant semiology do not preclude successful surgical outcome following standard surgical resections, neither do always necessitate implantation of intracranial electrodes. Such EEG features may represent activation of ''remote propagation areas'' or additional, potentially epileptogenic pathology, not enough on its own to manifest itself with seizure activity, at least fro the reported postoperative follow-up duration.

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CLINICAL AND SEEG CHARACTERISTICS OF PATIENTS WITH INSULAR RESECTIONS FOR REFRACTORY FOCAL EPILEPSY

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Purpose: To evaluate the characteristics and outcome of refractory epileptic patients in whom surgery including the insula was performed.

Method: A retrospective review of the medical charts and stereo-electroencephalographic (SEEG) records of 7 patients (4 males, 3 females) who underwent resective surgery including the insular cortex was done. The semiological seizure characteristics and ictal SEEG patterns were assessed.

Results: One patient had cryptogenic, and 6 symptomatic focal epilepsy. All patients have been implanted in the insula because the ictal semiology included initial or early and very prominent signs suggestive an insular origin or involvement (dysgeusia; marked hypersalivation; laryngeal/pharyngeal discomfort and/or constriction; paresthesias and/or piloerection with specific distribution). The ictal SEEG pattern was the primary reason for the decision to perform a resection of the insular cortex as the low voltage fast activity was first found on insular electrode contacts, or a very early spread to them was obvious, or they showed the same type of discharge as that of the ictal onset zone. Based on the electroclinical data the patients were classified as having pure insular (n = 1), insulo-frontal (n = 1), temporal plus (n = 2), insulo-fronto-temporal (n = 3) epilepsy. Five patients became seizure-free after targeting or including the insula in the resection. None presented postoperative deficit.

Conclusion: Our results suggest that an insular origin or involvement should be suspected in specific ictal semiological signs. The use of SEEG electrodes exploring the insular cortex could expand the possibility to reveal the epileptogenic network and to perform a successive tailored epilepsy surgery.

Poster session: Neuroimaging I
Monday 28th June 2010
13:30–14:30

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IMAGING TRANSPORTER-ASSOCIATED PHARMACORESISTANCE: DIFFERENCE IN THE IMPACT OF THE P-GLYCOPROTEIN MODULATOR TARIQUIDAR ON THE BRAIN KINETICS OF [^{18}F]-MPPF IN PHARMACORESISTANT AND -SENSITIVE EPILEPTIC RATS

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Purpose: Multiple studies have indicated a correlation between P-glycoprotein (Pgp) over-expression and pharmacoresistance. Pgp modulators like tariquidar (TQD) efficaciously inhibit Pgp function. Successive PET scanning using a Pgp substrate radiotracer with and without TQD pretreatment will probably allow a precise determination of blood-brain-barrier (BBB) Pgp function. Therefore, we evaluated whether subsequent [^{18}F] MPPF-PET scanning with and without TQD is suitable to image differences in Pgp function between pharmacoresistant and -sensitive rats.

Method: Experiments were performed in a chronic rat model with spontaneous recurrent seizures (SRS), in which it was previously demonstrated that phenobarbital (PB) nonresponders exhibit Pgp expression levels significantly exceeding those in PB responders. Based on a PB selection phase epileptic rats with SRS were selected in responders and nonresponders. Paired [^{18}F] MPPF-PET scans with and without TQD (15 mg/kg) were compared. Mean parametric maps of the [^{18}F] MPPF K_1 influx rate and the k_2· efflux rate were calculated.

Results: [^{18}F] MPPF-PET scanning following TQD pretreatment revealed significant differences in the impact of the Pgp modulator on [^{18}F] MPPF kinetics in the hippocampus. TQD increased the magnitude of [^{18}F] MPPF K_1 by a mean of 142% in nonresponders, which was significantly greater than the 92% increase seen in responders. TQD decreased [^{18}F] MPPF k_2 by 27% in nonresponders, whereas it did not exert an effect in responders.

Conclusion: In conclusion, the data rendered proof-of-concept for a novel approach to evaluate BBB Pgp function in individuals. As a diagnostic tool [^{18}F] MPPF-PET with TQD pretreatment renders a basis to further explore the clinical relevance of Pgp over-expression.

p146
BRAIN PATHOLOGY ASSOCIATED WITH EPILEPSY, DISCLOSED BY MRI: OUR EXPERIENCE

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Objectives: Magnetic resonance imaging (MRI) is an essential component of a multidisciplinary diagnostic evaluation of children and adolescents with epilepsy.

Patients: A group of 284 clinical outpatients (male 168, female 116), aged 3–36 years with epilepsy was studied for etiology and results of MRI examination in a period of 2004–2008.

Results: Malformations of cortical development (MCD) were disclosed by MRI techniques in 91 (32.1%) patients. Various congenital anomalies of the brain were seen in additional 28 (9.8%) patients. Phacomatoses were found in 21 (7.4%) patients: tuberous sclerosis (14), neurofibromatosis type I in 4 and Sturge-Weber syndrome in 3 patients. Periventricular leukomalacia and/or porencephalic cyst as result of the neonatal hypoxic ischemic injury was shown in 31 (10.9%) patients. Epilepsy in them is mainly associated with cerebral palsy (26 cases). Hippocampal sclerosis as underlying pathology of temporal lobe epilepsy was found in 13 (4.6%) patients. Ten patients (3.5%) with late posttraumatic epilepsy after head trauma presented on imaging with brain injury of various severity. Focal, unilateral or generalized cortical/subcortical atrophy associated with CNS infection was shown in 25 (8.8%) patients. Demyelization in 8 (2.8%), tumors in 3 (1%) and arterial-venous malformations in 11 patients (3.9%) were diagnosed. Normal MRI findings were found in 43 patients (15.2%) mainly in patients with idiopathic epilepsy.

Conclusion: The most common brain pathology, disclosed by MRI and associated with epilepsy in our patients are MCD, periventricular leucomalacia, congenital anomalies, postinfection atrophy and lesions characteristic for some phacomatoses.

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DIAGNOSTIC YIELD AND PREDICTIVE VALUE OF PHARMACOLOGICALLY PROVOKED ICTAL SPET IN PRESURGICAL EVALUATION OF TEMPORAL AND EXTRATEMPORAL EPILEPSIES

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Purpose: To demonstrate the efficacy of provoked ictal SPET in defining the EZ in both temporal and extratemporal epilepsies and its predictive value on long and short-term surgical outcome.

Methods: 100 drug-resistant epileptic patients: 34 cryptogenic and 66 symptomatic (46 temporal, 33 extratemporal, and 21 multifocal), underwent the following presurgical diagnostic protocol: anamnestic evaluation, neurological examination, MRI, neuropsychological and psychodynamic assessments, scalp-video-EEG monitoring, interictal and ictal SPET with ^{99m}Tc-ECD (740 MBq) and invasive recordings if necessary (Stereo-EEG or subdural grids. Ictal SPET was performed during seizure provoked with pentylenetetrazol slow injection and recorded by scalp-video-EEG and/or intracranial-EEG. Seizure onset, ^{99m}Tc-ECD injection time and seizure duration were assessed reviewing video-EEG recordings. Visual interpretation of interictal and provoked ictal SPET images was performed blind to clinical data. In selected patients SPM analysis of individual ictal SPET scans in comparison with a normal brain was also performed.

Results: SPECT hyperperfusion area as assessed by visual analysis was concordant with the epileptogenic zone in 2/3 of the patients. 70 patients were operated on: 55 underwent ablative surgery, 15 were submitted to vagal nerve stimulation. After 2 years 44 out of 55 patients were seizure-free, 2 patients in class II, 4 in class III while 5 in short follow up. 27 patients showed a follow-up of more than 5 years.

Conclusion: This study demonstrated the localising ability and the predictive value of pharmacologically provoked ictal SPET in refractory temporal and extratemporal epilepsies as supported by the satisfying short and long-term surgical outcome.

p148
NEUROPHYSIOLOGICAL ACTIVITY UNDERLYING ALTERED BRAIN METABOLISM IN EPILEPTIC ENCEPHALOPATHY WITH CONTINUOUS SPIKE-WAVES DURING SLEEP: A MULTIMODAL FUNCTIONAL IMAGING STUDY

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Purpose: Children at the acute phase of epileptic encephalopathy with continuous spike-waves during sleep (CSWS) may show the association of hypermetabolism and hypometabolism in distinct brain areas. This study investigates the neurophysiological correlates of these regional cerebral glucose metabolism abnormalities using magnetoencephalography (MEG).

Method: Five boys (aged 3.5–8 years) with CSWS and cognitive deterioration (Landau-Kleffner syndrome, three cases and frontal syndrome, two cases) were investigated by positron emission tomography using ^{18}F-fluorodeoxyglucose (FDG-PET) and MEG. Patients' FDG-PET data were compared to a control group of young adults using the statistical parametric mapping (SPM8) voxel-based method. Epileptic discharges observed on MEG during induced sleep were reconstructed using conventional equivalent current dipoles. For each patient, FDG-PET and MEG results were then coregistered on his cerebral magnetic resonance imaging.

Results: In all patients, the primary sources of spike-waves discharges were associated to significant focal hypermetabolism. The propagation of epileptic discharges to other brain areas was associated with focal hypermetabolism (two patients), focal hypometabolism (two patients) or the absence of any significant metabolic change (one patient).

Conclusion: This study shows that focal hypermetabolism observed at the acute phase of CSWS can be related to the primary source or the propagation of spike-wave discharges. It also shows that spike-wave discharges propagation can be associated with different types of metabolic changes, suggesting the occurrence of various neurophysiological mechanisms at the cellular level. Multimodal functional cerebral imaging is crucial to better approach the functional repercussions of CSWS activity on normal brain function.

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DIFFUSION TENSOR IMAGING CHARACTERISTICS OF THE ARCUATE FASCICULUS ARE NOT RELATED TO A DECLINE IN LANGUAGE FUNCTIONING FOLLOWING TEMPORAL LOBECTOMY

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Purpose: Diffusion tensor imaging (DTI) provides information about magnitude (ADC; diffusivity) and directionality (FA, fractional anisotropy) of water diffusion and allows mapping of the arcuate fasciculus (AF). Patients with temporal lobe epilepsy (TLE) may experience language difficulties, which often worsen after dominant anterior temporal lobectomy (ATL). We explored the relationship between DTI measures of the AF and change in language functioning following ATL.

Method: Preoperative DTI was used to reconstruct the AF in 22 left TLE patients with seizure-free outcome and coregistered to pre and postoperative T_1 MRI. Spearman correlations were conducted to examine the relationship between AF DTI measures and changes in language performance after ATL. Area of resection was visually inspected in 18 patients to determine if it impinged on the AF.

Results: FA was positively correlated with presurgical semantic fluency ($r = 0.613$, $p < 0.05$), but not with the Boston Naming Test (BNT, $r = 0.103$). Pre/postoperative scores were available on the BNT for 11 patients (raw change range −26 to +5) and on semantic fluency for 7 patients (raw change range −14 to +7). There were no significant correlations between DTI measures and change in language scores following ATL. In 4 of 18 patients, left TL resection impacted on the anterior extent of the AF; however, this was not consistently related to decline in language functioning.

Conclusion: Preliminary data suggest DTI measures are related to reduced preoperative semantic fluency scores in left TLE patients but, in our limited dataset, DTI measures were not related to language decline after ATL.

p150
'FUNCTIONAL CONNECTIVITY' IS A SENSITIVE PREDICTOR OF EPILEPSY DIAGNOSIS AFTER THE FIRST SEIZURE

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Purpose: The EEG is an important tool for epilepsy diagnosis and classification, but the sensitivity of interictal epileptiform discharges (IEDs) on the first EEG is only 30–50%. 'Functional connectivity' refers to synchronization between neurophysiological time series, and may be pivotal for epileptogenesis and seizure propagation. Does the use of 'functional connectivity' improve the diagnostic sensitivity of the first interictal EEG in the diagnosis of epilepsy?

Method: Two patient groups (matched regarding age and gender) were selected from a database with 390 standard EEGs of patients after a first suspected seizure: 1) patients who were later diagnosed with epilepsy, and 2) patients who did not have another seizure at least 1 year later and received another diagnosis. The synchronization likelihood (SL) was used as an index of functional connectivity of the EEG, and average SL per patient was calculated in seven frequency bands.

Results: In total, 114 patients were selected. Fifty-seven patients were diagnosed with epilepsy, 20 of whom had IEDs on their EEG, and 57 matched patients received other diagnoses. Epilepsy patients had significantly higher SL in the theta band than non–epilepsy patients. Furthermore, theta band SL proved to be a significant predictor of a diagnosis of epilepsy. When only those epilepsy patients without IEDs were considered (n = 74), theta band SL could predict diagnosis with specificity of 76% and sensitivity of 62%.

Conclusion: Theta band functional connectivity may be a useful additional tool in diagnosing epilepsy, especially in those patients who do not show IEDs on their first EEG.

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USE OF MULTICOMPARTMENTAL SPECT IMAGE ANALYSIS IN TEMPORAL LOBE EPILEPSY

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Purpose: This study assesses the utility of compartmental analysis of SPECT data in lateralizing ictal onset in cases of a putative mesial temporal lobe epilepsy (mTLE).

Methods: An institutional archival review provided 29 patients (10M, 19F) operated for a putative mTLE who achieved an Engel class Ia postoperative outcome. This established the standard to assure a true ictal origin. Ictal and interictal SPECT images were separately coregistered to a T_1-weighted (W) magnetic resonance (MR) image using a rigid transformation and the intensities matched with an L1 norm minimization technique. The T1W MR image was segmented into separate structures using an atlas-based automatic segmentation technique. Mean SISCOM intensity values were calculated for select subcortical structures and the accuracy of lateralization evaluated using a linear classifier.

Results: Hippocampal SPECT analysis yielded the highest lateralization accuracy (93%) followed by the amygdala (86%), putamen (72%) and thalamus (52%). Comparative FLAIR and volumetric analyses yielded 86% and 79% accuracies, respectively.

Conclusions: A quantitative anatomically compartmented SISCOM approach to SPECT analysis yields a particularly high lateralization accuracy in the case of mTLE. Hippocampal segmentation in this regard correlates well with ictal origin and shows good reliability in the preoperative analysis.

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PROTON MR SPECTROSCOPY OF METABOLITE CONCENTRATION IN YOUNG PATIENTS WITH CRYPTOGENIC PARTIAL EPILEPSY

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Purpose: To determine whether the intensity of 1H MRS signals is different in patients with cryptogenic partial epilepsy with good and bad response to treatment.

Method: We analyzed 48 patients aged 5–24 years, both genders, with cryptogenic partial epilepsy. Group A consisted of 17 patients with intractable seizures (FLE = 8, OLE = 3, TLE = 3) and group B consisted of 31 patients with good response to the treatment (TLE = 12, FLE = 15, PLE = 3). MRI and ^{1}H MRS were performed using GE 1.5T scanner, equipped with a transmit/receive head coil. The spectra (TE = 35 ms, TR = 1500 ms) were recorded from the volumes of interest located bilaterally in the frontal and temporal lobes.

Results: In FLE partial least squares – discriminant analysis revealed higher glutamate+glutamine and lower N-acetylasparatate in the patients from group A compared to group B. Multivariate analysis of metabolite ratios also resulted in a model separating significantly both groups. The separation is explained by higher glutamine+glutamate/creatine, choline/creatine and lower N-acetylaspartate/creatine and N-acetylaspartate/(creatine+choline) ratios in group A compared to group B. N-acetylaspartate was found to be the major metabolite that distinguishes group A from group B both ipsilaterally and contralaterally to the epileptogenic area.

Conclusion: Multivariate analysis of metabolite levels and ratios seems be helpful in classification of the spectra acquired from patients suffering from intractable epilepsy and patients responding well to the treatment. Presented approach could be the first step to determine the usefulness of ^{1}H MRS as the predictor of pharmacoresistence.

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MULTIMODAL APPROACH TO PHARMACORRESISTANT FOCAL EPILEPSY: PET/MRI/SISCOM COREGISTRATION

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Purpose: The aim of this study was to investigate the usefulness of PET/RM/SISCOM coregistration localizing the epileptic zone.

Method: We included, prospectively, 35 patients with refractory focal epilepsy. Presurgical evaluation included a FDG-PET and an ictal SPECT/SISCOM, which were coregistrated with the structural MRI of each patient using SPM2. The studies were interpreted by qualitative visual analysis, and the results were compared with the potential location of the ictal onset zone determined by long-term video-EEG, invasive EEG monitoring, and surgical results, in those patients who were operated.

Results: MRI was normal in 15 patients. Of those, PET showed a focal hypometabolism in 5 (30%), but PET/RM coregistration showed an hypometabolism concordant with ictal onset zone in 80% (12/15). SISCOM showed an hyperperfusion concordant with ictal onset zone in 7/12 (58%) patients with normal MRI, and in 10/13 (77%) of lesional patients. In 6 of 7 non lesional patients whose PET/RM showed a focal hypometabolism not identificated by PET, PET/RM/SISCOM fusion was concordant with hypometabolism. The hyperperfusion observed in SISCOM was less extensive than hypometabolism shown by PET. 15 patients underwent surgery. Of them, 7 patients were studied by invasive-EEG monitoring. Ictal onset zone was concordant with PET/RM in all cases. PET/RM/SISCOM fusion was performed in 5 of these patients, and was concordant in 4/5. 13/15 (86%) patients are seizure-free after epilepsy surgery.

Conclusion: PET/RM/SISCOM coregistration could be useful to locate and delineate the potential, and, therefore, to plan invasive EEG studies more precisely, especially in patients without lesion in MRI.

p154
LOCALIZING VALUE OF ICTAL LOCAL HYPERPERFUSION MRI CHANGES

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Purpose: Cases describing ictal MRI perfusion changes are scarce in single epileptic seizures. We describe two cases of local hyperperfusion in single focal seizures, where the perfusion changes matched the epileptogenic area.

Results: Case 1: A 39-year-old left-handed man was accepted to the ER with new onset audiogenic focal seizures. Early EEG showed PLEDs activity over the posterior right temporal region. Inmediately after EEG, a MRI was performed. It showed a tumoral lesion in the right temporal gyrus. Perfusion weighted imaging (PWI) showed local hyperperfusion matching the tumor. Simultaneously, an ictal SPECT injection was performed. Control MRI showed normalization of perfusion patterns. Substracted ictal-interictal SPECT Corregistrated with MRI, demostrated an ictal hyperperfusion matching the tumor as well.

Case 2: A 32-year-old right-handed man with posttraumatic epilepsy, had complex partial seizures characterized by ictal verbalization (congruent speech) and hand automatisms.

During a 3-TESLA MRI examination the patient started having one of his typical spells. A PWI was obtained during the ictal speech. Ictal MRI, showed local right temporal hyperperfusion that recovered in a control MRI performed 2 weeks later while the patient was assymptomatic. Echo-gradient slides showed chronic axonal damage in the right parietal lobe. Language functional-MRI demostrated a left hemisphere language dominance. Interictal EEG showed right temporal slow waves over the right temporal region.

Conclusion: According to our results hyperperfusion local changes observed in Ictal-MRI in single focal seizures, may have localizing value; since they are well correlated with the ictal semiology localization and recovered after clinical-EEG resolution.

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MULTIVOXEL MAGNETIC RESONANCE SPECTROSCOPY AT 3 TESLA IN PATIENTS WITH IDIOPATHIC GENERALIZED TONIC–CLONIC SEIZURES

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Purpose: The objective of our study was to gain further insight into the extent of local metabolic alterations in patients with idiopathic generalized epilepsy (IGE), respectively the subgroup with generalized tonic–clonic seizures (GTCS). The extent of regional metabolic involvement perhaps indicates the key structures in generation of seizures and involvement of specific network of dysfunction.

Method: Using the multivoxel technique at a 3 Tesla MRI Scanner metabolite levels of 25 age-matched healthy controls and 18 patients with GTCS were obtained from the basal ganglia, insular cortex, cingulum, hippocampus and along both hemispheres in the fronto-parietal white and gray matter.

Results: Group analysis of GTCS patients versus healthy controls revealed accentuated significant ($p < 0.05$) decrease of tNAA in the cortex of the central region and cingulum, but also in the thalami. Glx was elevated broadly in both hemispheres, in particular in central region, cingulum, insular cortex and left putamen, yet also in the right thalamus. Cho and mI demonstrated a significant coincidental decrease pronounced in the gray and white matter of the central region. Significant metabolic correlation ($p \leq 0.05$) based on tNAA, respectively Glx occurred between the thalamus and the central region, cingulum, putamen and medial frontal cortex. In patients with >2 tonic–clonic seizures in the last 12 month a trend towards higher Glx and lower tNAA levels was observed.

Conclusion: Our results demonstrate the altered metabolic interconnection of cerebral anatomic regions in patients with GTCS, in particular the major role of basal ganglia-central region relay in seizure generation.

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IMPACT OF P-GLYCOPROTEIN ON THE DISTRIBUTION OF [^{18}F]MPPF IN PHARMACORESISTANT TEMPORAL LOBE EPILEPSY

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Purpose: The multidrug transporter P-glycoprotein (Pgp) is thought to contribute to pharmacoresistance in temporal lobe epilepsy (TLE). [^{18}F]MPPF is a selective antagonist of 5-HT$_{1A}$ receptors, but also a substrate for Pgp. The aim of our study was to assess the expression of Pgp using [^{18}F]MPPF-PET before and after blocking Pgp, in patients with TLE.

Method: Ten patients with pharmacoresistant TLE (7 with MRI signs of hippocampal sclerosis) had paired 60-min [^{18}F]MPPF PET scans with and without continuous infusion of 2.5 mg/kg/h of cyclosporine A (CsA), a blocker of Pgp. A simplified reference tissue model with a cerebellar reference region was used to generate parametric images of 5-HT$_{1A}$ receptor binding potential (BP_{ND}) and k2.

Results: At baseline, all patients showed a major reduction of [^{18}F]MPPF BP_{ND} for 5-HT$_{1A}$ receptors in their epileptogenic temporal lobe. CsA serum concentrations were 4305 ± 1368 mcg/l at 60 min (scan start) and 5008 ± 2256 mcg/l at scan end. The concurrent infusion of CsA was associated with 1) a significant reduction of [^{18}F]MPPF k2 (by 22%), and 2) a significantly increased [^{18}F]MPPF BP_{ND} (by 14%) in most brain regions, regardless of their involvement in seizure generation or propagation.

Conclusion: CsA infusion had a significant impact on [^{18}F]MPPF binding and efflux, and these changes were comparable within and outside the epileptogenic temporal lobe. With the caveat that the exact percentage of Ppg blockade is unknown, our data so far do not suggest selective increases of Pgp in the epileptic focus. Instead, drug resistance could partly reflect baseline whole brain expression of these proteins.

Poster session: Status epilepticus
Monday 28th June 2010
13:30–14:30

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THREE YEARS IN THE TREATMENT OF STATUS EPILEPTICUS WITH INTRAVENOUS LEVETIRACETAM

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Purpose: We assessed the efficacy of IV LEV in the treatment of various types of status epilepticus (SE).

Method: LEV IV was administered at dosages of 1000 or 2000 mg either as an infusion (1000 mg in 100 ml NaCl 0.9% in 15 min) or fractionated in smaller volumes (500 mg in 20 ml NaCl 0.9%, given twice or

four times). Efficacy was assessed using termination of SE as the effectiveness criterion. Tolerability was assessed by evaluating treatment-related adverse events.

Results: Since its launch in 2006, we have used LEV IV to treat 60 patients with various types of SE. In general, LEV was administered as second-line therapy, after benzodiazepines. SE could be terminated in 31 of 60 patients (51.1%). LEV was more effective in simple partial (7/12), complex partial (16/25) and myoclonic status (2/2) than in nonconvulsive (5/11) or subtle (1/2) SE. In no case was (secondary) generalized convulsive SE terminated (0/8). Intravenous LEV was also well-tolerated when injected in fractionated form. No severe adverse events were observed.

Conclusion: LEV IV in moderate doses may represent an efficacious and well-tolerated alternative for the treatment especially of simple focal, complex focal and myoclonic SE.

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EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS OF NONCONVULSIVE STATUS EPILEPTICUS IN A TERTIARY-LEVEL HOSPITAL IN THE NORTHWEST OF SPAIN

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Purpose: Nonconvulsive status epilepticus (NCSE) is an under-diagnosed condition with sparse and variable incidence rates due to clinical heterogeneity and lacking of firm electroencephalographic (EEG) criteria. Our purpose is to document the incidence and clinical profile of NCSE in adults in the area covered by our hospital.

Method: A descriptive retrospective analysis was performed of adults diagnosed from NCSE between April 2008 and April 2009 in a tertiary-level hospital with 24-h neurological and neurophysiological assistance for over 400,000 people. Strict EEG and clinical criteria were defined. Patients in a coma were excluded.

Results: We identified 29 episodes of NCSE in 26 patients, with an incidence of 7 cases per 100,000 inhabitants. Male/female ratio was 1:4 with a median age of 71 years (59–80). Median length of stay was 9 days (6, 12). 63% had no previous history of epilepsy. The most frequent clinical presentations were depressed level of consciousness (48%) and dysphasia (24%). Complex partial status epilepticus (CPSE) was the most common subtype (69%) followed by simple partial with no major motor signs (28%). One absence status was identified. A symptomatic cause was found in most cases (65%). Benzodiazepines were the preferred first-line antiepileptic drug (52%). Mortality was 17% (67% of whom were symptomatic). Among the survivors, 75% were asymptomatic upon discharge.

Conclusion: NCSE in our sanitary area predominantly affects non-epileptic elderly population. Symptomatic causes are more common and related to a higher mortality, whereas nonsymptomatic cases have a better prognosis.

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STIMULUS-SENSITIVE POSTANOXIC FOCAL MOTOR SEIZURES EVOLVING INTO GENERALIZED MYOCLONIC STATUS EPILEPTICUS: A VIDEO-EEG STUDY

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Purpose: To describe the case of an adult who developed stimulus-induced focal motor seizures after prolonged cardiac arrest which progressed into a massive generalized myoclonic status epilepticus (GMSE).

Method: We carried out two video-electroencephalographic studies while the patient was admitted to the intensive care unit. Electroencephalograms (EEGs) recordings were performed according to standard techniques. Video-EEG was obtained for at least 30 min including photic, sensory, painful and verbal stimulation.

Results: Video-EEG showed a background activity constituted by low voltage diffuse alpha-theta activity suggestive of a severe anoxic encephalopathy. Painful stimulation provoked rhythmic clonic twitching on the right hand which progressively evolved into massive generalized myoclonic jerks. Twenty-four hours later, a second v-EEG revealed a nearly flat recording without evidence of epileptiform discharges. When the technician carried out painful stimulation on the right nipple, she provoked rhythmic clonic movements of the right hand. These motor manifestations were associated with transient stimulus-induced bilateral low-voltage rhythmic spikes more accentuated over the left hemisphere. These EEG changes were compatible with stimulus-induced rhythmic periodic ictal discharges (SIRPIDs). Rhythmic generalized epileptiform discharges increased in frequency and amplitude and, finally, clinical and EEG features were compatible with the diagnosis of massive GMSE.

Conclusion: This rare case describes the possibility that reflex partial motor seizures may evolve into a picture of GMSE in patients with severe cortical damage supporting the hypothesis that post-anoxic myoclonus represents an ictal state of epileptic nature.

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PRACTICAL CLASSIFICATION OF STATUS EPILEPTICUS

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Purpose: Aim of our work is to present simple classification for practical physicians reflecting prognosis and therapy particularity of SE.

Method: 214 patients with SE were observed, clinical-EEG, cardiovascular, respiratory, homeostatic and hemostatic systems investigation were used.

Results: Patients were divided into two large groups: with SE per se (124 ps) and symptomatic SE (90 ps). The other criterion was the type of epileptic seizures, according to which the patients were divided into four classes of SE: convulsive, myoclonic, nonconvulsive partial seizures and absence status. In this presentation only patients with SE per se are being analyzed. Serious consciousness (coma), homeostatic and hemostatic disorders were revealed only in patients with convulsive SE. The drugs of choice were diazepam and depakine IV, thiopenton, mascular relacsants with APV, local and general brain cooling. Mortality was 8.5%. In patients with myoclonic SE consciousness was presented. The drug of choice was high doses of valproates with piracetam, later, levetiracetam. Mortal exit was in 1 patient with Dravet syndrome. Consciousness of patients with partial SE remained or clouded. Drugs of choice were carbamasepine, valproates. Prognosis is benign. We have shown variants of absence SE and role of prefrontal lobe as structures of it's origin (Epilepsia 1997; 38, Suppl 3: 214). Level of consciousness was stupor. The choice of drugs is: diazepam, valproates, ethosuximide. Prognosis depends on type of epilepsy and age of patients.

Conclusion: Four main clinical classes of SE in epilepic patients are qualified, which are distinguished by somatic and homeostatic status, prognosis and therapy.

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SPECTRAL MODULATION OF THE SLOW COMPONENT OF RHYTHMIC EEG ACTIVITY BEFORE THE END OF ICTUS IN NONCONVULSIVE FOCAL STATUS EPILEPTICUS

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Purpose: Nonconvulsive focal status epilepticus (NCFSE) is a prolonged state of uninterrupted seizure activity, whose ictal EEG is dominated by continuous spike- or polyspike-and-wave discharges. NCFSE is not associated with convulsions and may occur in a wide range of symptomatic, probably symptomatic and idiopathic focal epilepsies. The neuronal mechanisms that contribute to the spontaneous end of this state are unknown.

Method: We investigated the spectral progression of NCFSE in five patients – four with complex partial status associated with temporal lobe epilepsy (TLE) and one diagnosed with Panayiotopoulos syndrome (PS) – by means of FFT-based time-frequency analysis (TFA).

Results: We focused on the time-course of the slow wave component of the continuous discharges that formed a clear stable spectral line at the beginning and the first part of the status in the range of 2.5–3.5 Hz. However, towards the late parts or immediately before the end of the status episode, we observed a strong modulation of this low frequency band in all patients (4/5 within the 2.0–4.0 Hz spectral window and 1/5 with TLE from 1.0–5.0 Hz). This modulation was generalized in space and oscillated smoothly with a period varying from 15 s to 250 s. The duration of the raw EEG slow waves was observed to be changing in consistency with the TFA modulation.

Conclusion: The time of occurrence of this modulation suggests that it may represent a neuronal mechanism of instability in the basic slow rhythm of the EEG activity and it may thus contribute to an eventual stop of the status.

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SYMPTOMATIC NONCONVULSIVE STATUS EPILEPTICUS CONTROLLED AFTER ORAL TREATMENT WITH ZONISAMIDE AND LEVETIRACETAM

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Purpose: Oral antiepileptic drugs are not commonly used to treat status epilepticus (SE). We wanted to study the efficacy of some of the new antiepileptic drugs, for oral administration, in nonconvulsive status epilepticus (N.C.S.E.)

Method: 8 patients consecutively admitted to our hospital for continuous epileptic seizures, from January to June 2009, entered our study.

2 of them suffering on N.C.S.E. received oral doses of levetiracetam or zonisamide in add on therapy.

Results: The first patient was a 54 year old woman, who had an absence status after neurosurgical treatment for a skull meningioma involving frontal and temporal right lobes.

Ictal video-EEG registered continuous epileptiform activity on the right hemisphere. She was treated with Phenobarbital 200 mg/day without any benefit.

When Levetiracetam, 2000 mg/day per os, was added, seizures disappeared.

The second case was a 62 year old man with a left hemiparesis because of an ischemic attack occurred 6 years before, admitted for continuous arrests in speech and staring while his head and his eyes turned on the left side.

RMI showed a right hemisphere wide ischemic lesion and the ictal video-EEG registered epileptiform discharges on the same site.

Valproic Acid 2000 mg/day; Valproic Acid+Oxcarbazepine 600 mg/day + Phenobarbital 400 mg/day; where ineffective.

Seizures disappeared when zonisamide (140 mg/day) was added to Valproic Acid.

Conclusion: In our experience levetiracetam and zonisamide could be useful in controlling non convulsive status epilepticus.

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CLINICAL AND ELECTROENCEPHALOGRAPHIC FEATURES OF APHASIC STATUS EPILEPTICUS

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Purpose: Ictal aphasia is infrequent as sole manifestation of status epilepticus. Early identification of aphasic status epilepticus is clinically important because it commonly misleads false diagnosis such as acute stroke or other causes of acute language disturbance. We report on clinical, neuroimaging findings as well as electroencephalography (EEG) features of patients with aphasic status epilepticus.

Method: Five patients presented aphasia as sole or most predominant symptom of status epilepticus were included. MRI and ictal EEG were obtained in all and ictal single photon emission computed tomography (SPECT) was done in two patients.

Results: Two patients presented global aphasia, but the others showed sensory type. Diffusion-weighted imaging failed to reveal any significant changes in all patients. Fluid-attenuated inversion recovery MRI showed cortical hyperintense signal in the left parieto-occipital region in one patient. Ictal EEG showed continuous widely spread left hemispheric delta slowing in the two patients with global aphasia. The sensory-type aphasic patients presented periodic lateralizing epileptiform discharges in the left hemisphere. There was no definite classic evolving feature of ictal EEG. Ictal SPECT, done in the two patients with sensory aphasia, disclosed increased blood perfusion in the left temporal or parieto-occipital region. The aphasic symptom was improved shortly after antiepileptic drug treatment in all patients.

Conclusion: Atypical ictal EEG pattern commonly occurred and MRI was usually negative, but showed cortical signal in the selected patient. Ictal SPECT and the clinical responsiveness to antiepileptic drug seem helpful to correct diagnosis of aphasic status epilepticus.

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NON-RASMUSSEN, NONSTROKE EPILEPSIA PARTIALIS CONTINUA (EPC)

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Rasmussen syndrome and stroke-related EPC are well-established subtypes of EPC. We studied cases belonging to neither.

Methods: Retrospective collection of cases with continuous focal epileptic symptoms, persistent for a minimum of 1 day or recurring in episodes of identical semiology each lasting ≥1 h.

Results: Of 60 cases 46 had motor, 5 each sensorimotor or somatosensory, and 4 visual EPC. 9 had a single episode, 17 repetitive episodes, 28 had EPC persistent for 1–25 years, in 6 EPC started with episodes and became persistent after 3 months to 4 years. Single episodes occurred as acute symptomatic events or in preexistent epilepsy. Concomitant seizures were simple focal in 44 pats, GTC in 29, complex focal in 14, other in 5 and absent in 6. Symptoms were restricted to one limb in 25, more widespread in 23 and indicated >1 focus in 9.

Etiologies were identified in 75% including local morphological lesions in 22 cases (9 cortical dysplasias), inflammatory causes in 14 (9 tick-borne encephalitis) and systemic pathologies in 6 (5 M. Alpers). 3 had idiopathic rolandic childhood epilepsy.

External triggering and inhibitory mechanisms were frequent.

Resistance to multiple AEDs was high. TPM had sometimes a positive effect with dysontogenetic etiologies.

Conclusions: Several time courses exist.

The most common accompanying seizure type in EPC patients is simple focal, indicating that strong inhibition of seizure spread is a general feature of these patients' ictogenesis.

Nonmotor EPC is probably underdiagnosed.

A prospective study should clarify various open questions.

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REFRACTORY STATUS EPILEPTICUS WITH LETHAL OUTCOME: A CASE REPORT

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Purpose: Status epilepticus (SE) may occur both in patients with known epilepsy, and in the case of the first manifestation of the disease. SE represents always a life threatening condition with a mortality ranging between 8–32% in adults.

Case report: A 25-year-old female with a negative history was admitted due to somnolence, fever and positive signs of meningeal irritation. During hospitalization, the unconsciousness progressed to coma, fever persisted and GTCS occurred. Three intravenous antiepileptic drugs and also antiedematics, antibiotics, virostatics and antimycotics were administered. The frequency of GTCS increased and progressed to SE within 3 days. Continual generalized epileptic activity was present in EEG monitoring. Patient was intubated and thiopental coma was used to achieve burst suppression. However, the clinically manifest GTCS persisted, although the burst suppression was achieved in EEG. Patient developed mineral dysbalance and cardiovascular dysfunction. Continual suppression of electric activity was observed in the EEG at the end of hospitalization. Patient died after 3 weeks. Intoxication, injury, stroke and brain tumor were excluded, using the repeated brain and spinal cord MRI, toxicology, complex examination of cerebrospinal fluid and serum. Brain edema and bacterial bronchopneumonia were found in autopsy, although the findings in brain MRI and chest x-ray were negative.

Conclusion: Refractory SE is a rare, but life threatening condition, occurring even in the case of the first manifestation of the disease.

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REPETITIVE SEIZURES AND STATUS EPILEPTICUS: CLINICAL PRESENTATION AND PROGNOSIS BASED ON PROSPECTIVE ANALYSIS OF PATIENTS TREATED AT THE DEPARTMENT OF NEUROLOGY; MEDICAL UNIVERSITY OF LUBLIN (2006–2009)

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Purpose: Repetitive seizures (RS) and status epilepticus (SE) are associated with increased risk of mortality. Identification of outcome-predictive factors could lower the risk of serious complications. Recently, a prognostic score STESS (Status Epilepticus Severity Score) was proposed to predict mortality in status epilepticus. The aim of the study was to prospectively analyze a cohort of patients presenting with RS and SE in order to identify the risk factors correlating with the outcome. In addition, STESS was applied to determine its utility in the early assessment of patients.

Method: The study group consisted of 50 subjects with RS (n = 27) or EEG confirmed SE (n = 23). Outcome at discharge (mortality, return to baseline clinical conditions) was analyzed in relation to demographics, clinical features, and etiology.

Results: The study group consisted of 42% of females and 58% of males with median age of 53 (23–78) years. The most frequent risk factors of RS and SE were: metabolic abnormalities (40%) and acute craniocerebral insult (22%), while the cause was undetermined in 18% of cases. RS were associated with good prognosis. Similarly, in those cases where RS transformed into SE (n = 8), the outcome was favorable. In the total SE subgroup (n = 23) the mortality rate was 10% and death was associated with age≥65 ($p = 0.02$) and coma or stupor at presentation ($p = 0.01$). STEES score significantly correlated with outcome ($p < 0.001$).

Conclusion: The early identification of patients at risk of mortality is crucial for proper management. The STEES scale has relevant prognostic value for patients suffering SE.

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NURSING INTERVENTION IN STATUS EPILEPTICUS

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Introduction: Generalized convulsive status epilepticus (GCSE) is a medical emergency which needs rapid and aggressive treatment to prevent neuronal damage. It is associated with high mortality and is largely contingent on the duration of the condition before initial treatment, the etiology of the condition and the patient's age. Yet, within the Greek Health Care System (GHCS) management of GCSE is seen as a purely medical task.

The aim of this presentation is to present and critically appraise the state-of-the art nursing interventions in status epilepticus for use within the GHCS.

Methods: A critical literature appraisal was undertaken. Key words included: epilepsy, nursing, protocol, management and a thorough Medline and Cinhal search using the following prefixes: ''and, or,'' 34 papers were retrieved and after correcting for publication within the last 5 years, 10 papers were finally selected.

Findings: The international literature revealed 8 protocols. A checklist of 10 parameters was compiled, and each protocol was compared against it. These parameters included: scientific evidence for the protocol's items, clarity, patient age spectrum, level of analysis, multidisciplinary

approach, and degree of evidence. Close examination and comparison showed that the latest protocol by Epilepsy Foundation of America committee's protocol is best for use within the GHCS as it was detailed and analytic.

Conclusions: Good management of patients with epilepsy can result in a significant reduction in seizures and improved patient management. Nurses should be trained in using shared protocols of evidence based care that guarantee quality assurance in the delivery of contemporary care.

Poster session: Clinical neurophysiology I
Monday 28th June 2010
13:30–14:30

p168
THE EPILEPTIC SEIZURES DIAGNOSIS BY ECHOENCEPHALOGRAPHY AND TELEMEDICINE

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Purpose: The aim of the present working out to study the value of A-mode echoencephalography and telemedicine at ictal epileptic evidence in clinical practice.

Method: We are using BIOSS A-mode echoencephalography tool Angiodin-portable with video-recording by a personal laptop. The ultrasound transducer was fixed above the root of the ear. At the same time was made video – monitoring of A-mode echoencephalography patterns by a personal laptop video-camera. These data in electronic form were sending to the virtual consultation by the Internet.

Results: We are testing 25 patients at generalized tonic–clonic seizures (TCGS), 13 patients at hemiclonic epileptic seizures (HCS), 14 patients at non–epileptic seizures (NES). Age range was 18–53. At GTCS was fixed the multiple echo-spikes (MES) during ictal evidence. At epileptic HCS was fixed 4–5 mm midline echo-spike shift (MSS) to clonic site of body during ictal evidence. At non–epileptic seizures (NES) not fixed MES and MSS. The MES and MSS at ictus are strong evidence of the increase regional cerebral blood flow. Its the equivalent epileptic activity. The diagnosis of NES was expelled after telemedicine virtual consultation.

Conclusion: A-mode echoencephalograph Angiodin-portable with personal laptop and virtual telemedicine consultation is diagnostic tool at clinical practice. This echo-encephalography diagnostic method of application is covered by patent 2182463 (2001) registered in Russian Federation.

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CLINICAL UTILITY OF EEG IN ALCOHOL-RELATED ACUTE SYMPTOMATIC SEIZURES IN HOSPITAL

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Purpose: To study whether electroencephalogram (EEG) shows specific changes in acutes symptomatic alcohol-related seizures and if it is useful and when to perform EEG exam to patients hospitalized after acute symptomatic alcohol withdrawal seizures.

Method: Alcohol withdrawal seizures was defined as the first time generalized tonic–clonic seizures during 48 h after stopping alcohol use, without any signs of focality in neuroradiological or neurological findings. We included 83 patients who were hospitalized in Riga East University Clinic, ''Gailezers'' neurological department from 2004 to 2009. EEG was recorded within 10 days (82% within 3 days).

Results: We noticed increased prevalence of low-voltage EEG activity and alpha amplitude reduction and increased beta activity. In group of patients with recurrent seizures during 24 h and in group when EEG were recorded within 1 day after seizure episodic low voltage slowing in frontal regions and increased sweating artefacts were noticed. Only in two cases the focality with epileptiform activity was found.

Conclusion: Low-voltage EEG without significant slowing is the most typical post actual pattern in acute symptomatic alcohol related seizures and there are not significant differences in which day within 10 days after seizure EEG is performed. EEG is not so useful predictor of alcohol related seizures as medical history.

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RESPIRATORY CHANGES WITH SEIZURES IN LOCALIZATION-RELATED EPILEPSY: ANALYSIS OF PERIICTAL HYPERCAPNIA AND AIRFLOW PATTERNS

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Purpose: The rate of sudden unexpected death in epilepsy (SUDEP) approaches 9 per 1000 patient-years in patients with refractory epilepsy. Respiratory causes have been implicated in SUDEP. We have shown that ictal hypoxemia occurs in one-third of seizures in localization-related epilepsy (LRE). We now report on respiratory changes in the periictal period including changes in end-tidal CO2 (ETCO2) that correlates directly with alveolar CO2, allowing a precise evaluation of seizure-related respiratory disturbances.

Method: 187 seizures were recorded in 33 patients with LRE, with or without secondarily generalized convulsions, undergoing video-EEG telemetry with recording of respiratory data.

Results: The periictal ETCO2 increase from baseline was 14 ± 11 mmHg(11,-1-50) (mean ± SD (median, range)). ETCO2 increase was ≥50 mmHg with 35 of 94 seizures, ≥60 mmHg with 15 seizures and ≥70 mmHg with 5 seizures. The duration of periictal ETCO2 increase above baseline was 424 ± 807 s (154.4–6225). The duration of ictal apnea was 49 ± 46 s (31.6–222); most ictal apneic events were central. Oxygen desaturation to 60% or less occurred with ten seizures including five that did not progress to generalized convulsions. Respiratory rate and amplitude increased in the immediate postictal period. The peak ictal ETCO2 change and duration of change were not significantly associated with apnea duration or seizure duration. Peak ETCO2 change was significantly associated with contralateral seizure spread.

Conclusion: Severe and prolonged periictal increases in ETCO2 occur with seizures in LRE. Postictally, respiratory effort is not impaired. Ictally-triggered ventilation-perfusion inequality, such as from pulmonary shunting or transient neurogenic pulmonary edema, may account for these findings.

p171
THE SLOW-WAVE COMPONENT OF THE INTERICTAL EPILEPTIFORM EEG DISCHARGES

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Purpose: The interictal epileptiform discharges (EDs) consist of a fast component (spike or sharp-wave) followed by a slow-wave component (SC). Our goal was to assess the intraindividual variance, the diagnostic significance and the possible effect of sleep on the SC.

Methods: EEG recordings from 50 consecutive patients with EDs were analyzed. Eleven patients had 1 recording, 9 patients had 2 and 30 patients had 3 or more recordings. The frequency of the SC was calculated as the reciprocal of the duration. The amplitude of the SC was divided by the amplitude of the fast component yielding a normalized value (amplitude-ratio). Intraindividual, intra- and interrecording coefficients of variation (CV) were calculated for frequency and amplitude-ratio. The correlation with the diagnosis, and the effect of sleep was analyzed.

Results: The frequency and the amplitude-ratio had low CV (<27%). The frequency was not correlated with the diagnosis. The amplitude-ratio was significantly higher in the patients with generalized epilepsies as compared with the localization-related ones ($p = 0.008$), and it was higher in the patients with idiopathic epilepsies as compared with the symptomatic ones ($p = 0.03$). These predictors were independent. Frequency and amplitude-ratio of the SC were not significantly different during sleep.

Conclusion: The frequency and amplitude-ratio of the SC are stable parameters. The amplitude of the SC in relation to the fast component is larger in patients with generalized and idiopathic epilepsies, suggesting higher degree of cortical inhibition in these patients, possibly corresponding to specific protective mechanisms.

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SENSITIVITY AND SPECIFICITY OF ELECTRIC SOURCE IMAGING IN FOCAL EPILEPSY: A PROSPECTIVE STUDY OF 150 OPERATED PATIENTS

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Purpose: An increasing number of studies report about the potential utility of electric source imaging (ESI) to delineate the irritative zone in patients with focal epilepsy, and promote its inclusion in the presurgical planning. However, the number of patients included in these studies has been relatively low so far, and the validation by surgical resection and outcome was often not provided.

Method: We prospectively studied the yield of ESI in 150 operated patients. In all patients ESI was applied to spikes recorded with standard clinical Video-EEG of less than 30 channels (LR-EEG). In addition, high-resolution EEG (HR-EEG) with 128–256 channels was analyzed in 55 patients. The individual MRI was used as head model whenever available.

Results: In 132 patients with successful surgery (Engel I or II), ESI localized correctly in the resected area in 71%. Taking only the 46 patients with HR-EEG, the correct localization increases to 83%. Worst results were found when ESI was based on LR-EEG and on standard MRI (59%). In the 18 patients without successful surgery (Engel III and IV), ESI correctly localized outside the resected zone in 61% (high resolution EEG: 67%, low resolution EEG: 55%).

Conclusion: This study shows high sensitivity and specificity of ESI if optimal technical equipment is used. Given that even HR-EEG equipments are readily accessible and affordable and that structural MRI is nearly always available in these patients, the result of this study clearly recommends the use of ESI in the presurgical evaluation of patients with focal epilepsy.

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QUANTITATIVE ANALYSIS OF UPPER LIMB AUTOMATISMS IN TEMPORAL AND FRONTAL LOBE EPILEPSY

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Purpose: To evaluate the lateralization of ictal upper limb automatisms in patients with temporal (TLE) and frontal lobe epilepsy (FLE).

Method: Ictal upper limb automatisms of 38 patients with TLE were quantified and compared to similar automatisms of video recorded seizures from 20 patients with FLE. Duration of automatisms in relation to total seizure duration, movement speed, extent, length and predominant frequencies of the movements were analyzed for both upper extremities separately and compared to the lateralization of the epileptogenic lobe. The movements were two dimensionally quantified according to a published protocol (Li et al., *IEEE-TBME*, 49(6), 565–73, 2002; O'Dwyer et al., *Epilepsia*, 48(3):524–30, 2007).

Results: The maximum speed of upper limb automatisms was statistically significantly slower contralaterally to the epileptogenic temporal lobe (median contralateral 84 vs. ipsilateral 173 pixels/s; $p < 0.02$) whereas in FLE there was no difference in the maximum speed between sides (median contralateral 428 vs. ipsilateral 511 pixel/s). The maximum speed of upper limb movement was significantly slower in TLE than FLE automatisms (ipsilateral:median TLE 173 vs. FLE 511 pixels/s; $p < 0.001$; contralateral:median TLE 84 vs. FLE 428 pixels/s; $p < 0.001$). Total seizure duration was significantly longer in TLE than in FLE (median 82 s vs. 40 s; $p < 0.001$). The duration of ictal automatisms in relation to the total seizure duration was significantly lower in TLE than in FLE (36% vs. 63%; $p < 0.001$).

Conclusion: In contrast to FLE, ictal upper limb automatisms in TLE show an asymmetry of movement parameters. The quantitative movement analysis provides information to differentiate TLE and FLE seizure semiology. 3D technique should be applied to overcome the limitations of the 2D analysis.

Acknowledgements: FCT&FEDER grants:PTDC/SAU-BEB/72305/2006,GRID/GRI/81833/2006,GRID/GRI/81819/2006.

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CORTICAL EFFECT OF ANTIEPILEPTIC THERAPY IN UNVERRICHT-LUNDBORG SYNDROME: A QUANTITATIVE EEG STUDY USING LORETA ANALYSIS

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Purpose: Progressive myoclonus epilepsy of Unverricht-Lundborg type (EPM1, baltic myoclonus) is the most common cause of progressive myoclonus epilepsy worldwide. Clinical symptoms are stimulus sensitive myoclonus, generalized tonic–clonic seizures, ataxia, tremor, depression and progressive cognitive impairment. The goal of the study was to analyze the background activity of resting EEG before antiepileptic therapy and the anatomical localization of the cortical effect of valproate (VPA).

Method: EEG was recorded in untreated condition and during monotherapy, when VPA treatment abolished the seizures. 19-channel EEG was recorded, and a total of 2 min artifact-free, waking EEG was processed for low resolution electromagnetic tomography (LORETA) analysis. Activity (that is, current source density) was computed in four frequency bands (delta, theta, alpha, beta), for 2394 voxels that represented the cortical gray matter and the hippocampi. Z scores were computed for the four bands and all voxels.

Results: Significant decrease of activity was found in the delta, theta and alpha bands. VPA decreased delta and theta activity in the entire frontal cortex, while alpha activity decreased in a smaller frontal cortical area.

Conclusion: VPA decreased activity in parts of the cortex that display ictogenic properties and contribute to seizure generation in idiopathic generalized epilepsy (IGE). These VPA-related changes might be related to the decrease of seizure propensity in EPM1 also.

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THE YIELD OF SLEEP-DEPRIVED EEG IN PATIENTS ADMITTED FOLLOWING A FIRST RECOGNIZED SEIZURE

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Purpose: To assess the yield of SDEEG in patients admitted following a first recognized seizure.

Methods: We retrospectively reviewed the EEG recordings and medical records of 78 patients admitted to the Neurology Department in Assaf Harofeh Medical Center due to a first recognized seizure during a 3-year period between 2006 and 2009, and who had an 8 h- SDEEG following a first routine EEG without epileptiform discharges (EDs).

Results: The study group included 42 (54%) men and 36 (46%) women, aged 18–78 years (mean-35 ± 17). Forty-six (59%) patients were admitted due to a primary generalized tonic–clonic seizure (GTCS), 24 (31%) due to a secondary GTCS, and 8 (10%) had a focal seizure. Previous seizures were recognized through repeated history in 32 (41%) patients. EDs were recorded in the SDEEG in 16 (21%) patients: 13/46 (28%) with a SDEEG recorded 3 days or less following the seizure and 3/32 (9%) with a later SDEEG ($p = 0.042$); 10/32 (31%) patients in whom previous seizures were recognized and 6/46 (13%) with a first-ever seizure ($p = 0.05$).

Conclusions: EDs in the SDEEG following a first recognized seizure occur more commonly when the SDEEG is performed 3 days or less following a first-ever seizure or when previous seizures are recognized.

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DON'T CLOSE YOUR EYES FOR EPILEPSY! SELF-INDUCTION OF EPILEPTIC SEIZURES BY SLOW EYE-MOVEMENT

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Purpose: To elucidate the different mechanisms of visual self-induction as a form of reflex epilepsy and their psychophysiological background and therapeutic options.

Method: Clinical findings and video-EEG recordings were used to show the characteristics of four patients using self-induction by visual stimuli.

Results: Four patients in whom self-induction by visual stimuli through slow eye-closure occurred are described. All were on several antiepileptic drugs but proved drug resistant. The clinical and the EEG findings, including the typical oculographic artefact seen in the EEG in visual self-induction, are presented. Also, the ''sunflower sign'' which may accompany visual self-induction is presented. The underlying psychophysiological mechanisms of self-induction and their treatment are discussed. The relation with photosensitivity is discussed. The outcome of the individual patient after appropriate treatment of the underlying mechanism is presented.

Conclusion: Visual self-induction can be a reason for treatment failure in epilepsy, especially in patients with fotosensitivity. Probably, self-induction is more common than previously thought but may go unnoticed because of the subtle clinical signs and EEG findings. Recognition of this phenomenon may open other treatment options.

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PHOTOSENSITIVITY: THE ROLE OF DURATION OF ANTIEPILEPTIC DRUG TREATMENT

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Purpose: We performed a long- term study to evaluate disappearance of photosensitivity (PPR) in relation to the response to antiepileptic drugs (AEDs) and duration of AEDs treatment.

Method: All patient were investigated with EEG at the onset of PPR, and follow up after 6, 12, 36, 60 months (respectivelly) of PPR detection.

Results: Fifty five photosensitive patients, 37 female(67%), 18 male (33%) were enrolled in the study, giving a female/male ratio of 3:1. The average age of onset photosensitivity was 13 years 6 months (range 5–21 years). The age range was between 6 and 31 years. Of the patients, 48 (87%) were treated with valproate (VAL) monotherapy, one with Lamotrigine (LTG) monotherapy, and six received VPA in combination with other AEDs. During follow up period (between 1 year and 12 years) PPR was reduced as follows: after 6 months PPR was not present in 29 (53%) patients, after 1 year in 34 (62%) patients, after 3 years in 67%, and after 5 years of follow up period in 40% of patients. Medication was withdrown in 9 out of 23 patient with PPR follow up 5 years and more.

Conclusion: Our findings show that VPA either monotherapy or in combination with other AEDs suppresses PPR. Disappearance of PPR also depend on time of follow up, and most prominent is after 3 years follow up period (67%). Increasing percentage of PPR after 5 years of follow up is probably due to withdrown of AEDs in 40% of patients.

p178
NEUROPHYSIOLOGIC INDICATORS OF EPILEPTOGENESIS AND SURGICAL TREATMENT OF TEMPORAL LOBE EPILEPSY

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Purpose: Over 35% of epileptic patients suffer uncontrolled by medication seizures. Our aim was to study dynamics of epileptogenesis in temporal epilepsy and to optimize surgical treatment.

Method: EEG-monitoring in preoperative, ECoG-SEEG via deep electrodes in postperative period. Electroclinical examination and surgical treatment of over 300 resistant temporal epilepsy patients aged 18–53.

Results: Investigation into epileptic syndrome forming in postneurotrauma patients revealed a number of critical electrographic patterns (criteria) denoting increasing surplus spatial synchronization and reflecting consecutive stages of brain epileptization in preclinical period. These neurophysiologic criteria help early diagnosis of epilepsy and seizure prevention. Further regularities of epileptogenesis were revealed at the level of morphofunctional organization of temporal epileptic foci and EEG-ECoG-SEEG analysis. The major group (79%) were patients with combined temporal neocortex and deep limbic structure (hippocampus, amygdala) damage, thus optimizing strategy of open surgical treatment

(anterior temporal lobectomy). EEG-SEEG data suggested extratemporal routes of epileptization: the hippocampus and amygdala enter the Papez and Livingstone-Escobar circle system via thalamic nuclei, which should be considered during stereotaxic intervention. Basing on EEG trait-markers, three clinical-neurophysiologic variants of temporal epilepsy reflecting dynamics of epileptogenesis at different stages of the disease were depicted: monotemporal, bitemporal and ''intermediate'' – monotemporal with initial mirror focus forming – that makes us reconsider the strategy and timing of surgery for epilepsy.

Conclusion: Neurophysiologic criteria appear a reliable method to evaluate regularities of epileptogenesis at the cortical, limbic and brainstem structure levels. The dynamics of epileptogenesis optimizes strategy of differentiated surgical treatment of drug-resistant temporal epilepsy.

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AUTOMATIC DIAGNOSTIC SYSTEM FOR PAROXYSMAL ACTIVITY DETECTION

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Purpose: The EEG signal displays summarized electrical brain activity which is nonlinear process. Today in hospitals methods ignoring nonlinear dynamics of the brain activity are used. The aim of our study was to create the assistant diagnostic system for EEG paroxysmal activity detection to revile epilepsy remission stage.

Method: We used the Neural-Net Method to make the assistant diagnostic system and examined this system on real EEG data. The largest Lyapunov's exponent is used as a criterion for the paroxysmal activity detection. In our research we used 18 registrations of the EEG signals taken from ten patients.

Results: At first we found a border value of the largest Lyapunov's exponent equaled 0. Therefore a value of the largest Lyapunov's exponent was positive for chaotic behavior of a system and decrease when the epilepsy activities occur. There were about 96.7% of epileptiform activity detection ant not big percent of the false detection 5.0% ($p < 0.05$). In a case when we had false detections it might be epileptiform activities which were invisible on EEG signals. It is significant that there were no false detections in EEG signals characterized only normal activity.

Conclusion: The present diagnostic system will be applied for the automatic epileptiform activities detection. We hypothesize about possible using system to prognostic detect of preseizure changes in the EEG signal dynamic and to predict a seizure occurrence, to revile epilepsy remission stage and to estimate efficacy of treatment.

Poster session: Clinical neurophysiology III
Monday 28th June 2010
13:30–14:30

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SOURCE LOCALIZATION METHODS APPLIED TO SUBDURAL EEG RECORDINGS IN FRONTAL LOBE EPILEPSY

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Purpose: Recent simulation studies as well as single case reports indicate that the application of source reconstruction methods to intracranial (subdural) EEG recordings may provide additional information in planing resections. We attempted to define the scope of applicability for these novel methods investigating accuracy of inverse solutions and defining clinical significance of source reconstruction regarding postoperative outcomes.

Method: We retrospectively analyzed subdural grid and strip electrode data of 5 patients with refractory frontal lobe epilepsy due to an underlying focal cortical dysplasia. Coverage included a lateral grid, as well as intrahemispheric and basal frontal strips. Spikes visually identified and averaged served as a substrate for the realistic boundary element model (BEM) based sLORETA and MUSIC (MUltiple SIgnal Classification) algorithms. Results were visualized using T_1-weighted MRI prior and after surgical treatment.

Results: Solutions localized within the clinically and electrophysiologically suspect region in all cases with a distance of 0–7 mm between MUSIC and sLORETA maximums. In two cases total resection of the epileptogenic zone including inverse solution was possible, followed by Engel Ia outcome. In another two cases, epileptogenic zone/solution localized partly within eloquent cortex areas and subtotal resection with additional multiple subpial resections led to Engel Ia and Engel IIb outcomes respectively. In a patient with Engel Ia outcome solutions localized at resection border.

Conclusion: Reliable source reconstruction derived from subdural recordings can be achieved through the MUSIC and sLORETA algorithms. This complementary information enhances localization, especially regarding deep sources, and may assist in planing tailored resections and enhancing clinical outcomes.

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BESA EPILEPSY: A NEW CLINICAL SOFTWARE FOR FAST EVALUATION OF INTERICTAL SPIKES IN LONG-TERM EEG

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Purpose: Traditional spike detection programs mark detected events in long-term EEG but lack a good overview. BESA Epilepsy uses a new hypercluster technique to combine similar events over 24 h of EEG. The physician inspects each hypercluster and decides whether it is epileptiform or not. Optimized EEG displays, 3D maps, and event localization in a head scheme allow for fast decision and assessment of the likely region of origin.

Method: A new spike detection and clustering algorithm based on an EEG transformation into 29 regional brain sources was developed. Clusters were calculated in 2 h epochs and combined into daily hyperclusters using empirical rules on similarity in waveshape and topography. 24 h EEG data of 44 epilepsy patients (21 children) were evaluated by independent raters using traditional visual inspection versus fast hypercluster evaluation.

Results: Visual rating resulted in 107 epileptiform spike types. Hypercluster rating agreed in 85% (temporal lobe spikes 94%, extratemporal 78%). In a 24 h recording, about 15–25 hyperclusters had to be inspected to decide whether they reflected artifacts, normal EEG patterns, or epileptiform discharges. As a benefit of the rapid inspection tools, the decision and reporting process was typically completed within 5 min by an experienced physician.

Conclusion: The traditional hourly evaluation of 2–5 min epochs of long-term EEG can be readily supplemented by a computer-based hypercluster evaluation. This adds a fast, comprehensive overview and report, an independent control of the existence of one or multiple spike foci, and an estimation of their origin.

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HOW LOCALIZING ARE THE FOCAL EEG EPILEPTIFORM ABNORMALITIES? EEG/MRI CONCORDANCE STUDY

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Purpose: Focal EEG epileptiform abnormalities (*f*EEG*abn*) may be indicative of underlying lesion in the brain. We aimed to study concordance of *f*EEG*abn* on EEG done in an out patient setting to the neuroimaging.

Methods: We reviewed *f*EEG*abn* and neuroimaging findings in 24 patients and the concordance was calculated. In addition, information regarding patient demographics, reason for EEG referrals, type and area of focal epileptiform discharges were collected.

Results: We found 12 male and 12 female patients with mean (±SD) age of 41(±23.6) years. All but 2 had ''seizure'' as reason for EEG referral. Eighty three percent (n = 20) had sharp waves, 12.5% (3) had spike-waves and 4% (1) had electrographic seizures. Seventy five percent (n = 18) had discharges seen on frontal and parieto-occipital lobes in equal numbers, while in 25% (6) EEG abnormalities were seen in temporal lobes. MRI was performed in 20 patients while CT was done in the remaining. On neuroimaging, 8 patients had strokes, 5 were nonlesional, 5 with mesial temporal sclerosis (MTS), 3 had tumors, 2 with cortical dysplasia and 1 had ADEM. Sixty-three percent (15) had EEG abnormalities localizing to the same lobe on neuroimaging. In three patients the EEG lateralized to the ipsilateral hemisphere, but not to the same lobe. In five nonlesional patients, the focal abnormalities were seen in extratemporal regions (3-frontal, 2-parietal and 1- central). One patient with right MTS showed left temporal discharges.

Conclusion: Concordance of *f*EEG*abn* to ipsilateral hemisphere on neuroimaging was seen in 75% of the patients.

p183
2D VERSUS 3D APPROACHES TO MOVEMENT QUANTIFICATION IN EPILEPTIC SEIZURES: SIMULATIONS AND REAL SEIZURES COMPARATIVE EVALUATION

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Purpose: Following our pioneering work on movement quantification in epilepsy (Li and Cunha, 2002; Cunha et al., 2003) based on a 2D approach, we now present a comparative analysis between a 2D versus a 3D movement quantification technique tested in simulated movements and real epileptic seizures.

Method: We tested the two paradigms in simple motor simulations performed by a normal subject and in real epileptic seizures. We aim to prove that the information deduced from a motor execution (simulated or seizure) can be very different depending on the quantification method used (2D vs. 3D) and characterize the entropy associated to it.

Results: Mean errors between 2D and 3D quantification could go up to 77% in simulated movements and 161% in real seizures.

Conclusion: Results confirm 2D method as a valid tool ONLY if certain conditions are met. We imposed these conditions in previous studies (O'Dwyer et al., 2007; Cunha et al., 2009). However, the loss of information verified if these conditions are not fulfilled advises caution when correlating 2D movement analysis with the semiology of the seizure. We also show that our innovative 3D movement quantification approach offers a high resolution (1 × 1 × 1 mm voxel resolution) that is vital when relating all the multimedia data (EEG, events, etc.) used in an Epilepsy Monitoring Unit. Several clinical studies are under development using this new 3D technique.

Cunha J.P. et al. Proc. *IFBME World Congress* 2009; Munich, Germany, p. 1435–8.

O'Dwyer R et al. *Epilepsia*. 2007 March; 48(3):524–30.

Li et al, IEEE Transactions on Biomedical Engineering. 2002 June; 49(6):565–73.

Acknowledgements: FCT and FEDER grants: PTDC/SAU-BEB/72305/2006,GRID/GRI/81833/2006,GRID/GRI/81819/2006.

p184
DETECTION OF MAJOR EPILEPTIC SEIZURES WITH HEART RATE CHANGES: FEASIBILITY TEST OF A STATE-OF-THE-ART WEARABLE SENSOR

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Purpose: To develop and validate a wearable ultra-low power prototype device for ECG-based epileptic seizure detection.

Method: This observational study is a nonrandomized, open, single-site, clinical test in 10 subjects (30–50 seizures) previously diagnosed with frequent (>1/week) major epileptic seizures (tonic–clonic, generalized tonic or clonic) with heart rate changes. A wearable device running a previously developed algorithm [van Elmpt WJ et al. Seizure 2006; 15(6):366–75] for heart rate based seizure detection was tested at night during 1–4 weeks per patient. Objectives were the sensitivity, positive predictive value and technical feasibility. Results were verified by visual analysis of recorded video and comparison to previously analyzed EEG-video data.

Results: In the first 3 patients 100% of major seizures were detected; however at the cost of many false positives. Reanalysis of the data showed that optimizing parameter settings of the detection algorithm considerably improved positive predictive value. Exact results will be presented.

Conclusion: Heart rate–based detection of major seizures by the proposed wearable sensor system is feasible.

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A NOVEL IMPLANTABLE VAGUS NERVE STIMULATION SYSTEM (ADNS-300): PILOT TRIAL AT GHENT UNIVERSITY HOSPITAL

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Introduction: Vagus nerve stimulation (VNS) is a well known treatment for refractory epilepsy. The ADNS-300 is new vagus nerve stimulator which possesses a transcutaneous recharging system and is capable of recording compound action potentials (CAP) of the vagus nerve. We report for the first time CAP measurements in chronically implanted human vagus nerve.

Methods: Three patients with refractory epilepsy were implanted with a combined stimulation/recording spiral cuff electrode (ADNS-300) around the left vagus nerve. CAPs were recorded in patient 1 and 2 at

regularly intervals during 6 months following the implantation. The vagus nerve was stimulated at a rate of 1 or 2 Hz with bipolar charge balanced pulses with varying intensity and pulse duration.

Results: Large negative and polyphasic signals were recorded initially and disappeared within 4 weeks. Lower amplitude electrophysiological activity was recorded again from week 16 on. Latencies of the different peaks varied as a function of the stimulus intensity and time: N1 (0.35–0.5 ms), P1 (0.55–0.9 ms), N2 (1.3–1.65 ms), P2 (4.25–5.1 ms). Maximal amplitude of the CAPs (P1-N2) at the end of the follow-up period was increased in comparison to earlier values.

Conclusion: ADNS-3.00 successfully recorded CAP's from the human left vagus nerve. After implantation, there was an asymptomatic silent period, during which no CAP's could be recorded. This might be due to a temporary demyelinization or partial loss of function of the vagus nerve. Adjusting the stimulation during this period might be meaningless and perhaps lead to inappropriate stimulation settings.

Acknowledgments: This study was partially funded by Neurotech Belgium.

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INTERICTAL AND ICTAL DYNAMICS OF NETWORK TOPOLOGY IN FOCAL EPILEPSY: A CASE STUDY

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Purpose: To understand the mechanism (s) of spontaneous focal seizure generation and look for evidence of network plasticity.

Method: We used data from eight seizures recorded from a single epilepsy surgery candidate with periventricular nodular heterotopia. We took six to nine 10-s epochs over the preictal, ictal and postictal periods. We quantified the state of the system over the broad-band signal (1–45 Hz) and the physiological frequency subbands using Synchronization Likelihood (SL), and performed graph analysis involving the Clustering Coefficient (C) and the Path Length (L). We estimated the values of these measures as a function of time to seizure onset, time to seizure termination, and seizure duration.

Results: We found a sharp increase of all measures in all frequency bands during seizure onset. This decreased postictally to a level slightly higher than in the preictal period. These differences between the pre-, ictal and postictal states were significant for all measures in all frequency bands, except for the SL measure in the 1–4 Hz band. The strongest discrimination between pre- and postictal states was observed by the C values in the 13–20 Hz and 20–45 Hz frequency bands ($p < 0.05$).

Conclusion: The above findings are compatible with the multistability seizure generation hypothesis where the transitions are fluctuation-driven -rather than gradual- and may indicate that the transition onsets cannot be predicted with our analysis. The clear difference between pre- and postictal states, however, may point towards network plasticity during the seizure due to changes in functional connectivity and network topology in the brain.

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LANGUAGE LATERALIZATION IN CHILDHOOD-ONSET FOCAL EPILEPSY: EVIDENCE FROM fMRI

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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: Twenty-four children suffering from drug-resistant, left-sided, early-onset epilepsy underwent fMRI-scanning using a covert verb-generation task. Twenty-nine 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). Typical language lateralization (left-sided) was defined as $LI > 0.2$ and atypical language (right-sided or bilateral) as $LI \leq 0.2$. Factors contributing to atypical language distribution were investigated including: age at seizure-onset, seizure frequency, handedness, lesion location, lesion size, size and asymmetry of the planum temporale.

Results: There was no statistically significant correlation between age at seizure-onset, seizure frequency, handedness, lesion location or lesion size and an atypical language lateralization ($p > 0.05$). However, the correlation between PT-asymmetry and the fMRI language lateralization index was highly significant ($r = 0.823$, $p < 0.001$). A stepwise linear regression analysis including all variables revealed that asymmetry of the planum temporale was the only significant predictor for language lateralization, accounting for 50% of the variance (Beta = 0.723, $p < 0.001$).

Conclusion: In the presence of left-sided pathology the asymmetry of the planum temporale appears to indicate the efficacy of language reorganization to the right hemisphere.

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SERUM NEURON-SPECIFIC ENOLASE IN POSTTRAUMATIC EPILEPSY

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Purpose: Neuron-specific enolase (NSE) has been established as a reliable marker of neuronal damage in various neurological disorders. The aim of this study was evaluation of posttraumatic epilepsy-caused neuronal damage based on the serum level of NSE.

Methods: Forty five patients aged from 25 to 38 years were enrolled. Among them, 28 patients had generalized seizures, and 17 patients had partial seizures. The maximal seizure duration was 30 min. Blood samples for the measurement of serum NSE was obtained immediately after the seizure. The concentration of NSE was measured by enzyme immunoassay.

Results: The normal level of serum NSE in healthy volunteers was 7.1 + 2.5 ng/ml with the NSA level ranged between 3.3 ng/ml and 11.3 ng/ml. The NSE level in both groups of patients with generalized seizures and with partial seizures showed strong correlation with the seizure duration, but in patients with partial seizures the NSE level was higher than that in patients with generalized seizures (14.1 ± 5.7 ng/ml and 11.5 ± 4.9 ng/ml respectively) and ranged as 1.9–23.3 ng/ml after partial seizures and 9.1–18.8 ng/ml after generalized seizures.

Conclusions: From the results obtained, it can be concluded that NSE may serve as a sensitive marker of neuronal damage in posttraumatic epilepsy and that partial seizures result in stronger neuronal damage then generalized seizures do and hence the former may cause more severe neuronal loss.

p189
EVALUATION OF CARDIAC AUTONOMIC FUNCTION IN COMPLEX PARTIAL SEIZURES: A STUDY WITH HEART RATE VARIABILITY MEASURES

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Purpose: Autonomic imbalance is considered an important reason for Sudden Unexpected Death in Epilepsy (SUDEP). Autonomic imbalance has been noticed in generalized seizures, but studies probing the autonomic imbalance in partial seizures are few.

Method: 15 patients (M:F-12:3) with Complex Partial Seizures attending out patient department in Neurology in a tertiary reference hospital (NIMHANS, India), were diagnosed by a Neurologist and recruited after satisfying the inclusion /exclusion criteria. Age and gender matched healthy subjects were taken as controls (n = 15). Heart rate variability was done with an artifact free 5 min ECG recording. Analysis was done in time and frequency domain measures

Results: The mean age of the patients and the duration of disease were 27.8 ± 7.4 years and 15.6 ± 7.5 years respectively. Data were analyzed by independent sample t-test after square root transformation. The data are expressed in Mean ± SEM. A significant deviation ($p < 0.05$) of autonomic function in the study subjects were noted when compared to controls in SDNN (33.9 ± 3.3 vs. 49.9 ± 4.6), RMSSD (26.9.1 ± 2.5 vs. 46.2 ± 5.9), HF power (249.9 ± 49.6 vs. 850.2 ± 239.5), LF/HF ratio (2.2 ± 0.6 vs. 0.85 ± .13).

Conclusion: There was a reduction in heart rate variability in complex partial seizures. A significant reduction in the activity of parasympathetic nervous function was found as reflected by reduction in power of RMSSD and HF. The sympathovagal balance showed a relative increase of sympathetic function in the subjects which might predispose them for cardiovascular dysfunction and SUDEP.

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OVERCOMING THE UNPREDICTABILITY OF SEIZURES: PATIENTS' VIEWS TOWARDS EEG-BASED PREDICTION DEVICES

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Purpose: The unpredictability of seizures affects everyday life of epilepsy patients. Data on the subjective impairment, however, are scarce, and little is known regarding patients'acceptance of prediction devices on a long-term basis. We here report results of a bicentric study on patients' attitudes on ambulatory devices for seizure prediction from Freiburg, Germany, and Coimbra, Portugal, as part of the project EPILEPSIAE (EU-grant 211713).

Method: 100 outpatients of the Freiburg epilepsy center and 55 patients from the Epilepsy Center of Coimbra were asked to fill out a questionnaire. Items addressed the general role of unpredictability of seizures, patients' requirements on prediction devices, and practical issues of device implementation.

Results: Unpredictability was considered as very important or important in 66%/67% of German/Portuguese patients. 70% of German and 81% of Portuguese patients considered the development of seizure prediction devices very important. Sensitivity of prediction was considered more relevant than specificity. In practical terms, patients of both centers favored an acoustic warning, brief seizure occurrence periods, and accepted also indicators of seizure propensity. Wearing EEG scalp electrodes on a long-term basis was considered acceptable by the majority of Portuguese, but only by 12% of German patients. More than 50% of patients are interested in automatic prediction-based intervention.

Conclusion: The unpredictability of seizures strongly affects patients' life. Correspondingly, there is high interest in seizure prediction devices both, for warning and for closed-loop intervention. Sensitivity requirements of patients are hardly met by existing algorithms, however, and practical issues have yet to be solved.

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HEART RATE DECREASE ASSOCIATED WITH FAST SEIZURE COMPONENTS AND INCREASED VAGAL ACTIVITY IN RATS

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Purpose: Ictal bradycardia (IB) is a manifestation of seizures which occurs in epilepsy patients and animal epilepsy models. Although studies suggest that cardiac arrhythmias result from ictal autonomic changes, the mechanistic support of IB is not fully understood. This work investigates correlations between cortical discharges, vagal activity and heart rate decrease during seizures.

Method: In PTZ treated rats with intact vagus nerves (n = 10), a maximum heart rate decrease occurred seconds after the onset of ECoG high amplitude fast seizure components and was associated with an increase in the general and cardiac related activity of the vagus nerves. These manifestations were absent in saline-treated rats (n = 6) and in rats vagatomized prior to PTZ administration (n = 6).

Results: In PTZ treated rats with intact vagus nerves (n = 10), a maximum heart rate decrease occurred seconds after the onset of ECoG high amplitude fast seizure components and was associated with an increase in the general and cardiac related activity of the vagus nerves. These manifestations were absent in saline-treated rats (n = 6) and in rats vagatomized prior to PTZ administration (n = 6).

Conclusion: It is concluded that increased synchronization of cortical discharges during seizures results in increased vagal activity which leads to heart rate decrease.

Acknowledgments: This work was supported by the Danish National Advanced Technology Foundation and Neurodan A/S.

Poster session: Epilepsy syndromes in development I
Monday 28th June 2010
13:30–14:30

p192
RASMUSSEN SYNDROME (RS): SURPRISING DEVELOPMENTS. WHAT THERAPEUTIC DECISIONS ADOPTED?

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Introduction: RS is partial continuous epilepsy (PCE) and progressive syndrome that includes seizures of multiples types and evolving neurologic deficits such as hemiplegia and mental deterioration. Current opinion favors the presence of immunologic allergic mechanisms.

Case report: 5-year-old child without family history interest. Pregnancy, childbirth and neonatal period were normal. Normal childhood development. He was operated congenital hydrocephaly to 12-months-old. The first seizures were focal seizures of member upper left (MUL) in March of 2009. We started on a treatment OXC and controlled epileptic seizures. These reappeared 60 days later and they were increasing their frecuency and spread to the lower left limb and hemifacies ipsilateral until it constituted PCE. The video-EEG showed a motor partial electroclinical status in MUL with critical activity in right parieto-occipital region and slow background activity and the brain MR- 3T and

PET-FDG a cerebral atrophy diffuse predominance right with signs of edema postcritical in right central and Silviana region. The epilepsy evolved to refractory epilepsy (it was treated with VPA, ZNS, PHT, ACTH, prednisone, MDZ, barbiturate coma with Pentothal and IGB) and progressive deterioration of the cognitive and motor functions. So we raised a functional hemispherectomy. The neurometabolic study, serology, neurotransmitters and neurotropic virus in CSF and Karyotipe were normal. The seizures disappeared spontaneously at 2 months of its onset with standardization of the video-EEG register, brain MR-3T, PET-FDG and the motor and cognitive functions.

Discussion: The disappearance of the seizures and clinical recovery in the RS is surprising. We would require information on similar cases and attitudes therapeutic recommendable in this situation, because the surgery would have produced aftermath irrecovarable.

p193
WHICH PROGNOSIS FOR FOCAL EPILEPSIES WITHOUT KNOWN CAUSES IN INFANCY?

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Purpose: The authors report a retrospective study aimed at assessing long-term outcome in patients with nonsymptomatic focal epilepsies with onset in the first 2 years after birth without definite etiology.

Methods: Thirty-three children admitted in our Unit between 1996 and 2008 were enrolled in our study. They all had partial seizures before the age of 2 years and, when assessed following the onset of seizures, there was no evidence of clinical features, brain MRI changes or laboratory findings suggesting metabolic or genetic diseases. They were all followed up to the age of 5 years with serial assessments of the evolution of seizures and neurodevelopment. Epileptic, neurocognitive and behavioral outcome at 5 years was analyzed in relation to the following possible risk factors: family history, age of seizure onset, psychomotor development before seizure onset, seizure features at onset, interictal electroencephalogram (EEG) abnormalities, behavioral disorders.

Results: At 5 years of age, 16 of the 33 children were seizure-free and sixteen had a normal cognitive development. Epilepsy recovery was found in ten of the sixteen cases with normal cognitive development whereas only six out of the seventeen patients with cognitive disorders were seizure-free. Delayed development before seizure onset, seizure frequency at the onset, changing seizure semiology and family history of epilepsy correlated with poor developmental outcome.

Conclusions: Evolution of focal epilepsy without known cause in infancy remains difficult to predict. New assessment techniques are needed to reveal early signs of severe epileptic disorders and provide more precise prognostic information.

p194
CLINICAL AND ELECTROENCEPHALOGRAPHIC FEATURES OF RETT SYNDROME: DIFFERENCES BETWEEN CLASSIC FORM AND HANEFELD'S VARIANT

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Purpose: Rett syndrome is a neurodevelopmental disorder characterized by microcephaly, mental retardation, stereotyped hands automatisms, dyspraxia and breathing irregularities. Epilepsy is commonly associated with this disorder. Identify clinical and neurophysiological features of epilepsy and try to detect differences in the 2 major variants (MECP2 and CDKL5).

Method: 8 pts (mean age 6.7 years) with Hanefeld variant (CDLK5 mutated) followed in our centre were compared to 8 newly diagnosed consecutive pts with classic form of Rett syndrome (MECP2 mutated; mean age 5.9 years). All the patients were female and underwent clinical, anthropometric and ISS (international score system) evaluation, interictal EEG and autonomic study with neuroscope instrument. Details about seizures semiology were obtained by relatives.

Results: Seizures were reported in all patients with Hanefeld's variant whilst 3 out of 8 pts with classic variant experienced seizures. 5 out of 8 pts with HV are drug resistant compared to 1 out of 3 pts with CF. Mean age of seizures onset is 3 months for HV and 5.7 years for CF. Seizures semiology is variable in both groups. No specific EEG pattern for one of the 2 forms has been noted.

Conclusion: Our data suggest that epilepsy is more common, more difficult to treat and earlier in onset in HV than in CF of Rett syndrome. This, together with the more evident autistic features of HV compared to CF, suggests that HV and CF of Rett syndrome are 2 clearly distinct clinical conditions possibly with different evolution and prognosis.

p195
WEST SYNDROME: ETIOLOGICAL AND PROGNOSTIC ASPECTS IN 48 CASES

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Purpose: We analyzed etiological and prognostic aspects of patients with West syndrome (WS).

Method: 48 patients were enrolled in retrospective study. Mean onset of epileptic spasms was 6 month. All children were followed from 2 to 6 years (mean 3.7).

Results: Etiology of epileptic spasms was symptomatic 40 (83.3%). Idiopathic WS was concluded in 8 (16.7%). Family history for epileptic spasms was reported in two girls. Neuroimaging studies showed morphological abnormalities in more than 83%.

Symptomatic etiologies were divided into prenatal, perinatal, and postnatal causes.

Prenatal causes included intrauterine insults, infections, malformations of cortical development and neurocutaneous syndromes accounted in 17 (42.5%) of symptomatic cases.

The perinatal group enrolled hypoxic ischemic encephalopathy, obstetric trauma, and other birth complications accounted in half symptomatic patients. Postnatal etiologies include infection, trauma, and tumors accounted in 3 (7.7%) symptomatic cases. Normal psychomotor development was observed in only 4 (8.3%), slightly motor delayed and borderline intellectual functioning 6 (12.5%) patients. Other patients suffer a poor outcome with respect chronic epilepsy, severe to profound mental retardation, and other neurodevelopmental disabilities.

Conclusion: Although WS is regarded as one of the intractable epilepsies, the prognosis differs widely according to etiology. The majority of our patients have a poor prognosis.

p196
THE OCCURANCE OF EPILEPTIFORM ACTIVITY ON EEG AND EPILEPSY IN CHILDREN WITH HYPERKINETIC DISORDER: A RETROSPECTIVE STUDY

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Introduction: Hyperkinetic Disorder (HKD) is a neurodevelopmental disorder characterized by age-related inadequate rate of hyperactivity, impulsivity and attention deficit, the incidence of HKD in child population is estimated 5–10%. Several studies evaluated that the epileptiform activity on EEG and/or epilepsy is present in 6–51% of children with HKD.

Purpose: The purpose of the study was evaluation of EEG recordings in children with HKD.

Methods: We retrospectively evaluated the EEG findings and clinical documentation of 135 children meeting the criteria of hyperactivity disorder according to ICD-10. We focused on localization of the epileptiform activity on EEG.

Results: In the study of 135 children aged 6–18 years there were 105 males (77.78%) and 30 females (22.22%). We found epilepsy (clinical seizures with or without EEG pathology) in 57 patients (43.00%) and epileptiform activity on EEG without clinical seizures in 17 of them (12.59%).

The EEG pathology was found in 79 patients (58.52%), to precise – the epileptiform activity on EEG was described in 60 patients (44.44%) and nonspecific EEG pathology in 19 patients (14.07%). The localization of epileptiform discharges on EEG was generalized in 18 patients (30.00%), predominantly frontal in 17 (28.33%) and rolandic in 8 (13.33%), temporal in 16 patients (26.66%) and occipital in 1 patient (1.66%).

Conclusion: The co-occurance of HKD and epilepsy or/and epileptiform activity on EEG is common in children with HKD. These results are important for further understanding of the pathofysiology of HKD and the therapy management.

p197
FEBRILE AND BENIGN SEIZURE ASSOCIATED WITH ACUTE GASTROENTERITIS IN CHILDREN

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Purpose: Febrile and benign seizure associated with acute gastroenteritis are common seizure disorders in children. We would like to know the clinical characteristics and prognosis between febrile and benign seizure associated with acute gastroenteritis.

Methods: We reviewed retrospectively the medical records of 124 pediatric patients aged from 3 months to 5 years that admitted to the Wonju Christian Hospital from 2004 to 2007 for febrile (A group) and benign seizure (B group) associated with acute gastroenteritis.

Results: The mean ages were A; 1.51 ± 1.10 years, B; 1.14 ± 0.44 years. The most common seizure type was generalized seizure; A, 94.5%, B, 100%. The average frequency of seizure was higher in B than A (A; 1.53 ± 0.88, B; 2.12 ± 1.35 times/day, $p < 0.001$). The incidence of positive history of parents for febrile seizures was higher in A to B (A; 14.5%, B; 4.3%, $p < 0.05$). The positive rate of stool rotavirus antigen test was higher in A and B (A: 45.7%, B: 42.6%), but there was no difference between two groups. There were no statistically significant differences of sex ratio, duration of seizures, serum sodium level, rate of EEG and neuroimaging abnormalities among two groups. The recurrence rate of febrile seizure after the 1st seizure was A; 9.1%, B; 5.8%, and unprovoked seizure was A; 5.4%, B; 1.4%.

Conclusion: We consider prophylactic short term management of recurrent episodes of seizures within 24 h, especially in benign seizure associated with acute gastroenteritis.

p198
CONVULSIONS DURING GASTROENTERITIS IN THE SPECTRUM OF BENIGN PARTIAL EPILEPSIES IN INFANCY: A 30 CASE SERIES AND VIDEO-EEG ICTAL RECORDING IN TWO PATIENTS

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Purpose: Afebrile benign convulsions associated with mild gastroenteritis (CwG) are now recognized as a clinical entity, characterized by acute cluster of afebrile seizures during mild diarrhea with a excellent prognosis. We studied 30 children who experienced at least two seizures during mild gastroenteritis.

Method: The inclusion criteria were: afebrile seizures during gastroenteritis, dehydration ≤5%, normal neurological findings, normal psychomotor development, no underlying pathology by laboratory and neuroimaging study.

Results: Mean age was 21 months (range: 6–38). Familiarity for epilepsy was present in 3/30 (10%) and for febrile convulsions in 11/30 (36.6%). Seizure onset was mainly on the third day after beginning of gastroenteritis. Seizures were described as generalized by parents in 16/30 patients (53.3%). We observed partial seizures with secondarily generalization in 14/30 patients (47.7%), with tendency to repeat in clusters. In two patients video ictal EEG and one EEG recording showed a focal onset. 20/30 patients (66.6%) received AED's during the acute state (monotherapy in 14 patients and politherapy in 6). At the follow-up (mean duration 53 months) all patients, but two, withdrawed antiepileptic treatment; one had a isolated afebrile seizure and two, one febrile seizure. None developed epilepsy.

Conclusion: Our series confirms the excellent prognosis of CwG. Although the pathogenetic mechanisms of CwG are unknown we can hypothesize that, during mild gastroenteritis, an acute random transient brain dysfunction involve, at the same time, different cortical areas, in children with a genetically determined susceptibility for seizures.

p199
LEVITIRACETAM TREATMENT OF CHILDREN WITH SLEEP-ACTIVATED EPILEPTIFORM ACTIVITY: A PLACEBO CONTROLLED DOUBLE-BLIND CROSS-OVER STUDY

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Purpose:

1. Evaluation of levitiracetam (LEV) on sleep-activated epileptiform activity in children
2. Assesments of the clinical impact of epileptiform activity during sleep on cognitive functions, behavior, short time memory and quality of life (will be presented later).

Method: Twenty-five children 5–10 years of age, with normal IQ with at least a fourfold increase of epileptiform discharges during slow-wave sleep and affecting at least 30% of the total slow wave sleep was eligible for the study. Children with epilepsy should have been seizure free for at least 6 weeks before entering the study.

Twentyfour-hour ambulatory EEG recording at baseline and at the end of each treatment period was performed. Spike index (SI) was calculated as the fraction of time where there were less than 3 s to next spike in 10 min epochs. LEV 20 mg/kg/day or placebo was given according to a double-blind cross-over protocol.

Results: Up to 20 patients have finished the study and are analyzed. The mean SI at baseline was 54.4. From baseline to placebo treatment there was a reduction of 13.9 in SI. Between baseline and LEV treatment there was a mean reduction in SI of 25.6. This is a significant difference ($p = 0.03$).

Conclusion: A low dose LEV gives a significant reduction in sleep-activated epileptiform activity in children.

p200
NEONATAL STRESS INCREASES VULNERABILITY TO PILOCARPINE INDUCED SEIZURE

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Purpose: The pathogenesis of epilepsy is thought to begin in early life. Among the early life factors implicated in epilepsy causation, stress may be one important contributor. In rats, we tested the hypothesis that neonatal stress, in the form of maternal separation (MS), creates vulnerability to seizure in adult life.

Method: On postnatal days 2–9, we exposed male and female rats to either MS for 120 min twice daily, or early handling (EH) and brief separation (5 min twice daily). At 6 weeks of age, rats were injected pilocarpine (50–200 mg/Kg.SC.). Then, epileptic behaviors of rats were observed for 120 min.

Results: In both sex, lower doses of pilocarpine were required following MS than EH to reach the Maximal seizures. Mean duration of onset of first epileptic behavior of EH rats was 7.24 ± 1.12 and 6.68 ± 0.84 min which decreased to 4.41 ± 0.64 and 5.11 ± 0.76 min in MS female and male rats respectively ($p < 0.01$); no differences were observed between males and females. Significant differences were observed between males and females concerning mean duration of tonic–clonic attacks both in EH and MS rats. Mean duration of attacks in EH females was 0.42 ± 0.1 min which increased to 3.2 ± 0.56 in MS females ($p < 0.01$). It was 0.52 ± 0.1 in EH males in comparison to 6.68 ± 1.14 in MS males ($p < 0.001$).

Conclusion: We conclude that, MS stress increases susceptibility to seizure in both genders but, more severely in female rats. This has implications for human epilepsy, suggesting the involvement of gender-specific factors.

p201
GLIOMATOSIS CEREBRI PRESENTING AS EPILEPSIA PARTIALIS CONTINUA: A CASE REPORT

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Purpose: To revise an atypical clinical presentation of gliomatosis cerebri.

Method: We report the case of a 8-year-old child who presented with epilepsia partialis continua on the right side of his body. Neuroimaging was compatible with first stages of Rasmussen encephalitis. After clinical worsening, some months later a neuronavigator-guided brain biopsy was performed. Pathological study was compatible with gliomatosis cerebri.

Conclusion: Gliomatosis cerebri may present with epilepsia partialis continua. Confusing cases deserve brain biopsy.

p202
EPILEPSY IN ARTERIOVENOUS MALFORMATIONS

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Purpose: The authors analyzed the epilepsy in 34 patients with cerebral vessels malformations hospitalized in Child Neurology Department in Katowice, Poland in the years 2001–2009.

Method: The age of the children was between 4 months and 17 years. The biggest group of patients was that one with arteriovenous malformations- 18, among them 10 were diagnosed with Sturge-Weber syndrome.

Results: Cerebral arterial abnormalities were seen in 9 patients, 4 children Moyamoya disease was recognized. Venous malformations were present in 5 children. 19 children were admitted because of suspicion of epileptic seizures. The diagnosis of epilepsy was established in 17 children. Partial epilepsy predominated, only in 2 patients generalized seizures were present, usually well controlled with antiepileptic drugs. Most often epilepsy was connected with arteriovenous malformations (in 10 out of 18 patients).

Conclusion: The authors show the diagnostic and therapeutic difficulties in patients with epilepsy and cerebral vessel malformations.

Poster session: Neuropsychology I
Monday 28th June 2010
13:30–14:30

p203
THE WADA TEST: HERE TO STAY?

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Since the 1960s the Wada test has been used as an instrument to identify the hemisphere dominant for language and to evaluate the risk of global amnesia after surgery. Because of its invasive character, there is a growing tendency to replace the ''language Wada'' by language-fMRI. Assessment of memory risk takes contralateral lesions (MRI) into account as all cases of global amnesia after temporal resection coincide together with bilateral lesions. If neuropsychology and MRI are ''clean,'' a memory Wada test is no longer indicated.

1606 Wadas were performed in 920 patients (75% bilateral injections). Complications occurred in only 1%. In left-sided foci language was represented in the left hemisphere in 92% (including bilateral speech). This was 6% in right-sided foci in the right hemisphere. Standard resections in the dominant hemisphere can cause sizeable decrease in verbal memory, but language stays largely intact. In a standard resection a Wada test, or other language assessing technique such as fMRI, is no longer needed. In large resections, unless a resection procedure under local anesthesia is planned (Penfield), language has to be assessed by Wada or another technique like fMRI. The latter however, contradicts the Wada test in 10%, mostly in cases of bilateral language. Instead of a Wada, two noninvasive tests (TCD or language MEG) could be performed. If these are not congruent, a Wada test will have to be performed. A discussion of the (partial) replacement of the Wada test will be given based on an analysis of the Wada test data.

p204
COGNITIVE NETWORKS DYSFUNCTION IN LEFT TEMPORAL LOBE EPILEPSY

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Purpose: Recent volumetric neuroimaging studies have showed that structural abnormalities in unilateral temporal lobe epilepsy (TLE) might be beyond the ipsilateral mediotemporal lobe complex, involving contralateral mesial structures and ipsi- and contralateral frontotemporal cortical networks. From a neurofunctional point of view, our purpose is to determine whether this structural network dysfunction would be translated into a parallel cognitive impairment in left TLE.

Method: Considering memory performance as a measure of mediotemporal lobe functional integrity, 22 left TLE patients were divided into two groups according to their verbal episodic memory (11 ''Verbal Memory Preserved'' and 11 ''Verbal Memory Impaired''). Then, both groups were compared in a comprehensive neuropsychological battery made up of 29 measures of executive functioning, working memory, nonverbal episodic memory, language, praxis and visuospatial perception. According to literature, these variables have been considered as representative neuropsychological measures of extrahippocampal as well as right hippocampal functioning.

Results: Results showed that ''Verbal Memory Impaired'' group had also a significant ($p < 0.05$) worst performance in Nonverbal episodic memory task and some ''frontal lobe'' measures (i.e., attentional and motor inhibition measures). Furthermore, this deficient neurocognitive profile was not correlated to epilepsy-related variables (i.e., age of epilepsy onset, epilepsy duration, etc.) but to ipsilateral memory performance.

Conclusion: In sum, unilateral left TLE may be associated to a broader cognitive impairment, modulated by its ipsilateral hipocampal functioning (verbal memory performance) and explained by a structural network dysfunction beyond left mediotemporal lobe system.

p205
MAKING PLANS AND DECISIONS IN PATIENTS WITH SLEEP-RELATED HYPERMOTOR SEIZURES

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Purpose: Hypermotor/hyperkinetic seizure denotes a specific seizure type characterized by the emergence of stereotyped motor behaviors during sleep. This seizure type can be observed in symptomatic frontal lobe epilepsy, as well as temporal or insular lobe epilepsies, and in genetically determined syndromes (ADNFLE). It is believed that hypermotor behaviors reflect ictal discharge onset or spread to the medial prefrontal cortex. We tested if patients with sleep-related hypermotor seizures display deficits in frontal lobe functions, and especially in decision-making abilities, independently from the epilepsy syndrome or the location of the epileptogenic zone.

Method: 7 patients with overnight video-EEG recording of typical hypermotor seizures were studied. One patient had symptomatic frontal lobe epilepsy; one had symptomatic temporal lobe epilepsy; cryptogenic etiology (3-tesla MRI) was diagnosed in 5 patients. 18 normal subjects, matched for age and education, served as controls. The ''Hanoi Towers Task'' and the ''Iowa Gambling Task'' (preferred choice of advantageous cards) were used to test planning and decision-making abilities respectively. All subjects underwent a comprehensive evaluation of standardized test of memory, language, and executive functions.

Results: At group level patients showed deficits in both planning and decision-making abilities compared to controls. Planning and decision-making resulted impaired also at single-subject level. As far as other cognitive domain verbal memory was impaired in 5 out of seven patients.

Conclusions: Impairment in planning and decision making was common in this cohort of patients with hypermotor seizures, independently from epilepsy etiology and epileptogenic zone. These data have to be confirmed in a larger patients population.

p206
IMPAIRED INTELLIGENCE SCORES ARE FREQUENT IN CHILDREN WITH FRONTAL LOBE EPILEPSY

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Purpose: To study the intelligence profile in children with frontal lobe epilepsy (FLE) as determined by the Wechsler Intelligence Scale for Children (WISC-IIInl).

Method: We reviewed the medical files of children, aged 6–17 years, diagnosed with FLE in Epilepsy Centre Kempenhaege between 1998 and 2009. We analyzed the WISC data and investigated factors of influence on intelligence scores.

Results: Data of 67 children, 45 boys and 22 girls, were analyzed. Mean age at epilepsy onset was 69.6 months (SD 47.0). Mean duration from epilepsy onset until assessment was 54.7 months (SD 37.5). Total IQ scores ranged from 57.00 to 135.00 [mean total IQ-score 86.6 (SD 16.7)]. Ten children (15%) had total IQ scores between 50.00 and 79.00, 13 (19%) between 70.00 and 79.00, and 17 (25%) between 80.00 and 89.00. Verbal IQ scores ranged from 54.00 to 132.00 [mean verbal IQ 89.9 (SD 16.4)], and performance IQ scores ranged from 54.00 to 128.00 [mean performance IQ 85.6 (SD 16.1)]. Mean individual scores were below normative for 11 out of 13 WISC-subtests. Disharmonic intelligence profiles (VIQ-PIQ or PIQ-VIQ discrepancy score >15) were demonstrated in 15 children (22.4%). Age at seizure onset was the only factor of statistical significance; for PIQ ($p = 0.032$) and VIQ-PIQ discrepancy ($p = 0.010$).

Conclusion: Mean intelligence scores are low average in children with FLE in our study group. This contrasts with the literature which states that intelligence generally remains intact in children with FLE. Low age at seizure onset is a risk factor for intellectual decline.

p207
IMPAIRED OBJECT IDENTIFICATION PROCESSING IN CHILDHOOD IDIOPHATIC OCCIPITAL EPILEPSY

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Purpose: To study object recognition processes in patients with idiopathic childhood occipital epilepsy (ICOE) versus children with symptomatic posterior cortex epilepsy (PCE) and versus healthy controls as a function of both the semantic category and spatial frequency content of stimuli.

Method: Participants included 8 children with ICOE and 9 children with PCE (age range 5–13 years), age and gender matched with controls (n = 60). IQ was evaluated by WISC-R and WPPSI. The frequency and topography of EEG abnormalities were assessed through repeated video-EEG recordings.

Patients and controls underwent the following object identification task: 120 blurred stimuli (living and nonliving categories) were presented in an ascending sequence at increasingly less-filtered images up to a complete version of the image.

Results: Both groups of patients exhibited an impaired identification pattern in less-filtered images and a worse performance in total accuracy in comparison to controls; children with ICOE obtained better results than those with PCE.

Patients with ICOE with no or negligible EEG abnormalities obtained higher scores in the object identification task and in some visual processing and visual spatial integration tasks in comparison to patients with higher abnormalities frequency.

Conclusion: An impaired identification pattern in less-filtered images is present in patients with both PCE and ICOE, suggesting that functional disruption caused by EEG abnormalities can interfere with object identification processing, though to a lesser degree with respect to structural occipital lesions.

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DEPRESSION AND ANXIETY IN PATIENTS WITH EPILEPSY

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Purpose: The aim of the study was to investigate prevalence of depression and anxiety in patients with epilepsy and also to compare those whose epilepsy is well-controlled with refractory ones.

Method: A group of 60 patients with epilepsy were analyzed, 23 of them (average age 44.15 ± 8.73) suffering from refractory and 37 patients (average age 37.22 ± 12.01 years) suffering from well-controlled epilepsy. For detection of these emotional disorders we used scales of depression, generalized anxiety and somatized anxiety from Crown-Crisp Experience Index.

Results: In our study 60 patients with epilepsy out of 35 (58%) suffered from depression, 31 (51%) from generalized anxiety and 37 (62%) from somatized anxiety In the group with well-controlled epilepsy depression was found in 44%, generalized anxiety in 32% and somatized anxiety in 48% of patients. Among the patients with refratocry epilepsy depression was found among 75%, generalized anxiety in 75% and somatized anxiety in 80%. Prevalence of depression and anxiety in patients with epilepsy was greater than in the general population. Also in each group of patients these emotional disorders showed higher intensity in comparison with healthy population. Intensity of disorders is much more in the group with refractory epilepsy, with statistically significant ($p < 0.01$) on scales of depression and somatized anxiety.

Conclusion: Depression and anxiety have significant impact on the quality of life of patients with epilepsy and need to be treated with the same scientific rigor as antiepileptic treatment in the control of seizures.

p209
FACIAL EMOTION RECOGNITION IN CHILDREN WITH HISTORY OF FEBRILE SEIZURES

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Background: Chronic drug-resistant medial temporal lobe epilepsy is associated with impairment in facial expressions recognition (FER) [Meletti et al. 2003; 2009]. An important question is whether a critical period of life exists for establishing the neural network underlying FER ability.

Purpose: Medial temporal lobe epilepsy is associated with antecedent of febrile seizures (FS). We therefore investigate FER in a group of school-aged children with antecedent of FS. We considered FS as a potential marker of early brain damage.

Method: 37 children with at least one episode of FS without subsequent epilepsy (aged 6–10 years) were evaluated. A group of 51 children attending primary school served as controls. Children's IQ was evaluated by means of Raven's progressive matrices test. A simple face-matching test (T1) was used to control for subjects' basic visuoperceptual ability with facial stimuli. FER was assessed using an ad hoc test with Ekman & Friesen's pictures of facial affect.

Results: In FS group subjects with IQ below 50° p (n = 5) or with errors in T1 (n = 6) were excluded from further analysis. The FS group showed a lower recognition score across all emotions (71.1%) respect to controls (82%; $p < 0.001$). Moreover, FS group resulted impaired relative to controls in the recognition of ear (71.7% vs. 87.5%; $p < 0.001$), disgust (75.5% vs. 89.2%; $p < 0.001$), and sadness (66.6% vs. 79.4%; $p = 0.005$).

Conclusion: This study evaluates for the first time FER in children with antecedent of FS. Our results demonstrate that these children are impaired in recognition of facial expression of fear, disgust and sadness, suggesting an early dysfunction of medial-temporal structures.

p210
AUTOBIOGRAPHICAL MEMORY DEFICITS IN PATIENTS WITH UNILATERAL TLE

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Purpose: The impact of temporal lobe networks for consolidation and recall of remote autobiographical memories and its emotional valence is under debate.

Method: We used a modified version of the Autobiographical Memory Interview (AMI, Kopelman, Wilson & Baddeley, 1990) which allows the assessment of episodic and personal semantic memory of different time periods of the past. We studied 31 patients with mesial unilateral TLE (14 left, 15 right) and 12 patients with lateral TLE (4 left, 8 right). 38 healthy control subjects were recruited to match the patients in terms of age, sex and education.

Results: Episodic ($p < 0.001$) and personal semantic ($p < 0.01$) memory performance in TLE patients was significantly below the performance of controls. For episodic memory, these deficits were extended to early childhood ($p < 0.019$). Patients with left neocortical TLE demonstrated most severe deficits ($p = 0.038$). In contrast to episodic memory, personal semantic memory correlated significantly with anterograde memory in left TLE ($r = 0.54$). Considering the emotional valence of episodic memories, patients recalled more neutral memories and scored their memories as less emotional intense, independently of focus lateralization and localization. Furthermore the left TLE-group recalled less positive memories with high intensity.

Conclusion: Both hippocampal and neocortical pathology affect autobiographical memory and its emotional valence. Aggravated impairment is caused by lesions in the left temporal neocortex, which might serve an important role in the storage of remote episodic memories. Episodic memory seems to be independent of anterograde memory functions, deficits are due to impairment of long-term-consolidation or storage.

p211
IS EPILEPSY AFFECTING THE COGNITIVE FUNCTIONS IN CHILDREN WITH CEREBRAL PALSY AND NORMAL INTELLIGENCE?

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Purpose: As previously shown, there was no characteristic neuropsychological profile in patients with epilepsy. However, some cognitive functions, mainly memory and attention, are often impaired, especially in patients with underlying brain lesions.

Method: A cohort of 63 children with cerebral palsy (CP) and normal intelligence was investigated for cognitive functioning. We compared two samples of CP patients: 1) children with CP and epilepsy (Group I, N = 33; age range 6.9–17.7, mean age 12.6; 20 male, 13 female) and 2) patients with CP without epilepsy (Group II, N = 30; age range 6.4–17.1, mean age 12.1; 15 male, 15 female). All subjects reached IQ > 85, measured by age-appropriate Wechler's Intelligence scales. Large battery of neuropsychological tests was applied, investigating: attention, verbal and visual memory, language functions, praxia, gnosis, thinking processes and executive frontal lobe functions.

Results: Three degrees of patient's cognitive functioning were found: 1) no cognitive impairment; 2) moderate neuropsychological impairment, with underachievement in one to four cognitive functions and 3) severe impairment, if more than 4 of investigated functions were underscored. Average degree of cognitive impairment was moderate and similar in both groups, without statistically significant differences (Group I 2.91 ± 1.16; Group II 2.53 ± 1.20; $p < 0.05$), but severe impairment was more often found in children with CP and epilepsy (Group I 15 of 33; Group II 10 of 30 patients).

Conclusion: Various cognitive dysfunctions are frequent in most of patients with cerebral palsy, regardless of the presence of epilepsy. Individual approach in their neuropsychological assessment is therefore strongly recommended.

p212
SPATIAL NAVIGATION IN TEMPORAL LOBE EPILEPSY PATIENTS

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Introduction: Spatial navigation may be impaired in patients with temporal lobe dysfunction. The aim of the study was to compare spatial navigation in patients with temporal lobe epilepsy (TLE) and controls in a set of visuospatial subtests.

Material and methods: The procedure of Hidden Goal Task, an analogue of Morris Water Maze, was used to test the spatial navigation. The subjects were instructed to locate an invisible goal in four different subtests using both virtual version (computer) and real-space setting (enclosed cylindrical arena; 2.9 m in diameter). The subjects were asked to remember the location of the goal by its relationship to the starting position (egocentric navigation) or to the distal landmarks (allocentric navigation).

We included 20 left-speech dominant, pharmacoresistant TLE patients; 10 left-sided (mean age 31 years, FSIQ 97, VIQ 97, PIQ 98), 10 right-sided (35 years, FSIQ 99, VIQ 100, PIQ 94). Control group consisted of five subjects (27 years, FSIQ 117, VIQ 119, PIQ 98). Patients and controls did not statistically differ in IQ levels.

Results: Patients scored worse than controls in allocentric subtests. Left-sided and right-sided patients did not differ in any spatial navigation subtest. FSIQ correlated with allocentric navigation outputs. Scores of egocentric navigation subtest correlated with PIQ.

Conclusions: Selective spatial navigation impairment limited to allocentric cueing was found in our group of TLE patients. These results support the localization of allocentric navigation in temporal region. Egocentric navigation was not significantly impaired.

Poster session: Acute symptomatic seizures
Monday 28th June 2010
13:30–14:30

p213
EARLY SEIZURES IN PATIENTS WITH SPONTANEOUS INTRACRANIAL HEMORRHAGE: INCIDENCE, ASSOCIATED FACTORS AND INFLUENCE ON OUTCOME

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Purpose: In patients with a spontaneous intracerebral hemorrhage (ICH), the occurrence of early seizures (ES) may be a prognostic marker. Our aim was to identify incidence, associated factors and influence on outcome of ES in ICH patients.

Method: From 11/04 until 03/09, we prospectively recruited 595 consecutive adults with a spontaneous ICH (PITCH cohort). Patients with previous seizures were excluded. ES were defined as seizures occurring within 7 days of stroke onset. Associated factors were identified with Cox regression. For the subgroup of onset seizures, we used logistic regression. Data influencing outcome (mortality at Day-7 and Month-6; functional outcome at Month-6) were studied using survival analyses.

Results: ES occurred in 78 (14%; 95 CI 11–17) of 553 patients (285 male; median age 71 years, IQR 57–79). The only factor associated with ES was cortical extension of ICH (OR = 2.09; 95 CI 1.33–3.29). Regarding onset seizures (n = 41), associated factors were: previous ICH (OR = 3.81; 95 CI 1.27–11.48), cortical extension (OR = 1.95; 95 CI 1.01–3.78), a younger age (OR = 0.98 per 1 year increase; 95 CI 0.96–0.99) and initial severity of the neurological deficit (OR = 1.03 per 1 point increase of the NIHSS; 95 CI 1.01–1.06). ES did not influence vital nor functional outcome.

Conclusion: ES are frequent in patients with spontaneous ICH and mostly occur within the first 24 h. Interestingly, the occurrence of ES did not alter the short-term prognosis.

p214
THE RISK OF SEIZURES AFTER MINOR BRAIN INJURY

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Purpose: The frequency of traumatic brain injury (TBI) in the US is 1.8–2.5 per 1000 person per year and higher in Europe.

The risk of seizure is increased after brain injury, and depends on the severity of trauma and duration of follow up period. In civilian population, the overall risk has been estimated at 2–5%. It is known that the incidence of seizures is significantly lower in mild brain injuries.

We conducted a prospective study in order to examine the incidence of post traumatic seizures in patients with a very minor brain, or spinal whiplash injury within the first year from the trauma.

Patients and methods: The study population included patients from the E. Wolfson medical center emergency room with a minor head trauma or whiplash injury. The medical information was obtained from the records within the first 24 h of arrival in the ER.

A year later, the patients were interviewed by phone call in order to determine the incidence of seizure during this year.

Results: Out of 2000 patients included in the study we contact 1630 patients of whom 1 patient developed seizures and 1 patient suffered from an event of loss of consciousness but was not diagnosed as having seizures.

Conclusion: The incidence rate of seizures during the first year post very mild head trauma was 0.06% respect to the expected rate which is 0.07% (according to the CDC data). In this subgroup of seizures post trauma 'no significant difference was found.

p215
ETIOLOGIC FACTORS IN PATIENT WITH EPILEPSY IN THE DEPARTMENT OF NEUROLOGY IN PRISTINA, KOSOVO

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Purpose: The aim of the study is to determinate factors as a cause of epilepsy, and compares their participation.

Method: In this study are included patients with confirmed epilepsy that where treated in the Clinic of Neurology between the year 2000–2005. Study was based on the data generated from the clinical histories of patients, and diagnostic methods such as EEG, CT, MMR. Data were analyzed using statistical parameters: structure, prevalence, mean and standard deviation. Values of the results were tested with: t-test and chi-square test.

Results: During investigation were covered 15,933 patients, 10.80% of them were diagnosed as epilepsy. At 1108 cases it is confirmed the cause of epilepsy and at 617 (35.77%) the cause was idiopathic. The most common findings were: posttraumatic atrophy (22.00%), postvascular sequel (12.80%), postobstetric trauma (11.3%), and brain tumor (6.8%).

Conclusion: Epilepsy as a disease is very common but not always is as a result of an underlying brain disease. The use of newer imagine methods are the first choice in the detecting of the morphologic changes that cause epilepsy.

p216
ANALYSIS OF THE INITIAL ICTAL PHENOMENON IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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Purpose: We aimed to analyze the initial semiological elements in temporal lobe epilepsy (TLE) and to assess their localizing value.

Methods: Video-EEG-documented seizures of 97 adult TLE patients were studied in relation to seizure origin (left versus right; mesial versus extramesial).

Results: In general, seizures with mesial onset started with very few ictal phenomena, while extramesially originating seizures began with a larger variety of ictal elements. Noticeable distributions were observed for the following phenomena: 1) In the total collective, aura was the most common initial ictal phenomenon, occurring significantly more frequently in mesial than in extramesial seizure origin. 2) Restlessness represented the most common first ictal element occurring directly after aura in all subgroups, with a preference for extramesial right seizure origin. In patients without aura, restlessness as initial ictal phenomenon appeared exclusively in seizures of extramesial right origin. 3) Behavioral arrest was only rarely found as initial ictal element in the total collective; focussing on the first seizure element occurring directly after aura, there was a trend toward left-sided seizure origin. 4) Vocalization presented exclusively as first seizure element occurring directly after aura, with a trend toward mesial left seizure origin. 5) Oral automatisms occurred only rarely as first ictal element in the total collective. Focussing on the first seizure element occurring directly after aura, we found a trend towards mesial seizure origin.

Conclusion: In conclusion, the initial ictal phenomenon may add useful information concerning differentiation of seizure onset in TLE.

p217
POSTSTROKE SEIZURES: PROSPECTIVE STUDY FROM A TERTIARY REFERRAL CENTRE IN NORTH INDIA

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Background: Stroke is the most common cause of seizures in elderly. There is only one study reported till date from India on this, despite both Stroke and Epilepsy being major diseases in the country.

Objective: We conducted a prospective study to determine the incidence, outcome and risk factors for seizures after stroke.

Methods and results: The study followed 1238 patients with acute stroke for an average duration of 12 months [(86%) of patients]. Seizures occurred in 10.2% of patients (8%, ischemic; 12%, hemorrhagic); epilepsy occurred in 3% of patients (2% with ischemic; 3.5% of hemorrhagic strokes). Mean age of patients developing post stroke seizures was 56.41 ± 14.43 years. Seizures occurred in 34.8% of ischemic and 66.4% of hemorrhagic strokes, with in 24 h. Hemorrhagic stroke (3.2-fold enhanced risk on multivariate analysis), cortical location and Glasgow Coma Scale (GCS) at time of admission were significantly correlated with occurrence of seizures. Additional risk factors on univariate analysis were presence of hyperglycemia, institution of quinolone antibiotics for infections during early phase of stroke and venous strokes. Compliance of antiepileptic drugs (AEDs) was poor in the economically deprived patients leading to additional disability of poorly controlled post stroke epilepsy.

Conclusions: The study confirmed earlier reported literature on incidence of and risk factors for poststroke seizures from a developing country. Study also suggests that stroke is an important cause of seizures in both young adults and the elderly since prevalence of stroke in young is significantly high in India.

p218
HYPERFAMILIARITY FOR UNKNOWN FACES: A RARE POSTICTAL SYMPTOM OF ACUTE SYMPTOMATIC FOCAL SEIZURES

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Purpose: Hyperfamiliarity for unknown faces represents a rare clinical phenomenon observed in left temporo-occipital lesions, likely to result from an imbalance between reciprocal hemispheric functions in face recognition.

Method: Three young adults (aged between 25 and 35 years) were admitted for acute symptomatic secondarily generalized tonic–clonic seizures (2) and psychomotor status (1). The patients underwent full clinical, EEG, MRI study.

Results: During the days following the seizures the patients had no difficulty recognizing known people but spontaneously claimed about experiencing strong familiarity for unknown people, including other patients, visitors and hospital staff. They often asked the unknown person (s) where they had met before and did not believe that their feelings where incorrect. The phenomenon was almost continuous during the first days and then gradually decreased (lasting for a mean period of 10 days). Brain MRI showed left amygdalo-hippocampal lesions suggesting the etiology of encephalitis in 2 patients and multiple demyelinating plaques with contrast enhancement in 1 patient. The interictal EEGs showed slow and paroxysmal abnormalities over the left temporal region in the two patients with encephalitis and independent epileptiform abnormalities over the right and, to a lesser extent, left temporal regions in the patient with multiple demyelinating lesions. A neuropsychological study performed during the phase of hyperfamiliarity in one patient with a left temporal lesion showed a marked defect of verbal memory.

Conclusion: Hyperfamiliarity for unknown faces may occur as a postictal phenomenon after focal seizures and may suggest the existence of an acute epileptogenic lesion in the temporal lobe.

p219
AN OBSERVATIONAL STUDY ON THE INCIDENCE OF EARLY-ONSET POSTSTROKE EPILEPTIC SEIZURES

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Purpose: To evaluate the incidence of early-onset (≤14 days) PSES and potential predictors of PSES in an hospital-based study.

Method: A retrospective search of all cases of stroke diagnosed in ''Ospedali Riuniti'' of Foggia (Italy) during 2002–2005 was performed using the Hospital Discharge Diagnosis Data Bank. Patients with a prior history of seizures/epilepsy were excluded. Univariate analyses employed t-test or chi-square. Logistic regression analyses were used to study the association between PSES and clinical indicators.

Results: 1784 strokes were identified. 105 (5.9%) cases developed PSES. 37.1% of cases developed heraldic seizures. Acute seizures (within the first 24 h from the onset of stroke) were observed in 23 cases (22%), while PSES occurred after the 24 h and within 1 week in 66 cases (63%). Patients with PSES had a more severe clinical feature [coma at onset: 43/105 vs. 323/1679; $p < 0.0001$], a more frequent history of previous stroke [27/105 vs. 231/1679; $p = 0.001$]. Mortality at 15 days was higher in patients with PSES (26/105 vs. 201/1679; $p < 0.0003$). Coma at onset (OR:2.1; 95%CI:1.3–5.6; $p = 0.003$), cortical site of the stroke, isolated (OR:3.7; 95%CI:1.9–7.3; $p = 0.0002$) and associated with deep brain lesion (OR:5.8; 95%CI:2.9–11.5; $p < 0.0001$), hemorragic stroke (OR:1.8; 95%CI:1.1–3.2; $p = 0.03$) were independent predictors of PSES.

Conclusion: The incidence of early-onset PSES was similar to previous studies. In our results, the highest occurrence of PSES in the first week confirms the relevant role played by metabolic changes occurring after stroke, in determining PSES.

p220
GENERALIZED SEIZURE: A RARE AND IMMEDIATE PRESENTATION OF CARDIAC MYXOMA CEREBRAL COMPLICATION

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Purpose: Neurological complication can be the initial manifestation of cardiac myxoma. To characterize and discuss an unusual type of cardiac myxoma complication: generalized tonic–clonic seizure as a first manifestation.

Method: We reviewed the clinical findings and laboratory data of 8 patient hospitalized for cardiac myxoma complication in our service during past 5 years

Results: Brain ischemic infarct was the common complication of cardiac myxoma (8 cases). No patient had concomitant cardiac symptoms. 2 cases presented with early focal seizure and hemiparesis, 4 cases with focal neurological signs and 2 cases with immediate generalized tonic–clonic seizure as initial manifestation of similar brain infarct. We describe the case of seventeen young girl who had a history of 10 min TIA (aphasia) 2 month before a generalized tonic–clonic seizure followed by right hemiparesis and aphasia. Cerebral MRI revealed an ischemic infarct and echocardiography detected a large intracardiac tumor. Cardiac surgery, anticonvulsivant drugs emerge in a good outcome.

Conclusion: Seizures are associated with cardiac myxoma in some cases and they are caused usually by cerebral infarction in young adults. Rarely the seizure is provoked by cerebral myxomatous emboli. Given that most poststroke seizure is caused by focal lesion, they are typically focal at onset. The immediate occurrence of generalized seizure is probably caused by the addition to focal ischemia of a concomitant global hypoperfusion of cardiac origin which can cause seizure activity, especially in hippocampus. Despite the lack of neuroimagistic testing we can not exclude small myxomatous subcortical emboli.

p221
C-REACTIVE PROTEIN AND SEIZURE IN PATIENTS WITH FOCAL EPILEPSY: A VIDEO-EEG STUDY

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Purpose: To examine C-reactive protein (CRP) level in patients with refractory focal epilepsy undergoing a video-EEG compared to healthy controls and CRP change during 24 h after a seizure.

Method: CRP levels were measured in serum at the onset of video-EEG recording (CRP-0h) and at 3 h, 6 h, 12 h, and 24 h after index seizures (IS: First verified localized-onset seizure) in 31 patients during video-EEG monitoring by using high sensitivity measurement of CRP concentration. The patients were categorized into two groups: temporal lobe epilepsy (TLE) (n = 15), and extratemporal lobe epilepsy (XLE) (n = 16). Eighty healthy volunteers served as controls.

Results: Index seizure type was associated with CRP rise from baseline to maximum level after IS ($p = 0.005$). The most significant predictors of significant increase in CRP level were secondarily generalized tonic–clonic seizure (SGTCS; $p = 0.030$) and male sex ($p = 0.047$). After IS, CRP level decreased in 3 h and increased after 12 h [significant quadratic U-shaped trend in all patients, especially in men, TLE syndrome, epilepsy duration <20 years, seizure frequency <15/month, left lateralization, and IS duration ≥1 min]. CRP-0h level was significantly higher in

refractory focal epilepsy patients than in controls [sex- and age-adjusted geometric mean ratio: 10.1, 95%CI: 6.0–17.0]. Older patients and those on monotherapy had significantly higher mean CRP level both in baseline and other measurements ($p < 0.05$).

Conclusion: Higher CRP levels in epileptic patients than in healthy controls and significant change in CRP after seizure (especially SGTCS) emphasize the association between inflammation and epilepsy.

p222
TAKOTSUBO CARDIOMYOPATHY INDUCED BY EPILEPTIC SEIZURES: A CASE REPORT

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Purpose: Takotsubo syndrome or apical ballooning syndrome is an acute dysfunction of the left ventricle apex related to stressful events (general anesthesia, pheochromocytoma, subarachnoid hemorrhage, shock, emotional stress). The coronary angiography is negative, the electrocardiogram suggestive of myocardial infarction, constant increase of cardiac enzymes. The prognosis is good, no need prophylactic therapy. Rarely described his association with seizures.

Method: Description of clinical case.

Results: We describe the case of a male patient 73 years old, who reported, following a domestic incident, a severe head injury (acute left subdural hematoma, surgically evacuated). In ambulance, episode of ventricular fibrillation with cardiac arrest, with rapid recovery after defibrillation. Encountered in the emergency room increased cardiac enzymes and ECG abnormalities consistent with anterior myocardial infarction, but coronary angiography and echocardiography negative. After 6 months of the trauma, appearance of attacks compatible with complex partial seizures of right temporomesial onset; incomplete control with carbamazepine. During a further seizure he perceives and reports chest pain. In emergency department: ST elevation in anterior leads, and moderate increase in cardiac enzymes. A myocardial infarct was suspected, but coronary angiography and echocardiography were negative. The two events are therefore compatible with cardiac apical ballooning syndrome, the second induced by epileptic seizure.

Conclusion: The takotsubo syndrome, rare cardiac complications of seizures, may be a mechanism underlying some cases of sudden unexpected death in epilepsy (SUDEP).

p223
NEW-ONSET SEIZURES IN KIDNEY TRANSPLANT PATIENT: A CASE REPORT AND LITERATURE REVIEW

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Introduction: Among the most common reasons for kidney transplantation are glomerulonephritis, diabetes, and hypertensive renal disease. According to previous reports, seizures developed as a neurological complication in about 5% of adult kidney recipients.

Case presentation: We report a 55-old female kidney transplant recipient who was admitted to our hospital with severe arterial hypertension and headache. Over the next 1 week she presented with new-onset generalized seizures. Laboratory results showed uremia, anemia, and metabolic acidosis. Blood levels of immunosuppressive agent were in theurapeutic ranges. Kidney transplantant ultrasound was suggestive for infarction of the lower pole. Brain computed tomography demonstrated multiple intracranial calcifications and undefined hypodence region in left cerebral hemisphere. EEG changes corresponded to encephalopathy. Medical history revealed onset of nephrotic syndrome with renal failure 12 years ago. Kidney biopsy confirmed the diagnosis of membranous glomerulonephritis. The patient underwent a cadaver renal transplant in 1997 followed by long-term immunosuppressive and glucocorticoid therapy.

Conclusion: Based on our own findings and literature review, we suggest that metabolic and hypertensive encephalopathy as well as cerebral structural lesion and immunosuppressive agent toxicity may play crucial role as possible mechanisms of epileptogenesis in kidney transplant patients.

p224
SEIZURES AFTER DOXYLAMINE SUCCINATE OVERDOSE

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Purpose: Doxylamine succinate is an over-the-counter drug commonly used in the treatment of insomnia. It is in the ethanolamine class of antihistamine and is frequently involved in accidental and intentional overdoses. Seizures are rare but there are potentially serious complications, making early recognition and treatment essential.

Method: We reviewed the medical records of patients admitted for seizures after a doxylamine succinate overdose. We evaluated them with clinical characters and prognosis.

Results: Among the 146 doxylamine overdose patients, 11 patients developed seizures. Females accounted for 9 (81.8%) patients and the number aged between 20 and 40 years was also 9 cases (81.8%). All patients had taken doxylamine succinate with suicidal intent. The average time from ingestion to emergency room visit was 170 min (60–360). The average time from ingestion to development of seizures was 188 min (60–480). The amount of doxylamine succinate ingested was 750–4750 mg (mean = 2425 mg). Impaired consciousness was the most common symptom. The frequent anticholinergic symptoms combined with seizure patients were tachycardia (63.6%), vomiting (45.5%), mydriasis (36.4%), and hypertension (36.4%). Rhabdomyolysis and drug induced hepatitis were observed in 7 cases (63.6%) and 6 cases (54.5%), respectively. Primary treatment included administration of benzodiazepine and conservative care. After more than a 6 month follow-up, no patients developed further seizure.

Conclusion: The incidence of seizure after doxylamine succinate overdose is rare and prognosis is good. However, other serious symptoms are commonly combined, and we have to be aware that seizures are a potential complication and should be actively investigated and vigorously treated.

p225
THE INFLUENCE OF BIOMETEOROLOGICAL CHANGES ON TONIC–CLONIC SEIZURES FREQUENCY IN EPILEPSY IN BIELSKO- BIALA, SOUTH POLAND

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Aim: The influence of foehn wind and increase of air temperature on tonic–clonic seizures in epilepsy in the city of Bielsko-Biala, South Poland.

Material and Methods: The study includes 36 patients (18 women, mean age 54 ± 0.3 ranged from 18 to 88 years) from Bielsko-Biala. There were 1361 tonic–clonic epileptic seizures diagnosed with use of clinical examination, EEG, CT or MRI. The therapy was based on Neurotop Retard, Depakine chrono and Convulex. Patients were observed prospectively from 2006 to 2009 within 1361 days. There were 242 days

with foehn wind and 362 days with increase of air temperature of 5 or more Celsius degrees. Index of meteorotropism (de Ruder) JM and test chi-square were used to find statistical correlations.

Results: There was statistically significant increase of the epileptic seizures observed in the days with foehn wind and during the day before. This founding was strongly observed in woman patients within cold months. There was no correlation between the air temperature increase and the number of epileptic incidents.

Conclusion: Our results suggest that fohn wind in Bielsko-Biala causes a specific meterotropic situation for epilepsy occurrence.

Poster session: Drug therapy I
Monday 28th June 2010
13:30–14:30

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CLINICAL RELEVANCE OF GENETIC POLYMORPHISM OF THE CYP2C SUBFAMILY AND ITS EFFECT ON THE PHARMACOKINETICS IN CHILDREN WITH EPILEPSY

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Purpose: To evaluate prevalence of CYP2C9 and CYP2C19 genotype/phenotype in children with epilepsy and compare it with response to AED. Poor control of epilepsy is expected if CYP2C9 and CYP2C19 are damaged when receiving CYP inducers.

Method: CYP2C9 and CYP2C19 alleles (*1,*2 or *3) were done in Croatian children with epilepsy (N = 137): A (N = 48) received AED inducers of CYP metabolism (CBZ, PH); B (N = 52) received AEDs non-inducers (VPA, LTG, TPM, GBP, CLB, ESM, CZP, LEV); C (N = 37) genotyped before AED treatment.

Results: There were 64 girls and 73 boys, average 6.31 years. Genotyping of CYP2C9 revealed: 90 extensive metabolizers (EM) – *1/*1 and 6 poor metabolizers (PM) – *2/*2 (N = 1), *2/*3 (N = 2) and *3/*3 (N = 3). There were 41 heterozygous patients for CYP2C9 intermediate metabolism (IM) – *1/*2 (N = 27) and *1/*3 (N = 14). Genotyping of CYP2C19 revealed: 110 EM *1/*1, 24 heterozygous patients (IM) for *1/*2, and 3 PM – *2/*2. 16 patients in group A were substituted by non-inducing AEDs. In 24 patients in group B, VPA was substituted with LTG/TPM because of poor seizure control. Among patients in group C genotyping guided a first-choice AED with poor control in only 4 patients (10.8%) compared with 25 patients (25%) treated prior to genotyping. Extensive and/or intermediate metabolism is related to better control of epilepsy, receiving CYP inducers with damaged CYP2C9 and CYP2C19 poor control of epilepsy is expected.

Conclusion: In aiming for better treatment of epilepsy in children it is important to pay more attention to CYP2C9 and CYP2C19 genotype.

p227
PHARMACOKINETIC EVALUATION OF ORAL LACOSAMIDE IN PHASE II/III CLINICAL TRIALS: A POOLED ANALYSIS

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Purpose: Antiepileptic drug plasma concentrations are sometimes measured during routine medication management. This analysis estimates peak (C_{max}) and trough (C_{min}) plasma concentrations of the new antiepileptic drug lacosamide.

Method: Lacosamide C_{max} (1 h postdose) C_{min} (12 h postdose), and area under the plasma concentration time curve over a dosing interval at steady-state ($AUC_{tau,ss}$) were estimated using standard pharmacokinetic equations. Patient plasma samples were obtained in 3 similarly conducted Phase II and III clinical trials. Lacosamide dosing ranged from 100 mg/day to 600 mg/day (50–300 mg bid) based on trial and randomization group. All samples obtained during titration and maintenance phases were used. An elimination rate constant (k_e) of 0.05/h (corresponding to a 13–14 h half-life) was assumed based on Phase 1 and population PK evaluations. Total body clearance (CL/f) was calculated by dose/AUC for each patient.

Results: A total of 3552 plasma samples from 852 patients were available for analysis. Lacosamide C_{max}, C_{min} and $AUC_{tau,ss}$, showed dose proportional increase over the range of 100–600 mg/day (50–300 mg bid). For example, for lacosamide 200 (n = 641), 400 (n = 497) and 600 mg/day (n = 144): C_{max} (μg/ml) = 3.88 ± 1.82, 8.76 ± 3.31, 12.33 ± 4.69; C_{min} (μg/ml) = 2.48 ± 1.00, 5.28 ± 1.92, 7.41 ± 2.78; and $AUC_{tau,ss}$ (μg/ml*h) = 36.56 ± 17.18, 82.61 ± 31.19, 116.26 ± 44.21. Total body clearance was similar across doses: Cl/f (L/h) = 4.04 ± 8.57, 3.15 ± 5.96, and 3.37 ± 4.12 for lacosamide 200, 400, and 600 mg/day, respectively, consistent with first-order elimination kinetics.

Conclusion: Based on estimates from Phase II/III clinical trial data, lacosamide showed dose-proportional increases in C_{max}, C_{min} and $AUC_{tau,ss}$. Total body clearance was stable over the dose range evaluated.

p228
LACOSAMIDE SALIVA AND SERUM CONCENTRATIONS IN PATIENTS WITH EPILEPSY

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Purpose: Lacosamide (LCM) is a new third generation antiepileptic drug which has a novel mechanism of action, favorable linear pharmacokinetics and proven efficacy in the adjunctive treatment of partial onset seizures. The aim of this investigation was to ascertain the relationship between serum and saliva LCM concentrations so as to determine whether saliva may be a useful alternative to serum for therapeutic drug monitoring.

Method: Blood samples were collected from 101 patients with intractable epilepsy (51 male, 50 female; mean age 41 ± 13; range 19–76 years) prescribed LCM as adjunctive therapy. For 51 patients concurrent saliva samples were also collected. LCM concentrations in serum (free and total) and in saliva were determined by high performance liquid chromatography.

Results: Linear regression analysis showed a good correlation between LCM dose and both total (r^2 = 0.809; n = 33) and free (r^2 = 0.815; n = 29) serum concentrations and LCM serum total and free concentrations were linearly related (r^2 = 0.7353; n = 101). Additionally there is a good correlation between LCM saliva and both total (r^2 = 0.852; n = 51) and free (r^2 = 0.847; n = 51) serum LCM concentrations. Based on the saliva data the protein binding of LCM in serum is calculated to be 87 ± 4% and is comparable to the value calculated by direct measurement of the free and total LCM concentration in serum (91 ± 4%).

Conclusion: These data support the use of saliva as a viable alternative to serum for monitoring LCM therapy in patients with epilepsy.

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PLASMA LAMOTRIGINE LEVELS OF PATIENTS WITH POLYMORPHIC UGT1A4 ENZYMES

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Purpose: The group of polymorphic enzymes could play an important role in minimizing the adverse effects or maximizing the effectiveness of drugs by changing their plasma levels. Lamotrigine is metabolized by UDP-glucuronosyl transferase (UGT) 1A4, an enzyme present in hepatic microsomal fractions. In our study, single nucleotide polymorphisms, L48V and P24T, of the UGT1A4 enzyme have been investigated in a Turkish population that included epilepsy patients with lamotrigine monotherapy in order to detect the effect of the polymorphic enzymes on plasma concentrations of lamotrigine.

Method: High performance liquid chromatography was used for the measurements of the lamotrigine levels and the analyses of the UGT1A4*2 and UGT1A4*3 alleles for detection of P24T and L48V polymorphisms, were performed with a matrix assisted laser desorption-time of flight mass spectrometry method.

Results: The frequency of the UGT1A4*3 allele was 31.4% heterozygote only while none of the patients were positive for the P24T polymorphism. The lamotrigine levels of the monotherapy patients were found to be 29.4% percent lower for the L48V polymorphism. Also plasma lamotrigine levels were significantly lower for nonsmoking or smoking polymorphic alleles than for normal.

Conclusion: In conclusion the high frequency of the L48V polymorphism indicates that lamotrigine dose adjustments in patients with the L48V polymorphism should be carefully recorded and the L48V polymorphism can be checked, particularly when the drug is ineffective..

p230
EVALUATION OF LACOSAMIDE EFFICACY AND SAFETY AS ADJUNCTIVE THERAPY IN PATIENTS RECEIVING TRADITIONAL SODIUM CHANNEL BLOCKING AEDS

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Purpose: In vitro electrophysiological studies show that the new antiepileptic drug (AED) lacosamide selectively enhances slow inactivation of voltage-gated sodium channels. Analyses of pooled phase II/III data demonstrated that lacosamide provides additional efficacy regardless of concomitant AED. To further evaluate specific AED combinations, a post hoc exploratory analysis was performed including patients taking traditional sodium channel-blocking AEDs as part of their treatment regimen.

Method: Data were analyzed from pooled Phase II/III placebo-controlled trials evaluating adjunctive lacosamide in patients with partial-onset seizures. Patients treated with at least one traditional sodium channel blocking AED (lamotrigine, oxcarbazepine, carbamazepine or phenytoin) were included; patients could also be taking other concomitant AEDs. Efficacy measures included change in seizure frequency and 50% responder rates. Safety variables included incidence of treatment-emergent adverse events (TEAEs) and withdrawal due to TEAEs.

Results: Of 1308 patients in the overall safety population, 82% were using at least one traditional sodium channel-blocking AED. Median percent reduction in seizure frequency per 28 days was significant for all lacosamide dose groups (200, 400 and 600 mg/day) compared to placebo (33.3%, 39.0%, 42.7% vs. 18.9%; $p < 0.01$). Similarly, 50% responder rates were significantly higher in the lacosamide 400 and 600 mg/day dose groups compared to placebo [33.3% ($p = 0.06$), 39.9% ($p < 0.01$), and 42.4% ($p < 0.01$) vs. 22.7%]. The most common TEAEs (≥10%) were dizziness, headache, nausea, diplopia and vomiting.

Conclusion: Adjunctive treatment with lacosamide confers additional therapeutic benefits to patients treated with traditional sodium channel-blocking AEDs, consistent with a previous analysis showing lacosamide is effective regardless of concomitant AED used.

p231
RAPID TITRATION OF LACOSAMIDE WITH SIMULTANEOUS REDUCTION IN CONCOMITANT AEDs IS WELL TOLERATED AND EFFECTIVE IN REDUCING SEIZURES IN PATIENTS WITH DRUG-RESISTANT PARTIAL-ONSET EPILEPSY

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Purpose: Pivotal trials performed for regulatory approval typically use fixed doses of study drugs and concomitant AEDs and do not evaluate possible benefits of medication conversions. We evaluated whether rapid programmed titration of lacosamide to 400–700 mg/day with rapid tapering of concomitant antiepilepsy drugs (AEDs) limits side effects and reduces seizures in patients with drug-resistant partial-onset epilepsy.

Method: We evaluated patients exiting an intravenous lacosamide loading trial and patients taking oral lacosamide. Three-month baseline, 4–5 week titration and 3-month maintenance periods were evaluated for seizure frequency and occurrence of common CNS-related side effects Lacosamide was increased weekly by 100 mg to 400–500 mg/day while concomitant AEDs were tapered. Patients with persisting seizures had additional dose increases. Doses were tabulated and compared to seizure and side effect outcome for each of the three study periods.

Results: Twenty-six patients had a baseline median of 4.3 seizures/month, despite treatment with an average of 2.1 AEDs. Mean lacosamide dose was 562 mg/day. Concomitant AED doses were reduced by an average of 75% (22/26 patients had sodium-channel drugs decreased). Mild, non–dose limiting transient CNS side effects occurred in 42% during lacosamide titration, however, only 4% had symptoms during maintenance treatment. Average seizure frequency decreased 58% with a 50% responder rate of 61.5%, including 4 seizure-free patients in the 3-month maintenance period.

Conclusion: This study demonstrates that weekly lacosamide increases to 400–500 mg/day followed by individual increases up to 700 mg/day with simultaneous reduction of concomitant sodium channel drugs is feasible and well tolerated in patients with drug-resistant partial-onset epilepsy.

p232
LONG-TERM PROGNOSIS IN PATIENTS WITH EPILEPSY

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Purpose: The National General Practice Study of Epilepsy (NGPSE) was set up in 1984 and is one of the longest established community-based studies of epilepsy in existence. Its aims are to follow-up a large incident cohort of people with newly suspected or diagnosed epileptic seizures in

the community, as most studies have been performed in hospital cohorts, which may give a biased view of prognosis.

Method: A total of 1092 people including 792 patients with definite or probable epilepsy and 220 with febrile seizures who were notified to the study by their General Practitioners (GPs) have been followed. Questionnaires have been sent to the GPs to ascertain the seizure outcome of each person with definite or probable epilepsy, and also of those with febrile seizures. We are in the process of sending questionnaires after almost 25 years of follow-up, having obtained the necessary ethics and data protection approvals. This is the first time in over ten years that such complete follow-up has been attempted for this cohort.

Results: From the original cohort of 1092, 301 (28%) have died. Preliminary analysis of the first replies from GPs of the surviving patients in the cohort shows that a majority are in terminal remission, with few instances of seizure recurrence in the intervening years. Further analysis is planned of seizure outcome and use of antiepileptic drugs.

Conclusion: It is hoped that the results of this study will provide a more realistic view of the prognosis of epilepsy for people with epilepsy.

p233
PHARMACOKINETICS OF PERAMPANEL, A HIGHLY SELECTIVE AMPA-TYPE GLUTAMATE RECEPTOR ANTAGONIST FOLLOWING ONCE- AND MULTIPLE-DAILY DOSING

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Purpose: Perampanel is an oral, noncompetitive, highly selective alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA)-type glutamate receptor antagonist. Perampanel is being investigated in phase III clinical trials in patients with refractory partial-onset seizures. The objectives of these 2 randomized, double-blind, placebo-controlled phase I trials were to determine the pharmacokinetics and safety of once- and multiple-daily dosing of perampanel in healthy male subjects.

Method: The single-dose profile of perampanel was assessed using a sequential, ascending, single-dose design with 1 placebo and 7 dose-groups (0.2–8 mg; 8 subjects per group). The steady-state profile of perampanel was determined using a multiple-dose, parallel-group design with 4 groups of 8 subjects; 6 subjects received perampanel (1–6 mg) and 2 received placebo once-daily for 14 days. Safety assessments included adverse events (AEs), physical examinations, laboratory tests, and 12-lead electrocardiograms (ECGs).

Results: Perampanel was rapidly absorbed with a mean time to peak plasma concentration of <1 h (0.25–3.0 h). Exposure was dose-related and associated with a mean $t_{1/2}$ ranging from 52–129 h in the single-dose study and from 66–90 h in the multiple-dose study. Steady-state plasma concentrations were reached by Day 14. The most common AEs in both studies were dizziness, fatigue, and somnolence. No serious AEs or clinically significant changes in physical examinations, vital signs, ECGs, or laboratory tests were observed in either study.

Conclusion: Perampanel was rapidly absorbed and slowly eliminated with steady-state being reached by Day 14. Perampanel was well tolerated, with most AEs being mild to moderate in severity.

Support: Eisai Inc.

p234
EFFICACY OF RETIGABINE 600, 900 OR 1200 MG/DAY BASED ON BASELINE TOTAL PARTIAL-SEIZURE FREQUENCY IN ADULTS WITH REFRACTORY EPILEPSY

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Purpose: Assess efficacy based on baseline seizure frequency of retigabine, a first-in-class antiepileptic drug (AED) that reduces neuronal excitability by enhancing the activity of KCNQ (Kv7) potassium channels, in refractory partial-onset epilepsy.

Method: RESTORE 1/2 (NCT00232596/NCT00235755) were randomized, double-blind, placebo-controlled, parallel-group studies in adults with ≥4 partial-onset seizures/28-days, receiving 1–3 AEDs, with/without vagus nerve stimulator. Patients underwent forced-titration to retigabine 600 or 900 mg/day (RESTORE 2) or 1200 mg/day (RESTORE 1) or placebo t.i.d., followed by 12 weeks' maintenance. Responder rate (≥50% reduction in seizure frequency) during maintenance and percent change in total partial-seizure frequency/28-days from baseline to maintenance were assessed by baseline seizure frequency category (≤8 and >8/28-days).

Results: Of the intent-to-treat population, 256/305 and 471/538 entered maintenance in RESTORE 1 (placebo = 137/152, 1200 mg/day = 119/153) and RESTORE 2 (placebo = 164/179, 600 mg/day = 158/181, 900 mg/day = 149/178). Responder rate during maintenance was greater for retigabine (p-values versus placebo) in both seizure frequency categories (RESTORE 1: placebo ≤8 = 23%, >8 = 22%; 1200 mg/day ≤8 = 69%, >8 = 47%, $p < 0.001$; RESTORE 2: placebo ≤8 = 20%, >8 = 18%; 600 mg/day ≤8 = 43%, >8 = 36%, $p < 0.001$; 900 mg/day ≤8 = 52%, >8 = 44%, $p < 0.001$). A similar pattern was seen in median percent change from baseline to maintenance in total partial-seizure frequency/28-days (RESTORE 1: placebo ≤8 = −19%, >8 = −19%; 1200 mg/day ≤8 = −62%, >8 = −47%, $p < 0.001$; RESTORE 2: placebo ≤8 = −21%, >8 = −14%; 600 mg/day ≤8 = −47%, >8 = −30%, $p = 0.001$; 900 mg/day ≤8 = −51%, >8 = −40%, $p < 0.001$). Greater efficacy was seen in patients with baseline seizure frequency ≤8 than >8/28-days. Most common adverse events were dizziness, somnolence, headache, fatigue, and confusion.

Conclusion: Retigabine 600–1200 mg/day demonstrated efficacy in adults with baseline 28-day partial-seizure frequency rates of ≤8 or >8.

Poster session: Drug therapy IV
Monday 28th June 2010
13:30–14:30

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COMPARISON OF THE EFFICACY AND SAFETY OF USING ANTIEPILEPTIC DRUGS TOPIRAMATE AND PHENOBARBITAL IN TREATMENT OF SYMPTOMATIC FOCAL FORMS OF EPILEPSY IN CHILDREN

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Purpose: Comparison of the efficacy and safety of using antiepileptic drugs topiramate and phenobarbital in treatment of symptomatic focal forms of epilepsy in children.

Method: We observed 2 groups of children with focal forms of epilepsy: 1 group – 31 patient were treated by topiramate in dozes from 56 up to 500 mg/day, from 2.8 up to 17 mg/kg/day (on the average 6.6 mg/kg/

day). 2 group – 34 patients – received therapy by phenobarbital in dozes from 12 up to 300 mg/day, from 1.5 up to 12 mg/kg/day (on the average 6.4 mg/kg/day). The therapy was used in monotherapy and in combine therapy with other antiepileptic drugs.

Results: Seizure freedom was achieved in 8/31 patients (26%), used topiramate, and in 9/34 patients (26%), treated by phenobarbital. Reduction in seizure frequency more than 50% was observed in 19/31 (61%) cases in topiramate group and in 4/34 (12%) cases in phenobarbital group. The side effects (SE) were detected in 16/31(52%) of all cases, treated by topiramate: somnolence, anorexia and nervousness, salts in urine, but only 3 patients withdrawal therapy was necessary. Six patients had improvement in they development kognitive functions. The side effects (SE) were detected in 16/34 (47%) of all cases, treated by phenobarbital: aggressiveness, somnolence, decrease in memory and attention, decrease in progress at school.

Conclusion: This study has shown topiramate is more effective, well tolerated new antiepileptic drug for treatment focal forms of epilepsy in children than the oldest one phenobarbital.

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DESIGN AND CURRENT STATUS OF THE CATZ STUDY: A PHASE III, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED TRIAL TO ASSESS THE EFFICACY AND SAFETY OF ADJUNCTIVE ZONISAMIDE IN PEDIATRIC PATIENTS WITH PARTIAL-ONSET SEIZURES

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Purpose: To assess the efficacy and safety of adjunctive zonisamide (ZNS) in a pediatric population with partial-onset seizures receiving one or two antiepileptic drugs (AEDs).

Method: The CATZ Study is a Phase III, multicentre, randomized, double-blind, placebo-controlled study. Following an 8-week screening period, subjects age 6–17 years, weighing ≥20 kg, with ≥4 simple or complex partial seizures (±secondary generalization) per month and receiving one or two AEDs are randomized 1:1 to ZNS or placebo. ZNS is initiated at 1 mg/kg/day, up-titrated to 8 mg/kg/day over 8 weeks (one down-titration is permitted), and continued unchanged during the 12-week maintenance period. Changes in concomitant AEDs are not permitted. The primary end point is the proportion of responders (≥50% decrease in seizure frequency) in the maintenance period. Secondary end points include: assessment of changes in seizure frequency and the proportion of subjects who are seizure-free during the titration and/or maintenance period. Safety is measured by adverse events, clinical laboratory tests, physical and neurological examinations. The effect of ZNS treatment on cognition, growth or development is also being assessed.

Results: The study is expected to complete by June 2011 and the results will be available thereafter.

Conclusion: This study will provide the safety and efficacy information to support the marketing authorization application for adjunctive use of ZNS in pediatric patients with partial epilepsy.

This study is supported by Eisai.

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FOCAL ROLANDIC EPILEPTIFORM DISCHARGE TREATMENT IMPROVES BEHAVIOR IN CHILDREN WITH BEHAVIORAL PROBLEMS WITHOUT EPILEPTIC SEIZURES

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Objectives: The aim of this paper was to show that suppressing focal-rolandic epileptiform discharges (FRED) improves behavior in children with behavioral problems without epileptic seizures.

Study design: In the prospective study lasting from 2000 to 2008, 36 children with behavioral problems and FRED, without epileptic seizures, were followed. Ambulatory electroencephalographic recordings and behavioral scales were performed at baseline and each 12 months during the follow-up period. Children were followed up without antiepileptic medication (AEM) for one year, and then they were followed with active drug treatment (valproate 20 mg/kg/day, karbamazepine 20 mg/kg/day, or lamotrigine 5–8 mg/kg/day) from 12 months up to 5 years. The primary hypothesis to be tested was that the behavioral scales would improve in children by the suppression of FRED with AEM.

Results: The global rating of behavior improved only in patients who showed a complete electroencephalography normalization during antiepileptic drug medication, which was best during lamotrigine medication.

Conclusions: Our data show that suppressing FRED in children without epileptic seizures improves behavior, and that lamotrigine shows the best results.

Keywords: Children, behavior, focal (rolandic) epileptiform discharges, antiepileptic medication, lamotrigine.

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CLOBAZAM ADD-ON THERAPY FOR THE TREATMENT OF EPILEPTIC ENCEPHALOPATHY

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Purpose: Clobazam (CLB) is a 1, 5 benzodiazepine, which is known to be effective for treating refractory partial epilepsy. The aim of this study is to evaluate the efficacy and tolerability of CLB in patients with epileptic encephalopathy.

Method: Patients with epileptic encephalopathy who had received CLB add-on therapy were enrolled in this study. We retrospectively reviewed these patient's characteristics including the type of epileptic encephalopathy, use of CLB, efficacy, adverse events, and retention time.

Results: Of the 58 patients (34 males and 24 females, ages from 9 months to 21 years), seven had West syndrome and 44 had Lennox-Gastaut syndrome. The other seven patients had undetermined epileptic encephalopathy transformed from previous infantile spasms. CLB were initiated at a mean dosage of 0.4 mg/kg/day and titrated maximally to 1.76 mg/kg/day. After 1 month with CLB, 18 patients (31.0%) became seizure-free and 15 patients (25.8%) had >50% seizure reduction. Tolerance developed in 21.2%, 37.0%, 54.5%, and 62.8% at 2, 3, 4, and 6 months, respectively. However, nine patients (15.5%) maintained seizure remission for at least 6 months. Adverse events including sedation, behavioral change, and dizziness were reported in nine patients, but led to drug discontinuation in only one patient. The 2 year retention rate by Kaplan-Meier method was 75.9%.

Conclusion: Our study shows CLB add-on therapy is effective and tolerable in patients with epileptic encephalopathy.

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SECOND-LINE ANTIEPILEPTIC DRUGS IN CHILDREN WITH INTRACTABLE EPILEPSIES: CLINICAL AUDIT OF USES AND OUTCOMES FOR CLOBAZAM AND TOPIRAMATE

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Purpose: To systematically assess the use of 2 second-line antiepileptic drugs (AEDs) in children, their retention, perceived effectiveness, tolerability and safety over 12 months follow-up.

Method: A retrospective chart review of all children starting epilepsy treatment with clobazam (CLB) or topiramate (TOP) in a defined time period in one pediatric neurology department were ascertained from hospital pharmacy and pediatric neurology data bases and clinic letters. A standard data sheet was used to record clinical information, outcomes and adverse events at 2, 6, and 12 months follow-up. Simple statistical analyses were undertaken in SPSS on the full data set (intention to treat basis).

Results: One hundred thirty-two children aged 0.1–17 years have been studied to date: CLB (72), TOP (60). Epilepsies were similar: 33% idiopathic, 30% symptomatic, the remainder unspecified or probably symptomatic; evenly split between generalized and focal or undetermined epilepsies: with median age of epilepsy onset 3 years. The mean number of additional AEDs (concurrent or withdrawn) was 3.6.

There was a small difference in retention at 12 months: 62% for CLB and 52% for TOP, and in perceived efficacy by 12 months: >50% seizure reduction was evident in 46% on CLB, and in 30% on TOP. Probably drug related adverse events (AEs) were reported in about half those exposed to each AED. There were no serious AEs.

Conclusion: CLB and TOP appear safe and effective. The data support development of a controlled trial of CLB in children with epilepsies.

p240
EFFICACY OF LEVETIRACETAM IN TWO PEDIATRIC PATIENTS WITH REFRACTORY STATUS EPILEPTICUS

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Purpose: To describe the use of levetiracetam in status epilepticus in our department.

Methods and results: We report two cases in which it has been used.

Case 1: 26-month-old boy who suffered postinfectious encephalitis with complex partial seizures, paroxysmal activity with tips biphasic in temporal region. Treated with valproic acid from the onset of the status developed a nonconvulsive complex partial status refractory to treatment with diazepam and phenytoin. Levetiracetam was administered in bolus of 20 mg/kg to control the status both clinical and neurophysiologically. Case 2: 18-month-old boy diagnosed with primary pulmonary hypertension who suffered cardiorespiratory arrest, lasting approximately 20 min. After 48 h he began with very frequent generalized tonic–clonic seizures not controlled with diazepam, phenytoin and valproic acid. After administration of Levetiracetam at 20 mg/kg the crisis ended without further recurrence.

Discussion: Currently levetiracetam is not indicated for the treatment of status epilepticus although there have been reported cases, similar to our experience, where it has been effective. More reports are necessary to establish the benefits of this drug in status epilepticus.

Conclusion: Levetiracetam was effective in two cases of status epilepticus (complex partial and tonic–clonic) refractory to usual medications.

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SECOND-LINE ANTIEPILEPTIC DRUGS IN CHILDREN WITH INTRACTABLE EPILEPSIES: CLINICAL AUDIT OF USES AND OUTCOMES FOR LAMOTRIGINE AND GABAPENTIN

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Purpose: To systematically assess the use of 2 second-line antiepileptic drugs (AEDs) in children, their retention, perceived effectiveness, tolerability and safety over 12 months follow-up.

Method: A retrospective chart review of all children starting Lamotrigine (LAM) or Gabapentin (GAB) in a defined time period in one pediatric neurology department were ascertained from hospital data bases and clinic letters. A standard data sheet was used to record clinical information, outcomes and adverse events at 2, 6, and 12 months follow-up. Simple statistical analyses were undertaken in SPSS on the full data set (intention to treat basis).

Results: One hundred thirteen children aged 1–16 years had data on outcomes to date: LAM (89), GAB (24). Epilepsies were dissimilar: those treated with LAM had idiopathic (44%), symptomatic (16%), the remainder unspecified or probably symptomatic, evenly split between generalized and focal or undetermined epilepsies; while those treated with GAB had idiopathic (12%), symptomatic (58%), the remainder unspecified or probably symptomatic, with 77% focal epilepsies. The median age of onset was 5 years. The mean number of additional AEDs (concurrent or withdrawn) was 3.6.

There was no significant difference in retention at 12 months: 61% for LAM and 67% for GAB, or in perceived efficacy at 12 months: greater than 50% seizure reduction was evident in 52% starting LAM, and in 42% starting GAB. Probably drug related adverse events (AEs) were reported in about half those exposed to each AED. There were no serious AEs.

Conclusion: LAM and GAB appear safe and effective when used selectively.

p242
USE OF RECTAL DIAZEPAM IN ABORTING SEIZURES IN CHILDREN FOLLOWING CAREGIVER EDUCATION: SINGAPORE EXPERIENCE

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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 471 patients aged 0–15 years old who had either epileptic seizures or febrile seizures in the 3 year period from 1 March 2006 to 28 February 2009. Caregivers were taught how to identify convulsive seizures and to administer diazepam rectally if the seizures lasted longer than 5 min, 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 hospital's Children's Emergency department were recruited into the study.

Results: Sixty-three patients who had seizures that lasted longer than 5 min were reviewed at our Children's Emergency. Out of these, 59 (94%) had rectal diazepam administered at home. The seizures stopped after administration of rectal diazepam in 48 (81%); the remaining 11 (19%) required further intravenous anticonvulsant treatment in the hospital.

Conclusion: Following education by a pediatric epilepsy nurse, caregiver administration of rectal diazepam was effective in stopping 81% of subsequent seizure recurrences lasting more than 5 min. It is a reassuring safety net for patients who are prone to prolonged seizures.

Poster session: Drug therapy VII
Monday 28th June 2010
13:30–14:30

p243
PREGNANCY AND EPILEPSY

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Purpose: To establish any influence of epilepsy or antiepileptic drugs treatment on pregnancy and children of epilepsy mothers.

Method: We controlled the records of the Epilepsy Unit, Service of Neurology, UHC Mother Theresa, Tirana. We found 22 female patients with history of pregnancy. The age, history of previous pregnancies, concomitant diseases, seizure's type, delivery or abortion, the general state of the offspring, antiepileptic treatment, family history are recorded.

Results: Of 22 patients, two of them were still pregnant. 2 had a history of abortion at the 6th and at the 10th week. Both mothers had epilepsy plus history (cerebral palsy, diabetes mellitus). The mean age of patients is 26.6 years old, at the delivery or abortion time. The media of gestional weeks is 39. There are 9 primiparous women, 2 had previous abortion history and 9 had 1–3 previous normal pregnancies. The education level of mothers is evaluated as a mean of 10.8 years. There have been 8 normal deliveries and 10 cesarean interventions. One child passed away 1 week after delivery because of pulmonary infection. During the pregnancy there were 17 patients on monotherapy, 3 on polytherapy and 2 without any AEDs. Four of mothers with normal pregnancy and offsprings had: astrocitoma, cerebelar cavernoma, cortical displasia.

Conclusion: The abortion rate and the child mortality is higher in epilepsy mothers, but there is no correlation with the AEDs treatment, mother's age, frequency of seizures. The concomitancy of epilepsy with other diseases had a negative influence on the pregnancy.

p244
REDUCTION DEFECTS IN TWO FETUSES PRENATALLY EXPOSED TO CLOBAZAM

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Purpose: Most antiepileptic drugs (AEDs) are associated with teratogenic side effects. Publications on clobazam (CLB) and human pregnancy outcome are few. We present two cases with reduction defects after prenatal exposure to CLB.

Method: Descriptive study of two cases registered in EURAP-Netherlands. EURAP is an international registry of antiepileptic drugs and pregnancy.

Results: The first case was a child born after exposure throughout pregnancy to 10 mg CLB and 375 mg phenytoin (PHT) daily. At birth, a terminal transverse reduction defect of the left lower arm was present. On x-ray, a normal left humerus, normal proximal ulna and radius of 1 cm, converging into a single fibrotic strand were demonstrated. No other skeletal abnormalities were present.

The second case concerned an ongoing pregnancy of 24 weeks with exposure throughout pregnancy to 40 mg CLB daily and 600 mg carbamazepine (CBZ) daily. A defect of the left lower arm was diagnosed by ultrasound. The structures of the lower part of the arm, wrist and hand are missing. Prenatal diagnosis was a terminal transversal reduction defect of the arm. Family history in both cases was negative for limb or skeletal defects.

Conclusion: These two cases of a rare skeletal defect in association with a infrequently prescribed antiepileptic drug raise the possibility of a rare effect of CLB alone or in combination with CBZ and PHT due to metabolic interactions. The chronic use of CLB might have been an additional risk factor, and indirectly point towards a potential teratogenic effect of CLB.

p245
MAJOR MALFORMATIONS ASSOCIATED WITH MATERNAL USE OF ANTIEPILEPTIC DRUGS IN SAMARA REGION

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Purpose: To find relationship between fetal major malformations and mothers using antiepileptic drugs (AED).

Method: We evaluated outcomes of 164 pregnancies of women with epilepsy in Samara region, Russia. Eighty-six women received monoterapy AED, 31 women used AED combination therapies and 47 women did not use AED at the first trimester of pregnancy.

Results: Eight congenital malformations in the offspring of women with epilepsy were found (5 of them had been prenatal diagnosed). 6 pregnancies had normal outcomes and 2 pregnancies were eliminated for medical reasons. There were similar congenital malformations in 2 children of one mother. They both had multicystic kidney. It was probably dependent on monogenic abnormality. Other malformations were congenital heart defects (3), neural tube defect (1), facial cleft lip (1) and multiple major malformations (1). Most of the women had taken folic acid before and during pregnancy. Risk of fetal major malformation has been 4.9% under study, 2.3% for women on monoterapy (excluding monogenic abnormality) and 6.5% for women on antiepileptic drug combinations. Risk of major malformation in general polulation of Samara region during that period was 2.6%.

Conclusion: There is an increased risk of congenital malformation in the offspring of women with epilepsy, particularly those using antiepileptic polytherapy. Prenatal detections may help improve perinatal care.

p246
SURVEILLANCE OF CROATIAN PREGNANT WOMEN WITH EPILEPSY AND EFFECTS OF ANTIEPILEPTIC DRUGS EXPOSURE IN THEIR OFFSPRING

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Purpose: To follow up pregnancies exposed to antiepileptic drugs (AED) and their offspring in order to assess teratogenic and neurodevelopmental effect of particular AED of newer generation.

Methods: The prospective surveillance (May 2003–May 2009) obtained the data about pregnancy planning, folic acid (FA) intake, seizure frequency and

AED therapy in 68 pregnancies from 52 Croatian women with epilepsy. The results were compared with 147 healthy controls (mother/newborn pairs).

Results: About 35% of women with epilepsy planned their pregnancies and 20% took FA, while 90% of controls planned their pregnancies and only 2.7% took FA properly. About 91% of pregnancies were exposed to monotherapy: 33 to LTG – 9 LB, 2 premature deliveries, 3 spontaneous abortions (SA), 1 artificial abortion, 1 intrauterine death and 7 ongoing pregnancies (OP). Eleven LB and 2 SA were exposed to CBZ; 1 LB to PHT; 1 SA and 2 LB to PB. One LB and 1 preterm LB with ASD, psychomotor delay and epilepsy was exposed to GBP; 5 LB and 1 OP were under VP. Six pregnancies were under polytherapy: TPM/VP (1 LB, 1 SA, 1 OP); CBZ/PB (stillbirth) TPM/CBZ/PHT (LB – IUGR and dysmorphism); VP/CZP (1 OP). Four pregnancies without AED resulted in LB.

Conclusion: We have surveyed pregnancies exposed to LTG, VP, PHT, PB, GBP, TMP, CBZ and CZP. AED polytherapy resulted in larger proportion of complications. Preconceptional counseling in women with epilepsy resulted in higher proportion of FA intake. Further follow up of LB till school age will be provided.

p247
OBSTETRIC AND NEONATAL OUTCOME OF PREGNANCIES IN WOMEN WITH EPILEPSY. PROSPECTIVE STUDY

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Purpose: To evaluate obstetric and neonatal outcome in cohort of woman with active epilepsy (WE) in comparison to general pregnant women population in Poland.

Method: Prospective study conducted in 3 centers for WE included 390 WE (mean age 27.4), who delivered between 2002–2009. Demographic, epilepsy and obstetric data were collected and compared with controls consisted of 361 440 deliveries in central part of Poland (Mazovia County) in this period.

Results: Out of 390 women, 326 (83.6%) gave birth (including 4 stillbirths) and 64 (16.4%) had spontaneous abortion. Two hundred four births (62.6%) were natural and 118 (36.2%) by caesarean section (cs). In Mazovia it was 71.2% and 26.9% respectively. The reasons for cs were obstetrical (59.3%), seizure related (17%) and other disorders related (16.1%). In 76.9% Apgar score in 1 min. was 10 points and in 4.1% <7 points. Compared to controls more children of WE had low-birth -weight (10.3% vs. 6%). Frequency of premature labour was similar (8.3%) to control group. The frequency of major malformations was 5.6% and minor 2.9%. Monotherapy was used in 70% of WE, most frequently CBZ, VPA, LTG and OCBZ with mean dosage in I trimester of 728.6 (100–1800), 773.2 (300–1800), 254.75 (50–450) and 1012.5 (150–1800) mg, respectively.

Conclusion: In majority of WE pregnancy and neonatal outcome was good. Frequency of caesarean section and low-birth-weight were slightly increased in WE. The number of patients was to small to correlate rate of malformations with AED dosage.

p248
TWO SISTERS WITH MENSTRUAL CYCLE MENARCHE INDUCED BY LEVETIRACETAM

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Reproductive endocrine disorders are reported to be more common in women with epilepsy than in the general female population. Epilepsy itself may affect reproductive endocrine function, as also some Anti Epileptic Drugs (AEDs). We report two sisters, with primary amenorrhea and epilepsy, in whom levetiracetam (LEV) treatment induced the appearance of menses. F.C. and F.F., respectively 34 and 22 years-old sisters, both born on term with normal delivery, microcephalus and mild mental retardation, without febrile seizures or a family history of epilepsy. Both experienced from the age of 1 year about one generalized tonic–clonic seizure/month, on addition to absences, more than once a day in F.C., most rare in F.F. Brain magnetic resonance imaging (MRI) revealed in both the presence of an empty sella and the gynaecological surveying hypogonadotropic hypogonadism. F.C. underwent LEV treatment (1000 mg/bid) with a marked reduction of seizures frequency and appearance of menarche at the age of 32, with successive menses regular. Her sister used from the beginning phenobarbital (PB), which was ineffectual, then oxcarbazepine (OXC), discontinued for leukopenia, and finally was successfully treated with LEV 1000 mg/bid, with the appearance of regular menses. In conclusion, the endocrine effects of the new AEDs have not been widely studied, and these are the first reported cases in literature of menses induced with LEV treatment, although the possible underlying mechanism is not understood. Furthermore, we stress the coexistence in both sisters of empty sella, microcephalus with mild mental retardation, amenorrhea and epilepsy, never described before.

p249
VALPROATE AFFECTS THE NUMBER OF CORTICAL CELLS IN THE DEVELOPING RAT BRAIN

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Purpose: Human studies have demonstrated that maternal use of valproate during pregnancy is associated with increased risk of long-term cognitive and behavioral dysfunction of the offspring. In this study we aimed to evaluate the total number of neocortical neurons in newborn rats exposed to valproate in utero and during the first 3 weeks postpartum corresponding to 2nd and 3rd trimester of human pregnancy.

Method: The maternal rats were given intraperitoneal injections of low or high dose valproate (20 mg/kg and 100 mg/kg, respectively). After sacrificing the pups at age 21 days, we determined the total number of neocortical neurons with use of an unbiased optical fractionator.

Results: The pups exposed to both low and high dose valproate had statistically significant higher total number of neurons in neocortex compared to controls ($p < 0.01$). There was no statistical difference between the two valproate groups. The total number of neocortical neurons in the control group amounted 15.5×10^6 which is in consistency with the results for the control group in our previous study which strengthens the power of our findings.

Conclusion: These results make it most likely that valproate interfere with brain development by decreasing normal neuroapoptosis.

Poster session: Drug therapy VIII
Monday 28th June 2010
13:30–14:30

p250
EFFECTIVENESS OF RUFINAMIDE IN DIFFERENT EPILEPSY SYNDROMES

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Objective: Since 2007 rufinamide is licensed in Germany for the treatment of seizures in Lennox-Gastaut syndrome (LGS). We report our experiences with rufinamide in different epilepsy syndromes.

Patients and methods: Eighty-five adults were treated with rufinamide (age 19–68 years, mean 33.4 years). All suffered from pharmacoresistant epilepsies (52 pats. with LGS), frequent seizures (31 pats. daily) and cognitive impairment (67 pats.). All had antiepileptic polytherapy (2–4 AEDs, mean 2.0 AEDs), 26 pats. nervus-vagus-stimulation.

Rufinamide was titrated slowly (+200 mg/3–7 days, target 1200–3400 mg/day), follow up ranges between 3 and 26 months (mean 18.2 months).

Results: 14 patients (16.4%) had side effects, predominantely nausea (7 pats.) and sedation (5 pats.). Side effects led to withdrawal in 7 pats (8.2%), in 7 pats. sideffects could be abolished either by reduction of comedication or rufinamide.

Effectiveness was assessed in 72 patients (6 pats. follow up <6 months), 26 of 72 pats. responded to rufinamide (>50% reduction of seizure frequency; 11 pats. >75%, no freedom of seizures, worsening in 1 pat.). The proportion of responders was higher in partial epilepsies (12/28 pats., 42.8%) than in LGS (15/44 pats., 34.1%), the difference was not significant (Fisher's exact test).

Discussion: Rufinamide is effective in partial epilepsies, maybe even more than in LGS. This result is not unexpected with respect to the difficult treatment of seizures in LGS.

It is well tolerated even in complex polytherapy, pharmacokinetic interactions are insignificant. Further investigations are necessary to assess the role of rufinamide in the treatment of different epilepsy syndromes.

p251
A META-ANALYSIS OF RETENTION RATE AND A COMPUTATIONAL MODELING OF RETENTION OF SECOND GENERATION ANTIEPILEPTIC DRUGS IN PEOPLE WITH PARTIAL ONSET SEIZURES

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Purpose: A computational retention model from clinical trial publications on second-generation antiepileptic drugs (AEDs) as adjunctive therapy in partial onset seizures (POS) was developed. Retention measures long-term treatment success on a multidimensional level. The current meta-analysis develops a methodology to analyze the time-course of retention, allowing the inclusion of multiple studies and data points.

Method: A comprehensive literature search of POS studies yielded >300 references; 44 publications for 4 drugs were selected for analysis (topiramate, 12; levetiracetam, 15; lamotrigine, 10; gabapentin, 7). Baseline demographics, retention and key efficacy data were tabulated for each. When necessary, Kaplan-Meier curves were digitized to obtain data points. The analysis weighted studies by size, and by repeated time points in the survival curve. A constant hazard model was chosen for patients who discontinued treatment.

Results: Weighting studies by size resulted in good model fit of the retention profiles over time for each of the drugs. Meta-analysis showed that discontinuation rates leveled off after 2 years. For levetiracetam, estimated 1 year retention rate ranges from 54–77%, with 9% trial-to-trial variability and 5% residual variability. The other AEDs also showed high consistency and good fit to the modeled Kaplan-Meier curves suggesting each drug has a consistent and distinct retention profile, with the following rank order lamotrigine~levetiracetam>topiramate>gabapentin.

Conclusion: The nonlinear, constant hazard model worked well in describing the time-course of retention for 4 s generation AEDs. The analysis suggests that each drug has a distinct retention profile.

Acknowledgment: Support was provided by Johnson & Johnson Pharmaceutical Research & Development, LLC.

p252
ITALIAN VERSION OF THE ADVERSE EVENTS PROFILE QUESTIONNAIRE IN PATIENTS WITH EPILEPSY: TRANSLATION, RELIABILITY AND STABILITY

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Purpose: To translate the Adverse Events Profile (AEP) Questionnaire into Italian and to evaluate its reliability and stability.

Method: The original 21-item questionnaire was translated by two independent specialists who agreed on a single version, and translated back into English by an independent mother-language translator. The original and back-translated versions were compared and corrections made to obtain the final version. This was tested in a prospective study in 104 adults with epilepsy treated with stable doses of antiepileptic drugs. The questionnaire was readministered 1 week later to a subset of 36 clinically stable patients without change in health status and drug therapy. The score distribution of the AEP scale was determined by calculating the score range and ceiling/floor effects. Reliability and stability were assessed by test of internal consistency (Cronbach's α coefficient) and test-retest reliability (Intraclass Correlation Coefficient (ICC)). Statistical analysis was performed by SPSS 8 program.

Results: The score distribution was satisfactory (Theoretical and Observed range for 19 and 21 items: 19–76, 21–84; 19–59, 21–67). Ceiling/floor effects were negligible (0%, 1.9%), suggesting that the questionnaire covered adequately the specific adverse events occurring in the study population. Internal consistency and test-retest reliability were also satisfactory: the Cronbach's α coefficient was 0.87 for 19 items and 0.89 for 21 items, and the ICC was 0.89 for 19 items and 0.87 for 21 items.

Conclusion: These results support the reliability and stability of the Italian translation tested.

Acknowledgments: Supported by grant FARM52K2WM from Agenzia Italiana del Farmaco (AIFA).

p253
CLINICAL EXPERIENCE WITH TOPIRAMATE IN KOREAN PATIENTS WITH EPILEPSY

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Purpose: This study aims to evaluate the clinical experiences, including efficacy and adverse events, of topiramate in Korea during the past 10 years.

Method: This was an open-label, retrospective observation with post marketing surveillance data of topiramate. 4535 epilepsy patients were enrolled in this study. The subjects were only included from epileptologists whose data included studies of at least a 16-weeks' duration period. The survey contained various issues, such as efficacy (responder rate, seizure-free rate), safety, adverse effects and the quality of life in patients.

Results: Of the total 4535, there were 56.3% men 43.7% women, and the mean age was 24.9 ± 16.4. The mean duration of epilepsy was 9.8 ± 8.9 years. We divided the subjects into two groups, the pediatric group (<18 years old, 1737 (38.3%)) and the adult group (≥18 years old, 2798 (61.7%)). The monotherapy ratio is higher in the pediatric group, 43%, than in the adult group, 33%. In the pediatric group, the response rate was 75% with partial seizure and 72% with general seizure, with 80% in monotherapy and 69% in polytherapy. In the adult group; the response rate was 65% with partial seizure and 67% with general seizure, with 68% in monotherapy and 64% in polytherapy. One or more adverse effects were reported in 19.2% of patients, with anorexia, vertigo, somnolence, memory difficulty, paresthesia, etc.

Conclusion: The efficacy and adverse rate of topiramate in Korean epilepsy patients is comparable to western countries. These results provide valuable information to clinicians regarding the clinical use of topiramate.

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THERAPEUTIC HABITS AND PRACTICES IN TREATMENT OF EPILEPSY IN SLOVAK REPUBLIC

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Purpose: The objective of this study was to determine therapeutic habits and routine practices of the neurologists in Slovak Republic in treatment of epilepsy. Other objective was to map a proportion of the patients with epilepsy in neurological practices.

Method: Quantitative questionnaire with 31 questions. Total of 125 responders – neurologists (1035 patients) from clinics and with their own private practice.

Results: On average, there are 196 patients with epilepsy in each practice. Total of 42% practices have <100 patients with epilepsy and in only 19% practices are registering more than 200 patients with epilepsy. Achievement of the seizure freedom is considered as the most important objective for over 75% of the neurologists. Total of 61% of neurologists consider monotherapy with new AED as having low importance. The most serious reason of the noncompliance of the patients is large number of the drugs (54%). The results has demonstrated, that the average number of the drugs is 1.6, therefore neurologists would like to have a drug which does not require combination with other drugs. The most prescribed drug is valproic acid (85%), the drug of the second choice is lamotrigine (59%) with the third most prescribed drug being levetiracetam (44%). The drug with the best characteristics for neurologists is levetiracetam. Valproic acid has the longest effect and is the most price available (63%).

Conclusion: Therapeutic habits and routine practices in treatment of the epilepsy of the neurologists in Slovak Republic correspond to standard therapeutic algorithms, with to requirements of the health insurance companies.

p255
A NATIONAL AUDIT OF EPILEPSY SPECIALIST NURSE PRESCRIBING PRACTICE IN THE UNITED KINGDOM (UK)

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Purpose: Recent advances in legislation have enabled nurses in the UK to become Independent and Supplementary Prescribers (NISP). The NISP can assess, diagnose and independently prescribe any licensed medicine within their area of competence (DOH 2005). This change has meant the number of nurse prescribers in disease specific areas has increased. This study aims to assess the number of Epilepsy Specialist Nurses (ESNs) prescribing and the context in which they do so.

Methods: A draft questionnaire was piloted with 10 ESNs. Minor amendments were made. In April 2009 all known ESNs were invited via letter to complete the questionnaire. One month later a follow up reminder was mailed to all ESNs to encourage participation. Data was analyzed using percentages and cross tabulation.

Results: Twenty-three ESNs were working as independent nurse prescribers and/or 9 as supplementary nurse prescribers. Of the 29 nurses who had completed the prescribing course, 25 were using the qualification. Prescribing practice demonstrated that 21 (29%) sign prescriptions, 28 (36%) make recommendations to other prescribers, 14 (19%) prescribe or amend ward/in patient drug prescriptions and 10 (14%) use clinical management plans. The medications prescribed by ESNs include antiepilepsy medication, folic acid, vitamin K, antidepressant drugs, steroids, rescue medication and the contraceptive pill. Most ESNs wrote a prescription for a new drug at least once a week whilst most nurses titrated medication daily.

Conclusions: A small number of ESNs are prescribing in the UK but are doing so in an appropriate manner.

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OXCARBAZEPINE IN BRAIN TUMOR-RELATED EPILEPSY: EFFICACY, SIDE EFFECTS AND IMPACT ON QUALITY OF LIFE

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Purpose: We conducted a prospective, observational study to evaluate the efficacy, side effects and impact on quality of life (QoL) and depression of oxcarbazepine in patients with BTRE followed for 12 months.

Method: We recruited 25 patients (14 m, 11 f; mean age 49.7 years) affected by BTRE (17 naive patients and 8 in monotherapy with other antiepileptics) and introduced oxcarbazepine monotherapy. At first visit patients underwent neurological examination, tests' administration:

Qolie 31P V2, EORTC QLQC30, Zung Self Depression rating Scale (ZSDRS) and Adverse Events Profile. Seizure diary was given.

Results: Follow up duration was 1–12 months (mean 6.8 months, because 6 patients died, 11 dropped out). Sixteen patients underwent both chemotherapy and radiotherapy, 4 chemotherapy, 1 radiotherapy and 4 did not undergo any systemic therapy. Mean dosage of oxcarbazepine was 1230 mg/day (min 600 max 2100 mg/day). Monthly mean seizure frequency before oxcarbazepine was 10.3, at follow up was 8.8. Ten patients were seizure-free. Mc Nemar test showed a significant difference on seizure freedom rate between baseline and final follow up ($p = 0.002$). Four patients had uncontrolled seizures during follow-up. Six patients (24%) had serious side effects and 1 patient (4%) mild. The tests' evaluation at final follow-up showed a significant improvement at ZSDRS (39.5 ± 10.8) ($p = 0.002$). Also distress related to energy, emotions and antiepileptics statistically diminished ($p = 0.02$; $p = 0.037$; $p = 0.009$).

Conclusion: Oxcarbazepine seems to be efficacious in controlling seizures in patients with BTRE. Also the mood and the distress related to antiepileptics, physical and emotional well-being significantly improves at follow up.

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THE COGNITIVE CONSEQUENCES OF RESECTING NONLESIONAL TISSUES IN TEMPORAL LOBE EPILEPSY SURGERY: EVIDENCE FROM MRI AND HISTOPATHOLOGICALLY NEGATIVE PATIENTS

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Purpose: We hypothesized that surgery in MRI and histo-pathologically negative patients with temporal lobe epilepsy (TLE) may serve as a proof of principle about the cognitive consequences of resecting nonlesional tissues.

Method: Verbal and figural memory outcomes of a group of 15 MRI and histopathologically negative patients (MRH-) were compared to 15 MRI and histopathology positive patients (MRH+). In the MRH- group 53% were males, 66% were resected on the left side, 13% underwent selective amygdalohippocampectomy, and 20% became seizure-free. MRH+ patients were selected from >1000 TLE patients, they had different types of lesions and were matched pairs in regard to age, sex, IQ, duration of epilepsy, side and type of surgery, and seizure outcome. Combined standardized scores ($m = 100$ $SD = 10$) for verbal/figural memory and attention/executive functionwere evaluated. Impairment or change were rated with standard scores <85 or changes >10 points.

Results: Preoperative memory was significantly better and less frequently impaired in MRH- patients as opposed to MRH+ patients (91 ± 9 vs. 79 ± 11 and 33% vs. 100%). After surgery, both groups improved in executive function ($t = -2.5/2.6$ $p = 0.022/0.023$). Memory deteriorated in the MRH- ($t = 3.7$ $p = 0.002$) but not in the MRH+ group ($t = -0.3$ $p = 0.70$). Both groups ended at similarly low performance levels.

Conclusion: Absence of MRI and histological pathology is a risk factor for highly significant postoperative memory loss. However, the postoperative memory outcome is not inferior to the MRH+ group. The findings confirm the significance of the resection/preservation of nonlesional functional tissues for cognitive outcome in epilepsy surgery.

Poster session: Drug therapy X
Monday 28th June 2010
13:30–14:30

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LONG-TERM MAINTENANCE OF EFFICACY WITH RETIGABINE 600–1200 MG/DAY IN ADULT PATIENTS WITH REFRACTORY EPILEPSY: EXTENSION STUDY OF RESTORE 1

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Purpose: To evaluate the maintenance of efficacy and safety of retigabine, a first-in-class antiepileptic drug (AED) that reduces neuronal excitability by enhancing the activity of KCNQ (Kv7) potassium channels.

Method: Study 303 (NCT00310375) is an ongoing, long-term, open-label extension of RESTORE 1, a Phase III, placebo-controlled, double-blind study of retigabine 1200 mg/day or placebo (t.i.d.), adjunctive to 1–3 AEDs, with/without vagus nerve stimulator. Patients in Study 303 underwent forced-titration to, or were maintained at, retigabine 1200 mg/day over a 6-week transition period. Retigabine dose (600–1200 mg/day) and background AEDs could then be modified. Efficacy evaluations included responder rate (≥50% reduction from baseline in 28-day total partial-seizure frequency).

Results: 181/224 (81%) patients who completed RESTORE 1 transitioned into Study 303, receiving ≥1 dose of retigabine (mean dose 1052 mg/day) over a median 357 days as of this interim data cutoff (30 June 2008). Responder rate was 57%, and 29.6% of patients experienced seizure reductions of 75–100%. Median reduction in 28-day total partial-seizure frequency was 57%. 10% of patients with ≥6 months of open-label treatment were free from seizures for any continuous 6-month period. Median percentage of seizure-free days was 86% during the extension period. The most common adverse events were dizziness (24%), somnolence (17%), urinary or renal disorders (12%), and headache (10%). Urinary or renal disorders included one patient each with urinary retention and urinary hesitation, both of which were severe and required discontinuation.

Conclusion: Retigabine maintained effectiveness and an acceptable safety profile during long-term, open-label, adjunctive therapy in adults with partial-onset seizures.

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LONG-TERM MAINTENANCE OF EFFICACY WITH RETIGABINE 600–1200 MG/DAY IN ADULT PATIENTS WITH REFRACTORY EPILEPSY: EXTENSION STUDY of RESTORE 2

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Purpose: To evaluate the efficacy and safety maintenance of retigabine, a first-in-class antiepileptic drug (AED) that reduces neuronal excitability by enhancing the activity of KCNQ (Kv7) potassium channels.

Method: Study 304 (NCT00310388) is a long-term, open-label extension of RESTORE 2, a placebo-controlled, double-blind study of retigabine 600 or 900 mg/day or placebo (t.i.d.) adjunctive to 1–3 AEDs, with/without vagus nerve stimulator. Patients underwent forced-titration to, or were maintained at, retigabine 900 mg/day over a 4-week transition period. Retigabine dose (600–1200 mg/day) and background AEDs could then be modified. Efficacy evaluations included responder rate (≥50% reduction from baseline in 28-day total partial-seizure frequency).

Results: 375/409 (92%) patients who completed RESTORE 2 transitioned to Study 304 and received ≥1 dose of retigabine (mean

doi: 10.1111/j.1528-1167.2010.02658.x

dose = 861 mg/day) over a median 275 days as of this interim data cutoff (30 June 2008). Responder rate was 54%, and 24% experienced seizure reductions of 75–100%. Median reduction in 28-day total partial-seizure frequency was 53%. 8% of patients with ≥6 months' open-label treatment were seizure-free for any continuous 6-month period. Median percentage of seizure-free days was 88% during the extension period. The most common adverse events were dizziness (19%), somnolence (17%), headache (12%) and fatigue (9%). Through December 2008, three treatment-emergent deaths were reported as possible/probable sudden unexplained death in epilepsy (SUDEP), resulting in an overall possible/probable SUDEP rate of 6.1/1000 patient-years of treatment, which falls within the range of disease-related mortality.

Conclusion: Retigabine 600–1200 mg/day maintains effectiveness and an acceptable safety profile during long-term, open-label use in adults with partial-onset seizures.

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THE RELATIONSHIP BETWEEN PREDICTED RETIGABINE EXPOSURE AND EFFICACY/SAFETY END POINTS: A POOLED PHARMACOKINETIC/PHARMACODYNAMIC ANALYSIS OF RESTORE 1 AND 2

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Purpose: To evaluate the relationship between predicted steady-state exposure and efficacy/safety end points for retigabine, a first-in-class antiepileptic drug (AED) that reduces neuronal excitability by enhancing the activity of KCNQ (Kv7) potassium channels.

Method: RESTORE 1/2 (NCT00232596/NCT00235755) were randomized, double-blind, placebo-controlled, parallel-group Phase III trials in adults with refractory epilepsy with ≥4 partial-onset seizures/28 days, receiving 1–3 AEDs, with or without vagus nerve stimulator. Patients underwent forced-titration to retigabine or placebo (t.i.d., p.o.) to 600, 900 or 1200 mg/day. Average steady-state area under the curve over the dosing interval ($AUC_{0-\tau}$) during the 12 weeks' maintenance was predicted for each patient and used to evaluate, by logistic regression, the relationship between exposure and probability-of-efficacy (≥50% reduction in baseline seizure frequency), and the probability of the most commonly observed adverse events (AEs: ataxia, dizziness, dysarthria, somnolence, tremor and blurred vision).

Results: $AUC_{0-\tau}$ values increased linearly over 600–1200 mg/day, although $AUC_{0-\tau}$ values overlapped between dose groups. Over the entire $AUC_{0-\tau}$ range, the probability-of-efficacy was higher than the probability of any AE. The slope of the exposure-response relationship for probability-of-efficacy was similar to that for dizziness and ataxia, whereas the slope of the exposure-response relationship for dysarthria, somnolence, tremor and blurred vision was less steep.

Conclusion: The probabilities of improved efficacy and the occurrence of common AEs increases with systemic exposure to retigabine. Dysarthria, somnolence, tremor and blurred vision were less sensitive to changes in exposure. This evaluation highlights the need to dose-titrate retigabine based on individual patient response for efficacy and tolerability/safety.

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EFFICACY OF RETIGABINE 600–1200 MG/DAY IN PATIENTS WITH REFRACTORY EPILEPSY WITH PARTIAL-ONSET SEIZURE: INTEGRATED ANALYSIS OF THREE RANDOMIZED STUDIES

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Purpose: Retigabine is a first-in-class antiepileptic drug (AED) that reduces neuronal excitability by enhancing the activity of KCNQ (Kv7) potassium channels. This integrated analysis of three randomized trials assessed the efficacy of retigabine as adjunctive therapy in adults with refractory epilepsy with partial-onset seizures.

Method: Study 205 (Phase IIb), and RESTORE 1/2 (NCT00232596/NCT00235755; Phase III) were randomized, double-blind, placebo-controlled, parallel-group studies in adults with refractory epilepsy, ≥4 partial-onset seizures/28-days, receiving 1–2 (Study 205) or 1–3 (RESTORE 1 and 2) AEDs, with/without vagus nerve stimulator. Patients underwent forced-titration to retigabine 600 or 900 mg/day (Study 205, RESTORE 2) or 1200 mg/day (Study 205, RESTORE 1) or placebo (t.i.d.) followed by 8 (Study 205) or 12 (RESTORE 1 and 2) weeks' maintenance. Responder rate (≥50% reduction in baseline seizure frequency) in maintenance phase and percent change in 28-day total partial-seizure frequency from baseline to maintenance were assessed in the pooled populations.

Results: Retigabine 600 mg/day (n = 241) and 900 mg/day (n = 223) were compared with placebo (n = 242) in Study 205 and RESTORE 2; retigabine 1200 mg/day (n = 187) was compared with placebo (n = 215) in Study 205 and RESTORE 1. Both responder rate and reduction in total partial-seizure frequency/28-days were significantly greater with all doses of retigabine than placebo. Responder rate: placebo = 21%, 600 mg/day = 35%, $p < 0.001$; 900 mg/day = 45%, $p < 0.001$; placebo = 24%, 1200 mg/day = 50%, $p < 0.001$; median percentage reduction in total partial-seizure frequency/28-days: placebo = 19%, 600 mg/day = 33%, $p = 0.004$; 900 mg/day = 40%, $p < 0.001$; placebo = 21%, 1200 mg/day = 51%, $p < 0.001$. Similar results were seen in the double-blind period.

Conclusion: Retigabine 600–1200 mg/day demonstrated efficacy as adjunctive therapy in adults with refractory partial-onset seizures.

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FIRST EXPERIENCES WITH ZONISAMIDE (ZNS) AS ADJUNCTIVE THERAPY IN REFRACTORY EPILEPTIC CHILDREN AND YOUNG ADULTS

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Purpose: To value efficacy and tolerability of zonisamide as add on therapy in a sample survey about 8 children and young adults with focal or generalized epilepsies.

Method: We retrospectively evaluated 8 epileptic children and young adults unresponsive to politherapy with old and new antiepileptic drugs exposed to ZNS as add on therapy. Neurological and physical examination, seizures type, EEG, serum concentration, CT or MRI were performed.Epileptic syndromes were classified according to I.L.A.E criteria, seizures frequency and adverse events were collected from patients family diary and results of clinical controls.Efficacy was valuated as seizures freedom, reduction >50% (responders), reduction <50% (non responders), unchanged or worsened with or without discontinuation.

Results: Patients received doses of ZSN between 2.5 and 7.5 mg/kg/die; 2 subjects discontinued treatment during the first 3 weeks through adverse events and inefficacy before completing drug titration.Among remaining patients 3 were seizures free and 3 experimented a seizures

reduction >50%.Tiredness and somnolence were more common side effects.

Conclusion: Although our sample is small, pediatric patients seem gain benefit from ZNS administration, according with literature data the drug shows a good efficacy and discrete tolerableness.

p263
A PROSPECTIVE AUDIT OF ADJUNCTIVE ZONISAMIDE IN AN EVERYDAY CLINICAL SETTING

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Purpose: This audit aimed to examine outcomes in patients prescribed zonisamide (ZNS) for various seizure types at a specialist epilepsy service.

Method: Adjuctive ZNS was prescribed for 203 patients (82 men, 121 women, aged 15–80 years [median 39 years]) with uncontrolled seizures following a 3-month retrospective baseline. Titration continued until one of the following end points was reached – seizure freedom for ≥6 months on a stable dose, ≥50% reduction in seizures, or <50% reduction in seizures for ≥6 months (marginal response) on the highest tolerated ZNS dose, or ZNS withdrawal due to adverse effects, lack of efficacy, or both.

Results: Overall, 42 (20.7%) patients remained seizure-free for ≥6 months on an unchanged ZNS dose. A ≥ 50% reduction was achieved in 37 (10.3%) patients. Those with primary generalized seizures (n = 24, 40%) were more likely to become seizure-free, compared to those with partial-onset seizures (n = 18, 12.7%; p = 0.000). Eight patients (5 seizure-free) were maintained on ZNS monotherapy. For patients also taking antiepileptic drugs (AEDs) which did not induce ZNS metabolism, seizure freedom was more likely than for those who also took enzyme inducing agents (p = 0.003). ZNS was discontinued in 72 (35.5%) patients (58 [28.6%] side effects, 11 [5.4%] lack of efficacy, 1 [0.5%] both, 2 [1%] adherence/seizure recording problems). Commonest side effects leading to discontinuation included sedation, nausea and vomiting, depression, rash, weight loss and poor memory. Twelve (5.9%) patients stopped the drug due to neuropsychiatric side effects.

Conclusion: ZNS is a useful broad-spectrum AED with a wide range of recognizable side effects.

p264
ZONISAMIDE IN THE TREATMENT OF DRUG-RESISTANT EPILEPSY: OBSERVATIONAL STUDY IN NORTHEAST ITALY

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Purpose: The aim of the study was to evaluate efficacy and effectiveness of zonisamide (ZNS) when used as an add-on treatment for patients with partial-onset seizure with or without secondary generalization in clinical practice.

Method: We recruited 118 patients (64 males) with cryptogenic (n = 56) or symptomatic (n = 62) drug-resistant partial epilepsy, mean age 45.3 ± 14 years 51 (45%) used another AED, 57 (50.5%) used two AEDs, and 5 (4.5%) used three AEDs beside ZNS. We considered responders the patients whose seizure's frequency decreased more than 50%.

Results: At 3 months, 42% patients were responders; responder rate at 6 and 9 months was 58% and 65%, respectively. The mean dose of ZNS was lower than the suggested therapeutic one; 49 patients (42%) had a dose lower than 300 mg. A significant association ($p < 0.05$) was found between the degree of clinical improvement and the type of epilepsy at 9 months. The cryptogenic epilepsy showed an improvement in 50%, 68% and 77% of patients at 3, 6 and 9 months: these percentages were respectively 33%, 49% and 53% in the symptomatic group. Fourty-one patients (35%) presented side effects. 15 patients (13%) had to discontinue ZNS either for side effects or inefficacy.

Conclusion: In our study ZNS appears to be effective in the treatment of partial epilepsy with or without secondary generalization. 65% of patients achieved at least a 50% reduction in seizure frequency at 9 months. We observed a higher effectiveness in criptogenic epilepsy than in secondary epilepsy.

p265
APPLYING RETROSPECTIVELY THE NEW DEFINITION OF DRUG RESISTANT EPILEPSY TO PATIENTS REFERRED FOR EPILEPSY SURGERY

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Purpose: The aim of this study was to apply retrospectively the new definition of drug resistant epilepsy to patients referred for epilepsy surgery to our Unit (reference center for refractory seizures).

Method: We examined clinical data available in last 40 patients admitted in our Unit. Ten patients had been seen regularly by our epileptologists, and 30 had been referred to us by other neurologists. All of them had been previously diagnosed with drug resistant epilepsy. We tried to verify if these patients met criteria for drug resistance according to new definition recently proposed by ILAE.

Results: 40/46 drug trials in the 10 patients followed up in our Unit were considered as ''informative,'' versus 8/150 in the 30 patients who were referred from other centers. Information available from the referring physicians included number and type of antiepileptic drugs tried, but mode of application, duration of exposure, efforts done to optimize dose and reasons for discontinuation (except severe side effects) were almost always absent; most patients could not provide this information by themselves. A diagnosis of drug resistant epilepsy could be made with appropriate chart review in our 10 patients but only in 3/30 patients referred from other centers.

Conclusion: The new definition proposed by ILAE requires significant information on drug trials to establish with certainty drug resistance. This information is often not provided by referring physicians. General neurologists need to get familiar with the new definition so this information is taken into account to establish drug resistance and refer patients appropriately.

Poster Session: Neurobiology and basic sciences III
Tuesday 29th June 2010
13:30–14:30

p266
STUDY OF THE ROLE OF T-TYPE CALCIUM CHANNELS IN A MOUSE MODEL OF TEMPORAL LOBE EPILEPSY

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Purpose: Recent studies indicate that T-type calcium channels may play a role in the development of temporal lobe epilepsy (TLE) and the associated hippocampal damage (*Becker et al J. Neurosci. 2008, 28:13341–53*). Our goal is to characterize further the implication of T-type calcium channels in TLE using mouse models.

Method: To investigate the role of these channels, we induced status epilepticus (SE) in wild-type (C57BL/6) and Cav3.1 knock-out mice. SE was triggered with an ip injection of pilocarpine (290–300 mg/kg). Sixty minutes later, diazepam (1 mg/kg) was given to control the seizures. Only animals that developed generalized seizures were considered. At 1, 15 and 30 days after SE, mice were sacrificed for the histological analysis of the hippocampus, to compare damage, gliosis and sprouting in both control and KO animals. Neuronal death was assessed on hippocampal sections stained with Cresyl violet, using a grading system described elsewhere (*Groticke et al Exp Neurol. 2007, 207:329–49*). Adjacent sections were immunostained with NeuN, GFAP antibodies, in order to evaluate neuronal death and gliosis in the CA3 area. Cav3 antibodies were used to estimate the expression Cav3.1 and Cav3.2 channels.

Results: Current experiments are in favor of minor alterations between control and Cav3.1 KO mice.

Conclusion: The expression properties of Cav3.1 and Cav3.2 channels in the hippocampus of the pilocarpine-treated mice will be presented and discussed in this poster.

p267
ISOXYLITONES (E/Z ISOMERIC MIXTURE) ATTENUATES CHANGES IN LEVELS OF BDNF AND C-FOS IN VARIOUS REGIONS OF MICE BRAIN UNDERGOING CHEMICAL KINDLING: IMPLICATIONS FOR ANTIEPILEPTOGENIC PROPERTIES

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Purpose: For the development of new drugs for untreatable epilepsy, it is necessary to clarify the basic pathophysiology involved and find the target site. Immediate early genes such as c-fos followed by expression of brain-derived neurotrophic factor (BDNF) have been evidenced as initial important phenomena in the cascade of molecular systems that develop and complement the neuronal excitation to long-term neuronal plasticity. Both have drawn much attention as a potential therapeutic target for epilepsy. In the present study we have focused on the expression of BDNF and c-fos as a target of novel antiepileptic compound isoxylitones (E/Z isomeric mixture) in the model of epileptogenesis.

Method: Kindling was induced by pentylenetetrazole. Levels of mRNAs and protein for BDNF and c-fos were analyzed in brain samples of mice using RT-PCR and Immunohistochemistry.

Results: After generalized grade 5 seizures, induced by chemical kindling, increased expression of BDNF and c-fos mRNA and protein was detected in amygdala, cortex, hippocampus and thalamus compared to normal group. In contrast, the treatment of isoxylitones not only retard the development of epileptogenesis but also exhibited a marked reduction in BDNF and c-fos levels. Furthermore, the test compound was more effective compared to diazepam since it did not produced signs of neuro- or muscular toxicity.

Conclusion: Ppresent data suggests that isoxylitones act at the molecular mechanism to control the seizure pattern, such as the suppression of BDNF and c-fos in various key regions of brain. Further investigations to explore the mechanism of action of this compound is under process.

p268
INTERLEUKIN-1 CHANGES IN EPILEPSY?

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Purpose: Expression of the proinflammatory cytokine interleukin 1beta (IL-1beta) is increased immediately after experimental seizures and epilepsy, especially when these are associated with neuronal injury. However, it is unclear if this expression is causal for the development of epilepsy or merely an epiphenomenon. Therefore, chronic expression of IL-1beta was evaluated in a nonneurodegenerative model.

Method: Rats were amygdala kindled. After reaching the fully kindled state, kindling was continued for 10 days. Forty-eight hours after the last kindling stimulus the animals were sacrificed and perfused with paraformaldehyde. Coronal 10 mm serial sections through the hippocampus were immunohistochemically stained for IL-1beta using two antibodies (one commercial polyclonal goat anti-rat (Santa Cruz Bio., CA, USA) and one monoclonal raised in mice against recombinant rat IL-1beta). IL-1beta immunoreactivity in the hippocampus and cortex was assessed by microscopic inspection of four sections per rat between Bregma levels -2.8 and −3.1.

Results: Twelve rats were kindled according to the above-mentioned protocol while 8 served as sham. The two antibodies gave similar results: no IL-1beta ir cells were found in the hippocampus or cortex, except from the cortex area where the EEG or kindling electrode pierced the dura mater.

Conclusion: IL-1beta is not chronically expressed in a nonneurodegenerative animal model for chronic epilepsy.

p269
HIPPOCAMPAL EXPRESSION AND DISTRIBUTION OF CB1 RECEPTORS IN THE AMAZONIAN RODENT PROECHIMYS: AN ANIMAL MODEL OF RESISTANCE TO EPILEPSY

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Purpose: This study aimed to investigate the distribution and expression of the CB1 receptor in the hippocampal formation of *Proechimys*. An animal considered crucial for the understanding of the mechanisms leading to chronic epilepsy following previous precipitating events.

Method: Immunohistochemistry and Western blotting techniques were performed to evaluate the distribution and expression of CB1 receptors in the hippocampal formation of Proechimys and Wistar rats.

Results: The immunoreactivity for CB1 was evident throughout the Ammon's horn and in the hilar region of both animal species. However, the distribution of these receptors was higher in the *stratum lucidum* of CA3 and in the hilar region of *Proechimys*. In addition, higher expression of CB1 receptors was observed in the *Proechimys* hippocampus.

Conclusion: These data could explain, at least partially, the natural resistance of this animal species to developing spontaneous seizures following epileptogenic precipitating events.

p270
ANTICONVULSANT ACTION OF ADENOSINE A1 RECEPTOR AGONIST CCPA IN IMMATURE RATS

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Purpose: Adenosine was proposed as an endogenous brain anticonvulsant. Agonists of inhibitory A1 adenosine receptors type may therefore be taken as potential antiepileptics.

Method: Two models of epileptic seizures were used. Convulsive seizures were induced by pentetrazol (100 mg/kg s.c.) in 12- and 25-day-old rats pretreated with CCPA in doses from 0.2–2 mg/kg. Cortical epileptic afterdischarges (ADs) were elicited by stimulation of sensorimotor cortex by means of implanted electrodes in 12-, 18- and 25-day-old rats. Stimulation was repeated six times with 10-min intervals, CCPA (0.5 or 1 mg/kg) was injected after the first AD.

Results: CCPA decreased the incidence of the tonic phase and increased latency of generalized seizures in both age groups, more efficiently in younger animals. Latencies of minimal clonic seizures were prolonged in 25-day-old rats. Repeated cortical ADs exhibit progressive prolongation, especially in 12-day-old rats. It was abolished by either dose of CCPA in12-day-old animals. The 18-day-old rats exhibited marked shortening of ADs after both doses. There was no clear anticonvulsant effect in 25-day-old rats. On the contrary, fourth to sixth ADs were longer than in control siblings. If ADs were affected, motor counterpart (clonic seizures) was more suppressed than EEG seizures.

Conclusion: Agonist of adenosine A1 receptors CCPA possesses an anticonvulsant action in both models used. The effects were more marked in younger rats than in 25-day-old ones. As a site of action is concerned, central as well as peripheral (neuromuscular junction) effects must be taken into account especially in suppression of motor seizures.

p271
THE INTERACTION OF MELATONIN AND AGMATINE ON PENTYLENETETRAZOLE-INDUCED CLONIC SEIZURE THRESHOLD IN MICE

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Purpose: Melatonin, the major hormone produced by the pineal gland, has a number of functions in mammals including anticonvulsant effect. Agmatine, a biogenic amine is formed from the decarboxylation of L-arginine has also showed anticonvulsant effect. This study investigated the interaction of melatonin and agmatine on seizure susceptibility in mouse model of pentylenetetrazole (PTZ)-induced clonic seizures. We further investigated the involvement of melatonin receptors in this interaction, using Luzindole, a Mel 1&2 receptors antagonist and prazocin, a Mel 3 receptor antagonist.

Method: The threshold of PTZ was determined by inserting a needle into the tail vein of mice and infusion of PTZ to unrestrained freely moving animals. Infusion was halted when forelimb clonus followed by full clonus of the body was observed.

Results: Melatonin and agmatine exerted anticonvulsant effect with doses as high as 20–80 mg/kg and 10–20 mg/kg respectively. Luzindole at dose of 2.5 mg/kg or prazocin at dose of 0.5 mg/kg did not change seizure threshold compared to saline treated mice. The anticonvulsant effect of melatonin was prevented by luzindole (2.5 mg/kg) but not prazocin (0.5 mg/kg), showing the possible involvement of Mel 1&2 receptors in the anticonvulsive effect of melatonin. Agmatine (5 mg/kg) increased the anticonvulsant effect of melatonin (10–80 mg/kg). Luzindole (2.5 mg/kg) decreased the anticonvulsant effect of agmatine (20 mg/kg). Luzindole (2.5 mg/kg) also decreased the seizure threshold when melatonin (10 mg/kg) administered simultaneous with agmatine (5 mg/kg); this decrease was significant compared to agmatine, melatonin or agmatine+melatonin groups.

Conclusion: Melatonin and agmatine show interactions on modulation of seizure susceptibility probably through Mel 1&2 receptors.

p272
VEGF: A NEW TARGET TO PREVENT BLOOD–BRAIN BARRIER DISRUPTION IN EPILEPSY?

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Purpose: In intractable temporal lobe epilepsy and in the pilocarpine model, we observed that BBB permeability was associated with an aberrant angiogenesis, assessed by an overexpression of vascular endothelial growth factor (VEGF) and its main receptor VEGFR2. Using an integrative in vitro model (organotypic hippocampal cultures: OHCs), we showed that VEGF was induced by seizures in neurons and astrocytes and was responsible for the neo-vascularization of the epileptic focus. In the present study, we investigated the role of VEGF/VEGFR2 signalling pathways in BBB disruption.

Method: Seizures were induced in OHCs by kainate (25 μM). At different time-points, we checked the expression of Zonula Occludens-1 (ZO-1), protein of tight junctions. We evaluated the activation of VEGFR2 and src pathway by measuring their phosphorylation. Then, to precise their roles in tight junction degradation after seizures, we tested the effects of a neutralizing monoclonal anti-VEGF antibody (1 μM) and of a selective inhibitor of Src: PP2 (10 μM).

Results: ZO-1 expression was significantly decreased in OHCs from 4 h to 24 h after seizures. At 4 h after seizures, immunofluorescence and western blot showed an increase of VEGFR2-P in microvessels, concomitant with Src activation. Both anti-VEGF antibody and PP2 inhibited the phosphorylation of VEGFR2 and prevented the degradation of ZO-1. However, VEGF neutralization, had deleterious effect (toxicity) but not Src inhibition.

Conclusion: These results demonstrate that VEGF/VEGFR2 system plays a pivotal role in BBB permeability, specifically via Src pathway. Targeting Src to protect the BBB could provide alternative strategies for intractable epilepsies.

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$GABA_A$-CURRENT RUN-DOWN IN THE HIPPOCAMPUS OCCURS AT THE TIME OF THE FIRST SPONTANEOUS SEIZURE IN THE PILOCARPINE MODEL

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We are previously found that the use-dependent decrease (run-down) of the currents evoked by the repetitive activation of $GABA_A$ receptors (I_{GABA}) is markedly enhanced in hippocampal and cortical neurons of patients affected by refractory temporal lobe epilepsy (TLE). Understanding the role of I_{GABA} run-down in the disease, and its mechanisms, may allow development of medical alternatives to surgical resection. Therefore, we have used an animal model (pilocarpine-treated rats) to identify when and where the increase in I_{GABA} run-down occurs in the natural history of epilepsy. By using voltage-clamp recordings in *Xenopus* oocytes microinjected with membranes isolated from rat brain tissues, we found: 1) that the increased run-down occurs in the hippocampus at the time of the first spontaneous seizure (i.e. when the diagnosis of epilepsy is made), and then extends to the neocortex and remains constant in the course of the disease; 2) that the phenomenon is strictly correlated with the occurrence of spontaneous seizures, because it is not observed in animals that do not become epileptic (resistant animals). Furthermore, initial exploration of the molecular mechanism disclosed a relative increase in alpha4- relative to alpha1-containing $GABA_A$ receptors, occurring at the same time when the increased run-down appears: this suggests that alterations in the molecular composition of GABA receptors may be responsible for the increased run-down. These observations disclose new research opportunities in the field of epileptogenesis that may lead to a better understanding of the mechanism whereby a previously normal tissue becomes epileptic.

p274
VAGUS NERVE STIMULATION-INDUCED ΔFOSB CHANGES IN THE RAT BRAIN STEM

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Purpose: Vagus nerve stimulation (VNS) is an effective treatment for intractable epilepsy, although the mechanism is poorly understood. Therefore, VNS in amygdala-kindled rats was investigated by studying ΔFosB immunostaining in projection nuclei of the vagus nerve.

Method: 31 rats were fully amygdala kindled (AK) after which kindling was continued for 10 days; 8 rats were sham kindled. Of the kindled rats, 8 received a 3-min train of VNS during the kindling stimulus, while 4 received sham VNS. ΔFosB expression was analyzed in the nucleus of the solitary tract (NTS), parabrachial nucleus (PBN) and locus coeruleus (LC).

Results: In VNS rats, the latency of the convulsive seizure increased >200% in 29% and seizure duration decreased >25% in 21%. In VNS rats, the highest ΔFosB-positive cell density was found in the NTS and PBN and right LC. In AK rats, the highest ΔFosB cell density was in the left LC. In VNS rats, NTS ΔFosB ir positively correlated with seizure duration reduction ($r = 0.800$; $p = 0.052$), while LC ΔFosB ir correlated negatively with latency ($r = -0.759$; $p = 0.040$).

Conclusion: VNS reduces seizure severity in fully kindled rats. Activation of the NTS correlates with VNS-induced seizure duration reduction, which suggests that VNS is effective because it activates specific vagal pathways, and not because it causes a random imbalance in the epileptic brain.

p275
STUDY THE EFFECT OF PRENATAL PREDATORY STRESS ON NEONATAL SEIZURES IN RAT

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Purpose: In regard with stress effect on epilepsy, both anticonvulsant and proconvulsant effects have been reported depending on the exact experimental conditions. Psychological stresses in prenatal might alter the brain maturation and precipitated the brain to epilepsy. The aim of present study is to investigate the effect of prenatal predator stress on epileptic behaviors in neonatal stage.

Method: Female rats (200 ± 20 g) were divided in two groups: 1- intact pregnant rats (control group) 2- stressed group. In the stressed group, at day 15 of pregnancy, rats in their cage were exposed to cage of a cat, once per day, 2 h per session for three consecutive days. Pilocarpine (150 mg/kg, s.c) was injected to pups of both groups, at 25th day of age to induce epileptic behaviors. Then, pups were observed for 120 min in order to evaluate the epileptic behaviors.

Results: Mean frequency and duration of partial attacks as well as mean frequency of tonic–clonic attacks in both groups did not show any significant differences. While, the mean duration of general attacks in control was 0.5 ± 0.1 which significantly increased to 16 ± 3.8 in stressed group ($p = 0.001$). Furthermore, mean duration of onset of first epileptic behavior of control group was 5.35 ± 0.57 min which significantly decreased to 3.2 ± 0.24 min in stressed group ($p = 0.005$).

Conclusion: Prenatal predator stress can decrease the threshold for onset of neonatal epileptic behaviors while increase the duration of general tonic–clonic attacks in rat. But, understanding the underlying mechanism requires further investigation.

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ICE/CASPASE 1 INHIBITION REDUCES SPONTANEOUS SEIZURES IN A MOUSE MODEL OF CHRONIC EPILEPSY REFRACTORY TO ANTICONVULSANT DRUGS (AED)

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Purpose: IL-1beta/IL-1R1 axis is activated in human TLE epileptogenic tissue. Acute seizures and kindling are inhibited by VX-765, selective inhibitor of ICE/caspase-1, the key enzyme specifically involved in the production of IL-1beta. We now studied the effect of VX-765 on chronic spontaneous seizures (SS) resistant to AED, using a mouse model of TLE.

Method: SS were induced in C56BL6 mice (n = 10) following status epilepticus (SE) caused by 200 ng kainate intrahippocampally. SS were quantified in epileptic mice, 2 months after SE, by 24 h/day EEG analysis. A stable baseline of SS was established by 2-weeks EEG monitoring, then 200 mg/kg VX-765 was given intraperitoneally, twice daily for 4 consecutive days, followed by a 3-day washout. One group of mice (n = 5) was also treated with 100 mg/kg levetiracetam and 50 mg/kg phenytoin.

Results: VX-765 progressively reduced SS during 4-days treatment. Maximal decrease of 65–75% in seizure number and duration was observed at 3rd and 4th days of treatment, then drug effects faded after 2-days washout. SS were unaffected by levetiracetam or phenytoin. Epileptic mice receiving vehicle (n = 5) showed increased IL-1beta in activated astrocytes in the hippocampus. Mice killed at the time of maximal VX-765 anticonvulsant effect (n = 5) showed no evidence of IL-1beta in activated glia.

Conclusion: A specific inhibitor of ICE/Caspase-1 strongly reduces SS and IL-1beta expression in mice with drug-resistant seizures, thus supporting a key role of ICE/Caspase-1 activation in the mechanisms of SS. ICE/caspase-1 inhibitors may represent a new class of drugs for controlling pharmacoresistant seizures.

doi: 10.1111/j.1528-1167.2010.02658.x

Poster Session: Neurobiology and basic sciences IV
Tuesday 29th June 2010
13:30–14:30

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EFFECTS OF GABAPENTIN, CARBAMAZEPINE, AND CNQX ON COGNITIVE FUNCTIONS AND BEHAVIOR IN RATS WITH PILOCARPINE-INDUCED STATUS EPILEPTICUS

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Purpose: We aimed to investigate the effects of intracerebroventricular (i.c.v.) gabapentin, carbamazepine and CNQX on learning and memory, anxiety, and locomotor activity in rats with pilocarpine-induced status epilepticus (SE).

Method: SE was induced by intraperitoneal injections of 3 mEq/kg LiCl preceeded by 45 mg/kg pilocarpine 24 h later. Three hours after the onset of SE, rats were divided into four groups and received gabapentin (100 μg/10 μl, two times a day; i.c.v.), carbamazepine (200 μg/10 μl; i.c.v.), CNQX (25 nmol/10 μl; i.c.v.) or saline (10 μl; i.c.v.) for 7 days. 6 weeks after SE, cognitive and behavioral performance were evaluated by Morris water maze, elevated plus maze, and open field tests.

Results: SE significantly impaired spatial learning and memory in the Morris water maze, and only gabapentin treatment prevented the deficits in learning but not memory performance. In the elevated plus maze, rats which received saline showed significantly lower anxiety levels, indicated by the increased frequency of entries to the open arms and the increased percentage of the time spent in the open arms with respect to the naive rats. None of the drugs significantly affected the decreased anxiety induced by SE. Locomotor activity and exploratory behavior did not seem to change due to SE, as assessed by the open field test.

Conclusion: Central injections of gabapentin, carbamazepine and CNQX do not have any significant effects on the cognitive and behavioral long term changes induced by SE, except the preventive effect of gabapentin on SE-induced spatial learning deficit.

p278
NEUROPROTECTIVE EFFECTS OF RECOMBINANT HUMAN ERYTHROPOIETIN IN THE DEVELOPING BRAIN OF RAT AFTER LITHIUM-PILOCARPIN INDUCED STATUS EPILEPTICUS

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Purpose: Status epilepticus is a neurological emergency which can lead to selective neuronal loss. Status epilepticus triggers a mixture of apoptotic and necrotic cell death within the hippocampus. This neuronal loss may induce the development of epilepsy and result in cognitive impairments. Erythropoietin mediates a number of biological actions within the central nervous system and has been shown to be neuroprotective. There is a few studies on neuroprotective agents in status epilepticus rat models in childhood. In the present study, we investigated the effects of recombinant human erythropoietin on the developing brain of rat after lithium piocarpin induced status epilepticus.

Method: Dam reared totally 21 Wistar male rats in postnatally 21 day were included in the study. Animals were classified into three subgroups: 1-Control group, 2-Lithium-pilocarpin induced status epilepticus group, 3-Erythropoietin and lithium-pilocarpin induced status epilepticus group. Morphological changes in the hippocampi of rats were examined with respect to neuronal loss and neuronal apoptosis via TUNEL and caspase 3.

Results: Histopathological examination showed that, erythropoietin treatment significantly preserved the number of neurons in the hippocampal CA1, CA2, CA3 and gyrus dentatus regions. The number of TUNEL and caspase-3 positive neurons in the status epilepticus group was higher than the control group. However, apoptotic cell count was found significantly reduced in the erythropoietin treatment group when compared to the status epilepticus group ($p < 0.05$).

Conclusion: Our results suggest that the possible use of erythropoietin in the treatment of status epilepticus may minimize neuronal loss and have neuroprotective effects on developing brain.

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SINGLE NUCLEOTIDE POLYMORPHISMS IN THE SPRAGUE DAWLEY CAMKIID GENE ARE ASSOCIATED WITH INCREASED SEIZURE SUSCEPTIBILITY

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Purpose: Epileptogenesis is associated with high intracellular calcium levels. Conditions associated with high intracellular calcium levels such as stroke or traumatic brain injury, can lead to epilepsy but it is unclear why some cases develop epilepsy while others do not. We aimed to establish if SNPs in a gene that regulates calcium homeostasis, the calcium/calmodulin dependent kinase II (CaMKIId gene), contributes to seizure susceptibility.

Method: 9-day old Sprague Dawley rat pups were subjected to hyperthermia (30 min; 39.5–42°C core temperature). For SNP analysis, genomic DNA was extracted from tail specimens of 26 animals that showed behavioral seizures during hyperthermia (HT+) and 66 animals without seizure behavior during hyperthermia (HT-). The SNP-containing gene fragment was amplified by PCR, followed by restriction fragment length polymorphism analysis.

Results: The T allele was observed in 48% of HT+ rats in contrast to 33% of HT- rats (c^2 (1) = 3.847, p = 0.05). Vice versa, 37% of the animals with a T allele developed seizures after hyperthermia, versus 23% percent of the rats with a G allele (odds ratio 1.9).

Conclusion: SNPs in the Sprague Dawley CaMKIId gene are associated with the susceptibility to seizures. Future studies should demonstrate whether this SNP can clarify the variability seen in other seizure models.

p280
A NEW SEIZURE MODEL OF TLE BY INTRAHIPPOCAMPAL INJECTIONS OF LOW-DOSE KA AND THE EFFECT OF FOCAL DBS

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Purpose: A new seizure model of TLE (temporal lobe epilepsy) in rats was developed that allows the investigation of both focal and secondary

generalized seizures. The effects of DBS (deep brain stimulation) near the focal zone on seizures were subsequently investigated.

Method: Wistar rats (n = 14) were implanted with an electrode-cannula complex in the hippocampus and a tripolar electrode in the contralateral motorcortex. Two weeks later rats were once per 1.5 h injected with KA (kainic acid) (0.1 μg/0.1 μl) for 2 or 3 days with an interval of 48 h. DBS (125 Hz, 100 μs) (n = 5) was delivered to the focal area at a predetermined intensity (100 μA~500 μA) when seizures were visually detected, while no stimulation was delivered in the control group (n = 2).

Results: All rats reached Stage V (Racine's scale) on day 1 and various severities of seizures were obtained (Stage I to V). 71.7% (43/61) of KA injections induced seizures and 51.1% (22/43) of them reached Stage IV or V. Preliminary results showed that the DBS group showed less generalized seizures (2.9 ± 0.8 vs. 4.5 ± 1.8) and longer intervals between seizures (1019 ± 342 vs. 581 ± 233) than the control group, while no effect was observed in seizure duration.

Conclusion: Focal and secondary generalized seizures can be reliably induced by repeatedly injections of low-dose KA into the hippocampus. The application of DBS suggested that DBS modulates temporarily the brain's excitability near the focus rather than disrupting ongoing seizures.

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EFFECTS OF CENTRALLY INJECTED GLUCAGON-LIKE PEPTIDE-1 ON PILOCARPINE-INDUCED SEIZURES, ANXIETY AND LOCOMOTOR AND EXPLORATORY ACTIVITY IN RAT

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Purpose: We aimed to investigate the effects of intracerebroventricularly (i.c.v.)-injected glucagon-like peptide-1 (GLP-1) on pilocarpine induced seizures, anxiety and locomotor and exploratory activity in rat.

Method: Rats were equipped with permanent cannulas for i.c.v. injections and were pretreated with GLP-1 (1–1000 ng/5 μl; i.c.v.) or saline (5 μl; i.c.v.) 30 min before seizure induction by pilocarpine (2.4 mg/5 μl; i.c.v.) and with GLP-1 (1, 10, 100 ng/5 μl; i.c.v.) or saline (5 μl; i.c.v.) 30 min before the open field test or the elevated plus maze test.

Results: GLP-1 did not produce any protective effect against pilocarpine-induced seizures and did not also change the number of squares visited or the number of rearings, compared to the saline-treated rats in the open field test. On the other hand, GLP-1 (1 ng and 10 ng; i.c.v.) induced an anxiogenic effect, indicated by a decrease in the time spent in open arms ($p < 0.05$), an increase in the time spent in closed arms ($p < 0.01$ and $p < 0.05$, respectively), and a decrease in the anxiety scores ($p < 0.01$ and $p < 0.05$, respectively) in the elevated plus maze test. Pretreatment with an arginine vasopressin V_1 receptor antagonist (125 ng/5 μl; i.c.v.) and L-NAME (100 mg/5 μl and 200 mg/5 μl) abolished the anxiogenic effect of GLP-1 (1 ng/5 μl; i.c.v.) ($p < 0.01$).

Conclusion: Centrally-injected GLP-1 produces anxiogenic effects via NO pathway and AVP V_1 receptors, but does not have any effects on pilocarpine-induced seizures or locomotor and exploratory activity in the open field test.

p282
COMPARISON OF FDG-PET FINDINGS BETWEEN GROUP WITH HUMAN UMBILICAL CORD BLOOD DERIVED MESENCHYMAL STEM CELL TRANSPLANTATION AND GROUP WITHOUT IN LITHIUM-PILOCARPINE MODEL OF EPILEPSY

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Purpose: Stem cell transplantations are one of possible treatment modalities in medically intractable epilepsy. The aim of this study was to assess the effects of mesenchymal stem cell (MSC) with FDG-PET in TLE model.

Method: Status epilepticus (SE) was induced in 81 Sprague-Dawley rats with lithium-pilocarpine. FDG-PET was performed at baseline, 1 day, 4 and 8 weeks after SE. Ten weeks after SE, rats were divided into group with MSCs transplantation (n = 8) or group without (n = 19). Group with MSCs transplantation was scanned with FDG-PET at 1, 4, and 8 weeks after transplantation, and group without MSCs transplantation at 18 weeks after baseline. Seizure frequencies and severity were monitored. Changes of glucose metabolism were assessed with voxel based analysis using statistical parametric mapping and voxel of interest analysis.

Results: Group with MSCs transplantation had increased glucose metabolism on cortical areas and basal ganglia at 1 week after transplantation compared to group without. Group with MSCs transplantation at 8 weeks after transplantation had increased glucose metabolism on the hippocampus compared to group without at 18 weeks after baseline. The percentage of injected dose in each ROI decreased in both groups, less decreased in group with MSCs transplantation, compared to that of baseline state. Group with MSCs transplantation had significantly decreased seizure frequencies compared to group without ($p < 0.035$).

Conclusion: MSC transplantation increases glucose metabolism on FDG-PET and reduces seizure frequencies compared to group without.

This study was supported by a grant (09-338) from the Asan Institute for Life Sciences, Seoul, Korea

p283
EFFECT OF 7-NITROINDASOLE A NEURONAL NITRIC OXIDE SYNTHASE INHIBITOR ON CORTICAL EPILEPTIC ACTIVITY IN RATS

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Purpose: Our recent findings show the importance of NO of neuronal origin in the initiation of the seizures in vitro. Available in vivo data show contradictory seizure susceptibility following administration of NOS inhibitors. The present study was designed to investigate the role of NO on neurovascular coupling in response to epileptiform activity after transcallosal electric stimulation in rats.

Method: Adult albino rats (250–350 g, n = 8) were anesthetized with isoflurane and epidural silver EEG electrodes were implanted over sensorimotor cortices. Regional cerebral blood flow during epileptic activity was measured by Laser Doppler flowmetery. We catheterized a common carotid artery to measure arterial blood pressure and arterial blood gasses. After postsurgical recovery animals were placed in a recording chamber. Biphasic constant current suprathreshold stimulus (8 Hz, 15 s) was applied after 15 min recording of background effect of intraperitoneally administered 7-nitroindasole (25 mg/kg).

Results: Results from acute in vivo EEG measuring display controversies. The administration of 7-nitroindasole led to a significant increase of blood pH. Transcallosal electrical stimulation produced cortical epileptic afterdischarges which were paralleled by facial and fore limb clonic seizures. A status similar to catalepsy was observed after the application of 7-nitroindasole.

Conclusion: The in vivo effect of NO is very complex and thus the anticonvulsive action is probably hidden by other systemic NO action.

Increased excitability due to systemic alkalosis seems to be one of the explanations for a lack of anticonvulsive effect in this model. The project was supported by grant from GACR no.P303/010/0999.

p284
THE EFFECTS OF VALPROIC ACID AND OXCARBAZEPINE ON RAT UTERINE IMPLANTATION

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Purpose: To determine the uterine implantation of valproic acid (VPA) and oxcarbazepine (OXC) on rats.

Methods: Twenty-four female Wistar rats were divided equally into four groups, which were given drinking water (controls), 300 mg/kg/day of VPA, 100 mg/kg/day of OXC and VPA + OXC (300 mg/kg/day of VPA and 100 mg/kg/day of OXC) via gavage, for 90 days. Then the female rats were put into the cages of male rats and were mated, and then they were applied daily vaginal smear. The day on which vaginal sperm was found in rats was taken as the 0th day of the implantation. On the 7th day, the uterus was removed with the fetuses. The tissue specimens were assessed immunochemically with laminin, collagen IV and vimentin.

Results: It was found that uterus implantation did not take place in the VPA group. Compared to the control group, it was found in the OXC group and VPA + OXC group that the laminin, collagen IV and vimentin immunoreactions in the trofoblast cells of the embryo and lumen epithelial cells of the uterus have a fairly low staining.

Conclusion: VPA has a serious negative effect on the uterine implantation in rats, while OXC, when used alone, has a mild negative effect; when used with VPA it probably has a protective effect.

p285
THE EFFECT OF A CHEMICAL ABSENCE MODEL ON THE PROGRESSION OF KINDLING IN WISTAR RATS

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Purpose: Thalamo-limbic circuits are thought to regulate limbic seizure activity whereas thalamo-cortical circuits are involved in expression and generation of spike-and-wave discharges (SWDs) in absence epilepsy models. Kindling, a well known model for temporal lobe epilepsies, causes secondary generalized seizures in rats. Recent studies have shown that there is resistance to kindling progress in animal models of genetic absence epilepsy, which relates to SWD activity. Gamma-butyrolactone (GBL) represents a chemical experimental model of generalized absence seizures. Here, we determined whether the resistance to the development of kindling in absence epilepsy can be independent of the genetic background.

Method: Electrodes were stereotaxically implanted into basolateral amygdala. Animals were stimulated 20 min after intraperitoneal administration of GBL at their afterdischarge thresholds twice daily until they reached stage 5 seizure state.

Results: The kindling rate was found significantly slower in GBL injected animals compared with control. Control animals had stage 5 seizures by 15 stimulations. However, GBL injected animals reached stage 5 by 30 stimulations. At first seizure stages 2, 3 and 4, kindling stimulations did not produce a significant change in SWD durations during post stimulation period. However, at the first stage 5 seizure there was a complete loss of SWDs.

Conclusion: Our data show a delay in development of kindling as well as a relation of SWD activity to the kindling progress after GBL administration. The resistance to limbic epilepsy in absence epilepsy rats seems to be partially influenced by absence epilepsy itself and possibly also to have a genetic background.

p286
SEPTO-HIPPOCAMPAL NETWORKS IN CHRONIC EPILEPSY

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Purpose: The elucidation of the pathophysiology of epilepsy requires both the identification of the neurons involved in both the production of epileptic activity and its control. We demonstrated that the medial septum inhibits the appearance of epileptic activity through theta rhythm generation in the pilocarpine model of temporal lobe epilepsy. Since the septal region receives a strong projection from the hippocampus and its neurons are highly vulnerable to epileptic discharges, their functional properties are probably altered by this disorder. In this study we examined the epilepsy-induced functional alterations of lateral and medial septal neurons.

Method: Chronic epileptic rats were anesthetized with urethane and simultaneous extracellular recordings of septal neurons and hippocampal field potentials were performed.

Results: Our results showed that: 1) the firing properties of lateral and medial septal neurons were altered by epilepsy, 2) a subset of lateral septal neurons increased their firing rates before and during hippocampal interictal spikes, 3) the discharges of those lateral septal neurons were well correlated to the hippocampal interictal spikes, 4) medial septal neurons discharges did not correlate with hippocampal epileptic activity. Our work provides strong evidence that both medial and lateral septal regions are functionally altered by the epileptic process and that the medial septum of chronic epileptic rats is functionally disconnected from the hippocampal-parahippocampal epileptic activity.

Conclusion: The elucidation of the roles of altered septo-hippocampal neuronal populations and networks during temporal lobe epilepsy will help to design new and effective interventions dedicated to reduce or suppress epileptic activity.

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BENEFICIAL EFFECTS OF SOMATOSTATIN ANALOGUES AGAINST KAINIC ACID-INDUCED SEIZURES IN THE RAT

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Purpose: The aim of the present study was to investigate the effect of somatostatin and its sst_1-, sst_2- and sst_4-receptor selective agonists CH-275, Octreotide and NNC269100, respectively on hippocampal neuronal alterations brought about by kainic acid (KA)-induced seizures.

Method: Drugs were delivered to anesthetized male Wistar rats through injection cannulas stereotaxically implanted in the CA1-hippocampal

field prior to KA administration. The effects of drugs on animals' motor/epileptic activity were assessed visually while their effects on hippocampal Nissl-staining, GABA-immunoreactivity, and NADPH-diaphorase activity (nitric oxide synthase-marker) were assessed 24 h later and compared to respective controls.

Results: *Saline/KA*-treated animals exhibited tremors, cloning movements and Racine stage V seizures, extensive loss of CA3-field Nissl-staining, ubiquitous decrease of GABA- immunoreactivity and upregulation of CA1-field and Dentate Girus NADPH-diaphorase activity, compared to saline/saline-treated animals. Somatostatin/saline-, CH-275/saline-, Octreotide/saline- and NNC269100/saline-treated animals demonstrated behavior, Nissl-staining and GABA-immunoreactivity similar to that of saline/saline-treated animals, while they exhibited an upregulation of NADPH-diaphorase activity similar to that of saline/KA-treated ones. Somatostatin/KA- and NNC269100/KA-treated animals demonstrated behavior and Nissl-staining similar to that of saline/saline-treated animals, while CH-275/KA- and Octreotide/KA-treated animals similar to that of saline/KA-treated ones. All drug/KA-treated animals exhibited an upregulation of NADPH-diaphorase activity similar to that of drug/saline- and saline/KA-treated animals.

Conclusion: These results confirm previous reports suggesting that somatostatin receptor-selective analogues play an important antiepileptic role and that hippocampus is a critical site of their action. Our data, further suggest the possible involvement of nitric oxide production in the intrinsic neuroprotective mechanisms triggered by KA and somatostatin analogues.

Poster session: Surgical treatment II
Tuesday 29th June 2010
13:30–14:30

p288
COMPARISON OF SELECTIVE TEMPORAL LOBECTOMY BETWEEN CHILDREN AND ADULTS WITH INTRACTABLE TEMPORAL LOBE EPILEPSY

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Purpose: To assess the difference of clinical characteristics and postsurgical outcome between children and adults undergoing temporal lobectomy (TL).

Method: We reviewed the medical records of 52 patients who had undergone TL between 2006 and 2008. Patients were classified as 19 childhood patients (≤18 years old) and 33 adults patients (>18 years old) according to ages when TL had been executed.

Results: Of 52 patients, 12/19 (63.2%) children and 24/33 (72.7%) adults became seizure-free. Rapidly secondary generalization such as generalized tonic or tonic–clonic seizures showed a tendency with more prominent in children (4/19, 22.0%) than adults (3/33, 9.1%). Childhood patients had significantly more multifocal discharges on interictal EEG (31.6%) compared to adults (6.1%, p = 0.014). The mean surgical extent of children and adults was 5.0 cm and 4.1 cm, respectively (p = 0.001). The incidence of hippocampal sclerosis, the most common pathologic finding in the two groups, was 57.9% (11/19) in children and 78.8% (26/33) in adults. Malformations of cortical dysplasia (MCDs) showed significantly more in children (9/19, 47.4%) compared to adults (7/33, 21.2%). Dual pathologies were found in 31.6% of children and in 12.1% of adults.

Conclusion: Patients who had undergone TL during childhood had distinctive interictal EEG findings, resectional extent, and pathologic findings.

p289
THE EFFECTIVENESS OF INTERICTAL EPILEPTIFORM ACTIVITY DURING ELECTROCORTICOGRAPHY AS PREDICTOR OF POSTSURGICAL OUTCOME IN PATIENTS WITH LESIONAL EPILEPSY

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Purpose: The value of electrocorticography (ECOG) regarding outcome of surgery for epilepsy is still controversial. The purpose of our study was to determine whether the presence of spikes following ECOG-guided resection in patients with structural brain lesion can be predictive of successful surgical outcome.

Methods: We conducted a retrospective study on 16 patients with lesional epilepsy who underwent intraoperative ECOG. The recordings were obtained before and after resection. The data from patients with residual interictal epileptiform activity (IEA) and patients without IEA were compared. Data included: gender, age, duration of epilepsy, seizure type, seizure frequency, MRI, PET, routine and video EEG and ECOG. Seizure outcome one year following resection based on the Engel classification was incorporated. The one way ANOVA and Fisher's exact test for independence were used.

Results: Data from 16 patients (M/F = 6/10, age = 27.6 ± 11.3 years) with (n = 10) and without (n = 6) residual epileptiform activity were analyzed. There was no statistically significant difference between the two groups relating to gender, age, seizure frequency prior to surgery, epilepsy duration or number of antiepileptic drugs. In the group of patients whose postoperative ECOG recordings showed IEA, 8/10 (80%) were seizure-free (Engel class I), and 2/10 (20%) had seizure recurrence (Engel class II-IV) one year after surgery. Among the group whose postoperative ECOG recordings showed no IEA, 3/6 (50%) were seizure-free (p = 0.3).

Conclusion: This study indicates that most probably the presence of residual IEA in ECOG does not preclude successful surgical outcome in patients with structural lesions.

p290
REFRACTORY TEMPORAL LOBE EPILEPSY DUE TO GANGLIOGLIOMA ASSOCIATED WITH FOCAL CORTICAL DYSPLASIA

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Purpose: Ganglioglioma (GG) is the most common benign tumor associated with refractory temporal lobe epilepsy (TLE). Coexistence of GG and focal cortical dysplasia (FCD) was repeatedly reported, but there is conflicting evidence concerning frequency and clinical relevance of this association.

Method: From a series of 133 adult TLE patients who underwent temporal lobe resection in the period 1999–2009, all patients with histologically confirmed GG were selected. Demographic, clinical, imaging and electrographic data were analyzed. Histological evidence of associated FCD was evaluated.

Results: GG was histologically confirmed in ten patients (7.5%; M = 5, F = 5; mean age at surgery = 31.1 ± 8.6 [SD]). All GGs were localized in mesial part of temporal lobe, with frequent involvement of amygdala and uncus of parahippocampal gyrus. Hippocampus was affected in three cases. Seizure semeiology and electrographic findings were congruent with this localization. Invasive exploration was not indicated in any patient. Tailored anteromedial temporal lobe resection was performed in all cases, and included hippocampus in three of them. In all but one patient, complete tumor removal was achieved. FCD (type 1) was found adjacent to tumor in eight patients. Follow-up data were available in all cases (mean f-up = 4.3 ± 2.5 year). Nine patients were seizure and aura free at last follow-up. Occasional seizures persisted in one patient with incomplete tumor resection.

Conclusion: In our series GG was frequently associated with FCD. Despite this fact the outcome of epilepsy surgery was excellent in most patients.

p291
PREOPERATIVE DEPRESSION AS A NEGATIVE PROGNOSTIC FACTOR IN EPILEPSY SURGERY FOR MESIAL TEMPORAL LOBE EPILEPSY

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Purpose: To investigate the prognostic value of preoperative depression for seizure outcome after epilepsy surgery in mesial temporal lobe epilepsy (mTLE).

Method: Retrospective data analysis was performed in a sample of 33 consecutive patients, who underwent anterior medial temporal lobectomy or selective amygdala-hippocampectomy for mTLE between 1995 and 2005. MTLE was diagnosed with intensive video-EEG monitoring (analysis of clinical seizure semiology, interictal and ictal EEG), high resolution MRI, and confirmed by pathological analysis of resected tissue. Beck Depression Inventory (BDI) was used preoperatively to detect depression and label patients as ''not-depressed'' (BDI < 11) or ''depressed'' (BDI > 11). Postoperative seizure outcome one year after surgery was classified according to the International League Against Epilepsy (ILAE) outcome classification. ILAE outcome classes were dichotomized into ''aura- and seizure-freedom'' (ILAE class 1) and ''presence of auras and/or seizures'' (ILAE classes 2–6). To compare frequencies of outcome subclasses in patients with and without preoperative depression, Fisher's exact test was applied.

Results: Postoperative outcome significantly differed in patients with and without preoperative depression. While 16 out of 18 (88.9%) patients without preoperative depression were rendered seizure-free after surgery, only 8 out of 15 (53.3%) patients with preoperative depression were completely seizure-free postoperatively (p = 0.047).

Conclusion: Preoperative depression was associated with an unfavorable postoperative seizure outcome. The presence of preoperative depression could be a potential marker for an extended epileptogenic zone indicating the need for an extended preoperative evaluation and/or a tailored resection in these patients.

p292
SEEG-GUIDED THERMOCOAGULATIONS FOR PERIVENTRICULAR NODULAR HETEROTOPIA TREATMENT: A CASE REPORT

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Purpose: Periventricular nodular heterotopia (PNH) is a malformation of cortical development (MCD) characterized by the presence of nodules of normal neurons mislocalized in periventricular white matter due to neuroblast migration abnormality. About 2% of patients with drug-resistant partial epilepsy present nodular heterotopia constituting 20% of MCD cases. Surgical resection after stereo-electro-encephalographic (SEEG) recordings may be proposed for unilateral PNH with good outcome.

Method/results: We report a case of a 19 years old student, who suffered, since age of 10, from drug-resistant partial seizures with frequency of two per week, symptomatic of an unilateral right temporal posterior PNH. Intrinsic epileptogenicity of PNH was demonstrated by SEEG recordings. To avoid the high risk of visual field deficit, SEEG-guided thermocoagulations were used as treatment instead of surgical resection. Five stereotactic thermolesions (three right parietal trajectories) in the PNH were performed. Three years after the procedure, the patient is still seizure-free without neurological deficit and he is studying for an international business master.

Conclusion: Within the framework of this case we report the clinical presentation, the imaging and scalp as well as intracranial EEG aspects of PNH. The different surgical options in treatment of this MCD type are discussed.

p293
COGNITIVE OUTCOME 10 YEARS AFTER TEMPORAL LOBE EPILEPSY SURGERY: A PROSPECTIVE CONTROLLED STUDY

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Purpose: There are few studies of long-term cognitive outcome after temporal lobe resection (TLR) for epilepsy and the results so far are not consistent. The aim of this prospective, longitudinal and controlled study was to explore late effects of TLR on general cognitive level and memory, and to investigate whether the verbal memory deterioration after dominant TLR is residual or progressive over time at group level.

Method: Fifty-one patients who had undergone temporal lobe epilepsy surgery (23 in the speech dominant temporal lobe, DTL; 28 in the non-dominant temporal lobe, NDTL) were assessed preoperatively, 2 and 10 years postoperatively. Twenty-three healthy controls were assessed at baseline and at corresponding intertest intervals. A battery of standardized tests was used for assessment of general cognitive level and memory.

Results: The DTL group showed decline in verbal memory at the 10 year follow-up compared to both the NDTL group and the controls. However, this verbal memory decline was disclosed already 2 years postoperatively, and no further decline occurred from 2 up to 10 years after surgery at group level. The NDTL group showed less improvement in performance IQ at the 10 year follow-up compared to the controls.

Conclusion: In this study the verbal memory decline in DTL patients found 2 years after epilepsy surgery was not progressive up to 10 years at

group level. This information on long-term cognitive outcome is important in the presurgical counselling process.

p294
CORPUS CALLOSOTOMY FOR INTRACTABLE EPILEPSIES IN EARLY CHILDHOOD

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Purpose: To analyze surgical outcome of corpus callosotomy for intractable epilepsies in early childhood.

Method: We indicated callosotomy for children with daily disabling seizures after multiple full-dose antiepileptics and meticulous presurgical evaluation for the possibility of resective surgery by EEG monitoring, MRI, MEG, PET and ictal SPECT. We experienced 34 consecutive cases under 10 years old; 8 month to 9 year (median 5 year 5 month) at the age of surgery from 2001. The etiology was cortical dysplasia in 13 (MRI negative 2), tuberous sclerosis in 2, encephalomalacia in 1, and unknown in 18 (all MRI negative) cases. The major seizure type was drop attacks in 6, nodding spasms in 8, tonic seizures/spasms in 16, and atypical absence in 4 cases. Total callosotomy was performed in 16 cases (47%). Resective surgery was indicated after callosotomy in 4 cases; i.e., 1 hemispherotomy, 1 posterior disconnection, and 2 frontal corticectomy as EEG/MEG findings were localized. Follow-up period was from 4 months to 8 years (median 2 year 10 month).

Result: Engel class I-II outcome was obtained in 7 cases (20.6%) after callosotomy (CSWS 3, multifocal spikes 4) and in 3 cases (8.8%) after additional resective surgery. Twenty-four cases (70.6%) were in class III-IV but 18 cases (52.9%) were free of target seizures. Neither significant morbidity nor mortality was experienced.

Conclusion: Although surgical indication of callosotomy for intractable epilepsies in early childhood is not established yet, a favorable outcome can be obtained in carefully selected cases with unresectable or hidden epileptogenic pathologies after callosotomy.

p295
THE USEFULNESS OF TRACTOGRAPHY INTEGRATED NEURONAVIGATION OBTAINING FROM DIFFUSION TENSOR IMAGE IN PEDIATRIC EPILEPSY SURGERY

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Purpose: Recently, diffusion tensor image and fiber tractography are the chosen method that can demonstrate the orientation and integrity of white matter tracts in vivo. Also, use of neuronavigation system in brain surgery has become more widely used as a means of accurately obtaining the localization of the lesions. The authors report the efficacy of diffusion tensor image (DTI)-neuronavigation (DiNN) for mapping of eloquent areas and identifying of important cortical fibers in pediatric epilepsy surgery.

Method: We performed 9 epilepsy surgeries using DiNN for the patients with intractable seizure where epileptogenic focus to the eloquent area such as motor, vision, or language cortex from November 2008 to October 2009. DTI based color maps were created from the fractional anisotropy values and the three vector elements using StealthViz with StealthDTI Application version 1.2. The vector maps were assigned to red (left-right), green (anterior-posterior), and blue (superior-inferior). Navigation MRI was fused to DTI tractography using a frameless neuronavigation system with mobile emitter.

Results: DTI based color maps were created from the fractional anisotropy values and the three vector elements using StealthViz with StealthDTI Applicaion version 1.2. The vector maps were assigned to red (left-right), green (anterior-posterior), and blue (superior-inferior). Navigation MRI was fused to DTI tractography using a frameless neuronavigation system with mobile emitter.

Conclusion: DTI could be reliably integrated into navigational datasets and FNN could provide more useful information than conventional neuronavigation for maximal safe resection of epileptogenic focus with functional preservation.

Poster session: Neuroimaging II
Tuesday 29th June 2010
13:30–14:30

p296
MR IMAGING AND SPECTROSCOPY IN PATIENTS WITH RASMUSSEN ENCEPHALITIS

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Purpose: The aim is to show main morphologic and neurometabolic features of Rasmussen encephalitis.

Method: Brain MR examination was performed in 4 patients with Rasmussen encephalits. Clinical presentation in two patients was epilepsia partialis continua, while seizures and ataxia were main findins in two patients with the history of measles and varicella in childhood, respectively. The presence of oligoclonal bands in cerebrospinal fluid was found in three patients. Brain MR spectroscopy was performed in two patients.

Results: Infiltration of the frontal lobe was evident in both patients with epilepsia partialis continua, mimicking glial neoplasm. However, detailed evaluation of the images detected mild widening of the surrounding sulci, suggesting chronic inflammatory process, most compatible with Rasmussen encephalitis. The presence of crossed cerebro-cerebellar atrophy was evident in a patient with seizures and a history of measles, while T2W hyperintense infiltration associated with contrast enhancement, most compatible with neoplasm, was present in the left cerebellar hemisphere, in a patient with ataxia. Follow-up examinations showed, apart from mass effect, the development of adjacent cerebellar folia widening. MR spectroscopy revealed marked elevation of choline/creatine ratio compatible with active inflammatory process, associated with significant concentration decrease of neuronal marker N-acetyl aspartate.

Conclusion: Widening of sulci adjacent to the infiltration process appears to be most important factor that helps in discrimination between glial neoplasm and Rasmussen encephalitis.

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DISADVANTAGES OF MR IMAGING IN DETECTION OF DISORDERS WITH CEREBRAL CALCIFICATIONS IN PATIENTS WITH EPILEPSY

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Purpose: The aim is to show disadvantages of MRI in detection of intracerebral calcium depositions.

Methods: MRI was performed on 1.5T MR scanner in three patients with seizures, and the images were correlated with CT study that was performed in one patient before and in two patients after MR examination.

Results: Completely normal appearing brain parenchyma was seen on T2W images in the first patient with while extensive intracerebral calcifications were noted after additionally performed CT of the brain. The diagnosis of pseudohypoparathyroidism was established after further clinical investigation. In the second patient, a child with seizures, marked left parietal cortical calcification was noted on CT, while MRI, including FLAIR and T_2 gradient-echo sequence was inconclusive. In the third patient with seizure attack, triangular nonexpansile lesion was noted on MR examination, most compatible with infarct. However, control MR study 6 months later revealed enlargement of the lesion. CT was immediately performed showing numerous intralesional calcifications, most consistent with oligodendroglioma. The neoplastic infiltration was surgically confirmed.

Conclusion: MRI, without CT, can be not only confusing, but even misleading diagnostic modality for detection of not only subtle, but also extensive cerebral calcifications. The benefit of gradient-echo T_2 sequence, that is usually included in MR protocol when intrcranial calcifications are suspected, is also rather limited.

p298
CONSEQUENCES OF OVERLOOKED PARENCHIMAL CT SIGN OF CEREBRAL VENOUS THROMBOSIS ASSOCIATED WITH EPILEPSY

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Purpose: To emphasize the connection between the seizures and cerebral venous thrombosis and to present the consequences of overlooked indirect CT sign of this disorder on CT examination.

Methods: Brain CT was ordered in an afebrile patient with neck pain and occipital headache.

Results: Since no abnormalities were noted on noncontrast CT study, the patient was discharged. However, the next day he developed myoclonic seizure compatible with focal motor status epilepticus. Another status epilepticus appeared within the MR scanner and the exam was discontinued. Imaging study, performed 2 days later revealed huge hemorrhagic venous infarct in the left cerebral hemisphere associated with extensive venous thrombosis. The presence of subtle curvilinear hyperdensity was detected in the left parietal cortical-subcortical border during the reevaluation of initial brain CT, most compatible with developing venous infarct. Lethal outcome appeared 11 days after initial CT scanning.

Conclusion: Detection of early parenchimal signs of cerebral venous thrombosis is extremely important, especially in patients with unclear direct signs of this disorder, since the delay of adequate treatment may have catastrophic consequences. Education of both radiology and neurology residents to detect both direct and indirect signs of cerebral venous thrombosis, is extremely needed in decreasing the rate of fatal outcome.

p299
FUNCTIONAL INTEGRITY OF POLYMICROGYRIA: AN FMRI STUDY

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Purpose: Functional reorganization of cerebral cortex occurs in subjects with polymicrogyria (PMG). We aimed to assess functional integrity of PMG in motor neural network in patients with epilepsy and PMG by use of fMRI.

Method: Fifteen patients (8 week/7 month) aged 17–76 years (mean 41.2) with PMG and epilepsy were selected at the Department of Neurology and Neurosurgery, Medical University Innsbruck, Austria. All subjects underwent MRI (1.5-T) and fMRI. PMG identified on MRI involved primary motor cortex (M1) in all cases. Single-subject fMRI image analysis was performed with statistical parametric mapping (SPM2).Simple motor tasks: tongue side-to-side movement, lip pursing, finger-to-thumb opposition and toe flexing were used for testing motor neural network. All subjects had been seizure-free for at least 48 h prior to fMRI study.

Results: Seven patients had unilateral PMG, eight – bilateral. In seven patients PMG was perisylvian; six had frontal PMG; one – fronto-parietal and one – temporal PMG.Eight patients (53%) had pharmacoresistant epilepsy. Mean age at seizure onset was 16 years (SD10.8); mean duration of epilepsy at the time of fMRI was 24.6 years (SD 17.5).PMG was activated in 13/15 (87%); activation was shifted from PMG in 2/15 cases. Neither shift of function from affected M1 nor its activation were influenced by age at seizure onset, epilepsy duration or seizure outcome.Ten patients (66%) had bilateral activation of cortices (either unaffected or dysplastic) irrespective of laterality of PMG.

Conclusion: Simple motor task fMRI suggests functional integration of PMG in motor neural network in the majority of cases.

p300
PREDICTIVE FACTORS OF ICTAL SPECT FINDINGS IN PEDIATRIC PATIENTS WITH FOCAL CORTICAL DYSPLASIA

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Purpose: Ictal SPECT could localize the seizure onset zone in patients with focal cortical dysplasia (FCD) and intractable epilepsy. Our goal was to verify a hypothesis that times of the radionuclide administration, durations and types of injected seizures predict ictal SPECT findings in pediatric FCD cases and eventually influence performing successful epilepsy surgery.

Method: We visually evaluated 42 ictal SPECT studies in 39 surgically treated children with FCD. SPECT findings were classified as ''nonlocalized,'' ''focal'' and ''extensive'' (multilobar or hemispheric) and compared with injection times, types and durations of injected seizures. The extent of the hyperperfusion zone resection was classified as ''completely resected,'' ''partially resected'' and ''nonresected'' and correlated with seizure outcome. Outcomes were regarded as ''favorable'' in patients with ≥90% and ''unfavorable'' in subjects with <90% seizure reduction.

Results: Eight of ten nonlocalized ictal SPECT studies were injected in simplex partial seizures. Patients with focal hyperperfusion zones (N = 16) had shorter mean duration of seizures (52 s) and injection time (23 s) than subjects with extensive hyperperfusions (N = 16, 88 and 42 s, respectively). The hyperperfusion zone was nonresected in four, partially resected in ten and completely resected in 18 localized ictal SPECT studies. Favorable seizure outcome was achieved in 50% of patients with nonlocalized, 25% with nonresected, 50% with partially resected and in 83% with completely resected ictal hyperperfusions.

Conclusion: Injection times, durations and types of injected seizures significantly influence ictal SPECT findings and may affect surgical planning in FCD patients.

Supported by Grant MZOFNM2005 and Kontakt Programme ME09042.

p301
NEAR-INFRARED SPECTROSCOPY AS A TOOL FOR STUDYING REFRACTORY

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Purpose: Near-infrared spectroscopy (NIRS) is a novel noninvasive imaging technique, which we have successfully used to lateralize language in epileptic children and adults. Using continuous multichannel NIRS-EEG monitoring in a young patient with refractory frontal lobe epilepsy, we have also successfully identified his epileptic focus. The purpose of this study was to study a greater number of patients to further assess NIRS' potential in the study of epilepsy.

Method: Simultaneous NIRS-EEG recordings were carried out in 27 patients (age 8–56 years, 18 male/9 female) with refractory partial epilepsy. The patients underwent prolonged EEG-NIRS recording using 19 EEG electrodes combined with 43 to 200 NIRS channels (ISS, USA) in order to record spontaneous seizures. Results were compared to the reference standard, i.e., the epileptogenic zone as determined by the multimodal analysis of ictal EEG (27/27), ictal SPECT (25/27), interictal PET (26/27), EEG-fMRI (26/27), MEG (25/27) and intracranial EEG recordings (12/27).

Results: During simultaneous EEG-NIRS recording, electrical and/or electroclinical seizures were recorded in 20 patients. Although seizure symptomatology differed across patients, all seizures were associated with hemodynamic changes maximum over a specific area. The most common pattern noted was an increase of rCBV, HbT and HbO. The areas of maximal hemodynamic changes were in good concordance with the reference standard in all patients except for one with seizures originating from the left anterior cingulate gyrus.

Discussion: This study suggests that continuous NIRS-EEG is feasible with the potential to regionalize the epileptogenic zone in epilepsy surgery candidates. Further evaluations are needed.

p302
DISRUPTIONS OF THE DEFAULT MODE NETWORK IN PATIENTS WITH PRIMARY GENERALIZED EPILEPSY

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Purpose: Active areas of the brain during periods of rest have only recently been designated the ''default mode network'' (DMN), which is comprized of the posterior cingulate cortex, prefrontal cortex, inferior parietal cortex and precuneus. Disruptions in this network characterized by BOLD signaling in fMRI have been noted in several disorders including Alzheimer's, schizophrenia, attention deficit disorder, and temporal lobe epilepsy. Given prior evidence for wide-spread cortical network abnormalities in patients with primary generalized epilepsy (PGE), we hypothesize that PGEs will demonstrate disrupted patterns of activation in resting state DMN during interictal periods.

Method: We obtained resting-state scans from 10 PGE patients and 56 controls using a Siemens 3.0-Tesla scanner. Each scan consisted of 197 contiguous EPI functional volumes (TR = 2000 ms; TE = 25 ms; 39 slices; acquisition voxel size = 3 × 3 × 3 mm). Data processing was done using FMRIB Software Library (FSL). Regions of interest were designated in the areas noted above and a correlation analysis of the low frequency oscillations (LFO) was performed to identify functional connectivity. Group averages of both extent and degree of correlation were compared.

Results: Resting state analysis of LFO correlation between areas of the DMN showed disruption in PGE patients. Interrupted connectivity between the PCC and PFC was seen in the PGE patients when compared to normal controls.

Conclusion: Our findings show functional resting state differences in the default mode network in PGE patients during interictal states, which may have implications for cognition or seizure initiation and spread in this group of patients.

p303
QUANTIFICATION OF OPIOID RECEPTOR FOLLOWING SPONTANEOUS EPILEPTIC SEIZURES; CORRECTION OF [^{11}C]DIPRENORPHINE PET DATA FOR THE PARTIAL-VOLUME EFFECT

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Purpose: Endogenous opioid peptides have been suggested to have anticonvulsant properties, hence the interest in positron emission tomography (PET) imaging of opioid neurotransmission in epilepsy. Previous studies with PET and with [^{11}C]diprenorphine ([^{11}C]DPN), however, have not corrected for the ''partial-volume'' effect (PVE), a confound that results from the limited resolution of the PET system. Here, the relationship between opioid receptor binding and seizures in refractory temporal lobe epilepsy (TLE) was accurately characterized using a novel PVE correction method.

Method: Eight denoised postictal/interictal (TLE), and seven test/retest (control) volume-of-distribution (VD) data sets were processed using SFS-RR (Shidahara M et al. Neuroimage 2009:44(2):340–348.). Anatomical information was obtained from 1.5T T_1-weighted MRI, which was anatomically segmented by multiatlas label propagation and decision fusion (Heckemann R et al. Neuroimage, 2006:33(1):115–26.

Results: Novel findings included postictal increases (ANOVA, $p = 0.019$) in [^{11}C]DPN VD in the ipsilateral parahippocampal gyrus (most evident in patients with hippocampal sclerosis; HS), and also bilaterally in the fusiform gyri ($p = 0.004$). Patients whose TLE was associated with HS also had a bilateral increase ($p = 0.018$) in [^{11}C]DPN VD in the pre–subgenual anterior cingulate (most evident interictally), relative to MRI-normal patients and controls.

Conclusion: This study provides direct human in vivo evidence for interictal and postictal alterations of opioid receptor availability in TLE. Patients whose TLE is associated with HS may have distinctive opioid neurotransmission derangements. Resolution recovery and precise anatomical segmentation can extract valuable information from PET studies that would be missed with conventional postprocessing procedures.

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ANATOMICAL ACCURACY AND FEASIBILITY OF PROBABILISTIC AND DETERMINISTIC TRACTOGRAPHY OF THE OPTIC RADIATION

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Purpose: Tractography (TG) of the optic radiation prior to temporal lobe resection (TLR) can predict the risk for a postoperative visual field defect. We aimed to determine the anatomical accuracy and feasibility of deterministic and probabilistic TG of the optic radiation.

Methods: Diffusion tensor imaging data from 11 controls and 7 patients (23 exams) were analyzed using a deterministic approach (Extended Work Station, Philips) and a probabilistic approach (FMRIB FSL-FDT v4.1). Distance from the tip of the temporal lobe to the anterior limit of Meyer's loop (TP-ML) was measured and compared using a paired t-test. TP-ML distances were compared to previous dissection studies.

Results: Mean TP-ML was 41 mm (range 32–51) for the deterministic TG and 30 mm (range 17–42) for the probabilistic TG, ($p < 0.001$). Deterministic TG found Meyer's loop (ML) to be a mean of 14 mm (range 8–21 mm) posterior to the tip of the temporal horn, whereas probabilistic TG found ML to be 2 mm (range (-10–15)) posterior to the tip of the temporal horn. Processing time for deterministic TG was 40 min and for probabilistic TG 520 min.

Conclusions: A considerable variability in the location of Meyer's loop was found, consistent with anatomical studies. Deterministic TG found Meyer's loop to be 12 mm more posterior than probabilistic TG and the latter showed better correlation to TP-ML distances reported in anatomical studies. Probabilistic TG is preferable over deterministic TG for localization of the optic radiation if processing time is not limited.

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COMPLEMENTARY USE OF GRADIENT MAGNETIC-FIELD TOPOGRAPHY (GMFT) AND EQUIVALENT CURRENT DIPOLE (ECD) FOR MAGNETOENCEPHALOGRAPHY IN PRESURGICAL EVALUATION OF INTRACTABLE NEOCORTICAL EPILEPSY

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Objective: We developed gradient magnetic-field topography (GMFT) for magnetoencephalography (MEG) to visualize the dynamic changes of gradient magnetic field of interictal epileptic discharges on the brain surface (Hashizume A, et al, 2007). This study is to elucidate whether GMFT complements equivalent current dipole (ECD) analysis for presurgical evaluation in patients with neocortical epilepsy.

Methods: We retrospectively analyzed MEG data in 10 patients who underwent resective surgery based on intracranial video-EEG (IVEEG). MEG was performed with Neuromag System (whole-head type, 306 channels, Elekta-Neuromag) including 204 channels of planar gradiometers. We selected the activating area of GMFT during the periods between start and peak of each interictal spikes as epileptic area. We compared the epileptic area on GMFT, distributions of ECD, and results of IVEEG.

Results: Eight patients had single cluster of ECDs. The clustered ECDs and IVEEG showed colocalized interictal spikes to demarcate the epileptogenic zone, which was concordant with the epileptic area on GMFT in all 8 patients. Two had scattered ECDs over the right frontoparieto-temporal and the right frontotemopral regions, respectively. A part of the scattered ECDs was colocalized to epileptogenic zone based on IVEEG. The GMFT of each spikes representing the scattered ECDs showed the overlapped epileptic area, concordant with the IVEEG in these 2 patients. Eight patients had excellent seizure outcome (Engel class I) and two had a greater than 90% seizure reduction (Engel class II).

Conclusion: GMFT may complement ECD analysis for preoperative evaluation particularly in patients with scattered ECD, difficult to demarcate epileptogenic zone.

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DIFFUSION TENSOR IMAGING WITH TRACT-BASED SPATIAL STATISTICS REVEALS WIDESPREAD WHITE MATTER DEGENERATION IN UNVERRICHT-LUNDBORG DISEASE (EPM1): TRANSLATIONAL STUDY IN HUMANS AND *CSTB*-DEFICIENT MICE

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Purpose: Unverricht-Lundborg disease (EPM1) is progressive myoclonus epilepsy caused by mutations in the *Cystatin B* gene. Cortical motor areas are affected, but white matter (WM) tracts have not been evaluated. Aims were 1) to characterize the WM changes in fractional anisotropy (FA) and directional diffusivity in patients, 2) to evaluate the congruence of changes between *Cystatin B*-deficient (*Cstb-/-)* mice and patients, and 3) to compare imaging data with histopathology.

Method: After diffusion tensor imaging (DTI) (1.5T, Siemens Avanto) voxelwise analysis with tract-based spatial statistics (TBSS, cluster-level inference at $t > 2.2$, $p < 0.05$) was used to compare FA, axial, radial and mean diffusion (AD, RD and MD) among 19 patients and 18 controls. Paraformaldehyde (4%) perfused brains from nine 6-months old *Cstb-/-* mice and 4 wild type controls were imaged at 9.4T MRI (Varian, DirectDrive) ex vivo and analyzed with TBSS. Brain slices from ten 6-months old animals (*Cstb-/-* n = 5, *Cstb+/+* n = 5) were stained with rat anti-myelin basic protein.

Results: TBSS revealed significantly reduced FA in all major WM tracts in patients compared with controls. There was no change in AD, but RD and MD were increased. In *Cstb-/-* mice, FA was significantly reduced in cerebellum, corpus callosum, external capsule and several thalamic nuclei. Immunostaining showed myelin loss in *Cstb-/-* mice in areas highlighted by TBSS.

Conclusion: We found a pattern of chronic WM degeneration in EPM1 patients and similar alterations in *Cstb*-deficient mice, providing further validation of this animal model. Immunohistochemistry indicated that myelin loss contributes to the decreased FA.

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PREOPERATIVE AND POSTOPERATIVE EVALUATION OF WHITE MATTER TRACTS IN PATIENTS WITH REFRACTORY TEMPORAL LOBE EPILEPSY

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Purpose: Patients with refractory temporal lobe epilepsy frequently need to be surgically treated. Traditional MRI usually depicts only structural abnormalities. Advanced MR imaging techniques (fractional anisotropy – DTI) may contribute in the preoperative identification of white matter tracts in the temporal lobes as well as possible secondary structural damage of subcortical fibers. Identification of white matter tracts preoperatively may contribute in the more accurate treatment planning.

Method: In our prospective clinical study, 15 patients (10 M/5 F) that have been operated during a 39 month period were included. Their ages ranged between 17 and 60 years (mean age 24.5 years). Preoperative evaluation included routine brain MRI, DTI, EEG, and interventional EEG in 2/15 (13,33%) patients. All MRIs were performed on a 3Tesla MRI scanner (HDxD, GE medical systems, USA). DTI imaging was performed using single shot EPI with 32 direction and was used to assess tract integrity of the cingulum, corus callosum, medial and inferior longitudinal fasciculi and the occipitofrontal fasciculus. All patients underwent temporal lobectomy and amygdalohippocampectomy.

Results: 12 patients (80%) underwent right temporal lobectomy and 3 (20%) left. 12 patients (80%) remained seizure-free one year after surgery (Engel class I), while 1/15 (6.66%) was Engel class II and 2 patients (13,33%) class III. Preoperative DTI modified the surgical planning in 4/15 (26.66%) patients.

Conclusion: DTI may contribute in the safer surgical planning of patients with refractory temporal lobe epilepsy. Further studies need to be done to estimate and establish functional maps and anatomic variations of white matter tracts.

Poster session: alternative therapies and epilepsy in the elderly
Tuesday 29th June 2010
13:30–14:30

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IMMUNOMODULATING THERAPIES IN REFRACTORY PARTIAL EPILEPSIES IN CHILDREN WITHOUT CLINICAL AND LABORATORY EVIDENCE OF INFLAMMATION

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Purpose: Estimation of immunomodulating therapies effect on refractory partial seizures in children without evidence of inflammation.

Method: A prospective open observational uncontrolled study was performed in 49 children with refractory symptomatic and cryptogenic partial epilepsies. The age ranged from 4 to 16 years (10.0 ± 4.8), seizure frequency – from 30 to 200 seizures daily (86.5 ± 15.4). 21 patient (43%) had neurological deficit, 25 (51%) were mentally retarded, 42 (86%) had MRI abnormalities (33 – brain malformations, 9 – neonatal stroke outcome). All patients had no clinical signs of inflammation or immunopathologic condition and blood and spinal fluid analyses were normal. 37 patients received prednisolone 0.5–1 mg/kg/day for 1 week and in case of good response the treatment (0.2–0.5 mg/kg/day) was prolonged for 1–6 month. 12 patient received plasmopheresis (4–6 procedures for total plasma exchange). The follow-up lasted 1–8 years (2,5 ± 1,3).

Results: After prednisolone treatment 2–6 months seizure-free period was achieved in 29 patients (78%), ≥50% reduction of seizure frequency – in 2 patients (5%). no effect – in 4 patients (11%). Long-term remission (2 and 5 years) was observed in 2 cases after prednisolone treatment. Plasmopheresis resulted in 2–8 months seizure-free period in 7 patients, ≥50% reduction of seizure frequency in 3 patients, no effect – in 1 patient; 6 year remission with subsequent AEDs withdrawal – in 1 patient.

Conclusion: Reduction of immunopathologic sequences of seizures results in reduction of seizure frequency or seizure-free period. In case of primary immunopathologic changes immunomodulation help to achieve a long-term remission.

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EVALUATION OF AN EDUCATIONAL PROGRAM FOR PATIENTS WITH EPILEPSY

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Purpose: To evaluate the effectiveness of a patient educational programme, in terms of knowledge acquisition and impact on quality-of-life, in adult patients with epilepsy.

Method: Patients with epilepsy, aged ≥18 years, recruited from 10 French neurology centers, underwent an educational programme conducted by specially trained healthcare workers. The programme, consisting of two individual meetings and three group sessions, was conducted over 1.5–2 months and focussed on educating patients about their disease and treatment, what to do/not do in a crisis, the implementation of support strategies, and reaction/adaptation to difficult situations. The primary measure was level of knowledge/understanding (defined as percentage of correct answers to a questionnaire) before (T0) and after (T1) completing the programme, and 3 months later (T2). The programme's impact on patients' quality-of-life was also evaluated, using the Quality-of-Life in Epilepsy-31 (QOLIE-31) questionnaire.

Results: Of the 73 patients enrolled (63% female, mean age 37 years), 60 (82.2%) were followed at T1 and 58 (79.5%) at T2. Level of knowledge/understanding increased significantly from 75.0% at T0 to 76.3% at T1 ($p = 0.0398$) and this level was maintained (78.0%) at T2 ($p = 0.0577$, T0 vs. T2). There were also significant improvements from T0 to T1 in global QOLIE ($p = 0.0467$), energy/fatigue ($p = 0.0264$) and social functioning ($p = 0.0159$) scores, but these were not maintained at T2.

Conclusion: Patients' knowledge/understanding of their disease significantly improved after participating in this educational programme, as did certain aspects of their quality-of-life. These findings may support the wider use of educational programmes.

This study was supported by Eisai.

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LONG-TERM OUTCOME OF VAGUS NERVE STIMULATION (VNS) IN CHILDREN WITH DRAVET SYNDROME (DS)

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Background: Although efficacy has been reported with various antiepileptic drugs (AEDs) and the ketogenic diet (KD), treatment is unsatisfactory and/or associated with unacceptable side effects in most patients with DS.

Purpose: To demonstrate the value of VNS – measured by reduction in seizure frequency, developmental progress and behavioral improvement – in patients with drug-resistant DS.

Method: We analyzed retrospectively changes in seizure frequency (patients diaries, Wieser criteria) and severity (Hague Seizure Severity Scale), deveopmental progress (neuropsychological testing, Child Behaviour Checklist/CBCL) and quality of life (Quality-of-Life in Childhood Epilepsy questionnaire).

Results: Nine children (3 female) with DS (proven clinically and by molecular genetics) were implanted at our centre. Mean age at implantation was 9 years (5–13 years), and mean follow-up after implantation was 5 years (3–9 years). Total seizure reduction was 65% (61% for generalized tonic–clonic seizures, 40% for myoclonic seizures). 1 patient became seizure-free. No patient showed increased seizure frequency. Parents reported significantly shorter duration of seizures and recovery phase. AEDs were reduced from an average of 2.7 to 1.5 per patient. Seizure reduction correlated with improvement in total quality-of-life, significant improvements were also detected in the social domain. There were no significant changes in cognitive functioning, but improvement over time regarding behavior and mood.

Complications included infection in 1 patient, and lead fracture in another. Side effects were mild and tended to diminish over time.

Conclusion: VNS seems to be a favorable and safe treatment option for children with DS.

Financially supported by the Anniversary Fund of the Central Bank of the Republic of Austria/ÖNB-12036.

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MODULATION OF SEIZURE SUSCEPTIBILITY BY SPINAL CORD STIMULATION

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Purpose: Stimulation of the anterior thalamus is currently evaluated as a clinical treatment for refractory epilepsy. An alternative nonintracranial way to stimulate the thalamus may be to stimulate the dorsal spinal cord (SCS), which projects to the ventral posterolateral thalamic nucleus. We have therefore investigated if SCS can modulate seizure susceptibility.

Method: Rats were divided in 3 SCS treatment groups: no treatment (NT, n = 8), low frequency (4 Hz) treatment (LFT, n = 6) and medium high frequency (54 Hz) treatment (MHFT, n = 8). In acute experiments and during anesthesia, tonic seizures were induced in the rats by 10 min intravenous infusion of pentylenetetrazole (PTZ, 5 mg/kg/min). SCS was started 5 min prior to, and continued during PTZ infusion. The time between PTZ-infusion start and the onset of tonic seizures was defined as the seizure onset latency (SOL) and used as a measure of seizure susceptibility.

Results: SOL was 289 ± 13 s, 169 ± 24 s and 317 ± 15 s (average±SE) for NT, LFT and MHFT groups, respectively. LFT significantly decreased SOL as compared to NT. In contrast, SOL increased in the MHFT group, but this change did not reach the significance level.

Conclusion: Although MHFT did not significantly reduce seizure susceptibility, our results show the same tendency as anterior thalamus stimulation since low and high frequency thalamic stimulation induces proconvulsant and anticonvulsant effects, respectively. Thus, seizure susceptibility can be modulated via SCS but further research is needed for optimizing stimulation parameters for decreasing seizure susceptibility.

Acknowledgments: This work was supported by the Danish National Advanced Technology Foundation and Neurodan A/S.

p312
TOWARD AN EASIER AND SAFER KETOGENIC DIET

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Purpose: The ketogenic diet (Johns Hopkins Hospital protocol) was introduced in 1996. The high ketogenic ratios (ratio of fats to protein + carbohydrate) used and the high plasma lipid levels often encountered were problematic. Our aim was to try lower ratios and normalize lipids.

Method: 141 patients with uncontrolled epilepsy (ages 5 months to 57 years) were put on the ketogenic diet. 57 patients were put on 3:1 or higher ratio and 84 patients were on lower ratios. The ratio used was the lowest required to maintain a stable urine ketosis of 4+. The lipid levels cholesterol, LDL, and triglycerides) were found to be high in those who were using solely or mainly saturated fats. We then changed them to a mixture of fats, namely, SFA: MUFA: PUFA in a ratio of 1:2:1.

Results: The high ketogenic ratios usually used (3:1–4:1) were not found to be necessary in all. Patients achieved as good seizure control with varying ratios. There was no significant difference in the seizure reduction in each ratio group. Seizure control of patients was also independent of age at starting diet, variation of calorie intake from the recommended 75% of RDA and variation of their initial weight from their Ideal Body Weight. The lipid levels remained within the normal ranges on a mixed fat KD.

Conclusion: Lower ketogenic ratios are as effective as higher ratios. Lower ratio diets are more palatable. Lipid levels can be maintained normal giving mixed fats.

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SUSTAINED EFFICACY AND TOLERABILITY OF VAGUS NERVE STIMULATION IN EPILEPSY: A 14-YEAR EXPERIENCE IN ITALIAN TERTIARY-CARE EPILEPSY CENTER

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Purpose: Vagus Nerve Stimulation (VNS) is indicated in the treatment of pharmacoresistant epilepsy. Albeit its general efficacy, the use of VNS remains undefined concerning two critical points: 1) there are only a few long-term studies; 2) there are no clinical markers, so far, which allow to predict in which cases VNS might produce the best efficacy. In order to explore these points, we report the long-term outcomes of VNS in 28 patients.

Method: Patients (20 M and 8 F, mean age 47.1 + 2.6) were implanted with VNS in the period 1995–2009. The follow up lasted up to 14 years (mean 4.7 + 0.8). Twenty-five patients showed symptomatic/cryptogenic partial epilepsy, while three subjects showed symptomatic generalized epilepsy.

Results: No significant adverse events were observed. VNS efficacy was enduring and increased significantly over time. Seizure frequency decreased by 32.5 + 3.8% after 1 year, 41.8 + 4.1% after 2 years,

47.2 + 4.6% after 3 years and 44.2%+5.1 at maximum follow up. A significant number of patients became responder between 2 and 3 years after VNS activation showing a delayed response. Seizures in symptomatic generalized epilepsy were reduced by more than 70% while more than 50% of patients with partial epilepsy responded at the longest follow up.

Conclusions: VNS is an effective and safe long-term therapy. VNS treatment has to be prolonged at least for 3 years before ruling out its efficacy. Among epileptic syndromes, generalized symptomatic and temporal lobe epilepsy seem to be associated to a better outcome to VNS, but additional data are required.

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LONG-TERM COGNITIVE OUTCOME AFTER BILATERAL CHRONIC STIMULATION OF ANTERIOR THALAMIC NUCLEUS IN PATIENTS WITH INTRACTABLE EPILEPSY

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Purpose: It is unknown over the cognitive and behavioral effects after deep brain stimulation (DBS) on the deep cerebral nuclei for epilepsy treatment. We investigated the cognitive outcome at least 6 months after DBS on bilateral anterior thalamic nucleus (ATN) for controlling intractable epilepsy.

Method: Nine, intractable epilepsy patients who are not candidates for resective surgery treated by bilateral ATN DBS underwent cognitive and behavioral assessments before implantation and around 1 year after DBS surgery. Postoperative cognitive assessments were carried out under continuous stimulation mode.

Results: Mean seizure reduction rate of our patients after ATN DBS was 71.8% (28.5~99.3%). There was a favorable results on verbal fluency tasks (letter and category, $p < 0.05$) and a significant improvement on immediate and delayed verbal memory ($p = 0.017$). But, there were no significant changes in general abilities (IQ, MMSE), information processing (digit forward & backward, trail-A, and digit symbol) or executive function (train-B and WCST). Interestingly, we could not observe any significant cognitive decline during ATN DBS for around 1 year (mean, 15.8 months). Also, no patient developed acute or severe cognitive decline after surgery.

Conclusion: Our findings showed that ATN DBS resulted in not only an excellant clinical efficacy but additional improvement of both a verbal recall and oral information processing, which may be related to the bilateral activation of fronto-limbic circuit following DBS surgery. Further controlled, long-term studies with larger population for elucidating clinical effects of ATN DBS should be warranted.

p315
ACUTE DRUG ADMINISTRATION AS PART OF TREATMENT STRATEGIES FOR EPILEPSY

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Ad hoc administration of Benzodiazepines (BZD) is well-established in status epilepticus, but intermittent BZD use in chronic epilepsy treatment is little known beyond catamenial epilepsy.

Material and methods: In 24 patients with epilepsy (IGE 9, focal symptomatic/cryptogenic 14, migraine-epilepsy 1) acute drug administration (ADA) was used for

1. Intervention at prodrome or aura,
2. Prevention of seizures at perceived risk, or
3. Prevention of clusters of seizures.

The standard ADA was 10 mg oral Clobazam; one patient received 10 mg rectal Diazepam. Concomitant antiepileptic drugs (AEDs) remained unchanged whenever possible. 10 patients used ADA always correctly, 7 mostly correctly, 7 sporadically or not at all.

Results: The outcome was positive in 44% of all patients (59% of those who actually used ADA): 5 patients seizure-free, 1 free of disabling seizures, 4 with >50% reduction in seizure frequency. 11 had only minor or no improvement, 3 patients could not be rated. 13 (of 19 possible) patients attempted prevention of seizures or clusters, 10 with full or >50% success. The best results were obtained in IGE patients whose seizures were habitually triggered by typical factors (sleep deprival, alcohol) but also some other patients were successful. The only adverse effect observed was gait ataxia in a multiple handicapped patient.

Conclusion: ADA is an elegant and often successful treatment option for selected patient groups where it can make the difference between becoming seizure-free or not. Depending on the individual case it can be applied as monotherapy or in combination with a basis AED.

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OPEN TRIAL OF THE OMEGA-3 FATTY ACID, EICOSAPENTAENOIC ACID, IN 10 PATIENTS WITH REFRACTORY EPILEPSY

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Purpose: Animal studies suggest that omega-3 fatty acids have antiseizure properties, but the results of clinical trials with combinations of omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have been inconclusive. Pure EPA without DHA appears to be more effective than combinations in studies of depression and schizophrenia. Here, we examine the effects of pure EPA in people with refractory epilepsy.

Method: This open study included a 12 week prospective baseline and a 12 week treatment period, during which patients received 1000 mg EPA daily. Patients continued their routine AEDs throughout the trial. The total number of seizures for each week was recorded.

Results: Ten patients (5 males) aged 23 to 75 with refractory focal seizures were included. All patients were taking between 1 to 4 AEDs. Median seizure frequency was 15 at baseline and 11 during treatment; 6 patients had fewer seizures with reductions of 12–59%. One patient with an increase in seizure frequency had reduced severity with seizures markedly shorter.

Conclusion: This is the first report of the use of pure EPA in people with epilepsy. With the very small numbers of patients and the open design of the study, no definitive conclusions can be reached. However, 7 patients can be considered to have gained benefit; hence EPA does not appear to aggravate seizures and may have beneficial effects. Further trials are required with more patients and higher doses.

Acknowledgement: PlusEPA capsules were kindly provided gratis by Minami Nutrition, Belgium.

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RISC FACTORS OF EPILEPSY IN WOMEN IN THE REPRODUCTIVE PERIOD

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Purpose: To identify the risk factors associated with development of epileptic seizures in women after 12 years old.

Method: A prospective and descriptive, randomized study was performed in Neurology Department, Emergency Hospital. During 5 years (2004–2009) were recruited 120 female patients from 470 stored in the data-base. According to the Classification of the International League Against Epilepsy (ILAE, 1981) were recorded different types of seizures. Every patient presented epileptic seizures starting after 12 years old. A special form for each patient was completed, including demographic, clinical, neurological, electroencephalographic (EEG) and brain Magnetic Resonance Imaging assessments.

Results: The risk factors that affected women with epilepsy were: trauma – 26 (21.6%) patients, metabolic or endocrine induced seizures – 18 (15%), perinatal injury – 12 (10%), arteriovenous malformations – 8 (6.6%), cortical dysplasia – 6 (5%), brain tumors – 2 (1.6%), hippocampal sclerosis – 4 (3.2%), idiopathic (probably polygenic) – 14 (11.6%), unknown cause – 30 (25%). The menstrual, sexual and reproductive dysfunctions didn't confirm the relationship between hormonal changes and EEG patterns. It is known that epilepsy is often multifactorial. Even when a major cause is identifiable, other factors are often involved in the clinical manifestations (S.Shorvon, Epilepsy, Oxford University Press, 2009, p. 29).

Conclusion: The majority of the patients had an unknown or idiopathic cause of epilepsy, along with trauma. To confirm or infirm the role of hormonal abnormalities in developing epileptic seizures and catamenial epilepsy are necessary detailed hormonal – EEG – drug monitoring research.

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ABSOLUTE BIOAVAILABILITY OF DIVALPROEX SODIUM EXTENDED-RELEASE IN ELDERLY PATIENTS WITH EPILEPSY BY A STABLE ISOTOPE TECHNIQUE

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Rationale: The relative oral bioavailability of extended-release divalproex sodium (Depakote-ER Abbott Labs, ER) compared to delayed-release divalproex tablets (DR) in healthy young adults is 89%. However, no bioavailability information is available for valproate from the ER formulation in elderly patients. Absolute bioavailability can be obtained by simultaneous administration of a stable isotope.

Methods: A dual-center, steady-state, crossover design (DR to ER, randomized) study in 12 patients (age 60–69, n = 6;>70 years, n = 6) was designed to assess ER bioavailability (F) relative to DR. Patients were initially on DR maintenance therapy. VPA was taken orally at 08:00 h (fasting). Simultaneous with the oral VPA dose, stable-isotope-labeled VPA ($^{13}C_4$-VPA) was administered (250 mg, i.v.) to assess absolute F. Fourteen blood samples were collected over 24 h and analyzed by GC-MS. AUC was calculated via trapezoidal curve, with F = oral $AUC_{0\text{-}24}$ / IV $AUC_{0\text{-infinity}}$, normalized for the mg dose difference. VPA metabolites are also being assayed to determine age dependent differences in metabolic pathways.

Results: The VPA absolute F in 7 elderly patients on maintenance therapy (500–3000 mg daily) were as follows: Mean FDR = 1.14 0.36, Mean FER 0.90 0.24. (Table). The relative F (AUC-ER/AUC-DR) was 0.79 0.31.Full data for 12 patients and relative F data for ER are forthcoming.

Conclusions: VPA from divalproex-DR tablets is completely bioavailable in the 7 elderly patients studied. Relative bioavailability in the elderly was very similar to younger patients (0.83 vs. 0.87, respectively). The VPA metabolite results will also be presented.

p319
EPILEPTIC SEIZURES IN PATIENTS WITH CEREBROVASCULAR DISEASE

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Purpose: Cerebrovascular diseases(CVD) are one of the most etiologic factor of the epileptic seizures. Seizures may appear in acute faze of the insult or during the reconvalesence.The aim of this paper is evaluation of the frequency, semiological classification and the types of seizures in comparison to the type of the CVD.

Method: In this prospective study, we evaluated patients with CVD who were hospitalized at the Department of Neurology in Nis, between January-December 2009. 108 (9.61%) of 1124 patients had seizures. Seizures occuring within the first 14 days after CVD were classified as early post-stroke seizures. Patients with a previous history of epilepsy and pulmonary diseases (who were on the therapy with teophylin) were excluded. Patients were evaluated and had the same investigations with medical history, laboratory, clinical, neurological, EEG and neuroimaging(CT, MRI) variables which were compared.

Results: 800 (71.17%) of 1124 patients with CVD, had ishic stroke, and 225 (20.02%) had hemorrhagic stroke. Mean age was 48 ± 31 years, male 45 and 47 female.108 of all the patients had seizures.75 of them had acute CVD, while 33 patients had seizures as a result of earlier CVD.57 (7.12%) of 800 patients with ishemic stroke had symptomatic seizures, while 14 (6.22%) of 225 patients with hemorrhagic stroke had seizures.Partial motor seizures(PMS) was registered in 47 (43.52%) patients, partial seizures with secondary tonic–clonic generalization in 39 (36.11%), primary GTC seizures were registered in 18 (16.67%) patients. Epileptic status was registered in 4 patients.

Conclusion: The frequency of symptomatic epileptic seizures is increased in patients with ishemic stroke. Partial motor seizures are a dominant feature.

p320
PREDICTING EPILEPSY IN PATIENT WITH OPEN HEAD INJURIES CAUSED BY WAR MISSILES

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Purpose: Detecting risk factors influencing the incidence of posttraumatic epilepsy after war missiles penetrating brain injuries.

Method: We analyzed sixty-five patients regarding the following parameters: age, traumatic mechanism, type, extend and localization of injury, presence of intracranially retained foreign bodies, neurological deficits, appearance of epileptic phenomena, cognitive dysfunction and Elecroencephalographic changes.

Result: Posttraumatic epilepsy was recorded in 14 patients (14/65 21.5%). Regarding the type of seizures there were six g.m., five complex partial and three motor partial seizures.

Elecroencephalographic recording showed: focal changes in 15, normal EEG in 26, unspecific in three, unspecific + focal changes in 2 patients. Nineteen patients had not done EEG.

Pathologic EEG changes are found in 11 of 14 patients who develop PTE (78.5% or 11/14).

Nine pathological EEG was registered in 51 patient who did not develop PTE (17.6% or 9/51). Wounds in the parietal region and in the frontoparetial region resulted in the occurence of PTE in 3 cases each.

Conclusion: The most important factors infuenting the incidence of PTE are: severity, extend and location of injury. The wounds in the frontal and parietal region were followed by epileptic seizures more frequently. Through-and-through brain injuries are more epileptogenic than others.

Evidence of nurological deficit has strong correlation with PTE.

There was no significant difference regarding the appearance of PTE in patients who are taking or those who are not taking AET.

Considering our analyses we can not find sure predictors or specific parameters decisive for the future development of PTE.

Poster session: Clinical neurophysiology II
Tuesday 29th June 2010
13:30–14:30

p321
EEG IN IDIOPATHIC GENERALIZED EPILEPSIES MISDIAGNOSED AS LOCALIZATION-RELATED CRYPTOGENIC EPILEPSIES TREATED WITH INAPPROPRIATE AEDS

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Purpose: The aim is to evaluate the EEG features in IGE previously misdiagnosed as cryptogenic localization related epilepsies (CLRE), treated with inappropriate AEDs.

Method: 155 patients diagnosed as IGE at tertiary level, 91 females and 64 males, on age of 10–60 years were evaluated: clinically, EEG and wake-sleep EEG after sleep deprivation (SD) features and imaging (brain CT/ MRI) findings.

Results: 45 patients were previously misdiagnosed as CLRE and were taking inappropriate AEDs. 20 patients were using CBZ and 10 Pb monotherapy, 15 polytherapy with either CBZ, Pb, PHY, even TPM and LTG with old generation AEDs. Seizure relapses of GTCS, absence status epilepticus, absences and myoclonic seizures happened in 36 patients. 9 patients were in remission, but those who used high doses of Pb and polytherapy, manifested cognitive, behavior and mood disturbances. EEG and wake-sleep EEG after SD, done after seizure relapse in most of the patients showed interictal/ictal discharges of spike wave (S-W) and poly S-W complexes of 3–4.5 Hz, with generalized or bilateral frontocentral appearance, occasional lateralization, even focal localization and normal background activity. Unspecific findings of spikes and sharp waves or normal EEG were registered in a few patients with rare seizures or in remission. VPA replaced inappropriate AEDs in 41 patients, resulting in EEG normalization and seizure remission. 4 patients continued their previous therapy and were seizure-free from GTCS.

Conclusion: EEG could contribute to a proper differentiation of IGE from CLRE, resulting in proper selection of AEDs.

p322
IN-PHASE SYNCHRONIZED GAMMA OSCILLATIONS PRECEDE SPIKE-AND-WAVE COMPLEXES IN HUMAN ABSENCE SEIZURE

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Purpose: Gamma oscillations (40–100 Hz) are considered for a binding measure of the neuronal activities between remote cortical areas. 3-Hz spike-and-wave complexes (SWCs) in childhood absence epilepsy (CAE) are the prototype of synchronized seizure activities in humans. Here, we investigated the existence of gamma oscillations before and during 3-Hz SWCs in a case with CAE.

Method: Five SWCs were recorded, and sampled (1.25 kHz) in a girl with CAE (Fp1-C3, C3-T3, T3-O1, Fp2-C4, C4-T4, T4-O2, C3-Cz and Cz-C4). First, the EEG data were notch-filtered at 50 Hz and its harmonic frequencies, then 5 segments (2048 points for a segment) were selected for the last segment to cover the first SWCs.

Results: Grand average of wavelet analyses on bilateral fronto-central and centro-temporal leads showed three gamma oscillations (around 60 Hz, 80 Hz and >100 Hz) pre- and during the SWCs. The gamma oscillations were extracted, and subdivided into 512 points. We applied Hilbert transform, and obtained two parameters (instantaneous amplitude and phase) of the gamma oscillations. Multiplied products of instantaneous amplitudes between the homologous leads are the measure for their synchronization; therefore, we collected the data exceeding a threshold (>25 microV^2), and calculated the phase difference between the leads. Results showed transient, but preceding and synchronized, gamma oscillations before the SWCs: -2.46 s in centro-temporal (around 60 Hz), −1.23 s in fronto-central (around 60 Hz, in-phase).

Conclusion: The preceding, in-phase synchronized, gamma oscillations probably bind the widespread cortical activities, and trigger the seizure in human CAE.

p323
A NOVEL PORTABLE SEIZURE DETECTION ALARM SYSTEM: PRELIMINARY RESULTS

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Purpose: The unpredictable and random occurrence of seizures is of the most distressful issue affecting patients and their families. Unattended seizures can have serious consequences including injury or death. The objective of this study is to develop a small, portable, wearable device capable of detecting seizures and alerting patients and families upon recognition of specific seizures' motor activity.

Methods: We prospectively obtained ictal data in consecutive patients admitted to two video-EEG Units. We included patients with a history of motor seizures, clonic or tonic, tonic–clonic seizures or patients with complex partial seizures with frequent secondary generalization. A ''motion sensor'' unit mounted on a bracelet was attached to one wrist. The ''sensor'' contains a 3-axis accelerometer and a transmitter. The 3-axis movements' data was transmitted to a portable computer. Algorithms specially developed for this purpose analyzed the recorded data. Seizure alerts were compared to the video-EEG data.

Results: Ictal data were acquired in 15 of the 31 recruited patients. The algorithm correctly identified 20 out of 22 (91%) captured seizures and generated an alarm within a median period of 17 s. All events lasting over 30 s. (i.e. 19 events) were identified. The system failed to identify 2 out of 22 seizures (9%). There were 8 false alarms during 1692 h of monitoring.

Discussion: Preliminary data suggest that this motion detection device/ alarm system can identify most motor seizures with high sensitivity and with a low false alarm rate.

doi: 10.1111/j.1528-1167.2010.02658.x

p324
THE ANALYSIS AND PROGNOSIS OF EPILEPSY IN PERIVENTRICULAR NODULAR HETEROTOPIA; AUDIT OF 14 CASES

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Purpose: Periventricular nodular heterotopia patients show heterogeneity of clinical, neurophysiological and neuroimaging features. We aim to document the features of those patients and to explore clues for prognosis.

Method: In this study we analyzed retrospectively the clinical, electrophysiological and imaging characteristics of the 14 patients who were diagnosed by means of magnetic resonance imaging.

Results: Of the 14 cases, 9 were men and 5 women. The mean age was 44 and the mean age at onset of seizures is 24.4 (range between 15 and 47). Three patients described febril convulsions, and 4 had epilepsy history in the family. Two patients were mentally retared, one of whom had also motor retardation. Ten patients (71%) had generalized tonic–clonic seizures, 9 (64%) had complex partial seizures, 4 (28.6%) had simple partial seizures. Only one patient reported status epilepticus. Three patients (21.4%) had isolated periventricular heterotopia, and 11 (78.6%) presented with additional migrational anomalies. Six had cortical dysplasia, 1 cerebellar hypodysplasia, 1 schizencephaly and 1 polymicrogyria along with callosal agenesis, 1 lissencephaly and 1 band heterotopia. Five (36%) patients had normal EEG and 9 (64%) had either focal or diffuse abnormalities. Eight patients were on monotherapy, 6 were on polytherapy.

Conclusion: Although isolated periventricular nodular heterotopia cases are associated with milder clinical and electrophysiological features, as previously reported, larger series are needed in order to identify specific prognostic factors.

p325
LOCALIZATION OF INTERICTAL SPIKE USING EEG-fMRI AND EEG SOURCE MODELING

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Purpose: It is very important to localize the epileptogenic zones in patients with partial epilepsy for successful surgical treatment. EEG Source imaging and EEG-fMRI have been recently used to localize epileptogenic zones as noninvasive new method. The aim of this study was to compare localization of epileptogenic zones using EEG-fMRI, dipole modeling and distributed modeling in patients with partial epilepsy.

Method: EEG-fMRI study was performed in 24 patients and BOLD changes were observed in 12 of 15 patients who showed interictal discharges. Finally we included 9 patients with partial epilepsy, whose epileptogenic zones were documented by traditional methods. EEG data of included patients were analyzed with source analysis program such as BESA for dipole modeling and LORETA for distributed modeling.

Results: Among EEG-fMRI, dipole modeling, and LORETA, the rate of correctly localizing the epileptogenic zone was 88.9% in EEG-fMRI study, 55.6% in dipole modeling with BESA, and 44.4% in distributed modeling with LORETA. The concordant rate to correctly localizing the epileptogenic zones among these 3 methods was high in cases with cortical developmental malformation or frontal lobe epilepsy, but low in cases with posterior cortex epilepsy. Especially in cases with posterior cortex epilepsy, EEG-fMRI was more useful to correctly localize the epileptogenic zone.

Conclusion: Source analysis with EEG-fMRI, dipole modeling and distributed modeling are useful to localize the epileptogenic zone and have complementary role among them. However, among these 3 methods, EEG-fMRI more correctly localizes the epileptogenic zone in our study.

p326
ELECTROCORTICOGRAPHY AND CORTICAL STIMULATION DURING AWAKE CRANIOTOMIES

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Purpose: Electrical cortical stimulation (CS) is considered the gold standard for functional mapping during resective surgery in eloquent areas. We assessed safety of cortical stimulation during awake craniotomies by reviewing electrocorticography (ECoG) recordings for afterdischarges (AD) or seizures following stimulation.

Method: We retrospectively analyzed 26 ECoG recordings. 21 patients underwent surgery for lesion resection (3 cavernous hemangiomas, 18 tumors), 5 for intractable epilepsy. All presented with seizures. A 6 contact strip was placed over the cortex with contacts 1 and 2 used for reference and earth. CS was performed using Ojemann stimulator with an Innomed probe. Stimulus parameters were: duration 0.5 ms, frequency 50 Hz and intensity between 4 mA and 14 mA peak to peak.

Results: Three patients with lesions (11.5%) developed AD. 6 patients (23%; 2 cavernous hemangiomas, 4 tumors) developed a seizure pattern time linked to cortical stimulation. Seizures were subclinical in 4 patients and clinical in 2 (speech difficulties known as part of seizure semiology). 50% of patients with stimulation induced seizures had ADs, whereas none of the patients without seizures had ADs ($p < 0.01$, Fisher's exact test 0.008).

Conclusion: Cortical stimulation during awake craniotomies is safe, with stimulation induced subclinical or short focal clinical seizures and ADs occurring in 23% of patients. In this small sample, we noted that 2 patients out of 3 with cavernous hemangioma developed a seizure. The presence of ADs may predict a higher risk for intraoperative seizures during CS. These findings need to be confirmed in a larger cohort.

p327
AMBULATORY EEG, A COST-EFFECTIVE SOLUTION FOR INCREASING NECESSITIES OF VIDEO EEG TELEMETRY IN ADULT POPULATION

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Purpose: To evaluate the diagnostic yield of ambulatory EEG recording in adults with epilepsy or with seizure-like spells.

Method: Over 2 years, patients that met the indications received ambulatory EEG monitoring without tapering the antiepileptic drugs.

Results: Thirty-three patients that were 37 ± 17 years old were monitored for 1 or 2 days with no complications. Of these, 67% had a recent normal EEG, 82% had more than 4 spells per month (1–600), and 48.5% were on one or more antiepileptic medications (0–4). The indications for recording were characterization of spells (82%), epilepsy surgery workup (12%), measuring the frequency of seizures or identification of spikes (6%). The question was answered in 24 (73%) patients in whom events were recorded. Of these, 12 (37%) had epileptic, 9 (27%) had nonepileptic, and 3 (9%) had both events. The main results were: nonepileptic events 17 (52%), epilepsy confirmed 5 (15%), potential surgery candidate-VEEG telemetry required 3 (9%), seizures quantified 1 (3%), generalized epilepsy-not a surgery candidate 1 (3%), no event recorded-question unanswered 6 (18%).

Conclusion: Despite the short recording, ambulatory EEG monitoring had a high diagnostic yield (73%) comparable with previous studies in pediatric populations and with video EEG (VEEG) monitoring. Epilepsy surgery work up comprized a minority of patients compared to VEEG monitoring. We conclude that ambulatory EEG is a cost effective solution for increasing necessities of VEEG in adult patients when the selection is accurate such as for characterization of frequent spells, diagnosis of epilepsy and quantification of epileptiform activity.

p328
MAGNETIC SOURCE IMAGING STUDY ON THE ROLE OF SUPPLEMENTARY MOTOR AREA IN READING EPILEPSY

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Purpose: Reading epilepsy is an idiopathic reflex epilepsy syndrome mainly characterized by orofacial myoclonus during quiet or aloud reading. Interictal EEG is normal, and ictal EEG shows fronto-temporal spike-waves (SW), generally lateralized towards the left side. This paper aims to characterize the pathophysiology of epileptic orofacial myoclonus in a case of reading epilepsy using magnetic source imaging (MSI).

Method: A 46 year-old woman with primary reading epilepsy underwent two whole-head magnetoencephalography (MEG) recordings (Vectorview, Elekta) within two months while reading aloud. MEG data were preprocessed off-line using the spatiotemporal signal-space-separation method to suppress external interferences and correct for head movements, and band-passed filtered at 1–40 Hz. Forty-one SW associated with orofacial myoclonia were averaged (within and across session) with respect to SW peak power. Single and averaged epileptic discharges were reconstructed using conventional equivalent current dipoles and distributed sources using sLoreta method.

Results: The spike discharges started from a left supplementary motor area (SMA) source at −30 ms, followed by a source in the left sensorimotor face area at −20 ms and yet another SMA source at −10 ms. The main spike peak (0 ms) and the slow wave (35–330 ms) sources were located in the left sensorimotor face area.

Conclusion: This case shows that orofacial myoclonus in reading epilepsy is related to a crosstalk between left SMA and sensorimotor face area regions with a primary onset in the SMA. These data underline the pivotal pathophysiological role of SMA in the generation of SW discharges in this idiopathic reflex epilepsy syndrome.

p329
INTRAOPERATIVE EPILEPTIC SEIZURES IN A SERIES OF PATIENTS AFFECTED BY PRIMARY BRAIN TUMORS

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Purpose: Surgical procedure and mapping techniques may induce intraoperative seizures, which represent a complication, especially during awake craniotomy.The aim of our study is to evaluate ictal electrocorticographic (ECoG) characteristics in patients undergoing neurosurgery, with respect to history of epilepsy, type of stimulation, lesion localization and interictal ECoG features.

Method: The occurrence of intraoperative seizures was evaluated in 118 patients, with glial tumors, both in temporal and extratemporal regions. The majority of patients (68/118) were under chronic antiepileptic treatment at the moment of surgery. ECoG was performed before and during resection and reviewed by two different neurophysiologists independently.

Results: Intraoperative seizures occurred in a subgroup of 35 patients, mainly affected by gliomas localized in motor or premotor areas (21/35). Related seizures were characterized by sudden onset with fast rhythms, often undistinguished from stimulation artefacts, fast recruiting epileptiform activity and rapid bilateral diffusion. Seizures arising from temporal lobe or insular region presented more often with ECoG unusual features, dominating by fast activity and recruiting slow waves. Patients with history of tumor-related epilepsy and interictal epileptiform EcoG activity were more likely to experience seizures during surgery. Seizures occurred mainly during surgical procedures and direct electrical stimulation (31/35).

Conclusion: Seizures during surgery are more likely to occur during mapping technique with direct electrical stimulation, in patients with history of epilepsy and interictal highly epileptiform activity at ECoG. Electrocorticography provides real-time information regarding changing in brain electrical activity and patients' behavioral state, which may interfere with subjects' compliance during awake craniotomy.

p330
ROLE OF A STANDARDIZED PARTIAL SLEEP-DEPRIVED EEG PROTOCOL IN THE DIAGNOSIS OF EPILEPSY, AND ITS CORRELATION TO CLINICAL AND NEUROIMAGING DATA

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Purpose: Electroencephalogram after sleep deprivation (dep-EEG) still represents a key diagnostic tool for epilepsy. Yet, sleep deprivation protocols vary among different centers, most of published date back to the preneuroimaging era, and a detailed electromorphological/clinical correlation often lacks.We evaluated the usefulness of a standardized method of dep-EEG in a wide population of patients evaluated at our University Epilepsy Center in 2006–2008.

Method: Among all patients submitted to dep-EEG, we selected only those with:

1. a baseline EEG negative or not specific;
2. a brain MRI;
3. a follow-up and a final diagnosis by our team.

Dep-EEG protocol consisted in wake up at 2:00 AM, and laboratory EEG+polygraphy from 8:00 AM to 10:30 AM. Data analyzed were:

1. electrical abnormalities during baseline EEG and dep-EEG;
2. type and localization of EEG abnormalities;
3. neuroimaging data;
4. clinical features.

Results: 151 patients out of 305 were selected for analysis. Epilepsy was confirmed in 64.9% of them. The protocol of partial dep-EEG used, significantly increased the yeld of epileptiform interictal abnormalities (IIA) in all of the epileptic syndromes examined and the diagnostic sensitivity, especially in probably symptomatic focal epilepsy. The yeld in IIA was significantly higher than mere repetition of a routine EEG or hypoerpnea. In patients with normal dep-EEG, specific IIA were never observed at baseline EEG.

Conclusion: Apart from confirming the usefulness of dep-EEG, our analysis reveals other potential correlations of EEG findings with specific syndromic and neuroimaging findings in epileptic patients. Further analysis on patients recruited before 2006 is ongoing.

p331
AN INEXPENSIVE ALTERNATIVE FOR OUTPATIENT VIDEO-EEG RECORDING

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Purpose: Many commercial EEG recording systems are available that provide electronically synchronized digital video and digital EEG. The cost ($6-7000 CDN per recording station) of digital video may be a significant impediment to routine use in outpatient EEG laboratories (either as part of the initial installation or addition to a preexisting system). We describe an inexpensive method for capturing patient behavior during routine EEG recordings.

Method: The EEG laboratory at the QEII Health Sciences Centre in Halifax, Nova Scotia, Canada is an integral part of a tertiary level adult epilepsy surgical program. In addition to inpatient video-EEG telemetry admissions, there are 1800 routine patient recordings/year. The first digital EEG recording system was installed in 1995. In early 2008 each routine recording station was equipped with a simple webcam (LifeCam NX−6000, resolution 800 × 600 pixels, cost = $100.00 CDN for camera and cable). A standard wall clock is included in the field of view of each recording. The video file (each approximately 500 MB in size) is stored on the recording station. The technologist notes any behaviors of interest (BOI) requiring review by the electroencephalographer and the time of their occurrence.

Results: From April 2, 2008 to November 30, 2009 54 BOI were captured (7 epileptic seizures, 28 nonepileptic seizures and 19 other).

Conclusion: This recording system captured, with acceptable video quality, BOI that obviated an expensive inpatient admission for diagnosis. A video recording system can be implemented in any EEG laboratory at minimal cost.

p332
IDIOPATHIC GENERALIZED EPILEPSIES SHOW GREATER OCCIPITAL EEG ALPHA POWER AFTER SLEEP DEPRIVATION

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Purpose: To check if some EEG indicators differ idiopathic generalized epilepsies from partial ones and control if no epileptic potentials exist in standard EEG.

Method: The alpha attenuation test (AAT) was applied at the total of 151 subjects. Therein where 117 patients with at least one episode of loss of consciousness and 34 controls. All patients underwent EEG after one night sleep deprivation and AAT was performed before the sleep onset. According to the later established diagnosis, three patients groups were established: 27 with idiopathic generalized epilepsies (IGE), 34 with the partial ones and 56 with unknown cause of loss of consciousness. A total of 36 logarithmic transformed variables underwent the parametric statistical analysis: six relative and six absolute alpha powers from each of the two channels (O2-A1 and O1-A2) after eyes-open (EO) and eyes-closed (EC) conditions, as well as six alpha attenuation coefficients (AAC).

Results: In the group of IGE absolute AACs were significant greater (F from 4.439 to 4.72), relative AAC slightly lower (F from 4.9 to 5.46) as well as absolute and relative alpha powers greater after EC measured in EC/EO conditions.

Conclusion: Greater alpha powers after EC and EO during the state of decreased vigilance before sleep onset after sleep deprivation among the patients with IGE might be of diagnostic value.

p333
USING ELECTROCORTICOGRAPHIC SIGNALS IN A BRAIN-COMPUTER INTERFACE (BCI) PARADIGM

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Purpose: A brain-computer interface (BCI) system allows individuals to communicate and control devices using their brain waves. Visual-evoked BCI paradigms have mainly used scalp EEG signals. We hypothesize that ECoG-translated BCI control signals will provide superior speed and accuracy over scalp-recorded EEG for a symbol selection matrix paradigm.

Method: Four epilepsy patients with implanted intracranial grid and depth electrodes were studied.

A 16- to 32-channel subset of each patient's intracranial electrodes was monitored using a separate EEG amplification system and BCI2000 software. Subjects focused on a prescribed character from a 6 × 6 square matrix of alphanumeric characters and counted as the prescribed character randomly flashes. A character string is presented on a monitor and the current prescribed character is highlighted behind the character string. Sessions consisted of eight to ten experimental runs composed of a series of characters forming a word.

For each patient, data from the first four runs were preprocessed and used to train a linear classifier using Stepwise-Linear-Discriminant-Analysis. This classifier was tested using the four subsequent runs to determine the classifier's ability to predict the intended target from independent data.

Results: For all four patients, the classifier predicted the intended target character at or near 100% accuracy using fewer than 15 stimulation sequences.

Conclusion: This preliminary analysis is one of the first to demonstrate that all patients could quickly and accurately control the P300 Speller using ECoG signals. The results indicate accurate BCI is attainable using a much more localized brain region than scalp-recorded EEG.

Poster session: Sleep and epilepsy
Tuesday 29th June 2010
13:30–14:30

p334
NIGHTTIME MONITORING OF CHILDREN AND YOUNG PEOPLE WITH COMPLEX EPILEPSY AND LEARNING DISABILITY—THE IMPACT ON PARENTAL SLEEP AND THE FAMILY'S PHYSICAL AND PSYCHOSOCIAL WELL-BEING

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Purpose: To investigate the impact of nighttime monitoring of seizures on sleep patterns and social well-being in the families of children and young adults with complex epilepsy.

Method: A total 103 parents of young people (age range 6–20 years) at a residential centre providing educational, social and medical management of epilepsy were requested to complete a questionnaire at the end of the school/college holiday period about their perception of nighttime monitoring and its effect on family's wellbeing. 45 (44%) responses were obtained.

Results: Seventy-five percent reported a high level of worry about the possibility of seizures and of sudden unexpected death during sleep. Parents woke up 2–5 times per night (range 2–10) to check on or assist the child/young person. The average duration of sleep of parents was 4–6 h (range 2–8) with all reporting an impact on their quality of sleep. 33% used a seizure monitoring device, but complained of the poor predictability of these. Sleeping arrangements were altered in 81%. Parents reported that nighttime monitoring had a great impact on organizing family holidays (50%), family activities (43%), social life (46%), job status (39%), marital relationship (32%) and overall health (34%).

Conclusion: The frequency of sleep problems in parents and its effect on the family's physical and psychosocial wellbeing is high which may in turn affect the quality of life and impact negatively on family function. Clinicians and services need to recognize and address these concerns to support and promote functioning of the family. A detailed prospective study is merited.

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DREAM RECALL AND SEIZURES IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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Purpose: To evaluate dream recall frequency (DRF) and characterize dream content in temporal lobe epilepsy patients (TLE), according to their epileptogenic zone and lesion type.

Method: Fifty-two TLE concluded a written dream diary every morning for 5 days and continuous seizure recording in video-EEG monitoring (V-EEG). Number of dreams recalled and nonrecalled dream mentation, collected. DRF calculated. Distributions of seizures and DRF during V-EEG, analyzed. Hall and Van Castle dream analysis, performed. A control group matched for age and gender completed the same diary 5 consecutive days. Nonparametric statistics used.

Results: TLE had lower values of: mean number of dreams recalled (MNDR), DRF and mean number of long dreams (MNLD). Female patients: a higher mean number of nonrecalled dreams. Left TLE: a higher MNDR and DRF. Mesial TLE: a higher MNLD. Mesial temporal sclerosis patients (MTS): also a higher MNDR and DRF. The lower MNDR was coincident to the peak of the mean seizure frequency. In content analysis, TLE had a higher familiarity of characters and settings and a lower dream involved success, striving and sexuality. MTS and Right TLE: a higher percentage of animals in their reports. MTS patients: also a lower percentage of aggression in dream social interactions.

Conclusion: There are differences in TLE dream mentation in comparison to controls and according to gender, epileptogenic zone and lesion. The role of temporal structures in dream experience can explain this variability. Content differences can be supported by psychopathological and life quality indexes but also by mesial temporal lobe dysfunction.

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MELATONIN IN INTRACTABLE EPILEPSY: A POSSIBLE POSITIVE EFFECT

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Purpose: Melatonin is beneficial for sleep-wake cycle disturbances and occasionally improves seizure control. This study is the first to examine the effect of melatonin administration on seizures, sleep and behavior of patients with intractable epilepsy using a double-blind, placebo controlled design.

Method: The study group included 12 patients aged 9–32 years with severe intractable epilepsy. The antiepileptic drug regimen remained unchanged during the study period. The study was divided into three stages. 1. Three-week treatment with melatonin or placebo. 2. One week washout period, and 3. Three-week treatment with placebo or melatonin. Seizure frequency was monitored by clinical evaluation and EEG recordings. Behavior parameters, including daytime sleepiness, difficulty getting up and falling asleep, agitation and concentration levels were graded on a scale of 0 (very low) to 7 (highest). Polysomnography studies were performed during the last week of the study.

Results: Two patients withdrew from the study and the statistical analysis was conducted on data from the remaining 10 patients. Diurnal seizure frequency decreased significantly during melatonin therapy compared with placebo (from 7.75 to 4.26 in average; $p = 0.034$). No change was demonstrated in the frequency of generalized seizures, maximal number of seizures per day, and seizure duration. No major side effects were noticed during the period of melatonin treatment. No significant changes on behavioral parameters were reported.

Conclusion: Melatonin may be effective and safe in decreasing daytime seizure frequency in young patients with intractable epilepsy. Further studies are needed to determine its efficacy and safety.

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SLEEP ARCHITECTURE AND DAYTIME SLEEPINESS IN PHARMACORESISTANT EPILEPSY

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Purpose: Patients with epilepsy suffer from disrupted sleep and daytime consequences, is generally accepted statement being supported by several questionnaire studies. Our study was performed to clarify the changes in macro and micro sleep architecture and daytime sleepiness in epileptics.

Method: In the retrospective analysis we examined night video-EEG recordings of 8 epileptic patients (32.88 ± 13 year) with intractable seizures and 8 controls (29.63 ± 14.5 year), assessing the sleep architecture characteristics (sleep stages, K-complex index and cyclic alternating pattern -CAP- rate during NREM-sleep in the first cycle). The modified Epworth Sleepiness Scale-ESS (the question exploring the situation while driving was withdrawn) was used to assess the daytime sleepiness.

Results: Sleep stages proportions: 1NREM (epileptics: 4.54 ± 2.9% vs. controls: 4.56 ± 5.06%), 2NREM (epileptics: 47.23 ± 10.55% vs.

controls: 52,46 ± 7.39%), SWS (epileptics: 14.99 ± 7.26% vs. controls: 15.99 ± 7.68%), REM (epileptics: 19.36 ± 5.52% vs. controls: 20.46 ± 5.03%) did not varied between the groups, nor microsleep characteristics did: K-complex index (epileptics: 2.97 ± 1.73 per min of 2NREM vs. controls: 3.82 ± 1.5 per min of 2NREM), and CAP-rate (epileptics: 38.46 ± 24.66% vs. controls: 54.55 ± 15.69%). Mild statistic difference was in the wake-time proportion during sleep (epileptics: 13.86 ± 12.17% vs. controls: 5.65 ± 4.88%, p = 0.0491). The scores in modified ESS did not vary (epileptics: 5.13 ± 2.42% vs. controls: 5.38 ± 3.12%).

Conclusion: The evaluation of the sleep architecture in the meanings of micro and macro characteristics and the sleepiness scores failed to prove the expected differences in patients with pharmacoresistant epilepsy and normal population. Further studies are needed to explore the prevalence of subjective and objective sleep abnormalities in the larger sample of epileptic patients.

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NREM OF THE FIRST SLEEP CYCLE IN JUVENILE ABSENCE EPILEPSY IS MARKED BY THE LACK OR SIGNIFICANT ATTENUATION OF SLEEP SPINDLES

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Purpose: In the category of idiopathic generalized epilepsies, juvenile absence epilepsy (JAE) is hallmarked by recurrent typical absences. The spike-wave discharge EEG pattern appearing during absence seizures has been proposed as a product of sleep spindle transformation under experimental conditions, and therefore has been related to abnormalities across the thalamocortical circuit. In order to see whether the epileptic activity affects the spindles' profile, we investigated the quality of sleep spindle generation during the descending NREM branch of the first sleep cycle.

Method: Nine JAE patients, who underwent EEG investigation after partial sleep deprivation, were compared against nine age-matched normal controls. FFT-based time-frequency analysis was used to assess spindle production during NREM sleep.

Results: In the JAE patients, we observed a dramatic defect in sleep spindles: In 8/9 patients slow spindles (frontal-Fz) were completely absent and fast spindles (central-Cz) were either absent (3/8) or had substantially lower power than in controls (5/8). At the same time, the cyclic alternating pattern (CAP) A-phase/B-phase ratio of those 8 patients was markedly increased. Only in 1/9 cases spindles had a normal profile with a CAP characterized by a lower ratio of CAP A/B phase.

Conclusion: Since sleep spindles are normally part of the B-phase of the CAP, the lack of normal fast and slow sleep spindle spectral profile in the JAE patients is more likely to be attributed to the increased CAP A-phase density rather than a specific thalamocortical abnormality.

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INTERICTAL EPILEPTIC ACTIVITY TOPOGRAPHIES DETECTED IN MORNING AND AFTERNOON POST-SLEEP DEPRIVATION EEGS

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Purpose: Despite the increasing evidence suggesting that different seizure topographies have different circadian rhythms, little is known about the corresponding interictal epileptic activity (EA) rhythms. Therefore, the present study aimed at studying the influence of the time of the day in which post–sleep deprivation electroencephalograms (EEGs) were made on the topography of EA detected.

Method: The last 212 post–sleep deprivation EEGs with EA detected were selected. The exams were made either in the morning (M), at 8 h 30 AM, or in the afternoon (A), at 13 h 30. All patients were given the same standardized instructions for sleep deprivation. The EEGs reports were retrospectively analyzed for the EA topography. Topographies were classified into generalized, frontal, fronto-temporal, medial temporal, central and posterior (parietal, posterior temporal or occipital). EA topography detected in the M and A period were compared with chi-square test, p;0.05.

Results: There were 246 EA topographies detected (M group 114; A group 110). The epileptic topographies distribution was: generalized M 57.7%, A 42.3%; frontal M 47.8%, A 52.2%; fronto-temporal M 50.6%, T 49.4%; medial temporal M 42.9%, T 57.1%; posterior M 62.5%, T 37.5%. This distribution was not significantly different.

Conclusion: EA topography was similarly detected in post sleep EEGs made in the early morning or early afternoon. This data is relevant for scheduling post–sleep EEG in epilepsy patients. Further studies with a more precise definition of the epileptogenic zone are necessary to better define the circadian variation of interictal EA.

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USE OF SLEEP MEDICATIONS PRIOR TO PRESENTATION TO SLEEP CLINIC IN PATIENTS WITH EPILEPSY AND INSOMNIA: A RETROSPECTIVE STUDY

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Rationale: Insomnia in patients with epilepsy has been described. However, there have been no studies documenting sleep medication usage of patients with epilepsy and insomnia. We would like describe the frequency and type of medications this population is using before presenting to a Sleep Medicine specialist.

Methods: We performed a retrospective chart review and included patients with epilepsy and insomnia who presented to the New York Sleep Institute over a 1-year period.

Results: There were 50 patients included in our study. The average age was 48.4 years-old. Twenty-five patients reported trouble falling asleep. Five patients reported difficulties staying asleep. Twenty-one patients were on one antiepileptic drug (AED) and 20 patients were on two AEDs. Twenty-one patients (42%) took medications for sleep before presenting to a Sleep Center. Thirteen patients took zolpidem; three patients took diphenhydramine; two patients took melatonin. Three patients took more than one medication. Ten of 21 patients on one AED (47.6%) took medications for insomnia. Nine of 20 patients on two AEDs (45%) took medications for insomnia. Two of eight patients on three or more AEDs (25%) took medications for insomnia.

Conclusion: Many patients with epilepsy and insomnia take sleep medications prior to presenting to a sleep medicine physician. Patients on one or two AEDs were more likely to take medications for insomnia than patients on three or more AEDs, which suggest that patients on multiple AEDs may be hesitant to take additional medications.

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NOSEY PARKA—NOCTURNAL SEIZURES IN YOUNG PEOPLE: PRECAUTIONS AND RESCUE TREATMENT KNOWLEDGE AUDIT: EARLY RESULTS

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Purpose: Nocturnal seizures are common in children with refractory epilepsies. The aim of this audit was to explore the practical and emotional impact of these seizures on families, particularly in regard to the use of rescue medications and monitoring for nocturnal seizures.

Methods: We developed pilot questionnaire for supervised completion with parents of children who have had nocturnal seizures. The study was registered as a clinical audit. The questionnaires were completed opportunistically e.g. while waiting to be seen in clinics. Simple descriptive statistical analysis was used.

Results: Twenty-four parents with children who had nocturnal seizures responded. 13/24 children were male and they ranged from 1 year to 17 years of age (median 10 years). 17/24 (71%) parents had negative feelings regarding nocturnal seizures and reported that they became scared or concerned about their occurrence. 12/24 (50%) had used some form of monitoring equipment and 18/24 (75%) had stayed awake to observe their child at night, and 10/24 (42%) had slept in the same bed.

18/24 (75%) parents had used buccal midazolam at home for prolonged seizures with 2 parents also had rectal diazepam. 6/18 (33%) had felt unconfident or scared to use emergency treatment.

Conclusions: Most parents found that night-time seizures in their children were very frightening and stressful and adapted using a variety of strategies, including sleeping in the same room or bed as their child. Further acquisition and analysis of data is ongoing.

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GEORGIAN EPILEPSY PATIENTS WITH SLEEP DIFFICULTIES

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Purpose: Sleep difficulties are common in general population, and the individuals having different neurological diseases, in particular. Epilepsy and its treatment may exacerbate different sleep disorders. This study was aimed to investigate sleep complaints distribution in Georgian epilepsy patients.

Method: One hundred seventy-five volunteer subjects aged 18–69 years (mean age: 33.33 years, SD = 12.91), consisting of 91 healthy individuals and 84 outpatients with epilepsy (60 taking antiepileptic drugs (AEDs) and 24 not-taking AEDs) completed self-reported questionnaire which contained items concerning sleep-wake schedule and habits and nocturnal sleep complaints. The demographic and socioeconomic factors that we used were: age, gender, education, marital status and employment. Data analyses were performed by SPSS 13.0 for Windows.

Results: 67.9% out of 84 subjects with epilepsy and 76.9% out of 91 healthy individuals have had no sleep complaints. Insomnia symptoms were detected in 32.1% (27 out of 84) of outpatients having epilepsy and in 23.1% (21 out of 91) of subjects not having epilepsy. The difference was statistically significant ($p < 0.05$). 35.0% (21 out of 60) of treated with AEDs epilepsy patients had nocturnal sleep difficulties that was prevalent among the 25.0% (6 out 24) of untreated patients having epilepsy.

Conclusion: The findings of the present study are in the agreement with the literature data on the interrelation of epilepsy and sleep disturbances. The prevalence of insomnia seems to be much higher among the epilepsy patients than healthy individuals. Compared with untreated epilepsy patients sleep complaints were more often found in the epilepsy patients with AEDs medication.

p343
CAN RECORDING OF SLEEP DURING THE DAY TIME REPLACE FULL NIGHT RECORDING IN NOCTURNAL EPILEPTIFORM ACTIVITY?

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Purpose: Focal nocturnal epileptiform activity (FNEA) in the EEG occurs in children with Landau-Kleffner syndrome (LKS) and other cognitive disorders. The activity has often been called continuous spike wave during slow sleep (CSWS) and has been linked to specific syndromes, but is also seen in several other traits, such as autism and ADHD. By definition, one must record EEG throughout the night to calculate spike index (SI). Epileptiform activity during daytime sleep is common in these patients. This study was set up to test the feasibility of replacing full night recordings with daytime sleep recordings.

Method: Nine children aged seven to twelve years with known FNEA and SI above 30% are currently included in the study. They had no mental retardation or known MR-pathology. All children had a 24-h ambulatory EEG recording. Unlike the ordinary ambulatory recordings these children were woken up at 3:00 A.M. and kept awake until morning. At 7:30 A.M. the children were allowed to sleep. The recordings were stopped at 10:00 A.M. The SI during NonREM and awake were calculated and used in the analysis.

Results: Seven of nine children fell asleep and slept from 20 min to 2 h. The maximum SI during night and daytime sleep were near identical.

Conclusion: The preliminary results are promising and currently support the hypothesis that daytime EEG recording after sleep deprivation may replace full night recordings in patients with FNEA.

Poster session: Epilepsy syndromes in development II
Tuesday 29th June 2010
13:30–14:30

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THE USE OF TOPIRAMATE IN IDIOPATHIC INFANTILE SPASMS

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Purpose: Infantile spasm presents one of the most refractory types of an age-related, catastrophic childhood epilepsy syndrome. The aim of this study was to evaluate the efficacy and tolerability of treatment with topiramate for idiopathic infantile spasms.

Method: We reviewed the medical records of treatment with topiramate for all children with idiopathic infantile spasms between 2003 and 2008 at our institution. Topiramate were treated with an initial dose of 1 mg/kg/day, with a progressive titration of 1 mg/kg a week until their spasms were controlled and a maximum dose of 10 mg/kg/day was achieved. The evaluation of the treatment efficacy was based on the spasm frequency data that was obtained by EEG and by the parental count of spasm.

Results: 11 children were included in this review. Age of onset of spasms ranged from 3 to 10 months (mean 5.6 ± 2.5 months). Four of 11 patients (37%) became spasm free and disappearance of hypsarrhythmia as seen via EEG. Three of 11 patients (27%) achieved a seizure reduction of more than 50%. The spasm frequency decreased from 10.3 ± 7.3 to 3.9 ± 2.8 spasm/day. Mild adverse effects during treatment included rash, oligohidrosis, lethargy, irritability.

Conclusion: Our results suggest that topiramate monotherapy should be considered as an option for treating idiopathic infantile spasms.

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IS EPILEPSY A COMMON FEATURE IN ISOLATED AND ASSOCIATED CORPUS CALLOSUM AGENESIS

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Purpose: Corpus callosum agenesis (CCA) is the most common brain malformation, characterized by developmental delay, behavioral disturbance and epilepsy. However the phenotype is different whether an etiology (chromosomal, viral, metabolic, or syndromic) can be found or not. As CCA diagnosis is now currently done prenatally, giving a prognosis remains challenging: if fetal assessment (ultrasound, Magnetic Resonance Imaging, virus screening and karyotype) shows anomalies, CCA is said associated (ACCA) and the prognosis is usually poor (severe mental retardation, autistic features, epilepsy). On the opposite if CCA is isolated (ICCA) children may be asymptomatic or with mild phenotype.

Method: We retrospectively analyzed 155 cases of prenatal diagnosis of CCA in order to evaluate the frequency of epilepsy in isolated and associated CCA.

Results: In 62 cases, pregnancy was terminated. Among the 93 babies born, there were 36 ACCA and 57 ICCA; follow up (3–8 years) was known for 24 (71%) ACCA and 45 (76%) ICCA. Epilepsy occurred in 7 cases of ACCA (29%) infantile spasms (n = 2), partial seizures (n = 2), tonic–clonic seizures (n = 3), mainly within the first year, and in 3 cases (7%) of ICCA (febrile seizures (n = 1); Aicardi syndrome (n = 1) and sub telomeric chromosomal anomaly (n = 1)).

Conclusion: Epilepsy is not frequent in isolated CCA and if present, - except in case of simple febrile seizures - an underlying etiology has to be searched.

Francesco P, Maria-Edgarda B, Giovanni P, et al. Prenatal diagnosis of agenesis of corpus callosum: what is the neurodevelopmental outcome? Pediatr Int. 2006;48: 298–304.

p346
THE FREQUENCY OF ABNORMAL EEGS AND EPILEPSY IN A POPULATION-BASED COHORT OF CHILDREN WITH AUTISM IN ROCHESTER, MINNESOTA

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Purpose: Autistic children are reported to have epilepsy in the range of 25–46%. However, current studies on the prevalence of epileptiform EEGs and epilepsy in children with autism have variable results and are not population-based. Therefore, the aim of this population-based study was to determine the frequency of abnormal EEGs and epilepsy in autistic children.

Method: Subjects included a previously identified cohort of 121 children who met DSM-IV research criteria for autism during 1976–1997 in Olmsted County, Minnesota and 1:2 gender-and age-matched controls. The medical records of this cohort were reviewed retrospectively to determine whether these children had abnormal EEGs or epilepsy prior to age 21 years.

Results: 121 autistic children and 242 controls were identified. Epilepsy was present in 16% (n = 19) of the autism cohort, 1.2% (n = 3) of controls ($p < 0.001$). EEGs were obtained in 53 autistic children and 11 controls and were not significantly more likely to be abnormal in the autism group (25/53 vs. 7/11, $p = 0.32$).

Conclusion: In this population-based study, epilepsy occurred significantly more often in the autism cohort, but less often than the 25–46% previously reported. In the autism cohort, 47% of EEGs were abnormal, similar to previous studies. This was not significantly different than controls, likely due to the small number of EEGs performed in the control cohort. EEG abnormalities occurred more frequently in this autism cohort than in previously reported cohorts of normal children. Thus, epilepsy and abnormal EEGs occurred more frequently in autistic children, although epilepsy occurred less often than previously reported.

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ASPECTS OF THE INTELLIGENCE PROFILE OF CHILDREN WITH (NOCTURNAL) FRONTAL LOBE EPILEPSY

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Purpose: To describe the intelligence profile of children with (nocturnal) frontal lobe epilepsy who have either nocturnal seizures, daytime seizures or both.

Method: We performed a retrospective patient file study of 67 children with frontal lobe epilepsy seen at the outpatient clinic of Epilepsy Centre Kempenhaeghe. Children with frontal lobe epilepsy were divided into 3 groups; children with nocturnal seizures only, children with daytime seizures only and children with seizures both during nighttime and daytime. Wechsler Intelligence Scale for Children (WISC-III-nl) was performed in these children.

Results: Mean total IQ-score is 80 (SD 12.2) in children with nocturnal seizures only versus 85.3 (SD 11.2) in children with daytime seizures only. Mean verbal IQ-score is 82.6 (SD 13.2) in children with nocturnal seizures only and 89.1 (SD 12.6) in children with daytime seizures only seizures. Performance IQ-score is 80.5 (SD 13.6) in children with nocturnal seizures only and 84.2 (SD 11.8) in children with daytime seizures only. The largest difference in IQ-score between children with nocturnal seizures only and children with daytime seizures only is the verbal IQ-score.

Conclusion: Children with only nocturnal seizures have on average lower IQ-scores than children with only seizures during wakefulness. Nocturnal seizures will have a negative effect on verbal IQ-score.

p348
SEIZURE SEMIOLOGY CHANGES WITH AGE

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Purpose: We aimed to elucidate the interaction between seizure semiology, aging, and structural brain lesions.

Methods: This retrospective study included 83 children with symptomatic or cryptogenic partial epilepsy who were referred for presurgical evaluation. We related changes in seizure semiology with age in each patient. Changes in serial (inter)ictal EEGs and MRIs were related to changes in semiology.

Results: Median age at seizure onset was 14 months. Most patients presented with a single seizure type. An older age was related to presence of somatosensory and autonomic auras ($p < 0.001$; 0.015), psychic symptoms other than dysphasia and/or laughing ($p = 0.003$), ictal sensory symptoms ($p = 0.032$), dystonia ($p = 0.004$), orofacial automatisms ($p = 0.022$) and postictal dysphasia ($p = 0.030$). Seizure semiology changed in 79 of the 83 patients, at a median age of 66 months. Changes were judged to originate from new epileptogenic zones in only 8 patients. Structural abnormalities changed in 21% of the MRIs, with tumor growth and development of hippocampal sclerosis being most prevalent. Epileptiform activity was localized in 20% of (inter)ictal EEG recordings. Ictal

EEG changes were found in 38% but did not distinguish patients with and without suspected new epileptogenic zones.

Conclusion: Change in seizure semiology with age occurs in the vast majority of children with intractable epilepsy, partly explained by improved expression of subjective symptoms, but new symptoms do occur. A suspected new epileptogenic zone could not be explained by changes in structural brain lesions including dual pathology.

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COGNITIVE OUTCOME OF CHILDHOOD EPILEPSY IN ADOLESCENCE: UTILITY OF THE EPILEPSY SYNDROME SEVERITY SCALE FOR CHILDREN (ESSS-C)

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Purpose: The Epilepsy Syndrome Severity Scale for Children (ESSS-C) is a 10-point measure for seizure severity, response to treatment as well as long-term prognosis, ranging from 1 (least) to 10 (most) severe (Dunn et al., 2004). However, the authors point out that in the middle ranges of the scale, outcome variability may be large. We condensed the categories into low (scores <5), moderate (5–7) and severe (>7) epilepsy. We tested the utility of the original and the shortened scale to predict cognitive outcome.

Method: Youngsters with childhood-onset epilepsy (n = 73, age of onset 0.3–10.6 years), tested in adolescence (mean = 13.6 years) with the Dutch WISC-R/WISC-III (mean FSIQ = 83.7, range 50–128). Nine had low, 52 moderate, and 12 had severe epilepsy. Stepwise regression analysis was performed to predict outcome on IQ-Scales and Factor Indexes based on the original and adapted ESSS-C.

Results: Chi-square revealed no differences between severity groups for sex, handedness, positive MRI-findings, number of AEDs, or WISC-version used. For the shortened scale only, with significant negative correlations, higher severity was associated with lower scores on the PIQ, Perceptual-Organization, FSIQ and Freedom-from-Distractibility (but not VIQ, Verbal-Comprehension or Processing-Speed). For PIQ, $F = 7.38$, $p = 0.008$; explained variance: 9.4% and for FSIQ, $F = 6.03$, $p = 0.017$; 7.8%. FSIQ-range was restricted (53–86) for the severe and wide (50–128) for the moderate group.

Conclusion: Increased syndrome severity on the shortened ESSS-C predicted worse cognitive outcome for the Perceptual-Organization/Performance Scale and Full Scales. Indeed, as reported by the Dunn, outcome was variable in the middle ranges of the scale.

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INCIDENCE OF CHILDHOOD EPILEPSY IN ESTONIA: A PRELIMINARY DATA

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Purpose: The aim of the study is to establish the incidence rate (IR) of childhood epilepsy in Estonia and to describe the structure of childhood epilepsy.

Study group and method: This study is a part of population-based prospective epidemiological study of childhood epilepsy in Estonia. Study was carried out from January 1, 2009 to December 31, 2009 in southern Estonia in six counties, with population of children during the study period 78,877 (www.stat.ee). All consecutive patients (age range of 1 month to 19 years) with newly diagnosed epilepsy were included. A diagnosis (according to ILAE, 1989) was confirmed by neurologist and EEG-specialist. Eighty-one children met the study criteria (38 males and 43 females).

Results: The total incidence rate was 103/100,000. The IR was the highest, 198/100,000, in the age group from 5 to 9 years, and in the age group from 1 month to 4 years the IR was 123/100,000. 20% of patients had generalized seizures, 60% focal seizures. 51% of cases presented with idiopathic epileptic syndromes, 16% symptomatic epileptic syndromes and 13% cryptogenic syndromes. In 20% of cases epileptic syndromes were unclassified. A family history of epilepsy was present in 17% of cases.

Conclusion: Incidence rate of childhood epilepsy in present study is approximately twice higher compared with first epidemiological study of childhood epilepsy in Estonia (45/100,000, Beilmann et al 1999), what can be explained with better case collection and improved diagnostic possibilities.

p351
A RARE CAUSE OF MYOCLONIC ABSENCE EPILEPSY: GLUT-1 DEFICIENCY

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Purpose: Metabolic disorders should be in mind in the etiological examination of myoclonic absence epilepsy.

Case: A 7 year-old girl was referred to our hospital for tremors and ataxia. The previous history was unknown since she was adopted at the age of 2.5. She was diagnosed as epilepsy when she was 3-year old and the initiated valproate therapy has failed . The neurological examination revealed continous head titubation, clumsiness in cerebellar tests and dull intelligence. The full blood and urine metabolic screenings were unremarkable as well as the cranial magnetic resonance imaging. The video-EEG analysis revealed 3-Hz spike-and-wave complexes synchronous with several attacks of myoclonic jerks in the upper extremities and head in addition to partial impairment in conciousness. She was diagnosed as myoclonic absence epilepsy and ethosuximide therapy was initiated. The cerebrospinal fluid (CSF) analysis performed for etiological examination of myoclonic absence epilepsy revealed a glucose level of 33 mg/dl while serum glucose level was 105 mg/dl. Since the CSF/serum glucose ratio was 0.31, she was diagnosed as glucose transporter deficiency-1. Significant improvement in cognitive functions and seizure cessation was obtained soon after the initiation of ketogenic diet. Blood sample for SLC2A1 mutation analysis was sent for definite diagnosis.

Conclusion: The case was found interesting as a rare cause of myoclonic absence epilepsy and presented to emphasize the importance of CSF analysis in the etiological examination of all intractable epilepsy in childhood.

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INFANTILE CONVULSIONS WITH MILD GASTROENTERITIS: EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS AND OUTCOME

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Purpose: The aim of this study is to analyze the epidemiological, clinical and evolutional characteristics in patients who presented convulsions associated with mild gastroenteritis (CwG).

Method: Twenty-four medical records of patients hospitalized with CwG between January 1, 2000 and December 31, 2008 were reviewed. The criteria defined by Uemura et al (2002) were used in the diagnosis.

Results: A family history of epilepsy was presented in four patients (16.6%). PD prior to the onset were normal in all patients. The age at onset ranged from 9 to 65 months (mean: 18.1 months). The average interval between the onset of gastroenteritis and that of seizures was

3.8 days (range, 1–6 days). Throughout the follow-up of the 24 patients included in this study, 64 seizures were recorded. Seizures were mostly brief (<1 min) and apparently generalized, and often repetitive occurring in cluster (2.2 seizures per episode). Rotavirus antigen was positive in stools in 55.2% of cases. There were no abnormalities in serum biochemistry tests, including for the glucose level and electrolytes. CSF studies in all 10 episodes were normal. The interictal EEG was normal in all patients. Neuroradiological studies were performed in 11 patients with a normal result. The period of the follow up was 4.2 years, ranging from 1.5 to 9.8 years. Five patients (20.8%) experienced a recurrence episode of CwG during follow-up and one patients developed epilepsy.

Conclusion: CwG also occur outside Asia. This entity must be well recognized among pediatric neurologists as well as general pediatrician. Prognosis is excellent;

p353
CASE REPORT: EPILEPTIC SEIZURES IN A CHILD WITH PORENCEPHALY

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Purpose: To present a case of a child with porencephaly and simple motor partial seizures. Porencephaly as a presence of abnormal cavities or cysts in the brain tissue is a result of destructive lesion or damage from infection, loss of blood flow, stroke during brain development or genetic disorders. There is an enhanced capacity about epilepsy appearance in porencephaly during early development.

Method: The file of a girl, 10 years old is checked; it contains anamnestic data, neuropediatric examination, psychological, speech therapist and psychiatric explorations, EEG records and presentation of NMRI of the brain.

Results: There are significant anamnestic data of traumatic birth with considerable peri and neonatal problems; neuropediatric examination reveals coordination problems, left-side paresis, strabismus and persistence of simple motor partial epileptic attacks, light delay in mental and psychomotor development, EEG records bilateral epileptic changes, and the most significant are extensive morphologic changes of CNS. Lamotrigine has shown significant effects, an important reduction of seizure attacks is marked and improvement of intellectual development.

Conclusion: Prevention is of great importance: regular gynecologic controls during the pregnancy in order to discover and treat the risk factors, avoid the traumatic obstetric manipulations, and realization of a safe neonatal period. One of the key points in the treatment of epileptic attacks are antiepileptic drugs, in this case Lamotrigine, which has shown reduction in number of spike and wave episodes on EEG and improvement of mental, psychomotor and speech development.

Poster session: Genetics I
Tuesday 29th June 2010
13:30–14:30

p354
MDR1 POLYMORPHISMS IN CHILDHOOD DRUG RESISTANCE EPILEPSY

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Purpose: Despite considerable progress in pharmacotherapy of epilepsy, more than 30% of the patients are resistant to antiepileptic drugs. In recent years, overexpression of multidrug transporters in blood–brain barrier, have frequently been investigated. One of the frequently investigated genes that is found to be responsible for drug resistance in epilepsy is multidrug resistance 1 (MDR1) gene. In this study we aimed to screen the MDR1 gene for the most common polymorphisms C3435T and G2677AT in drug resistant epilepsy patients and control group.

Method: Thirty-nine children with drug resistant epilepsy and 95 control samples were involved in the study. The polymorphism detection was performed by PCR-RFLP and Pyrosequencing.

Results: We found no associations between C3435T and G2677AT polymorphisms and multidrug resistant epilepsy. Haplotype analysis including these 2 polymorphisms showed no significant association. Compound genotype analysis showed that CC^{3435}/GG^{2677} compound genotype found to be statistically higher in control group. As a conclusion, when analyzed seperately, these 2 MDR1 polymorphisms are considered not to be responsible for the responsiveness to either different or combined antiepileptic drug therapy in our study group.

Conclusion: CC^{3435}/GG^{2677} compound genotype might be considered to have a protective role in drug resistant epilepsy.

p355
A LARGE ADPEAF FAMILY NEGATIVE FOR LGI1. RESEARCH FOR A NEW LOCUS

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Purpose: Autosomal dominant partial epilepsy with auditory features (ADPEAF) is an idiopathic focal epilepsy syndrome with auditory auras as major ictal manifestations. Mutations in LGI1 gene were found in only 50% of ADPEAF families suggesting genetic heterogeneity. An highly informative pedigree with many affected members suitable for linkage analysis has not yet been found.

Method: Recently we observed a large ADPEAF pedigree of brazilian origin. The proband was a 46 year old woman presenting partial seizures with auditory features since the age of 8 years. All family members but the proband live in Brazil.

Results: The family comprises 176 members (excluding spouses) of whom 16 had epilepsy (3 deceased). We collected detailed information and blood samples from 68 family members. Direct sequencing and linkage analysis excluded the role of LGI1 in this family. The pair-wise simulation study for linkage analysis has been performed with the SLINK program, which yielded a mean and a maximum LOD score (at recombination fraction = 0) of 2.4 and 3.8 respectively. In the multipoint simulation, the SLINK and SUP programs together were used. Mean and maximum location scores were calculated, the mean score (3.4) as the mean of maximum location scores per simulation, the maximum score (4.7) as the maximum location scores over the 100 simulations.

Conclusion: We describe a large pedigree with the typical phenotype of ADPEAF and 13 living affected members. This family promises to be highly suitable for linkage analysis and subsequently for the identification o a gene other than *LGI1* responsible for ADPEAF.

p356
PHOTOSENSITIVITY IN A PATIENT WITH HALLERMANN-STREIFF SYNDROME: A CASUAL RELATIONSHIP?

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Purpose: Hallermann-Streiff Syndrome (HSS) is a rare genetic disorder, associated with a mutation in the GJA1 gene (6q) in some cases. It is characterized by dyscephalia, congenital cataracts, microphthalmia, proportionate dwarfism, abnormal dentition, hypotrichosis and skin atrophy. HSS is not known to be associated with epilepsy. We observed epileptic photosensitivity in a 23-year-old normally intelligent girl with typical HSS features.

Method: The girl, who showed congenital R-eye microphthalmia, bilateral strabism, cataract, nystagmus and glaucoma, was referred by her ophthalmologist because of photophobia especially for surgery-theatre lamps. A clinical-diagnostic workup included CT, MRI, VEP, screening for infectious causes, genetic counselling and dysmorphological evaluation. Video-EEGs were performed with standardized Intermittent Photic Stimulation (IPS) and pattern stimulation.

Results: HHS was diagnosed clinically. CT, MRI were normal. Since age 8 she had three occipital seizures (one GTCS), induced by flickering sunlight. She complains since childhood of cephalalgia and visual hallucinations during intense visual stimuli. EEG recordings showed besides normal background, spontaneous bilateral (R > L) epileptiform discharges over the temporal-occipital regions. Both focal and generalized Photoparoxismal Responses were elicited (8–35 Hz) with concomitant visual and vegetative symptoms. Flash-VEPs showed normal latencies, but low amplitude (R > L).

Conclusion: This is the first report of epileptic photosensitivity in a visually severely handicapped girl with HSS. The underlying pathogenetic mechanism is not yet clear. The photosensitivity can represent a visual cortical pathway reorganization, secondary to early visual deprivation. Otherwise, we can hypothesize that the same genetic alteration is responsible for both clinical pictures, in parallel or sequentially.

p357
IS THERE A LINK BETWEEN SCN1A MUTATIONS AND DEFICIENT THERMOREGULATION WITH HYPERTHERMIA AND ANHIDROSIS UNDER TOPIRAMATE TREATMENT? REPORT OF TWO CASES

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Background: Topiramate exerts its anticonvulsant effect through enhancement of GABA-activated chloride channels, blockage of voltage-dependent sodium channels and inhibition of excitatory neurotransmission and carbonic anhydrase. Anhidrosis is a possible side effect of topiramate, but the underlying mechanism is not fully understood.

SCN1A mutations are found in patients with various epileptic conditions, such as Dravet syndrome and generalized epilepsy with febrile seizures plus (GEFS+).

Cases: Patient A had GEFS+, patient B suffered from Dravet syndrome. Both had fever-induced seizures and SCN1A mutations (A: p.Leu1854-Ser, B: p.Arg701Stop). Hyperthermia in the summer and anhidrosis was noticed under topiramate treatment.

Discussion: The mechanism of anhidrosis through topiramate is not entirely clear. In the literature, inhibition of carbonic anhydrase isoenzymes in the eccrine glands has been suggested to be the underlying mechanism, but remains unproved. Sweat production is related to the core temperature sensed by the anterior hypothalamic peroptic nucleus. Our two SCN1A mutated patients developed anhidrosis under topiramate treatment. We hypothesize that anhidrosis in these patients is more a central thermoregulatory problem due to voltage-dependent sodium channel-blockage in the hypothalamic structures. In our patients this blockage is accentuated through dysfunctional, SCN1A mutated sodium channels (not expressed in the skin), leading to a lack of normal responses. This phenomenon may explain the increased tendency of patients with SCN1A mutations to hyperthermia and with it a higher vulnerability to fever. Further studies will be needed to confirm our hypothesis.

p358
FREQUENCY AND INHERITANCE OF MICRODELETIONS 15Q13.3, 15Q11.2 AND 16P13.1 IN IGE-PATIENTS WITH PHOTOPAROXYSMAL RESPONSE

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Purpose: Recently, a 1.5 Mb deletion at 15q13.3 has been shown to be associated with idiopathic generalized epilepsy (IGE) with a high risk for disease (OR ~50) n odds ratio of ~50. The same deletion was shown to be associated with other neurological disorders, but often with lower odds ratios. A similar observation was made for deletions at 15q11.2 and 16p13.1. The cause of the pathogenic effect, and the reason why the associated phenotype is so clinically varied is unknown. To further study the relationship between these deletions and epilepsy phenotypes, and to identify patients for follow-up studies, we have typed these deletions in a cohort of epilepsy patients who also show photoparoxysmal response.

Method: From various Mediterranean countries, we have collected a cohort of 132 patients with IGE, who also show photoparoxysmal response, along with their parents. Their parents were also phenotyped. We tested this cohort of probands and parents for the presence of the microdeletions, using realtime PCR assays.

Results & conclusion: The results will show the frequency of the different microdeletions in this cohort and in parents of these patients, enabling us to compute the penetrance and inheritance patterns.

p359
COEXISTENCE OF HIPOMELANOSIS OF ITO AND MOSAIC TURNER SYNDROME IN A 3-YEAR-OLD GIRL – A CASE REPORT

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Purpose: Hypomelanosis of Ito is a rare phacomatosis. The most typical for the syndrome are linear hypomelanotic skin lesions localized along Blashko lines. Among neurological signs most frequent are epilepsy (60% of the patients) and hemimegalencephaly. Genetic analysis may reveal mosaicism.

Method: The girl was born from the second pregnancy, at term, through surgical delivery, with appropriate weight, and received 10 points in

Apgar score. Neonatal TSH screening showed hypothyroidism. At the age of 9 months she was admitted to neurology out-patient department because of psychomotor delay. Physical examination revealed: dysmorphic features (short stature, microcephaly, hypertelorism) and linear hypomelanotic skin lesions on right side of the body. From the age of 2.5 years she began to experience night, partial epileptic seizures, preceded by febrile seizures. On EEG generalized spike and waves discharges and spikes at fronto-parietal regions were recorded. Brain MRI examination was normal. She was diagnosed as having a hypomelanosis of Ito and cytogenetic examination was done revealing karyotype: 45, X[50%]/46,X,r(X)(p22q28)[50%], typical for mosaicism in Turner syndrome. She was commenced on valproic acid and than switched to polytheraphy with lamotrigine, with good effect. She still presents slight psychomotor delay especially in aspect of speech development.

Conclusion: Linear hypomelanotic skin lesion with Blashko lines may be the only sign of hypomelanosis of Ito. Coexistence of this phacomatosis with genetic or chromosomal mosaicism is known from the literature. Unique is the accompanying mosaic Turner syndrome in the presented case.

p360
EXPRESSION PROFILE ANALYSIS OF PERIPHERAL BLOOD MONONUCLEAR CELLS IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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Purpose: The purpose of our study was verifying of usefulness of the peripheral blood mononuclear cells (PBMCs) gene expression profiling in diagnostics of human epilepsy.

Method: The study material was the peripheral blood mononuclear cells of 10 patients with temporal lobe epilepsy. The control group the 10 healthy adults was established. From PBMCs the total RNA was extracted. Our study was conducted using the Agilent Whole Genome Microarray Kit. Whole-genome microarray analysis was performed and verified by real-time quantitative RT-PCR.

Results: 43 376 human biological features was investigated. At False Discovery Rate adjusted $p < 0.05$ 1557 genes were significantly altered. To the most important upregulated genes belong: histone cell cycle regulation defective homolog, transketolase, G protein-coupled receptor 153 et alteres. To the most important downregulated genes belong: activating transcription factor 3, general receptor for phosphoinositides 1, CD 69 molecule et alteres.

Conclusion: We concluded that PBMCs profiling may be useful for diagnosis of patients with temporal lobe epilepsy.

p361
RITSCHER-SCHINZEL SYNDROME - 3C (''CRANIO-CEREBELLO-CARDIAC'') SYNDROME: A FIRST CASE REPORT IN CROATIA

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Purpose: Ritscher-Schinzel or cranio-cerebello-cardiac (3C) syndrome is rare autosomal recessive syndrome characterized by craniofacial, cerebellar and cardiac anomalies. Central nervous system anomalies include Dandy-Walker malformation, cerebellar vermis hypoplasia and enlargement of the cisterna magna. Ritscher-Schinzel syndrome is listed as a very rare disease by the Office of Rare Disease (ORD) of the National Institutes of Health and so far only about 30 cases are reported all over the world, mostly from North America and Europe. We present a first reported case of Ritscher-Schinzel syndrome in Croatia.

Case presentation: A young male patient born in 1972 clinicaly presented with craniofacial, cardiac and central nervous system abnormalities, but he also has syndactylia of 1st and 2nd finger on his right foot and abnormalities of vertebra. Soon after his birth, he was operated because of cleft palate, and in 1996 because of ventricular septal defect. In 1989 diagnosis of epilepsy (complex partial and grand mal seizures) was estimated. In March of 2009 he was hospitalized in University Hospital Centre Zagreb, Department of Neurology, where MRI of the brain was performed and showed Dandy-Walker malformation, cerebellar vermis hypoplasia and enlargement of the cisterna magna, but X-ray examination of the vertebra showed congenital block of C6-C7 and scoliosis of thoracal segment.

Conclusion: Based on clinical examination, neuroradiologic and radiologic diagnostic procedures we belive that our patient fill all necessary criteria for the diagnosis of this syndrome, and so far he is the oldest patient described in literature, and first described in Croatia.

p362
RARE STRUCTURAL GENOMIC VARIANTS IN NON-SYNDROMIC EPILEPTIC ENCEPHALOPATHIES WITH AND WITHOUT MRI-DETECTABLE STRUCTURAL BRAIN ABNORMALITIES

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Purpose: Structural genomic variations are frequently observed in neurodevelopmental disorders including idiopathic epilepsies. This study aims to determine whether such alterations may also contribute to the etiology of nonsyndromic epileptic encephalopathies with and without brain anomalies detectable by magnetic resonance imaging (MRI).

Method: One hundred twenty-one patients with nonsyndromic epileptic encephalopathies from six cohorts in three European countries were clinically evaluated, investigated by MRI and screened by genome-wide array platforms including bacterial artificial chromosome arrays, oligonucleotide arrays or single nucleotide polymorphism arrays.

Results: In addition to already known microdeletions, we found numerous losses and gains suspected to contribute to the disease. In 12 of the 64 (19%) patients with MRI-detectable brain anomalies and 4 out of 57 (7%) patients without MRI-detectable structural brain abnormalities, a previously not described structural genomic variation spanning one or more genes was found. While the frequency of rare structural genomic variants was not significantly different between groups, it is considerably higher than in control populations.

Conclusion: Our results indicate that genome-wide screening methods for rare structural genomic variants may provide clues for the genetic etiology in patients with an otherwise intractable form of epilepsy.

Performing such genome-wide screens might be considered as part of the diagnostic workup in patients with a broad range of epileptic encephalopathies, including patients with brain anomalies detectable by MRI. Results of these investigations may have important implications for genetic counseling of patients and family members.

p363
GENETICALLY DETERMINED EPILEPTIC SYNDROME

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Purpose: The last 6 years we examined seven patients, who belong to two different families, with epileptic seizures. (three males, four females, from 17 to 64 years old). Every patient's battery included EEG, brain CT scan, visual and auditory control, blood examinations and we sent all of them to the video EEG laboratory. All patients were short, with splints to the articulations of all extremities, they had troubles with their visual and auditory capacity and two of them had mental deficiency (IQ index from 76 to 90). All patients had presented epileptic seizures since their childhood. Although we looked to the epileptic seizure's classification there isn't any known genetical syndrom, presenting all those manifestations.

The antiepileptic drugs we perscripted to the patients were valproic acid, as monotherapy, or with topiramate. The frequency of the seizures reduced from 30% to 90%. The EEG findings also improved. All patients are still in the same AEDs, they keep doing the same job and we perform to them an EEG examination every 6 months. The serial blood examinations, are anormal, and the valproic serum blood level is therapeutic. We sent all other healthy members of the same family to the neurogenatical laboratory, in order to find out if there is any detectable genetical sign of this syndrome. Since now we don't have any result.

We keep looking for any new detail about the clinical manifestations of those patients. All laboratory examinations (EEGs, CT and MRI scans, blood examinations) are available.

p364
TERMINAL DUPLICATION OF CHROMOSOME 21 IN A PATIENT WITH MENTAL RETARDATION, FACIAL DYSMORPHISM AND SEVERE EPILEPSY

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Purpose: The percentage of epilepsy in patients with trisomy 21 (Down syndrome) range from 1–13%. Of this group, 32% have infantile spasms with or without classical hypsarrytmia. The chromosome 21 locus responsible for the infantile spasms is unknown. We report a 19-year-old female patient with mental retardation, facial dysmorphism and epileptic seizures carrying a 0.9 Mb duplication of 21q22.3-qter.

Method: Array-CGH on purified DNA from peripheral blood was performed using standard protocols.

Results: A terminal 0.9 Mb duplication of 21q22.3-qter was detected in a 19-year-old female patient without clinical features of Down syndrome. The patient had mental retardation, facial dysmorphism and epilepsy with different seizure types. Epilepsy started as infantile spasms with classical hypsarrhythmia at the age of 10 months, and later in life progressed into focal epilepsy with rapid secondary generalization.

Conclusion: This is the first report of a patient with duplication of 21q22.3 having infantile spasms and focal epilepy. We suggest that duplication of 21q22.3 may cause epilepsy in patients with trisomy 21.

Poster session: Neuropsychology II
Tuesday 29th June 2010
13:30–14:30

p365
NEUROPSYCHOLOGICAL FUNCTIONING IN A GROUP OF CHILDREN WITH BENIGN EPILEPSY WITH CENTROTEMPORAL SPIKES (BECTS)

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Purpose: The aim of the current investigation is to discriminate the neuropsychological functioning of children with BECTS from that of children with no health problems.

Method: Neuropsychological status was examined in 20 children with BECTS (6 males, 14 females), aged 7–14 years and compared with 20 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 neuropsychological assessment: Memory (List Learning, Rey Complex Figure, Corsi Test), Language (Rapid Naming, Phonological Awareness, Comprehension of Instructions, Verbal Fluency), Attention and Executive Functions (Cancellation Task, Trail Making Test, Tower of London) and Motor Function (Pegboard Test).

Results: Children with BECTS present deficits in language (semantic verbal fluency, and phonological awareness) and attention (sustained and divided).

Conclusion: This empirical research underlies the importance of assessing children with BECTS with neuropsychological assessment protocols that include several measures of language and attention. So that we can establish adequate and timely school intervention plans namely for those with school difficulties.

p366
ASSESSMENT OF DEPRESSIVE SYMPTOMS IN PATIENTS WITH EPILEPSY IN ROUTINE CLINICAL SETTING

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Purpose: To assess and to compare depressive symptoms in outpatients with epilepsy using two different scales for evaluation of depression.

Method: 199 outpatients (mean age 34.5 ± 15.2 years, 56.3% women) with epilepsy (mean duration of illness 10.0 ± 10.1) were assessed using a sociodemographic and clinical questionnaire, Lithuanian version of Hospital Anxiety and Depression Scale (HADS) and Beck Depression Inventory Scale (BDI) (individual interview).

Results: Severe depressive symptoms were determined in 39(19.6%) of patients using HADS and 39(19.6%) – BDI. Only 29.3% of patients with severe depressive symptoms were sent to psychiatrist because of depression, 34.8% used antidepressants before, and 10.4% used antidepressants during assessment. 32.1% of depressive patients referred suicides in first-line family members (7.0% in nondepressive group), and 25.0% had first-line family members with depression (7.7% in nondepressive group).

In 26 patients, who had family history of suicides, 7(26.9%) were referred to psychiatrist, 8(30.8%) had diagnosed depression, and 34.6% used antidepressants. In this group severe depression was determined in 11(42.3%) patients using HADS and BDI. Patients with significant depressive symptoms more frequently were unemployed (87.3%). We didn't find correlation between depressive symptoms and sex, duration of epilepsy, frequency of seizures and family status.

Conclusion: Depressive symptoms are frequently disregarded in patients with epilepsy in routine clinical setting. Depressive symptoms are more frequent in patients who have family history of suicide and depression and are unemployed. Both scales are equal for evaluation of depressive symptoms.

p367
EMOTION RECOGNITION IN MEDIAL TEMPORAL LOBE EPILEPSY IN THE VISUAL AND AUDITORY DOMAIN

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Purpose: Patients with chronic medial temporal lobe epilepsy (MTLE) can be impaired in different tasks evaluating so called emotional or social abilities. Among these, the recognition of facial emotions can result especially affected (Meletti et al. 2003, 2009). To better understand the nature of emotion recognition (ER) deficits in MTLE we investigated the decoding of basic emotions in the visual (facial emotions) and auditory modality (emotional prosody).

Method: Study population: 37 MTLE patients with MRI evidence of medial temporal sclerosis (mean age 38.7 years); 50 normal subjects served as controls. ER was evaluated by tasks of facial expressions recognition and emotional prosody recognition. Statistical analysis (MANOVA) was conducted comparing performances of MTLE versus controls with education and age as covariates.

Results: Overall MTLE patients were impaired in the recognition of both facial end vocal expressions ($p < 0.05$). As far as basic emotions, sadness and fear recognition was defective in both modalities ($p < 0.05$). On the contrary, the recognition of disgust and happiness was not significantly different from controls performance neither for faces nor for prosody. Anger recognition resulted defective for the visual modality alone ($p < 0.01$). Correlation analysis of recognition in both modalities resulted highly significant: Pearson 0.6 ($p < 0.001$).

Conclusions: we observed deficits both in the recognition of facial and vocal expression of emotions. A strong correlation of performances in two modalities was evident suggesting that ER impairment in MTLE is not dependent from the sensory channel through which the emotional stimulus is presented.

p368
EXECUTIVE FUNCTIONS IN GENERALIZED IDIOPATHIC EPILEPSIES

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Purpose: The aim of our study was to assess the cognitive and intellectual functions in different idiopathic generalized epilepsies with special consider on executive functions (EF).

Method: Assessment was performed in a group of patients at The Department of Developmental Neurology in University of Medical Science in Poznan: 20 with diagnosis of juvenile myoclonic epilepsy (JME), 30 with childhood and juvenile absence epilepsies and control healthy children. Beside classical cognitive tests we use computerized neuropsychological battery ''FEPSY.'' Awaking EEG and sleep EEG were analyzed.

Results: Our results show different cognitive impairment depend on idiopathic generalized epilepsy syndrome. The more impairment we found in memory and vigilance. The executive functions were most disturbed in all epileptic groups. The results of intellectual functions did not correlate with cognitive deficits.

Conclusion: Our results postulate that dysfunctions in EF are not the distinguish parameter between the cognitive profile's in different epilepsy syndromes particularly in IGE. Perhaps explanation of that fact is that EF appear as the last in cognitive development and they are built on other functions, they highly correlate with vigilance and memory. Thus, observed in our group disturbance in the ontogenetically earlier developed functions hamper typical progress in EF in studied group. There is a deep need for systematic neuropsychological assessment of cognitive functions in group of children with generalized idiopathic epilepsy.

p369
POSTSURGICAL MEMORY DEVELOPMENT—A COMPARISON BETWEEN YOUNG AND MIDAGE GROUPS

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Purpose: We have found significant variability in memory development after temporal lobe epilepsy surgery. We aimed to explore the possible effect of age on postsurgical memory outcome with respect to etiology, duration of disease, surgery in dominant hemisphere and preoperative Wada test results.

We observed memory development in patients after temporal lobe epilepsy surgery to find and explain difference in memory change in groups of patients up to 30 years and over 45 years of age.

Method: We selected 6 male patients aged over 45 years who underwent temporal lobe epilepsy surgery. The patients were balanced by 12 males between 17 – 30 years who were similar to the first group in duration of disease, surgery in dominant hemisphere, preoperative Wada test results and Engel's outcome.

Both groups were observed for 5 years. The memory quotient was examined immediately before surgery, one year after surgery and five or more years after surgery. Memory changes in two periods of time were evaluated.

Results: We did not find significant differences between the groups in MQ changes between presurgical and a year after surgery examinations. On the contrary, we found significant deterioration in the group over 45, compared to young men, when the memory changes between 1 – 5 years after surgery had been taken into account.

Conclusion: Our data prove the expectation that the postsurgical memory of surgically treated patients aged over 45 decreases. It seems probable that the deterioration does not follow surgery immediately but rather in long-term development.

p370
DMS 48: A VISUAL MEMORY TEST SENSITIVE TO DIFFERENTIATE LEFT FROM RIGHT TEMPORAL LOBE EPILEPSY

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Purpose: Typical language representation provided, memory deficits are expected for verbal material in left temporal lobe epilepsies (LTLE)

and for nonverbal contents in right temporal lobe epilepsies (RTLE). The first one is already well established. Diagnostic tools such as word lists and short story recalls are well established. However, visual memory diagnostics have been questioned concerning the validity of the material-specific hypothesis. This study investigated if the DMS 48 visual recognition memory test might be a valuable tool to differentiate LTLE from RTLE.

Method: 38 adult patients with TLE (17 LTLE and 21 RTLE) with average intellectual levels (>25 on the Raven Matrices), treatment with one or two AEDs, and a typical language representation according to fMRI, were investigated at two measuring points by means of the DMS-48. This visual recognition memory test demands the patient to look at 48 repetitive abstract and concrete stimuli and to estimate if the picture has more or less than 3 colors. Immediately and 1 h post encoding the subjects are asked to recognize the previously presented stimuli among a set of distractors.

Results: Concerning immediate recognition, the differences between the two groups were significant with lower scores for the RTLE patients ($t = 6.66$, $p < 0.0001$). At the delayed measuring point, the discrepancy was even more pronounced ($t = 8.86$, $p < 0.0001$). One hour post encoding, 19 out of 21 RTLE patients had pathological results.

Conclusion: This study suggests that the DMS 48 is a sensitive instrument to seize mesiotemporal lobe dysfunctions in the nondominant hemisphere.

p371
SEVER PROGRESSIVE NEUROPSYCHOLOGICAL IMPAIRMENT IN A CHILD WITH CEREBELLAR VERMIS HYPOPLASIA AND EPILEPSY: 10-YEAR FOLLOW-UP

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Purpose: Study presents a 10-year-follow-up neuropsychological data of the 12-year-old boy diagnosed with febrile seizures, epilepsy and inferior cerebellar hypoplasia. In the age of 3 the child was referred for neuropsychological consultation due to delayed speech development.

Method: Neuropsychological assessment was based on: Terman-Merrill Scale, chosen subtests from Wechsler Intelligence Scale for Children, Raven Matrices Test, neuropsychological testing battery, clinical observations and interviews collected from 10 years regular follow-up visits. Genetic, metabolic, magnetic resonance and electroencephalographic diagnostics were administered.

Results: Focal seizures, secondarily generalized with loss of consciousness and occasionally mild tonic–clonic component with low-voltage single spikes intermittently observed bilaterally in the centro-temporal areas during sleep. Seizures were treated with topiramate and carbamazepine. Remission periods (1–6 months) alternated with periods of refractory seizures (2–12 months). MRI revealed hypoplasia of the inferior cerebellar vermis. No specific etiology was confirmed. Intellectual functioning revealed metal retardation: I – 3 to 5 years of age – (IQ 70 – 51) mild; II – age 6–8 – (IQ 48 – 44) moderate; III – age 9–12 – (IQ < 34) severe. Out of cognitive functions, the speech production, visual-motor integration, graphomotor skills and attentional processes were particularly impaired. In the emotional sphere occurred selective mutism, emotional lability, anxiety, strong separation reactions and aggressive behaviors.

Conclusion: Despite antiepileptic treatment and multimodal neuropsychological stimulation dramatic decline in global intellectual level and progressive cognitive impairment continued. Authors debate weather the cause of deteriorating neuropsychological status is refractory epilepsy, pharmacotherapy or progressive degradation due to the cerebellar defect.

p372
DOUBLE DISSOCIATION BETWEEN ANTERO- AND RETROGRADE AMNESIA IN TWO CASES WITH BILATERAL HIPPOCAMPAL DAMAGE

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Purpose: We studied the dissociating anterograde and retrograde memory profile of two patients with bilateral hippocampal sclerosis in order to address the diversity of performance in two individuals with almost similar lesions.

Method: A.O. is a 23-year-old right-hander with a basic education level. Epilepsy onset was at age 10 years. The history was without significant medical insults. A bilateral hippocampal sclerosis was proven on MRI. The second patient, M.A. is 40 years old. He is also right-handed and has a similar education background. The first seizure occurred at the age of 38 following limbic encephalitis that had destroyed both hippocampal regions. Neuropsychological assessment of anterograde episodic and retrograde semantic and episodic memory was carried out.

Results: A double dissociation between antero- and retrograde memory performance was found: A.O. scored average on verbal and visual anterograde recall while he had a poor performance on both, the episodic and semantic retrograde memory examination. M.A. failed all anterograde tasks, however the results for the retrograde parts were spared.

Conclusion: The double dissociation described demonstrated that similar structural lesions may cause contrary dysfunctions. We hypothesize that the different age othe underlying insult was the crucial factor to determine the adaptation process and thus the different cognitive performance.

p373
COGNITIVE FUNCTIONS IN EPILEPSY

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Purpose: Considering antiepileptic drug intervention, not only absence of seizures, but also preservation of cognitive performance and psychosocial health are of prime importance. Therapeutic interventions may alter the cognitive profile. Unwanted cognitive and mood side effects of antiepileptic drugs may seriously compromise the patients ability to work, his quality of life, and affect his compliance. These unwanted effects vary considerably. To avoid these drawbacks, the individual cognitive and mood changes in the course of therapy should call our attention.

Method: We developed a computerized cognitive test battery (CCTE), evaluated by standard neuropsychological tests, which allows the standardized assessment of cognitive functions at risk of antiepileptic medication (attention, cognitive speed, verbal and visual working memory, verbal and spatial memory). Emotional variables like depression, anxiety, irritability, sleep quality and subjective performance are recorded by means of visual scales. 200 epilepsy patients and 80 normal controls were investigated.

Results: We could demonstrate significant cognitive changes ($p < 0.05$) related to titration and withdrawal of different antiepileptic treatments (topiramate, levetiracetam, lamotrigin). In addition the appropriateness to detect focus lateralization in epilepsy was proofed. Thirty patients with mesial temporal lobe epilepsy (mTLE) from our epilepsy presurgery program were investigated. Significant differences ($p < 0.05$) in specific verbal and spatial subtests were revealed between patients with left and right mTLE.

Conclusion: We could demonstrate medication related changes in the individual's cognitive and mood profile, indicating that a regular assessment of these functions is essential to keep track of unwanted side effects and to optimize therapeutic interventions.

Poster session: Epileptic encephalopathies
Tuesday 29th June 2010
13:30–14:30

p374
EPILEPSY AT THE AGE OF SEVEN YEARS IN CHILDREN WITH NEONATAL HYPOXIC-ISCHEMIC ENCEPHALOPATHY

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Purpose: Neonatal hypoxic-ischemic encephalopathy (HIE) is the most common cause of long term neurologic deficits in children. The survivors with HIE were prospectively studied for long-term prognosis and neurological outcome.

MethodA cohort of 103 full-term infants with HIE were assessed during the neonatal period. All infants were followed until aged 7 years for incidence of epilepsy and long-term neurological deficits.

Results: The neurological outcome at the age of seven years was normal in 84%of infants, moderately abnormal in 7% and severely abnormal in 9%. Seizures occured in 9 patients (9%) and were associated with severely abnormal neurological outcome. Seizures were classifield as infantile spasms (4 infants), complex focal (3) and generalized tonic–clonic (2). Analysis of HIE severity showed grade I HIE in 42% of infants, grade II in 24% and grade III in 34%.EEGs recorded in the neonatal period and during the follow up were normal in 65%, moderately abnormal in 22.5% (intermediate pattern) and severely abnormal in 12.5% (low-voltage slow-wave background activity, spike-waves discharges). All infants were treated with different antiepileptic drugs (AED): valproates (5), steroids (4), carbamazepine (2), vigabatrin (3) and lamotrigine (2). In 7/9 a complete seizures control and stable remission was achieved. Epilepsy developed in infants with grade III HIE and severely abnormal EEG and in none with grade I HIE and normal EEG.

Conclusion: Term infants with perinatal grade III HIE and severely abnormal EEGs had the greatest risk for developing epilepsy.

p375
A HIGHLY EVOCATIVE ICTAL AND INTERICTAL EEG PATTERN IN ALPERS' DISEASE WITH *POLG1* MUTATIONS AND ONSET BY STATUS EPILEPTICUS

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Purpose: The main purpose of this report is to draw attention to a thus far poorly reported EEG pattern which is highly evocative of Alpers' disease with *POLG1* mutations.

Alpers' disease is an autosomal recessive disorder of early childhood. Clinical signs are refractory seizures, particularly epilepsia partialis continua, neurological deterioration and progressive or rapidly fatal hepatic failure. Electroencephalographic workup has identified a characteristic pattern, recently termed RHADS (rhythmic high-amplitude delta waves with superimposed poly-spikes). A causal relationship between Alpers' disease and mutations in the polymerase γ gene, a major disease gene in mitochondrial disorders, has now been established.

Method: We present the electroclinical characteristics of a boy who developed normally until the age of 17 months when he experienced a first episode of refractory status epilepticus followed by intractable seizures. *Epilepsia partialis continua* was not present. Two months later he experienced a second episode of status and a fatal liver dysfunction.

Results: At onset, encephalitis was suspected but biological and CSF parameters were normal. Since the first recording, EEG monitoring showed unusual, high amplitude delta wave activity with superimposed (poly-)spikes, intermixed with more rhythmical delta and spike sequences. This pattern was identical to RHADS. Molecular genetic analysis revealed that the patient was compound heterozygous for two missense mutations in the *POLG*1 gene.

Conclusion: RHADS can be considered as an early and distinctive EEG pattern highly evocative of Alpers' disease due to POLG1 mutations even when there is atypical onset by status epilepticus.

p376
EPILEPTIC SPASMS IN CEREBRAL PALSY: PRELIMINARY RESULTS

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Infantile spasm is an age-dependent epileptic syndrome associated with many underlying conditions and characterized by specific ictal manifestation and specific pattern EEG.

Purpose: To evaluate the epileptic and developmental evolution in infants with symptomatic infantile spasm and cerebral palsy and to determine early predictors of outcome in this form of epilepsy.

Method: We have retrospectively valued the clinical and electroencephalogram (EEG) characteristics of symptomatic infantile spasm, with a follow-up at 2 years

Results: 35 patients of which 14 boys and 21 girls were included in the study. The average age at onset of epileptic spasm was 6.3 months (SD ± 4.18) and at the onset all patients showed a psychomotor delay. At the onset, higher prevalence of other seizure types occur with epileptic spasms in 42% of patients; 25.7% of patients showed other generalized seizures. At the follow-up at 2 years, 48% of patients was epileptic spasms-free, 52% of patients showed high epileptic spasms frequency. 51% of patients had other seizure types and 28% showed focal seizures. 91% of patients showed a mental retardation at the follow-up. Early onset and initial high frequency of epileptic spasms, initial high frequency of other seizure types, EEG slowing, white matter damage and brain malformation were associated with an increased risk of intractable epilepsy at the follow-up ($p < 0.05$).

Conclusion: Our data suggest that there are complex relationships between underlying etiology, clinical features and clinical outcomes and that children at greater risk of developing intractable epilepsy can be identified early.

p377
EPILEPSY, PRECOCIOUS PUBERTY, IMMUNE RELATED DIABETES MELLITUS, AND TEMPORAL LOBE PATHOLOGY

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We present two cases, one with limbic encephalopathy and the other with mesial temporal lobe epilepsy sharing clinical findings of immune mediated diabetes mellitus, precocious puberty, behavioral problems along with the presence of anti-GAD antibodies.

Case A presented at the age of 4½ years old with right facial and limb tremors along with behavioral problems. The initial EEG showed left side slowing and the MRI increased T_2 and Flair signal mainly on left hippocampal area. The patient was treated with steroids and IVIG without significant improvement. She also developed focal seizures with secondary generalization partially controlled with antiepileptics. During the course of the disease she developed an insulin dependent diabetes mellitus with positive anti-GAD, anti-Insulin and anti-Islet antibodies, as well as precocious puberty.

Case B presented at the age of 5 years old with auras and psychomotor spells and autonomic symptomatology. The initial EEG showed periodic runs of left temporal θ activity and the MRI left hippocampal atrophy. In the course of the disease she developed precocious puberty, hypothyreoidism with positive antithyreoglobulin antibodies and diabetes mellitus with anti-GAD, anti-Insulin and anti-Islet antibodies. The patient received four courses of IVIG and she is currently on antiepileptic medication with a good seizure control but problematic behavior.

Our index patients share epilepsy due to temporal lobe pathology, immune mediated endocrinopathies and positive anti-GAD antibodies. We believe that the sequence of the clinical findings is not accidental but the result of a common immune mediated process that alters both neurochemical excitabilty and hormonal functions.

p378
TWO PATIENTS WITH MALIGNANT MIGRATING PARTIAL SEIZURES IN INFANCY

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Purpose: Malignant migrating partial seizures in infancy is devastating age specific epileptic encephalopathy which still presents an etiologic, pathophysiologic, clinical and therapeuric problem. We report the clinical course of two patients.

Method: Patients were diagnosed and treated in the Neurologic Department of Mother and Child Health of Serbia during 2006 and 2008. Both patients came at two months of age, and were extensively investigated (imaging, metabolic investigation). First patient was treated with numerous conventional and new AEDs before bromides, stiripentol, and levetiracetam were introduced. Second parient was diagnosed on the day of arrival, and was treated with combination of mentioned AEDs in the first month.

Results: Diagnosis was made on the basis of nearly continuous motor seizures with lateral eye deviation, blinking, chewing, drooling, flushing and elevation of one arm. Ictal EEG showed rhythmic Beta, sharp Theta or sharp slow wave of different duration shifting from one to another hemisphere. The first patient responded to combination of bromides, stiripentol, and levetiracetam introduced after 4.5 months, and had only short multifocal seizures afterwards. The features of the syndrome persisted until 20 months of age when she died of pneumonia. Second patient showed therapeutic response to administered AEDs and after a month had only four to five clinically recordable seizures, and now is 13 months old. Both patients did not show any developmental progress.

Conclusion: Antiepileptic drugs previously reported to be beneficial in case reports of this epileptic encephalopathy when given concomitantly may substantially reduce the number and severity of seizures.

p379
UNILATERAL HEMISPHERIC POLYMICROGYRIA ASSOCIATED WITH PHARMACORESISTANT ELECTRICAL STATUS EPILEPTICUS DURING SLEEP (ESES) IN CHILDREN: EFFICIENCY OF VERTICAL PARASAGITTAL HEMISPHEROTOMY (VPH)

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Purpose: To study clinical and electrophysiological features in a population of 12 children operated on by VPH for pharmacoresistant ESES due to unilateral polymicrogyria

Method: From a population of 150 children who underwent VPH for pharmacoresistant epilepsy at our institution, we studied a series of 12 patients with ESES due to unilateral polymicrogyria. Clinical charts and electrophysiological data were retrospectively reviewed. The postsurgical outcome is reported.

Results: Mean age at seizure onset was 29 months (range 7–51) and mean age at diagnosis of ESES was 4.7 years (range 4–7.8). Seizures associated with ESES were partial motor seizures, atypical absences and drop attacks. All patients had some degree of developmental delay associated with a hemiparesis; during ESES all of them evidenced a cognitive decline and 7 had a worsening of the hemiparesis. In all, ESES was pharmacoresistant to antiepileptic drugs, including corticosteroids. VPH (7 left and 5 right) was performed at a mean age of 8 years (range 5–11). The outcome of epilepsy, with a mean follow-up of 4 years (range: 2–6) showed that in all patients ESES disappeared whereas 11 (91%) became seizure-free. An improvement of behavioral and cognitive condition was observed in all.

Conclusion: ESES is often encountered in polymicrogyria and responsible for an aggravation of the neurological condition when accurate medication fails. In the cases where the malformation involves one hemisphere, VPH can be proposed as a safe treatment leading to the relief of ESES.

p380
A FIVE-MINUTE SLEEP SEGMENT MAY BE SUFFICIENT TO DIAGNOSE ELECTROGRAPHIC STATUS EPILEPTICUS OF SLEEP (ESES)

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Purpose: ESES is characterized by a dramatic sleep activation of continuous spike-wave discharges, occupying ≥85% of non-REM-sleep and an overnight EEG is considered the gold standard for its diagnosis. Previously, we demonstrated that the spike wave index (SWI) calculated from the initial 300 seconds of non-REM sleep (SWI300) is well-correlated with the SWI derived from an average of three evenly-distributed overnight 100-s non-REM segments. In the present study, we examined whether the diagnosis of ESES obtained by calculating an overnight SWI can also be determined by the SWI300 measured in the first 5 min of sleep.

Method: Overnight EEGs (N = 8) recorded from patients with confirmed ESES were reviewed by visual inspection. EEGs were systematically edited per hospital protocol to display the first 5 min of each consecutive hour. SWI was calculated as a percentage of 1-s bins containing at least one generalized spike-wave complex. SWI300 was compared to the overnight SWI which was previously calculated for clinical purposes.

Results: Profound sleep spike-wave activation was apparent on EEG at sleep onset in all cases with the SWI300 ranging from 85.0% to 99.3% (mean 93.1 ± 5.5%). Thus the SWI300 sensitivity in diagnosing ESES was 100%.

Conclusion: Our preliminary data suggest that ESES may be diagnosed by calculating the SWI from a relatively short non-REM sleep segment at sleep-onset, and that perhaps an overnight EEG may not be necessary for diagnosis. Further validation of this observation is ongoing at time of this writing.

p381
CHILDREN WITH SCN1A MUTATIONS AND EPILEPTIC ENCEPHALOPATIES TREATED WITH KETOGENIC OR ATKINS DIET

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Purpose: To investigate if children with medically intractable epilepsies due to SCN1A mutations would profit from dietary treatment.

Method: 9 children (4 females/5 males) with SCN1A mutations and classical Dravet syndrome (DS) (6), or nonclassical Dravet epileptic encephalopathy (3) were included in this study. The children were between born between 1992 and 2008, 1.5–17.5 years old and all had epilepsy onset at 4–5 months of age, (50% after 1st vaccination) and long lasting febrile seizures. All had tried 3–12 relevant AEDs and accepted treatment with either classical ketogenic diet or modified Atkins diet.

Results: Two of the 6 children with classical DS, had either more than 90% seizure reduction or became completely seizure-free. The two oldest children with classical DS had no seizure reduction from the diet but an improvement in the quality of life. The 3 children with nonclassical Dravet epileptic encephalopathy all responded to the diet – one with 50% seizure reduction, one with more than 90% seizure reduction and one became seizure-free.

Discussion: No previous studies have monitored the effect of diet on patients with SCN1A mutations. In our group the responder rate in children with classical DS and SCN1A mutation didn't differ from the responder rate in other investigated groups. On the other hand children with nonclassical Dravet syndrome and SCN1A mutation showed a 100% responder rate, suggesting the diet as a valuable early treatment option in this patient population. Relation to individual type of mutation will be discussed.

p382
INITIAL EEG FEATURES AND EFFICACY OF VIGABATRIN IN THE PATIENTS WITH WEST SYNDROME

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Purpose: This study was performed to review the early EEG features of West syndrome (WS) and to assess the efficacy of vigabatrin (VGB) in newly diagnosed West syndrome in relation to etiology.

Method: Sixty four patients were included. All patients were treated with VGB and had been followed up at least 6 months. The earliest available EEGs after the onset of WS were reviewed focusing on the severity of hypsarrhythmia and the presence of atypical patterns.

Results: Forty one (64%) patients were symptomatic and 23 (36%) were cryptogenic. Twenty five (39%) patients became spasm-free either with monotherapy (20, including 8 patients with tuberous sclerosis) or after add-on therapy (5) of VGB. Twenty seven (42%) EEGs showed atypical hypsarrhythmic patterns: voltage attenuation (19), asymmetry (7), constant focality (2), increased synchrony (2), or no epileptiform discharge (1). Mean hypsarrhythmia severity score was 5.9 (0–12). The severity of hypsarrhythmia in the initial EEGs did not affect response to VGB treatment. However, atypical hypsarrhythmia and hypoxic ischemic encephalopathy as an etiologic factor were associated with the poor response to VGB treatment.

Conclusion: This study demonstrates the efficacy of VGB as an initial treatment for WS. Initial EEG features may serve as prognostic factors predicting favorable response to VGB in the patient with WS.

Poster session: Epileptic encephalopathies and neonatal seizures/syndromes
Tuesday 29th June 2010
13:30–14:30

p383
SEIZURES AS A PRESENTATION OF NEUROBLASTOMA IN A 5 MONTH OLD CHILD

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Opsoclonus-myoclonus and acute cerebellar ataxia may be presenting features of occult neuroblastoma. Seizures and arrested development are unusual manifestations.

5-month old healthy male infant, admitted with acute onset of focal seizures. Improvement with administration of carbamazepin was observed, but some days later seizures recurred, with clusters of brief symmetric flexion jerks, occurring on awakening. Development was initially normal, followed by arrested milestones and regression. His first EEGs were well structured, with posterior focal spikes and spike-waves, predominantly in the left hemisphere. Shortly after his EEG worsened, with near-hypsarrhytmic features. Vigabatrin was started with some improvement. Pyridoxine administration did not change the seizures neither the EEG. Cranial MRI, cerebrospinal fluid, genetic and metabolic studies (organic acids, amino acids, neurotransmitters, lactate, biotinidase) were normal. On the 21st day of seizures a vanillmandelic and homovanillic peak in the urine was observed. Abdominal-pelvic ecography and MRI disclosed a presacral mass, measuring 55 mm x 40 mm. Diagnosis of neuroblastoma was confirmed by biopsy. Chemotherapy and monthly dexamethasone pulses were started. Seizures abruptly disappeared in 3 days. Two weeks later EEG became normal and he progressed. Vigabatrin was progressively stopped. He had never eye movements suggestive of opsoclonus-myoclonus. Extensive search for auto-antibodies, including anti-Hu, Ri and Yo antineuronal antibodies, was negative.

An immunologic mechanism of antibodies against neuroblastoma tumor antigens cross-reacting with CNS antigens is the hypothesis admitted in opsoclonus-myoclonus. In this infant, we speculate that neurological manifestations could have a similar pathogenesis. Epileptic encephalopathy may be a paraneoplastic neurological syndrome associated with neuroblastoma.

p384
INTRACTABLE EPILEPSY IN TUBEROUS SCLEROSIS COMPLEX: LONG-TERM EFFECTS OF VAGUS NERVE STIMULATION ON SEIZURE CONTROL, COGNITION AND BEHAVIOR

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Purpose: The aim of the present study was to investigate the long-term effects of vagus nerve stimulation (VNS) on clinical, cognitive and

behavioral variables in a population of patients with tuberous sclerosis complex (TSC) associated to intractable epilepsy.

Method: This retrospective study comprized 11 patients with TSC (age at implant time: 14.40; range; 3–35) who underwent implantation of VNS for treatment of intractable epilepsy, and were evaluated until 36 months after the implant (mean follow-up: 38 months). Neuropsychological testing was carried out before and 1 year after the implant.

Results: eizure reduction at 12 months after the implant was rated class IA (80–100% reduction) in 1 patient (10%), IIA and IIB (50–79% reduction) in 8 patients (72%), IIIB (<50% reduction) in 3 patients (27%), according to McHugh classification. One year after VNS implantation, two patients reported an improved cognitive functioning; all patients experienced a higher level of alertness/attention and reduced impulsivity and aggressive behaviors. Patients younger than 6 years at implant age (40%) reported greatest benefits in cognitive variables. Moreover, all patients reported some improvement in adapting behavior, especially in communication and socialization. Finally, both seizure reduction at 1 year and the age at implant time were positively associated to the improvement in the quality of life.

Conclusion: The findings suggest that VNS is an effective therapy in reducing seizure frequency and preserving or improving cognitive and behavioral development in patients with TSC and intractable epilepsy, especially when treated in early age.

p385
HYPERTROPHIC CARDIOMYOPATHY ASSOCIATED WITH ACTH THERAPY FOR CHILDHOOD SEIZURE DISORDER

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Purpose: Hypertrophic cardiomyopathy is a relatively rare, potentially fatal complication of ACTH therapy.

To evaluate the incidence, clinical symptoms and prognosis of hypertophic cardimyopathy during ACTH treatment for childhood seizure disorder.

Method: 16 children, aged 4–38 months, treated for seizure disorders with ACTH were included in the study. Echocardiography was performed prior initiating therapy and every month until treatment was discontinued. Other side effects of ACTH were also monitored.

Results: 3 children (18%) developed hypertrophic cardiomyopathy with asymetric septal hypertrophy. Blood pressure was high in those children and in 3 more children with normal echocardiography findings. Echocardigraphic changes resolved in all patients within 3 months after termination of therapy.

Conclusion: Hypertophic cardimyopathy occur more often than realized during ACTH treatment for childhood seizure disorder. A routine echocardiogram study should be done at least to children with high blood pressure. All changes were reversible after discontinuation of treatment.

p386
ELECTRICAL STATUS EPILEPTICUS DURING SLOW WAVE SLEEP: CLINICAL AND ELECTROPHYSIOLOGICAL CORRELATION

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Introduction: Encephalopathy with electrical status epilepticus during slow wave sleep (ESES) is a partly reversible, age related childhood epileptic encephalopathy with the triad of seizures, neurophysiological impairment and typical EEG findings.

Material and Method: 15 patients (male = 8, female = 7) followed up at Child Neurology Division of Ege University with the EEG findings of ESES were clinically and electrophysiologically evaluated.

Results: The mean age of ESES onset was 7.9 years (SD: ±20 months). The previous history was unremarkable in seven (46%) of the patients, while the others (54%) had history of asphyxia, prematurity, neonatal convulsions or febrile seizures. The seven (46%) of the patients had epilepsy history among the first or second degree relatives. The mean age at the first seizure was 4.2 years (SD: ±32 months) and the mean interval between the first seizure and ESES onset was 3.8 years (SD: ±32 months).Seizure types were complex partial (34%), generalized tonic (40%) and tonic–clonic (14%), focal clonic (6%), myoclonic (6%). Before the development of ESES, five patients were following as benign childhood epilepsy with centrotemporal spikes or childhood epilepsy with occipital paroxysms. Before ESES, the most frequent EEG abnormality was focal epileptiform activity (54%). Valproic acid and carbamazepine was the mostly used drugs before the onset ESES. Valproic acid, topiramate and ACTH was used in %60, 53% and 26% of the patients respectively when ESES was diagnosed. EEG patterns and cognitive abnormalities partially recovered only in half of the patients.

Conclusion: Early recognition of ESES development in epileptic children is essential both for seizure control and prevention of cognitive impairment.

p387
RUFINAMIDE FOR REFRACTORY EPILEPTIC ENCEPHALOPATHIES IN CHILDHOOD

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Introduction: Refractory epileptic encephalopathies are a challenge for child neurologist to manage and is very difficult to reach a full seizure control. Even to obtain a 50–75% of seizure control is a meaningful purpose for these patients. Rufinamide has demonstrated to be very effective in Lennox-Gastaut syndrome and recently have been used also in other generalized epileptic syndromes and in refractory focal epilepsies with promising results.

Purpose: In order to reach a maximum seizure control in epileptic patients with epileptic encephalopathies out of control of different etiologies we decided to use rufinamide as add-on therapy.

Method: Eleven children (7 girls and 4 boys) aged between 4–14 years were treated as add-on therapy with rufinamide 600–2400 mg per day. There were several etiologies: 4 cases were cryptogenic, 3 cerebral malformations, 3 secondary to perinatal hypoxia and the last one was traumatic. Every patient took previously at least one antiepileptic drug. Seizure type was chiefly generalized. All patients had daily seizures.

Results: All children but one had significant seizure reduction. Frequency episodes evolve from daily to weekly or monthly episodes, that is to say a 50–75% in seizure frequency reduction. As an add-on effect we observe a better cognitive performance in the majority of patients treated with rufinamide.

Conclusion: Refractory epileptic encephalopathies in childhood have an excellent response to rufinamide in seizure frequency and in neuropsychological aspects.

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NATURAL HISTORY OF TREATED NEW-ONSET EPILEPSY IN CHILDREN: A LONG-TERM FOLLOW-UP COHORT STUDY IN A SINGLE CENTER

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Purpose: Investigate the different patterns of seizure evolution and role of epilepsy syndrome on seizure outcome in new onset pediatric epilepsy.

Method: Evolution of remission and relapse in the course of epilepsy was examined in 326 children (<15 years of age). Etiology of epilepsy syndrome was classified as: idiopathic generalized epilepsy, idiopathic partial epilepsy, cryptogenic partial epilepsy, symptomatic partial epilepsy, and epileptic encephalopathy. Different remission-relapse patterns were determined in each patient and according to epilepsy syndrome. The probability of repeated remission and relapse was analyzed with Markov process.

Results: During follow-up (mean ± SD: 79 ± 25 months), early remission starting within the first year of treatment was seen in 289 patients (88.6%), and late remission was achieved in 20 patients (6.1%). Remission was not occurred in 17 patients (5.2%). Of 309 patients experienced remission, first, second, and third relapse was occurred in 127 (39%), 70 (21.5%), and 39 patients (12%). At the end of follow-up, 281 patients (86.2%) were in terminal remission. Of this, 194 patients (59.5%) showed remitting course, and 87 patients (26.7%) showed remitting-relapse course. 45 patients (worsening course in 28 patients; 8.6% and drug resistant course in 17 patients; 5.2%) did not show terminal remission. Markov process disclosed that children with epileptic encephalopathy and symptomatic partial epilepsy were less likely to remit than children with idiopathic partial or generalized epilepsy ($p < 0.001$).

Conclusion: Poor seizure outcome was found in small portion of new-onset pediatric epilepsy. Etiology of epilepsy syndrome is an important factor to determine poor seizure outcome.

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CLINICAL CHARACTERISTICS WITH RISK FACTORS FOR TERM NEONATAL SEIZURES

Suh E

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Purpose: Neonatal seizures reflects neurologic disorders, affecting neonatal morbidity and mortality. Nevertheless, risk factors for seizures in term infants have been less well defined. We studied risk factors and clinical manifestations associated with term neonatal seizures.

Method: We used retrospective case-control frequency matching study.We do not only identified risk factors for term neonatal seizure, also analyzes day of seizure onset, seizure types, findings of EEG and neuroimagings, and response to treatment.

Results: Our data showed the asphyxia is the most important risk factors for neonatal seizures in term infants. We could not find the relationship between the maternal risk factors and the rsik of term neonatal seizures. Day of seizure onset were diverse. The seizure caused by asphyxia occurred earlier, of which 90% did within the first 48 h. Various type of seizures were observed of which subtle seizures were the most common-type in neonatal asphyxia. EEG was diagnostically available. However, it did not provide critical eveidence to predict prognosis of their seizures. Neuroimaging studies were not helpful for clinical diagnosis. There are no sustained seizures in 48% of all cases who used phenobarbital only.

Conclusion: We confirmed neonatal asphyxia is the most important risk factors for neoenatal seizure. We should identify and establishe etiologic tisk factors for term neonatal seizures patricularly following neonatal asphyxia, and challenge to predict seizure onset and manage presumed seizures in advance.

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A RETROSPECTIVE ANALYSIS OF LEVETIRACETAM EFFICACY IN EPILEPTIC SYNDROMES WITH CONTINUOUS SPIKE WAVES DURING SLEEP (CSWS)

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Purpose: To evaluate the add-on effect of levetiracetam (LEV) treatment on the EEG and clinical status of children with CSWS.

Method: Clinical and electrographic data from 20 children with CSWS, who received LEV 50 mg/kg/day were evaluated.8- cryptogenic, 6-symptomatic and 6- atypical benign partial epilepsy (aBECTs) patients with CSWS were included. 24 h EEG recordings taken every 6 months, (minimum of 3 per child), were assessed. Children were categorized as responders, partial responders or nonresponders by comparing changes in the spike index (SI) during NREM-sleep with baseline SI before initiation of LEV. The clinical efficacy of LEV was assessed by comparing seizure frequency at the end of follow up with the baseline. The follow-up duration varied from 16 to 53 months.

Results: Electrographic response: 3 children from the symptomatic group showed a lasting response. 1 child showed no response.1 child from the cryptogenic showed a lasting response, 5 showed no response.1 child from the aBECT′s group showed a lasting response, 3 showed no response.Clinical response: 11 out of the 20 children were seizure-free at baseline and during the whole follow up. The rest, 6-symptomatic and 3-cryptogenic patients, had seizures prior to LEV treatment initiation. 6 became seizure-free after add-on therapy with LEV, and in 3 children a significant reduction of seizure frequency was observed.

Conclusion: This study suggests that treatment with LEV 50 mg/kg/day has a positive effect on children in whom CSWS results from a known underlying structural brain lesion (the symptomatic group).

Poster session: Drug therapy II
Tuesday 29th June 2010
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EPILEPSY, ANTIEPILEPTIC DRUGS AND PREMATURE OSTEOPOROSIS

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Purpose: We report on three young male patients with severe osteoporosis during use of antiepileptic drugs (AEDs) to draw attention to the need for screening for this treatable condition.

Method: Case reports.

Results: Three male patients aged 21, 27 and 44 years with epilepsy and long-term AED use were screened for low BMD with dual-energy X-ray absorptiometry (DEXA)-scan. One patient was wheelchair-bound, two were able to walk with aid. DEXA-scan revealed low T-scores of the lumbar spine and femoral neck in all patients, compatible with osteoporosis. Also all three patients had low serum levels of 25-hydroxy vitamin D, compatible with a vitamin D deficiency. Calcium and vitamin D supplementation and antiresorptive bone therapy were started in all three patients.

Conclusion: With these case reports we want to draw attention to the need for screening patients with epilepsy and (long-term) AED use. The negative effect of AEDs on BMD have been known for a long time, but systematic screening has not yet become common practice. Not only postmenopausal women, but also children and male patients are at risk. From the literature it is strongly recommended to screen for osteoporosis, especially when using enzyme-inducing AEDs. The severe osteoporosis at young age and severe vitamin D deficiency in our patients underscores this recommendation. Official international European or AAN guidelines on the management of AEDs and osteoporosis are still lacking, but should be developed on short notice in the best interest of this already vulnerable patient group.

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THE INFLUENCE OF LAMOTRIGINE THERAPY ON NITROSATIVE STRESS AND LIPID PEROXIDATION IN PATIENTS WITH EPILEPSY

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Introduction: Several studies have demonstrated the functional involvement of nitric oxide (NO) in both proconvulsant and anticonvulsant phenomena but no definitive conclusions are still available. Also, it has been proposed that NO mediated mechanisms are involved in the anticonvulsant efficacy of lamotrigine.

Purpose: To assess the level of nitrosative stress and lipid peroxidation in patients with epilepsy, during the treatment of lamotrigine mono and polytherapy.

Method: Fifteen patients with complex partial epilepsy were included in this study (10 men, 5 women), age 40 ± 11, treated at Clinic of Neurology in Clinical Centre Nis. They were divided into two groups: 7 patients on Lamotrigine monotherapy and 8 patients on politherapy (lamotrigine and valproate). The control group was composed of 11 healthy voluntary blood donors (5 men, 6 women), age 42 ± 11. Nitrite and nitrate concentration as the measure of NO synthesis, and malondialdehyde (MDA) as the measure of lipid peroxidation process, were estimated spectrophotometrically in plasma.

Results: The plasma level of MDA has been significantly lower in patients taking lamotrigine with valproate (polytherapy), than patients on lamotrigine monotherapy ($p < 0.05$) and than control group ($p < 0.001$). Nitrate and nitrite plasma level have not changed comparison between groups ($p > 0.05$).

Conclusion: The obtained results prove an possible important role of anticonvulsant mechanisms of lamotrigine polytherapy on lipid peroxidation process which is probably indirect consequence of modified nitrosative stress. This offers the new possibilities for modified combined approach in anticonvulsant therapy.

Keywords: Nitrosative stress, Malondialdehyde, Lamotrigine, Epilepsy

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COGNITIVE AND BEHAVIORAL EFFECTS OF LAMOTRIGINE AND CARBAMAZEPINE MONOTHERAPY IN PATIENTS WITH NEWLY DIAGNOSED OR UNTREATED PARTIAL EPILEPSY

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Purpose: Previous studies have examined the cognitive effects of lamotrigine (LTG), but there are limited data comparing the cognitive effects of LTG and carbamazepine (CBZ) in patients with newly-diagnosed epilepsy. We compared the long-term cognitive and behavioral effects of monotherapy with LTG and CBZ in epilepsy patients.

Method: This was a multicenter, open-label, randomized study that compared monotherapy with LTG and CBZ in newly diagnosed or untreated patients with partial or generalized tonic–clonic seizures. We employed an 8-week titration period and a 40-week maintenance period. LTG was administered at 100–500 mg/day and CBZ at 400–1200 mg/day. Cognitive functions, Symptom-Check-List-90, and QOLIE-31 were assessed at baseline, 16 and 48 weeks.

Results: A total of 110 patients were eligible and 73 completed the 48-week study (LTG, n = 39, 68.4%; CBZ, n = 34, 64.2%). Patients on LTG had better performance on most cognitive tests (71% of 17 variables) at 48 weeks, except for decreased performance in nonverbal drawing. However, the only significant difference between the two groups was better performance on verbal fluency in LTG group. The LTG group and CBZ group both experienced improvement in depression, anxiety, and quality-of-life at 16 weeks, but these improvements were maintained at 48 weeks only in the CBZ group. Except on the Obsessive-Compulsive subscale, these effects were not evident in a comparison of the two treatment groups.

Conclusion: Patients on LTG had better cognitive function, especially verbal fluency, than had patients on CBZ. However, patients on CBZ experienced better behavioral effects and quality-of-life than did patients on LTG.

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LAMOTRIGINE-INTOXCICATION ASSOCIATED WITH HEPATITIS C INFECTION: DIAGNOSTIC AND THERAPEUTIC CHALLENGES

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Purpose: In an individual patient pharmacokinetics of antiepileptic drugs (AED) depend on function of organs involved in drug absorption, distribution, metabolism and elimination. Therefore, a sudden change of AED serum levels under stable dosages points to diseases of these organs. We report on a patient who experienced a lamotrigine (LTG) intoxication under a stable combination therapy with valproate (VPA) as consequence of hepatitis C infection.

Methods: Case report.

Results: The 48-year-old man suffered from pharmacoresistant post-traumatic epilepsy. Combination therapy with LTG 550 mg/day and VPA 1200 mg/day enabled a tolerable seizure situation over two years with maximum LTG and VPA levels of 87 and 333 μmol/L, respectively. Then seizure frequency decreased accompanied by signs of a lamotrigine intoxication. At that time serum levels were 94 and 503 μmol/L, respectively. Therefore, the dosage of LTG was reduced. Mild elevations of GOT, GPT and Gamma-GT during the months before led to the diagnosis of hepatitis C. VPA was immediately discontinued and LTG dosage has to be increased again in order to stabilize the meanwhile detoriated seizure situation. During the following months hepatitis C was eradicated with peginterferon apha2a and ribavirin. Seizure frequency was finally tolerable with LTG 900mg/day and pregabaline 600mg/day.

Conclusion: In case of AED intoxication due to increases of serum levels under a stable drug regimen organs being involved in drug metabolism and elimination have to be investigated. Since VPA affects histone acetylation an effect of this drug on hepatitis C virus infection could be possible.

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INCIDENCE OF RASH AND HYPONATRAEMIA IN ADULT PATIENTS WITH REFRACTORY PARTIAL SEIZURES TREATED WITH ADJUNCTIVE ESLICARBAZEPINE ACETATE: RESULTS FROM THREE PHASE III STUDIES AND 1-YEAR OPEN-LABEL EXTENSIONS

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Purpose: Rash and hyponatremia are recognized adverse events associated with carbamazepine. We report the incidences of treatment-emergent rash and hyponatraemia among patients taking eslicarbazepine acetate (ESL), a novel antiepileptic drug chemically related to carbamazepine.

Method: A combined analysis of three Phase III trials of adjunctive ESL therapy in adults with refractory partial seizures was conducted, along with an analysis of the individual open-label extensions. Patients were randomized to 14 weeks' double-blind treatment with placebo (n = 290) or ESL 400 (n = 196), 800 (n = 284) and 1200 (n = 280) mg/day, followed by a 4-week tapering-off period (two studies only). Patients could then enter a 1-year open-label phase starting on 800 mg/day.

Results: A total of 1049 patients received ≥1 dose of study medication in the double-blind phase of the three trials; 833 entered the open-label extensions. Rash occurred in 13/760 (1.7%) patients on ESL and 2/289 (0.7%) on placebo during the double-blind phase. During the 1-year open-label extensions, rash occurred in 3/314 (1.0%), 4/325 (1.2%) and 1/194 (0.5%) in the three studies; overall incidence 0.96% (8/833). Hyponatraemia was reported in 6/760 (0.8%) patients taking ESL and no placebo patients during the double-blind phase. During 1-year open-label extensions, hyponatremia was reported in 1/314 (0.3%), 5/325 (1.5%) and 1/194 (0.5%) in the three studies; overall incidence 0.8% (7/833).

Conclusion: Phase III data show that the risk of rash and hyponatremia was low in patients taking adjunctive ESL, and did not increase in the 1-year open-label extensions.

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DEPRESSIVE SYMPTOMS IMPROVE WITH 1-YEAR ESLICARBAZEPINE ACETATE TREATMENT: A POOLED ANALYSIS OF 3 OPEN-LABEL EXTENSIONS OF PHASE III STUDIES IN PATIENTS WITH PARTIAL-ONSET SEIZURES

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Purpose: To understand the effectiveness of eslicarbazepine acetate (ESL) on depression risk in the pooled population of a 1-year open-label extension (OLE) of 3 Phase III randomized clinical trial (RCT) studies.

Method: Montgomery Asberg Depression Rating Scale (MADRS) was completed at RCT baseline and at 1-year treatment (or early discontinuation) OLE. Patients (n = 828) were stratified by baseline MADRS Total Score into four severity categories: Severe (score ≥ 31; n = 13); Moderate (25 ≤ score <31; n = 30); Mild (10 < score <25; n = 246); and No Symptoms (score ≤ 10; n = 539). For each MADRS category, results at end of treatment were compared with baseline, with 603 patients completing the MADRS after 1-year of treatment.

Results: In the intention-to-treat (ITT) population, highest mean decrease was reported in patients of MADRS Severe category (-18.8; $p < 0.0001$). Mean decrease was -10.1 ($p < 0.0001$) for patients in MADRS Moderate category and −5.4 ($p < 0.0001$) for patients in MADRS Mild category, with no change for patients with No Symptoms at baseline. Overall, the proportion of symptomatic (mild-severe depression) patients decreased from 35% at baseline to 24% at 1-year OLE adjunctive ESL treatment. There were no reported cases of suicide or suicide attempt. Most patients were treated with ESL 800 mg once-daily (range: 400–1600 mg).

Conclusion: Patients with mild, moderate and severe depressive symptoms were rated as having significant improvement (as measured by MADRS) during long-term open-label adjunctive ESL treatment. These data demonstrate the usefulness of ESL in treating comorbid depression that is a prevalent comorbidity with epilepsy.

Supported by BIAL- Portela & Co, SA.

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RUFINAMIDE AS ADD ON THERAPY IN CHILDREN & ADOLESCENTS WITH DRUG RESISTANT EPILEPSY AND LEARNING DIFFICULTIES

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Purpose: Describe the effectiveness of rufinamide as add-on therapy in children and young people with drug-resistant epilepsy in a residential care centre.

Method: Records of patients who were prescribed Rufinamide as add on therapy were retrospectively analyzed. Effect on the frequency of seizures and status epilepticus, the development of new seizures and behavioral changes was noted. Data was collected for at least 3 months after reaching a stable dose of rufinamide.

Results: A total of 15 patients (8 male, 7 female) received rufinamide. The mean age was 17.4 years (range 10–21).13 (86%) had Lennox-Gastaut syndrome. All were on polytherapy (2–4 antiepileptic drugs) and 13/15 had daily seizures (2–250/month). The mean duration of follow up was 6.4 months (range 3–18). Reduction in seizures was observed in 5 (33%) patients (one became seizure-free and 4 had >50% reduction). The median seizure frequency in responders was 65 per month (IQR 17–99) prior to Rufinamide and was 18 per month (IQR 8–90) afterwards, $p = 0.3765$ (Mann-Whitney U test). No increase in status epilepticus occurred.The drug was well tolerated but was withdrawn in 6 patients (40%), either due to a combination of worsening of seizures, lack of efficacy or behavioral problems. In one patient even though the seizures improved, it was discontinued due to the behavioral side effects. Behavior improved in 3 patients with preexisting behavioral problems.

Conclusion: Add on rufinamide therapy is beneficial in 33% of patients with epileptic encephalopathy. Main adverse effects were worsening of seizures or on behavior.

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VIGABATRINE INDUCED T_2 HYPERINTENSITIES IN CRANIAL MRI: NOT ONLY A NEURORADIOLOGICAL FEATURE BUT ALSO ASSOCIATED WITH ACUTE ENCEPHALOPATHY AND DYSTONIA?

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Purpose: Vigabatrine (VGB) is one of the first line agents in the treatment of infantile spasms. Recent studies demonstrated reversible T_2-weighted hyperintensities in cranial MRI which were associated with VGB therapy. Thus, no relevant clinical symptoms have been described so far.

Case report: Our patient developed infantile spasms at 4 months of age. Initially, neurological examination, cranial MRI and metabolic work up were unremarkable. He was treated with VGB, responded well and became seizure-free. 4 weeks later the spasms recurred, and hydrocortisone was added. The next day the patient suddenly became somnolent. 6 days later he showed a relevant dystonic movement disorder. Cranial MRI revealed symmetric T_2-weighted hyperintensities in the thalamus,

putamen, corpus callosum, dentate nuclei, and mesencephalon without lactate peak in MR-spectroscopy, and marked generalized brain atrophy.

Extensive investigations including analysis of mitochondrial, storage and neurotransmitter disorders were entirely unremarkable. Assuming a VGB side effect, VGB was withdrawn, hydrocortisone was continued. The spasms ceased rapidly, the patient slowly recovered. After 4 months the T_2 lesions disappeared completely. After 8 months of follow up the patient shows psychomotor retardation, but makes continuous progress. The dystonic movements have improved markedly.

Conclusion: The transient T_2-weighted hyperintensities in this case were assumed to be associated with VGB, but concurrently might also explain the encephalopathy and dystonic movement disorder. Though an association of these symptoms with VGB cannot be proven, it has to be considered, that the effect of VGB on specific brain areas might not only be limited to neuroradiological findings.

Poster session: Drug therapy V
Tuesday 29th June 2010
13:30–14:30

p399
ADJUNCTIVE TREATMENT WITH LACOSAMIDE: AN OPTION FOR GENERALIZED EPILEPSY?

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Purpose: Lacosamide (LCM) was licensed in Germany for the treatment of focal epilepsy in September 2008. We investigated the efficacy and tolerability in 10 patients with idiopathic generalized epilepsy who failed at least 3 approved antiepileptic drugs (valproate, lamotrigine, topiramate, levetiracetam) and subsequently received LCM 100–300 mg/day as off-label adjunctive treatment.

Methods: Ten consecutive patients (7 females, 3 males, 20–62 years) were included. Syndrome diagnosis was based on seizure semiology, EEG findings and absence of structural lesions. Efficacy was calculated comparing the seizure frequency to that of 6 months prior to LCM treatment. Assessment of tolerability was obtained from patient reports and neurological examinations.

Results: Three patients stopped LCM due to side effects (tiredness, n = 2) and lack of efficacy (n = 2). Two patients are seizure-free since starting LCM (for 10 and 15 months, respectively). These patients had 5 and 6 generalized tonic–clonic seizures (GTCS) during the 6 months before starting LCM. Two patients experienced >50% seizure reduction. Three further patients received LCM for 2–3 months so far. These patients had 3–6 GTCS during the 6 months before LCM and are all currently seizure-free on LCM adjunctive treatment. No increase in seizure frequency was observed in any patient. Tiredness was the most common side effect (4 of 10 patients).

Conclusion: Lacosamide may be a good option for adjunctive treatment of generalized epilepsies. LCM is well tolerated in most patients. A randomized, double-blind, placebo-controlled trial should be established to further evaluate the potential in treatment of generalized epilepsies.

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LEVETIRACETAM IN IDIOPATHIC GENERALIZED EPILEPSY SYNDROMES: OPEN-LABEL, NONCOMPARATIVE, MULTICENTER, LONG-TERM FOLLOW-UP STUDY

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Purpose: To evaluate the long-term efficacy and tolerability of adjunctive levetiracetam (LEV) in patients with idiopathic generalized epilepsy (IGE) syndromes: childhood and juvenile absence epilepsy (CAE + JAE), juvenile myoclonic epilepsy (JME) and generalized tonic–clonic seizures on awakening (GTCSA).

Method: Supplementary analysis of open-label, multicenter, noncomparative, long-term follow-up study (NCT00150748) in patients with IGE who completed one of two double-blind, Phase III studies. Patients received individualized LEV doses ≤4000 mg/day (≤80 mg/kg/day for children/adolescents <50 kg).

Results: Of the 217 patients enrolled [mean (min-max) age 28 (6–63) years; 58% female; median LEV exposure 771 (4–1668) days; mean dose 2918 (788–3993) mg/day], 189 were included in the current analysis (31 with CAE/JAE, 122 with JME and 36 with GTCSA) and 28 were excluded (22 with other IGE syndromes and 6 with unknown syndromes).

The ≥50% responder rates (all seizure types) were similar in patients with CAE + JAE (87.1%), JME (84.4%), and GTCSA (83.3%). Seizure freedom rate (100% reduction from baseline in all seizure types) was highest for CAE+JAE (58.1%) followed by GTCSA (25.0%) then JME (18.0%). Fewer patients with CAE + JAE (48.4%) reported ≥1 treatment-emergent adverse event (TEAE) compared to patients with JME (80.3%) or GTCSA (72.2%). Most TEAEs were mild to moderate in intensity. 0% (CAE+JAE), 9.0% (JME) and 5.6% (GTCSA) of patients discontinued treatment due to TEAEs.

Conclusion: Adjunctive LEV provided sustained efficacy and was well-tolerated during long-term treatment of patients with IGE syndromes (CAE+JAE, JME, GTCSA), supporting the broad spectrum efficacy of LEV.

UCB-sponsored.

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SAFETY AND EFFICACY OF SUSTAINED RELEASE LAMOTRIGINE AS MONOTHERAPY/ADD ON THERAPY IN THE TREATMENT OF EPILEPSY

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Purpose: Lamotrigine (LTG), a phenyltriazine derivative, is an antiepileptic drug (AED), with beneficial effects against partial and generalized epilepsies. Neurological side effects are normally seen at higher plasma concentrations. LTG_{SR} which will produce lower plasma levels and slow plasma concentration escalation, is expected to reduce the incidence of this troublesome side effect. Hence, the present trial (open label, noncomparative, multicentric) was designed and aimed to determine the safety and efficacy of the LTG_{SR} in Indian patients of epilepsy.

Method: Total 20 patients were enrolled. All patients completed the full (12 weeks) duration of the study. Patients in the age range of 16–70 years with diagnosis of Epilepsy, as defined in ICES were selected. Patient-categories included were: Category-I: Newly diagnosed patients (h/o ≥ 2 seizures in last 3 months), Category-II: Patients who did not achieve adequate seizure control (≥4 seizures in last six weeks) with other AED. Category-III: Patients who were on Lamotrigine Conventional release (IR) formulation, followed by exclusion criteria.

Results: LTG_{SR} treatment reduced seizure frequency in all patient-categories. Statistically significant reduction in seizure frequency (per 4 weeks) was seen in patient-Category -II. QOLIE-31 total score also significantly improved, in each patient-category. No serious adverse event (AE) was reported during the study.

doi: 10.1111/j.1528-1167.2010.02658.x

Conclusion: Lamotrigine (LTG_{SR}) is safe and effective in the Indian patients of Epilepsy. It offers the advantage of a better tolerability profile as compared to conventional LTG. It also offers a safe switchablility from conventional preparation at the same molar dose with better quality of life.

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ASSESSING THE CONSISTENCY OF THE PHOTOPAROXYSMAL EEG RESPONSE (PPR) OVER A 12-HOUR PERIOD IN PLACEBO-TREATED PHOTOSENSITIVE EPILEPSY PATIENTS: IS THERE A BLINK, CIRCADIAN RHYTHM OR PHYSIOLOGIC TEMPORAL DRIFT IN PPR?

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Purpose: Substantial placebo response over time has been noted in neuroclinical trials (Gold-*JClinPsych* 2007, Quessy-*Pain* 2008, Burneo-*EpilBehav* 2002, Whalen-*Epilepsia* 2009). The photoparoxysmal EEG response (PPR), an objective measure, should not be influenced by placebo, but this has not been tested. Diurnal rhythm in seizures has been detected (Labate-*Epil Research* 2007). We examined both the consistency of EEG-PPR response and presence of a diurnal pattern in photosensitive patients given i.v.-saline-placebo over 12 h.

Method: Data from a prospective, dual-center, placebo-controlled, nonrandomized single-blind study, N = 13 patients (9/13, stable AEDs), was used. Photosensitive epilepsy patients were tested (Kasteleijn-Nolst-Trenité-*Epilepsia* 1999) with hourly photic stimulation while receiving iv saline-placebo ×12 h. No patient had altered sleep the night before testing; EEG was analyzed blindly. The presence of a temporal, physiologic drift in high Hz and standardized photosensitive response (SPR) was tested by repeated-measures ANOVA; diurnal rhythm by comparison of values at 0 & 12 h.

Results: The Table lists the F-value/p-level for repeated-measure-ANOVA (hourly PPR determinations, 0–12 h, each eye condition) and t-values/p-level for t_0h versus t_{12}h. Each patient showed minimal variation (''blink'') in hourly PPR Hz vs. t_0. We did not detect a temporal drift, nor altered circadian pattern, in PPR within-day, within-patients.

Conclusion: The EEG PPR response in the photosensitive epilepsy model shows consistency during placbo administration, without diurnal pattern, over 12 h within the same day within patients.

	Eye closure	Eyes closed	Eyes open
High Hz, hourly,0–12h:	1.42;0.16	0.41;0.95	0.92;0.52
t_0h vs t_{12}h:	−0.69;0.49	−0.64;0.52	0.31;0.75
SPR, hourly, 0–12h:	0.93;0.52	0.59;0.85	0.95;0.50
t_0h vs t_{12}h:	−1.43;0.15	−0.13;0.89	−0.08;0.93

p403

LAMOTRIGINE AND COGNITIVE FUNCTION IN CHILDREN

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Purpose: Cognitive function in school children is an important issue because at that time children learn to deal with much more complicated tasks than those they were given before. Those tasks need a great deal of concentration and memory, which are impaired due to the treatment with antiepileptic drugs. It is one of adverse-effects of those drugs that requires further studies as it influence greatly the family and school lives of children treated with AEDs.

Method: Our study group was a group of 46 children with different types of epilepsy, age 8 to 12 years, treated with Lamotrigine, who didn't have any seizures since the beginning of treatment three years ago. Our control group was 34 healthy children in similar age. We measured their IQ at the beginning of treatment and three years later with WISC-R test. The results were compared with a statistic method. Primary IQ in both groups was >70.

Results: There were no differences between two groups in all IQ scales.

Conclusion: The therapy with lamotrigine have no effect on epilepsy children's IQ during three years of treatment.

p404

LAMTROGINE EFFECTIVE IN MYOCLONIC ASTATIC EPILEPSY (DOOSE SYNDROME) AS BASED ON ELECTRONIC DOCUMENTATION OF TREATMENT WITH EPIVISTA®

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Purpose: MAE is a severe IGE affecting previously normally developed children aged 7 months – 6 years. MAE is frequently pharmacoresistant, and about 50% of the patients develop mild or moderate mental retardation. There is no controlled treatment data and few uncontrolled evidence from case series indicating that LTG may be effective.

Method: We included all patients with MAE who were admitted between 7/2007–12/2009 and treated with LTG. Seizures were electronically documented with Epivista®, and analysis was done retrospectively.

Results: We included 10 patients (8 boys) aged 2.1–7.8 (median 3.7) years at the time when LTG was started in comedication. The onset of MAE had been at 1.5–4.3 (median 2.6) years. All patients were pharmacoresistent and had been exposed to 2–8 (median 3.5) AEDs without success. The most frequent AEDs used before LTG were valproate (n = 7), levetiracetame (n = 7), sulthiame (n = 6), and topiramate (n = 4). During baseline (4 weeks) 7–416 seizures (median 108) were documented. Seven patients became seizure-free after 28–145 (median 63) days with LTG between 1–7 (median 3) mg/kg and LTG serum levels between 1–5 (median 2) mg/L. One girl did not respond, and 2 patients were considered as ''nonresponders'' due to insufficient seizure documentation. There was no recurrence during follow up between 5–32 (median 12) months. Using electronic documentation with Epivista® follow up is ongoing in all patients.

Conclusion: Our promising preliminary data justify a prospective trial, possibly including early LTG treatment in MAE patients.

p405

THE LONG-TERM EFFECT OF LEVETIRACETAM IN THE TREATMENT OF IDIOPATHIC GENERALIZED EPILEPSIES

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Purpose: To assess efficacy and tolerability of Levetiracetam (LEV) in patients with idiopathic generalized epilepsies (IGE).

Method: Patients with IGE, documented by clinical criteria and video EEG, were prospectively recruited among adult outpatients between August 2001 and March 2009.

Results: Sixty one patients (66% women), with mean age of 32 years (SD 13.4) were followed for 2.3 years on average (range 0.4–7.6), totally for 140 years. LEV was add-on treatment in 49 cases. Twenty one patients had JME, 11 had juvenile absence epilepsy, 10 had generalized tonic–clonic seizures (GTCS) only, 5 had reflex epilepsy and 7 other syndromes; classification was not possible in 7. Fifty six subjects had GTCS, 36 had absences (TA), 29 myoclonic seizures (MS) and 12 other seizures; 26 were photosensitive. Mean epilepsy onset age was 13 years (SD 8.7) and mean duration 19 years (SD 13.9).Seizure freedom/seizure reduction over 50% was achieved by 36 subjects; seizure control was unchanged in 23 and worsened in two. Median seizure freedom duration was 1.6 years (interquartile range [IQR] 1.9) for GTCS (20 subjects), 2.6 years (IQR 4.1) for TA (7) and 1.5 years (IQR 0.5) for MS (5). Mean LEV daily dose was 1466 mg (SD 881, range 250–3500). Twenty seven patients experienced side effects; these were psychiatric/behavioral in 20. Sixteen patients discontinued treatment, due to side effects (12), inefficacy (2), or both (2). Efficacy and tolerability were not associated with any epilepsy characteristic.

Conclusion: LEV is effective and well tolerated in different syndromes and seizure types of IGE.

Poster session: Nonepileptic paroxysmal events
Tuesday 29th June 2010
13:30–14:30

p406
PSYCHOGENIC SEIZURES – DIAGNOSTIC IMPORTANCE OF VIDEO-EEG AND AMBULATORY LONG-TERM MONITORING

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Purpose: Psychogenic seizures(PS) are motor, sensitive or perceptive phenomena that can be similar to epileptic seizures but don't correlate with alterations on the EEG. They are frequent in neuropediatric clinics and lead to excessive and unnecessary investigations and therapy, thus the importance of a correct diagnosis and therapeutic strategy along with psychiatry. They occur mainly in adolescent females, isolated or coexisting with epilepsy.This work alerts for the high frequency of PS, the difficulties of diagnose and the usefulness of video-EEG, ambulatory long term EEG-monitoring and provocation of seizure using suggestion with placebo.

Method: Prospective study including patients with suspected PS, with or without previously confirmed epilepsy. In all patients were performed: a suggestion test with intravenous administration of physiologic serum under video-EEG; a standard EEG or an ambulatory EEG-monitoring(24 hours) to exclude or detect epileptic activity. Parameters analyzed: age, sex, test of provocation result, visual interpretation of EEG recordings.

Results: 24 patients were included, 7 boys and 17 girls. The mean age was 13.9 years. In 19 cases the suggestion test was positive. Six patients had both epilepsy and PS; 13 had only PS; 3 has epilepsy but no PS. A correct diagnose permitted to adjust antiepileptic therapy and appropriate psychiatric follow-up.

Conclusion: PS are frequent cause of misdiagnosis and unnecessary investigation and therapy.

Our results outline the role of video-EEG, of long term EEG-monitoring in ambulatory and of tests of provocation with placebo in the correct diagnosis and appropriate therapy by child neurologists together with psychiatrists.

p407
NONEPILEPTIC PAROXYSMAL EVENTS IN PATIENTS WITH VERIFIED LONG-TERM EPILEPSY

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Purpose: A lot of publication are devoted to the question of differential diagnose epileptic seizures and nonepileptic paroxysmal events. Combination epileptic and nonepileptic seizures in the same patient are investigated greatly rarely.

Methods: Four hundred sixty-three patients with long-term epilepsy were examined. All these patients had verified epilepsy during 2–8 years. Age of patients was 20–65 years. Nobody of them had full seizure control. Seizures frequency was from 2 in year to 8 in month. All patients had several partial seizures with or without secondary generalization.

Results: One hundred twenty-one patients from 463 had nonepileptic paroxysmal events. 36 patients had psychogenic seizures, which had conversion nature; these paroxysms imitated epileptic seizures and were demonstrative ones. 39 patients had syncope (36 – orthostatic and 3 – iritative vertebrogenic). 44 patients had panic attacks. 3 patients had combination panic attacks with psychogenic seizures and 2 patients with syncope. 1 patient had comorbidity epilepsy with ophthalmic migraine. 6 patients had nonepileptic abstinent paroxysms after benzodiazepine abolitions as one of symptom of drug abstinent syndrome.

Conclusion: Several nonepileptic paroxysmal events are not rare in epileptic patients with long-term epilepsy without full seizure control. 26% of these patients have various nonepileptic seizures and this fact need to be considering in therapeutic tactic selection.

p408
PACEMAKER IMPLANTATION AFTER ICTAL ASYSTOLES: A CASE REPORT

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Purpose: Events of ictal convulsive syncope caused by asystoles may be relevant in patients with related falls and injuries.

Method: A twelve years old patient was suffering from complex-partial and secondarily generalized tonic–clonic seizures with postictal aphasia since the age of nine. Six months before admission there was a change in seizure semiology with a new seizure type (paleness, myoclonic jerks, falls). Drug treatment with first line antiepileptic drugs did not lead to a sufficient seizure control. Therefore we initiated presurgical evaluation. MRI showed a lesion left frontal mesial, which was unchanged in a 2 year follow-up. During video-EEG-monitoring we detected an ictal asystole lasting 38 s with clinical signs of a convulsive syncope.

Results: A pacemaker was implanted to prevent further asystoles and the patient was readmitted for video-EEG. All of the four monitored seizures with staring and discrete oral automatisms showed a left frontotemporal pattern. Pacemaker was triggered during one of these seizures when bradycardia occurred. Because of the findings in presurgical evaluation the patient underwent epilepsy surgery of the left frontomesial lesion with the histopathological finding of a dysembryoblastic neuroepithelial tumor (DNET). 20 months after surgery the patient was still free of seizures and syncopes without any neurological deficits.

Conclusion: Pacemaker implantation may result in long-term freedom from convulsive syncopes and injuries in patients not responding to drug treatment.

p409
PAROXYSMAL NONEPILEPTIC EVENTS IN CHILDREN: A VIDEO ELECTROENCEPHALOGRAPHIC MONITORING RECORDS OF 15 YEARS

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Purpose: The aim of this study is to evaluate the relative frequency and clinical characteristics of paroxysmal nonepileptic events (PNE) in children who underwent prolonged video electroencephalographic (EEG) monitoring.

Method: During a 15-year period, 1108 pediatric patients were monitored in the Epilepsy Monitoring Unit of Seoul National University Hospital and 206 patients were suspected as having PNEs. Retrospective review of medical records and monitoring data resulted in a diagnosis of specific PNEs in 143 patients (13%).

Results: Mean age at the time of monitoring was 5.0 ± 4.5 years (range, 0.2–19 years). Epilepsy was concomitantly present in 43 patients (30%, 43/143). Developmental delay or mental retardation was found in 49 patients (34%, 49/143). The major groups of PNEs were different according to the age groups classified around 5 years of age at the time of monitoring. In the younger age group (<5 years, 82 patients), staring or inattention (18%), nonepileptic tonic posturing (18%), sleep disorder (9%), and stereotyped behavior (7%) were more frequently diagnosed. In the older age group (>5 years, 61 patients), psychogenic seizures (21%), hypnic jerk (16%), movement disorder (16%), and staring (11%) were major subgroup of PNEs. Thirty six patients (25%, 36/143) were on antiepileptic medications at the time of evaluation with the false impression of epilepsy.

Conclusion: Video EEG monitoring is useful for accurate diagnosis of PNEs in children, especially in the subgroup of population who were neurologically impaired or had concomitant epilepsy, possibly resulting in avoidance of unnecessary use of antiepileptic medication.

p410
TAKOTSUBO SYNDROME (TKS) IN EPILEPSY: A POSSIBLE MECHANISM OF SUDEP?

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Purpose: Takotsubo syndrome (TKS) is an acute cardiomyopathy happening after a stressful condition, including seizures and status epilepticus. We report one case and the review of the epilepsy literature.

Method: A 50-year-old woman in a stressfull personal situation suffers from a first secondarily generalized tonic–clonic seizure. In the Emergency Room, cardiac auscultation revealed galop, the troponin is 7.51 ng/ml and the EKC showed antero-septal Q waves. Echography showed transiently antero-infero-apical hypokinesia with ejection fraction estimated to 36%, and coronarography was normal. TKS was diagnosed, treated by acetylsalicylic acid, bisoprolol and perindopril. Valproate 1000 mg/day was added. The long-term EEG monitoring and brain MRI were normal, with no recurrence of seizure nor TKS.

Results: Seizures can induce TKS and 15 other cases can be found in the epilepsy literature, including relapsing TKS with repetitive seizures. However, most of the published cases of cardiac events linked to seizure do not mention TKS but describe ischemic cardiac attack secondary to seizures. TKS pathophysiology is mainly explained by a catecholamine discharge secondary to stress and is a functional problem. It can mimics myocardial infarction including abnormalities of EKG, elevation of troponin, left ventricular dysfunction and possible rhythm abnormalities, eventually fatal, but is not an ischemic event.

Conclusion: TKS should be part of the differential diagnosis of acute cardiac events in epileptic patients and should be considered as one possible mechanism of SUDEP. Systematic troponin dosage after a seizure with some cardiac event could help for the screening of potential SUDEP candidate.

Poster session: Drug therapy XI
Tuesday 29th June 2010
13:30–14:30

p411
EFFECTS OF CARBAMAZEPINE WITHDRAWAL ON SERUM LEVELS OF ROUTINE LAB TESTS IN PATIENTS WITH EPILEPSY: A PROSPECTIVE RANDOMIZED DOUBLE-BLIND WITHDRAWAL STUDY

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Purpose: Antiepileptic drugs (AEDs) may affect routine lab tests like serum levels of electrolytes, blood cells and liver function tests. The aim of this study was to evaluate the serum levels of such routine tests before and after double blinded withdrawal of AED treatment and see if a possible effect is reversible.

Methods: The study was prospective, randomized and double-blinded. 160 patients were included and randomized to withdrawal or not. One hundred fifty (80 females, 53%) patients went through the intervention and was included in the study which lasted for 12 months. Complete serum samples from before and 4 months after completed withdrawal/no withdrawal were obtained from 130 patients. 93 patients used carbamazepine (CBZ) prior to AED withdrawal.

Results: Following CBZ withdrawal, we found a significant increase in hemoglobin and a significant reduction in γGT after AED withdrawal in the withdrawal group. We also found a borderline significant increase in alkaline phosfatase in patients withdrawn from CBZ ($p = 0.09$). There were no other significant changes in routine lab tests.

Conclusions: As exspected, we found a reduction in γGT in patients withdrawn from CBZ due to nullifying the liver enzyme induction. Moreover, we found an increase in hemoglobin levels and, somewhat surprising, a boderline significant increase in alkaline fosfatase after withdrawal of CBZ.

p412
PREGABALIN VERSUS PLACEBO FOR THE TREATMENT OF PARTIAL ONSET SEIZURES IN PATIENTS TAKING CONCOMITANT ANTIEPILEPTIC DRUGS: AN ANALYSIS OF COMBINED CLINICAL TRIALS

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Purpose: To evaluate pregabalin as adjunctive therapy in patients taking multiple concomitant antiepileptic drugs (AEDs) for the treatment of partial onset seizures.

Method: Data from 6 double-blind, randomized studies of pregabalin vs placebo in patients with partial onset seizures who received ≥1 concomitant AED were pooled for analysis. The analysis included 1769 patients randomized to placebo (n = 562) or 150 mg (n = 185), 300 mg (n = 242), 600 mg (n = 530) or flexible dose (150–600 mg; n = 250) pregabalin. A 5-way factorial model was used to assess the influence of number and mechanism of concomitant AEDs on the 50% responder rate in pregabalin versus placebo treatment groups.

Results: Baseline clinical characteristics were comparable between pregabalin and placebo groups. The majority were taking 2 concomitant AEDs (45%) followed by ≥3 AEDs (33.5%) or 1 AED (21.5%). Most patients were taking ≥1 sodium channel modulator (81%) while fewer patients were taking ≥1 broad spectrum (64.5%) or ≥1 GABAergic (37%) agent. Overall, improvement with pregabalin exceeded placebo on the proportion of ≥50% responders (39% vs. 16%). When this efficacy parameter was stratified by number and mechanism of concomitant AEDs, modeling results suggested that the magnitude of improvement with pregabalin versus placebo remained generally consistent across subgroups. One exception occurred in patients receiving ≥3 AEDs of which ≥2 were sodium channel modulators where no difference was observed.

Conclusion: In general, pregabalin provided a consistent improvement in seizure reduction versus placebo in patients with partial onset epilepsy regardless of number and type of concomitant AEDs.

Funded by Pfizer.

p413

ASSESSMENT OF THE IMPACT OF ESLICARBAZEPINE ACETATE ON CARBAMAZEPINE PHARMACOKINETICS AT STEADY-STATE: A POOLED ANALYSIS OF THREE PLACEBO-CONTROLLED PHASE III STUDIES

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Purpose: Carbamazepine (CBZ) is associated with a high susceptibility to pharmacokinetic interactions. To assess whether eslicarbazepine acetate (ESL) affects CBZ pharmacokinetics (PK), plasma CBZ concentrations were evaluated in patients taking ESL or placebo as adjunctive therapy to CBZ in a pooled analysis of 3 Phase III studies in adults with partial-onset seizures.

Method: Trough (i.e., predose) blood samples for CBZ immunoassay (FPIA) were taken from patients with ongoing CBZ treatment at the time of randomization (i.e. before starting add-on treatment with once-daily ESL 400, 800, 1200 mg or placebo) and after 12 weeks of treatment. The metabolite CBZ-epoxide was not measured. Geometric mean ratios (GMRs) and 95% confidence intervals (CIs) of steady-state CBZ concentrations at the end/start of ESL/Placebo treatment were calculated.

Results: Among 1049 patients enrolled in the 3 Phase III studies, 611 (58%) were receiving CBZ as an underlying AED. Plasma CBZ concentrations were available for 414 (68%) CBZ-treated patients. GMRs and 95% CIs were 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] in CBZ + Placebo, CBZ + ESL 400 mg, CBZ + ESL 800 mg, and CBZ + ESL 1200 mg treated patients, respectively. The results did not identify any major influence of ESL on steady-state plasma CBZ concentration.

Conclusion: In this pooled analysis of 3 Phase III studies, no major influence of ESL on the PK of CBZ was observed.

Supported by BIAL – Portela & Co, SA.

p414

LACOSAMIDE EFFICACY AND SAFETY IN PATIENTS TAKING AEDS THAT ACT ON NON–SODIUM CHANNEL TARGETS

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Purpose: When monotherapy with an antiepileptic drug (AED) fails, a common recommendation for choosing an adjunctive AED is to consider mechanism of action as a means to maximize efficacy and tolerability. Lacosamide, a new AED for adjunctive treatment of partial-onset seizures, selectively enhances slow inactivation of voltage-gated sodium channels, distinguishing it from other AEDs. To evaluate the role that combination of specific AEDs may play in clinical outcome, post hoc exploratory analyses were performed on lacosamide Phase II/III trial data including patients only taking AEDs that act on non–sodium channel targets.

Method: Patients concomitantly taking only AEDs that act on non-sodium channel targets (e.g., valproate, levetiracetam, topiramate, zonisamide, gabapentin, pregabalin, phenobarbital, tiagabine, and/or lorazepam) were included. Efficacy measures included change in seizure frequency and 50% responder rates. Safety variables included treatment-emergent adverse events (TEAEs) and withdrawal due to TEAEs.

Results: Of 1308 patients in the overall safety population, 18% were taking only AEDs that act on non–sodium channel targets. Median percent reduction in seizure frequency per 28 days for lacosamide 200, 400, and 600 mg/day was 38.0%($p = 0.11$), 62.5%($p < 0.01$), 79.0% ($p < 0.01$) compared with placebo (28.0%). Similar results were observed for 50% responder rates (41.9%[$p = 0.20$], 62.3%[$p < 0.01$], and 79.2%[$p < 0.01$] vs. 25.0%). Lacosamide appeared well-tolerated with 8.6% withdrawing for TEAEs; TEAEs with incidence ≥10% (all lacosamide doses combined) were dizziness (15.3%), headache (12.3%), and fatigue (10.4%).

Conclusion: This post hoc exploratory analysis suggests that lacosamide can provide excellent efficacy and tolerability as part of a rational polytherapy regimen when combined with AEDs acting on non–sodium channel targets.

p415

PHARMACOKINETICS OF BRIVARACETAM IN SUBJECTS WITH SEVERE RENAL IMPAIRMENT

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Purpose: To compare the pharmacokinetics of brivaracetam (BRV) and its metabolites in subjects with severe renal impairment and matched healthy subjects.

Method: This open-label study comprized nine subjects with severe renal impairment (creatinine clearance <30 ml/min/1.73 m^2, not requiring dialysis) and nine matched healthy controls administered a single oral dose of 200 mg BRV. Plasma concentration and urinary excretion were determined up to 72 h postdose, and noncompartmental pharmacokinetic parameters were statistically compared.

Results: C_{max} of BRV was not altered relatively to healthy controls (mean ratio 0.997; 90%CI 0.85–1.17) whereas AUC∞ was increased (mean ratio 1.21; 90%CI 1.01–1.45). Renal clearance of BRV was reduced from 4.48 to 1.66 ml/min/1.73m^2 in the renally impaired group. Exposure to the pharmacologically inactive metabolites (acid, hydroxy, and hydroxy-acid) was markedly increased: C_{max} by 2.4-, 2.0- and

doi: 10.1111/j.1528-1167.2010.02658.x

11.7-fold, and AUC by 3.2-, 4.1- and 21.5-fold. Renal clearance of these rapidly cleared metabolites (healthy controls CL_R = 206, 61 and 365 ml/min/1.73 m^2) was decreased 10-fold in severely impaired subjects. Adverse events were mild with similar incidence in both groups. Preclinical toxicology studies concluded to the absence of safety issues with the increased levels of metabolites.

Conclusion: Severe renal dysfunction had a modest effect on plasma BRV while the toxicology studies indicated that the accumulating metabolite levels were nontoxic. Therefore, dosage adjustment of BRV should not be necessary at any stage of renal dysfunction.

UCB Funded.

p416

A MULTICENTER, OPEN-LABEL TRIAL TO ASSESS THE SAFETY AND TOLERABILITY OF A SINGLE INTRAVENOUS LOADING DOSE OF LACOSAMIDE FOLLOWED BY ORAL MAINTENANCE AS ADJUNCTIVE THERAPY IN PATIENTS WITH PARTIAL-ONSET SEIZURES

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Purpose: An IV loading dose of lacosamide is desirable when rapid titration is necessary but current dosing instructions recommend weekly titration. This trial examined safety and tolerability of a 15-min lacosamide intravenous (IV) loading dose, followed by oral maintenance treatment at common target doses, in patients with partial-onset seizures (POS).

Method: Subjects were 16–60 years old and taking 1–2 AEDs. Consecutive 25-subject cohorts were given three progressively increasing doses of lacosamide (200, 300, 400 mg) administered IV over 15 min. A fourth cohort of 25 subjects repeated the 300mg dose to provide safety data on 50 subjects at the highest well-tolerated dose at this infusion duration. Subjects received the loading dose followed 12 h later by the equivalent daily dose administered orally twice daily for 6.5 days. Safety evaluations included adverse events, 12-lead ECGs, vital signs and laboratory parameters. Lacosamide and AED plasma concentrations were measured.

Results: Overall, adverse events were dose-dependent. Within the first 4 h following infusion, dizziness, somnolence, nausea, and diplopia were common in subjects receiving 400 mg (44%, 26%, 19%, and 1% respectively); less common for 300 mg subjects (19%, 17%, 4%, and 0%); and infrequent for 200 mg subjects (4%, 0%, 0%, and 4%). Seven patients withdrew from the trial, all due to adverse events; 3 (6%) from the 300 mg cohorts, and 4 (16%) from the 400 mg cohort.

Conclusion: IV loading doses of 200 mg and 300 mg lacosamide administered over 15 min were best tolerated. The 400 mg loading dose was less well tolerated, due to a higher frequency of dose-related adverse events.

p417

ACUTE OXCARBAZEPINE-INDUCED HEPATOTOXICITY IN A PATIENT SUSCEPTIBLE TO DEVELOPING DRUG-INDUCED LIVER INJURY

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Oxcarbazepine (OXC) is generally accepted as a drug without risk of severe drug-induced hepatotoxicity, but according to recently reported pharmacovigilance data this statement has been challenged. Except for drug rash with eosinophila and systemic symptoms DRESS syndrome, in a recent study the case of OXC-induced liver adenoma has been reported. To our knowledge, there have been no reports of acute OXC-induced hepatotoxicity.

We present a female, with several partial complex seizures, 1 month after delivery who had borderline elevated liver enzymes prior to the initiation of OXC treatment. Two weeks after introducing OXC, highly elevated liver enzymes were found. After discontinuation of OXC the enzymes continued to rise for another week (maximum upper limits of normal values were: AST 11.6, ALT 17.3, GGT 10.4), and afterward gradually decreased. The causal relationship with OXC intake was determined to be highly probable. Two years later, the transitory elevation of liver enzymes was observed during the treatment of acute tonsilopharingitis with amoxicillin + clavulanic acid. The repeated elevation of liver enzymes related to use of different drugs might indicate patient`s susceptibility for drug induced liver injuries.

We suggest that monitoring of liver function tests would be clinically rational for early detection of acute OXC-induced liver hepatotoxicity in the patients with clinical and/or laboratory features which might be interpreted as possible risk factors of the increased susceptibility to drug induced liver injuries (e.g. previously known borderline values of laboratory liver tests, pregnancy, liver steatosis, elevation of liver enzymes during the treatment with other drugs).

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THE EFFECTS OF RETIGABINE ON THE PHARMACOKINETICS OF CONCOMITANTLY ADMINISTERED ANTIEPILEPTIC DRUGS

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Purpose: To measure trough concentrations of selected concomitant antiepileptic drugs (AEDs) before and during treatment with retigabine, a first-in-class AED that reduces neuronal excitability by enhancing the activity of KCNQ (Kv7) potassium channels.

Method: RESTORE 1 (NCT00232596) and 2 (NCT00235755) were multicentre, randomized, double-blind, placebo-controlled, parallel-group Phase III trials in adults with refractory partial epilepsy, ≥4 partial-onset seizures/28 days, receiving 1–3 AEDs, with/without vagus nerve stimulator. Patients underwent forced-titration to retigabine or placebo (immediate release tablets, t.i.d., p.o.) 600 or 900 mg/day (RESTORE 2) or 1200 mg/day (RESTORE 1) followed by 12 weeks' maintenance. The impact of adding retigabine to existing AEDs was investigated using confidence intervals (CIs) to compare trough concentrations of AEDs (carbamazepine, clobazam, clonazepam, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, pregabalin, topiramate, valproic acid and zonisamide) prior to and during concomitant administration of retigabine.

Results: Overall, retigabine had little or no effect on the trough concentrations of concomitant AEDs. The 90% CIs of most geometric mean ratios with and without concomitant retigabine fell within the 80% to 125% limits associated with bioequivalence. Although clobazam, clonazepam, gabapentin and lamotrigine all had 90% CIs that overlapped equivalence limits, only lamotrigine had a 90% CI excluding unity. Retigabine coadministration was associated with a 20% decrease in lamotrigine concentrations.

Conclusion: Retigabine does not affect oral clearance of most concomitant AEDs, with the exception of a modest decrease in lamotrigine concentrations. No pharmacokinetic requirements for dose adjustments of

concomitant AEDs are anticipated during treatment with retigabine as adjunctive therapy.

Poster session: Epilepsy syndromes in children and adults I
Tuesday 29th June 2010
13:30–14:30

p419
RASMUSSEN'S CHRONIC PROGRESSIVE FOCAL ENCEPHALITIS IN UZBEKISTAN

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Rasmussen's encephalitis (RE) - rare disorder of uncertain etiology usually occurring in childhood, characterized by the development of intractable focal seizures, progressive hemiparesis and increasing intellectual impairment. Under systematic review of the scientific work denoted RE, all more widespread becomes an autoimmune theory of the development disease. Findings antibodies to glutamate receptors 3-d class (GlyR3) in RE may explain some possible pathophysiological mechanisms. For the first time in Uzbekistan we describe the clinical case of the RE beside 12-year-old boy with analysis of the particularities clinical, paraclinical and laboratory data. Age at onset of epilepsy was 4 years. On clinical data, disease was in 2 stage on Bancaund J (1992). Particularity of the clinical current was absence myoclonical twitching on the same side, however periodical myoclonic twitching observed. Current of the seizures was with remission during one year. And beginning this disease don't be related with viral respiratory infection. In other respects, clinical description coinside Bancaund's clinical criteria. Neuroimaging (CT, MRI) shows the gradual development of progressive cerebral hemiatrophy. On EEG: the alpha rhythm is absent: the constant, steady peak-wave activity with frequency 5–6 Hz in right hemisphere, as much as possible expressed in temporo-occipital areas. Analysis of immunological data in the cerebrospinal liquid (CSF) increase of immunoglobulines (Ig) G – 59.1 mg/L and Ig M – 3.0 mg/L shown. Thus, there were some differences in clinical features of the case of the disease described in the present work and the other published data.

p420
PREVALENCE OF DRUG RESISTANT EPILEPSY IN CHILDREN – 1 YEAR PROSPECTIVE STUDY IN TWO POLISH EPILEPSY CENTERS

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Purpose: To evaluate the prevalence of drug-resistant epilepsies among children and adolescents with epilepsy.

Method: All epilepsy patients who entered the Developmental Neurology Departments (In and Outpatients Clinics) in the period between 01.10.2008 – 01.10.2009. were included in the study and followed prospectively. 1053 children and adolescents with dagnosed and treatet epilepsy entered the study. The diagnostic criteria for drug resistant epilepsy were: failure of adequate trials of two tolerated and appropriately chosen and used AED schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom. (Kwan et al. 2009)

Results: 9% of patients fulfilled the criteria for drug-resistant epilepsy. The most common types of seizures among drug-resistant patients were complex partial seizures or polymorphic generalized seizures (tonic, tonic–clonic and myoclonic).

Conclusion: This large population based study shows according to recently proposed definition the surprisingly high incidence of drug-reistant epilepsies among children and adolescents.

References: Kwan, P., Arzimanoglou, A., Berg, A.T. et al. Definition of drug resistant epilepsy. Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. (2009) *Epilepsia*

p421
THYROID FUNCTION AND LIPID PROFILE IN CHILDREN WITH EPILEPSY TREATED WITH OXCARBAMAZEPINE MONOTHERAPY: A PROSPECTIVE STUDY

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Purpose: Studies on the effects of oxcarbamazepine (OXC) on thyroid hormone and lipid profile in patients with epilepsy are conflicting. The aim of this study was to prospectively evaluate the changes and possible associations in thyroid and lipid profile in children treated with OXC monotherapy.

Method: Serum thyroxine (T4), free thyroxine (FT4), triiodothyronine (T3), thyrotropin (TSH), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TGs) levels were measured in 23 children with epilepsy, before and at 8 and 18 months of OXC monotherapy.

Results: FT4 levels were significantly decreased at 8 and 18 months ($p = 0.000$ and $p = 0.000$, respectively), whereas TSH levels were significantly increased at 8 and 18 months ($p = 0.003$ and $p = 0.001$, respectively) of OXC monotherapy. TC and LDL-C levels were significantly increased at 8 ($p = 0.015$ and $p = 0.001$, respectively) and 18 months ($p = 0.021$ and $p = 0.002$, respectively) of OXC treatment. There were no significant alterations in T4, T3, HDL-C and TGs levels during treatment with OXC. There were also no significant correlations between FT4 and TSH and TC or LDL-C levels, at 8 and 18 months of treatment.

Conclusion: Oxcarbamazepine monotherapy may cause significant and persistent alterations in TSH, FT4, TC and LDL-C levels in children with epilepsy. Therefore, it may be useful to measure serum thyroid hormone and lipid profile routinely in children with epilepsy taking OXC. Further prospective studies are required to determine the mechanisms and risk factors for development of thyroid and lipid disturbance in children treated with OXC monotherapy.

p422
RATIONAL THERAPEUTICAL OPTIONS IN EPILEPSY TREATMENT IN CHILDREN WITH METABOLIC DISORDERS

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Purpose: Epilepsy is common manifestation of mitochondrial cytopaties and other metabolic disorders in children and usually refractory to standard treatment. The purpose of our investigation is to find the optimal treatment options in epileptic patients having the metabolic disorders.

Methods: 20 children with epilepsy (mean age:6,4), among them 6 patients with mitochondrial diseases, confirmed with molecular analysis of mDNA, 3 children with storage diseases, and 11 children with another type of mitochondrial dysfunction. Patients take the metabolic therapy and special diet. Levetiracetam was given in monotherapy to 10 patients, among them to 4 children with mitochondrial diseases, or add-on therapy to valproic acid, phenobarbital or topiramate.

Results: In 6 months after starting the complex therapy: 9 patients are completely seizure-free, 6 had >50% reduction in seizure frequency, 9 had the EEG improvement, 2 had an EEG completely free of epileptiform discharges, 8 showed improvement in cognition function and/or behavior, but 2 presented the hyperactivity and 1 sedation with the improvement of EEG and/or seizure reduction. In 11 patients, taking another anticonvulsant treatment elevated serum ammonia level was observed. After changing therapy in 8 patient the serum ammonia level was decreased. The most adequate achievement in seizure control was in combination of new antiepileptic drugs—levetiracetam or levetiracetam and topiramate with metabolic therapy.

Conclusion: Levetiracetam is more helpful in epilepsy treatment of children with metabolic, especially, mitochondrial disorders. The early diagnostic of metabolic diseases need for providing adequate therapy options for these disorders.

p423
RISK FACTORS, CHARACTERISTICS, AND PROGNOSIS OF EPILEPSY IN PATIENTS WITH CEREBRAL PALSY

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Purpose: The aim of this study was to evaluate risk factors, the age of seizure onset, nature and prognosis of epilepsy in our patients with cerebral palsy (CP).

Method: The group of 49 children and adolescents, aged from 4 to 27 years (mean 11) with CP and epilepsy was studied retrospectively for clinical course and prognosis. Clinical follow-up of at least 3 years was required. There were 42 patients with spastic form (spastic hemiplegia - 16 patients, quadriplegia 11, diplegia 13, paraplegia 2) and 7 patients with mixed form of CP.

Results: Thirty-two of 49 (65%) patients had a history of early hypoxic-ischemic encephalopathy. Seizure onset ranged from 1 month to 9 years (mean 3.2 years). First seizure occurred before the age of 12 months in 31%, including all patients with spastic quadriplegia. Focal seizures with or without secondary generalization were by far the most common type (80%). Infantile spasms were observed in 4 of 11 children with spastic quadriplegia. CP was associated with mental retardation in 76%. AED monotherapy was applied in 57%, while others were treated with polytherapy. Intractable epilepsy occurred in 27% of patients with CP, while in spastic quadriplegia it was evidently higher (64%). Seizure freedom for ≥12 months was mainly achieved in children with spastic diplegia (12/13).

Conclusion: Hypoxic-ischemic encephalopathy was the most frequent etiological factor in our patients with CP and epilepsy. Focal seizures were the most common seizure type. Spastic quadriplegia was most often associated with pharmacoresistant epilepsy.

p424
EFFECT OF PREGNANCY ON SEIZURE FREQUENCY IN WOMEN WITH EPILEPSY

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Purpose: To evaluate if pregnancy induce a chance in seizure frequency (SF), percentage of subjects remaining seizure-free, risk of recurrent seizures in women with epilepsy (WWE).

Method: We recruited 108 WWE (36 cases = WWE during pregnancy and 72 controls = WWE not pregnant) referred to our tertiary epileptic centre. Controls were matched 2:1 with the cases for relevant clinical parameters. Both cases and controls had to be referred to our centre at last 9 months before-pregnancy/pregnancy/the-9-months-after-birth. Controls were followed for the correspondent periods of time: respectively control period 1-2-3.

Results: We recruited 36 cases and 72 controls [in both group mean age 28 years, partial epilepsy (80.6%), generalized epilepsy (19.4%)]. In the 9-months-before-pregnancy/control period-1, 83.3% of cases and controls were seizure-free; during pregnancy/control period-2, 24/36 (66.7%) cases and 57/72 (73.6%) controls and in the 9-months-after-birth/control period-3, 22/36 (61%) cases and 53/72 (73.6%) controls.

The mean seizure/month in the 3 time periods were respectively 0.68 (0–14.8)/0.65 (0–21.4), 0.49 (0–7)/0.59 (0–18) and 0.35(0–6)/0.72 (0–32.2). There were no differences in seizures/month across all the 3 time periods that were considered ($p = 0.952$, $p = 0.448$, $p = 0.581$, Wilcoxon test), and comparing cases versus controls. During pregnancy/control period-2, 3/36 (8.3%) cases and 5/70 (6.9%) controls experienced an increase in SF ($p = 0.79$); 7/36(19.5%) cases and 8.72 (11.1%) controls a reduction ($p = 0.24$); in 26/36 (72.2%) cases and 59/72 (81.94%) controls the SF was unchanged.

Conclusions: In this retrospective case-control, pregnancy does not affect SF in WWE. Less than 10% of subjects experienced an increase in SF and most of patients remained seizure-free.

p425
FRONTAL LOBE EPILEPSY: REVIEW OF A SERIES OF CASES IN A TERTIARY LEVEL HOSPITAL IN SPAIN

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Purpose: Frontal lobe epilepsy (FLE) represents a diagnostic challenge due to its complex semiology and nocturnal appearance which often mistaken it for pseudoseizures or parasomnias and lead to mistreatment. We describe clinical and electroencephalographic characteristics in our series of patients and establish video-EEG as a valuable tool to diagnose and optimize treatment of patients with FLE.

Method: Retrospective study of 31 patients with fulfilled criteria for FLE after video-EEG monitoring. Patients with diagnosis of nonrefractory FLE without video-EEG and patients with concomitant extrafrontal epileptogenic focus were excluded. Medical histories were reviewed remarking treatment adjustment in relation with video-EEG results and possibility of surgery. Improving ≥50% after vagus nerve stimulation (VNS) or Engel I after lesionectomy was considered good prognosis.

Results: 64% were males. Mean age at epilepsy onset was 10 years old and at video-EEG diagnose of FLE, 31 years old. Hypermotor seizures

appeared in 58% followed by tonic seizures (29%). Two patients presented concomitant pseudoseizures. 77% appeared predominantly during sleep. Electromyographic activity on ictal EEG obscured seizure pattern in 38.71% cases, with 32.26% of patients with localizable seizure onsets and bilateral or generalized activity in 25.81%. Treatment was adjusted in 8 patients according to video-EEG results, and 75% improved ≥75%. Other 3 underwent neurosurgery (2 VNS, 1 resective surgery) with good prognosis.

Conclusion: Video-EEG monitoring is useful for seizure depiction, with hypermotor seizure as the most common subtype, and helps to achieve better seizure control since it determines surgery feasibility and helps to pharmacological adjustment.

p426

A CLINICAL- AND RESEARCH-ORIENTED ELECTRONIC DATABASE FOR THE MANAGEMENT OF PATIENTS WITH EPILEPSY: FEATURES AND PERSPECTIVES

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Purpose: The computerization of medical records is not (yet) a standard practice in most medical institutions, but it appears as a key prerequisite for any systematic study. Concerning epilepsy, all of the patients'clinical and instrumental data can be transformed into numeric/categorical data after appropriate standardized simplifications, thus allowing their use both for clinical- and research-oriented purposes. The aim of this project is to create a versatile SQL-based database to fulfil these needs in a tertiary level Epilepsy Center.

Method: We used only open source tools. The relational database was designed following the specifications of the UML modelling language and implemented using MySQL, version 5.1. The scripting language php was selected to develop a custom web interface allowing the physician to easily manage the database.1) For developing a research-oriented database, we created ad hoc subcategories of entries for EEG, neuroimaging, laboratory and clinical data, modified to allow statistical comparisons of data which are usually handled merely qualitatively. 2) For creating a database for handling all data for our Epilepsy Center outpatients, we focused on ease of access to all data and on easy access to multiple versatile queries.

Results: We developed the database with the abovementioned requisites. The steps of projecting, developing, conceptualising and testing it represent the main topic of our presentation.

Conclusion: This database reveals as a versatile, powerful tool, both for clinical and research aims, and is the result of the fruitful collaboration by epileptologists and mathematicians with a strong background in creating research-oriented SQL databases.

p427

ICTAL WATER DRINKING AS THE PRESENTING EPILEPTIC PHENOMENON OF TEMPORAL EPILEPSY IN AN 8-YEAR-OLD GIRL

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Ictal water drinking is un unusual clinical epileptic semiology of temporal lobe epilepsy. No more than 30 cases of peri ictal water drinking have been reported in the literature so far and even less as the presenting feature of temporal lobe epilepsy especially in children. We report the case of an 8-year-old girl who for the first time in her life developed 5 fits of 10 to 15 min each, of intense feeling of thirst and water drinking in about a period of 8 h. Every crisis was characterized by agitation, tremor, elevated blood pressure and pulses and a strong feeling of dry mouth and thirst. The child during each crisis consumed one to two liters of water. Only after phenytoin loading the child regained his previous usual behavior. The first neurological and psychomotor evaluation of the child was normal as an emergency cerebral CT scan also. Hematological and biochemical profile were in the normal range either. The surface EEG revealed a normal background organization but a left temporocentral epileptic focus of spikes and generalized discharges of sharp slow waves, clearly with higher voltage on the left side. Cerebral MRI was normal. The child was treated with carbamazepine and 13 months later is still seizure-free with normal behavior, school performance and neurological evaluation. The last EEG, 6 months later, showed localized slow theta waves at the left temporo-centro-parietal area and rare theta waves at the same controlateral area. Unremarkable personal and family history for epilepsy.

Poster session: Epilepsy syndromes in children and adults III
Tuesday 29th June 2010
13:30–14:30

p428

HASHIMOTO'S ENCEPHALOPATHY PRESENTING AS STATUS EPILEPTICUS AND SUBACUTE PSYCHIATRIC DISORDER IN A 15-YEAR-OLD GIRL

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Hashimoto's encephalopathy (HE) is a rare neurological disorder based on an autoimmune mechanism associated with Hashimoto thyroiditis or, less frequently, Basedow's disease, responsive to steroid treatment. It comprises a heterogenous group of neurological symptoms including psychosis, confusion, seizures, stroke-like episodes, tremor, and myoclonus, variously associated. The most common immunological feature of HE is the presence of high titers of antithyroglobulin or anti-TPO antibodies without any connections to the thyroid function . We report on a 15-year-old girl affected with Basedow's disease, with normal levels of thyroid hormones but with very high levels of anti-TPO antibodies. She presented with a generalized tonic–clonic status epilepticus (SE), treated with i.v. DZP and Pb. The girl showed a moderate impairment of cognitive functions and behavioral and mood disturbances; according to her parents such condition had begun about two weeks before and had been gradually worsening until the onset of SE. While EEG was normal, brain vasculitis was diagnosed by means of MRI. Steroid treatment induced a dramatic and rapid improvement of clinical and neuroradiological manifestations. The concurrence of the present results supports the view of a possible vasculitic origin of HE and the efficacy of corticosteroid therapy.

p429

LATE ONSET RASMUSSEN'S ENCEPHALITIS: TWO CASES IN THE FOURTH AND SEVENTH DECADES OF LIFE

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Purpose: Rasmussen's encephalitis (RE) is a rare immune-mediated brain disease characterized by refractory epilepsy, progressive neurological disfunction and unilateral hemispheric atrophy. Usually, affects children and adolescents, although occasional reports of adult-onset RE have been reported. We present a woman (case-1) and a man (case-2) in whom RE manifested at 34 and 63 years old, respectively.

Method: Case-1. Three-year history of progressive epilepsia partialis continua involving left face and limbs. Case 2. One-year history of somatomotor and sensitive seizures, epileptic visual illusions and hallucinations, involving left part of his body and space, with progressive evolution.

Results: Case-1. MRI (several studies): progressive right anterior frontal atrophy with subcortical gliosis. EEG: continuous right frontal epileptiform discharges. Brain biopsy: T-cell perivascular encephalitis with gliosis. Treatment: five antiepileptic drugs, intravenous immunoglobulins and high doses of corticosteroids. Case 2: MRI (several studies): progressive right occipital and temporal atrophy with subcortical gliosis. EEG: continuous PLEDs in right posterior region. Brain biopsy: diffuse and perivascular encephalitis (T-cell predominant), gliosis, and vascular amyloid deposits. Treatment: three antiepileptic drugs, plasmapheresis and high doses of intravenous corticosteroids. In both cases, vasculitis, systemic, prionic, and neoplastic diseases were ruled out. Antibodies against GluR3 receptor were not done.

Conclusion: RE must be considered in adults and old people with progressive drug resistant lobar epilepsy and focal brain atrophy. To the best of our knowledge, our second case is the oldest RE reported in the literature. We emphasized the value of brain biopsy to confirm the diagnosis and to rule out other diseases.

p430
LANDAU-KLEFFNER SYNDROME: CLINICAL AND ELECTROENCEPHALOGRAPHIC FOLLOW-UP

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Purpose: To report the clinical and electroencephalographic (EEG) follow-up of Landau-Kleffner syndrome (LKS) of acquired aphasia with epilepsy in children from the onset til adolescence and young adulthood.

Method: During the follow-up lasting from 10–22 years, neurological and other clinical examinations, EEG recordings including video monitoring during both wakefulness and sleep and neuropsychological testing were performed repeatedly in all 8 patients with Landau-Kleffner syndrome.

Results: Seizure onset (at the age ranging from 3–7 years) preceded the aphasia in all patients. Video-EEG disclosed ictal findings even in 3 patients with subtle seizures. Antiepileptic drug therapy achieved seizure control in all patients. However, aphasia and EEG discharges, mainly bitemporal, outlasted seizure control in all patients. Whole night EEG recording have uncovered significant increase of epileptiform discharges in all patients, while bilateral continuous spike-waves during slow wave sleep occurred in three patients and focal electrographic status in left centro-temporal region in one patient. The index of bilateral spike-wave discharges during slow wave sleep and time period with severe aphasia were significantly correlated (Pearson $r = 0.8392$; $p < 0.01$). EEG normalization always preceded the improvement of behavioral disorders (evident in all patients) for a period of 2–5 years. The recovery from aphasia was moderate in 5 and almost complete in 3 patients. A favorable effect of adrenocorticotropic hormone or corticosteroid treatment cycles on aphasia was difficult to assess due to fluctuating course.

Conclusion: In spite of a favorable prognosis for seizure control and EEG normalization, a considerable degree of dysphasic disturbances persisted during adulthood.

p431
CURRENT MANAGEMENT OF WEST SYNDROME IN ARMENIA

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Purpose: To determine epidemiological characteristics of West syndrome and to compare treatment approaches in Armenia with management of this syndrome worldwide.

Method: We analyzed medical records of more than 1200 patients registered in Republican Children's Epilepsy Center (RCEC) from 2003 to 2006. We found 21 patients with WS (11M/10F).

Results: Ethiological classification of WS was possible only in 11 cases because of absence of full range of diagnostic investigations: 9-symptomatic, 1 – crypptogenic, 1 – idiopathic. the diagnostic criteria applied were those of the International League Against Epilepsy. As a first drug of choice Depakine was used in 47.5%, Phenobarbital in 33.3%, Prednisolone in 4,8%

Conclusion: Prevalence of WS among all pediatric epilepsies is 9% whereas in RCEC prevalence of WS among all patients with childhood epilepsies is 2.7% which reflect low awareness on WS and/or low admission rate. Analyzing treatment approaches we found out that it was not in accordance with international therapeutic guidelines. One child treated with nonepileptic drug - Pantogam.

p432
DUPLICATION (X)(P11.22-P11.23) ASSOCIATED WITH MENTAL RETARDATION, SPEECH DELAY, AND EEG ANOMALIES IN MALES AND FEMALES: DESCRIPTION OF A NEW SYNDROME

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Purpose: To describe in detail the clinical and instrumental features of one family and a sporadic case previously reported by Giorda et al. (Am J Hum Genet. 2009; 85:394–400) who identified a new syndrome characterized by mental retardation (MR), speech delay, EEG abnormalities and mild facial dysmorphisms related to a microduplication at Xp11.22–11.23.

Method: Neurological examination, brain MRI, EEG and a neuropsychological assessment specific for language disturbances have been performed.

Results: Three members of the family were affected (mother and two siblings): we directly investigated the two siblings (a 30-year-old man and his 35-year-old sister). The sporadic case was a 13-year-old female. All patients had the following characteristics: negative brain MRI; mental retardation with a moderate-severe global language deterioration; wake and sleep EEG showing epileptiform discharges especially activated during sleep in two siblings, whereas electrical status epilepticus

during slow sleep (ESES) was evident in the sporadic case. We also found a comorbidity for autoimmune disease in the familial cases (Wegener's granulomatosis in the female; ulcerative rectocolitis in the male).

Conclusion: This microduplication determines a new syndrome characterized by EEG abnormalities (ESES in childhood) and a MR mainly involving language function. Speech delay, without structural abnormalities in brain MRI, could be the result of a childhood ESES that disappeared in adulthood, or insufficient language development secondary to poor stimulation due to a social isolation in a child with MR.

p433
THERAPEUTIC APPROACHES IN CHILDREN WITH ANGELMAN SYNDROME

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Purpose: Angelman syndrome (AS) is a neurogenetic disorder caused by various 15q11–q13 abnormalities, characterized by severe developmental delay, speech delay, motor impairment, distinctive electroencephalographic features. Over 90% of patients have epilepsy. In this paper we present the therapeutic characteristics of our patients with AS.

Method: We analyze 7 children (5 boys and 2 girls) with AS, all with interstitial deletion of 15q11–13, with aged ranged between 6 months and 12 years. The study focuses on the characteristics of epilepsy and response to treatment.

Results: All the patients presented early-onset seizures, generalized seizures in 5 children and focal seizures in 2 cases. All the children presented an EEG pattern that was typical for the disease. Valproic acid was used in all patients; in one case this was associated with lamotrigine and clonazepam, and with levetiracetam in other case. In one case, corticotherapy was associated with valproate. Other antiepileptic drugs, like topiramate, carbamazepine, nitrazepame, were used, but disrupted because of their inefficiency. Four children are seizures-free; the children with polymorphic seizures have periods of refractory epilepsy and periods without seizures. The child with corticotherapy and valproate has a good control of seizures and a slight improvement of psychomotor development.

Conclusion: Epilepsy is a common feature in children with AS, often difficult to control. In our cases, valproate, alone or in combination with other antiepileptic drugs, was effective in most patients. Corticotherapy had a good effect, both on seizures and psychomotor development.

p434
GOOD RESPONSE TO POLYTHERAPY IN A PATIENT WITH 20 RING CHROMOSOME SYNDROME DRUG-RESISTANT EPILEPSY

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Purpose: Relatively few cases of the 20 ring chromosome syndrome have been reported. This syndrome is a well-defined chromosomal disorder almost systematically characterized with polymorphic seizures, frequently drug resistant, which lead to cognitive decline.

Method: We report a case of a 21 year old male, with epilepsy onset at 4 year old. The patient had daily polymorphic seizures: atypical absences, complex partial and generalized tonic–clonic seizures. Once an hospital admission due to nonconvulsive status was required. Cranial MRI was normal and EEG and video-EEG records showed bifrontal spike and wave activity. Ring chromosome 20 was found in 44% of examined metaphases.

Results: Several combinations with up to 4 antiepileptic drugs were prescribed (including valproic acid, clonazepam, carbamazepine, levetiracetam, topiramate, clobazam, ethosuximide, ACTH, lamotrigine), but a dramatic improvement was achieved only after adding zonisamide to the last treatment (clobazam, etoxusimide, lamotrigine).

Conclusion: Lamotrigine is being used in combination with good result, however zonisamide is hardly described in the literature. Its usefulness was dramatic in our patient, and could be considered as a therapeutic option in patients with 20 ring chromosome syndrome.

p435
A POPULATION-BASED STUDY ON EPILEPSY WITH ONSET IN THE FIRST YEAR: INCIDENCE AND SYNDROME CLASSIFICATION

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Purpose: The aim of our study was to investigate the incidences and etiologies of different epilepsy types and syndromes with onset in the first year of life.

Method: A population-based retrospective study was performed using the hospital diagnosis registry to select all infants who had epileptic seizures before the age of 12 months and were born in 1997 through 2006 in our hospital district with 127,730 live births during the study period. Hospital charts were reviewed to reevaluate and confirm the diagnosis and to collect data on etiological investigations and family history. In 21 cases who had two different epilepsies diagnosed in the first year, the results refer to the presenting type or syndrome.

Results: One hundred sixty infants met the study criteria. The overall incidence rate (IR) of epilepsy was 125/100,000. The incidence rate was higher among boys (58%; IR 143/100,000) than girls (42%; IR 107/100,000). Partial epilepsies (PE) accounted for 65% (IR 81/100,000), infantile spasms syndrome (IS) for 30% (IR 38/100,000) and other or unclassified epilepsies for 5%. The underlying etiologies were: partial epilepsy, 50% idiopathic and 50% symptomatic or probably symptomatic; infantile spasms syndrome: 19% and 81%, respectively.

Conclusion: The overall incidence is slightly higher than previously reported. This may be explained by improved diagnostic accuracy as the idiopathic partial epilepsy group, which may present with only a few seizures, was relatively large. The incidence and etiology of infantile spasms syndrome are very close to what has been reported earlier.

p436
MYOCLONUS FOLLOWING CARDIOPULMONARY RESUSCITATION

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Purpose: Myoclonus is defined as shock-like, involuntary, sudden jerks typically lasting 10 to 50 ms, with the duration of movement rarely longer than 100 ms. Can be irregular, rhythmic, or even oscillatory, and occur with dysfunction in cortical, brainstem or spinal motor system. Patients with diffuse cortical hypoxic injury may develop both focal motor seizures with central spikes and myoclonus.

Method: We would present three patient, two female and one male, age 21, 29, 46 years. All three of them survived cardio respiratory arrest and successful cardio respiratory resuscitation (CPR). As neurological com-

plication post anoxic myoclonus occur. We would revue data from our patient group, etiology, CPR, clinical, neurological data, EEG, time of occurrence after the successful resuscitation, treatment.

Results: Clinically hypoxic injury results in coma (low Glasgow coma Score), focal, multi focal or generalized miolonic movements (often manifest by eye blinking, chewing movements, or multi focal twitching). Electroencephalogram showed typical myoclonic potentials, burst suppression pattern and characteristic diffuse brain injury. Initially used paralytic agents, benzodiazepines show ineffective. Antiepileptic drugs valproic acid (VPA) and clonazepam (CZP) have been used.

Conclusion: Generalized myoclonus should be considered as predictor of poor outcome in patient following cardiopulmonary resuscitation (CPR).

Poster Session: Neurobiology and basic sciences V
Wednesday 30th June 2010
13:30–14:30

p437
CHOP (GADD153) PROTECTS THE HIPPOCAMPUS AGAINST SEIZURE-INDUCED NEURONAL DEATH

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Purpose: Prolonged seizures cause DNA damage and endoplasmic stress, and activate signalling pathways associated with apoptosis. C/EBP homologous protein (CHOP), also known as GADD153 is a small nuclear protein induced by a variety of cell stressors including endoplasmic reticulum stress. It can function as a positive or negative regulator of gene transcription, mediate cell cycle arrest and induce apoptosis via transcription of the proapoptotic Bcl-2 family protein Bim. We recently reported that prolonged seizures in mice caused endoplasmic reticulum stress and Bim induction in the hippocampus, and that mice lacking Bim were partially protected against seizure-induced neuronal death. Accordingly, we investigated the role of CHOP in this model.

Method: Status epilepticus was induced in adult C57BL/6 mice and *Chop*+/+ or *Chop*-/- mice by intraamygdala microinjection of kainic acid. Hippocampus or neocortex were extracted for Western blotting or whole brains processed for immunohistochemistry and histopathology.

Results: Status epilepticus caused a time-dependent increase in CHOP protein levels within the ipsilateral hippocampus, beginning 1 h after SE and continuing until 24 h. In contrast, CHOP was not induced in the ipsilateral neocortex. Seizure-like behavior of *Chop*-/- mice after kainate was similar to wild-types. However, seizure-damage in both the dorsal and ventral hippocampus was significantly greater in *Chop*-/- mice compared to wildtype mice. Seizure damage was not different in the neocortex between genotypes.

Conclusion: The present data demonstrate that CHOP is induced in the hippocampus following prolonged seizures and may contribute to neuronal survival.

p438
NEUROPROTECTIVE EFFECT AND BEHAVIORAL IMPROVEMENT BY TOPIRAMATE ON GLOBAL CEREBRAL ISCHEMIA IN YOUNG RAT

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Purpose: Topiramate (TPM) is a structurally novel compound which has been demonstrated a broad spectrum of antiepileptic activities both in experimental and clinical studies. Several pharmacological actions of TPM have been identified. These include a potentiation of GABAergic transmission, antagonism at AMPA-kainate receptor sites, blockade of voltage activated sodium channel and calcium channel, and an inhibition of carbonic anhydrase. We tested whether treatment of TPM could reduce global cerebral ischemic injury and functional impairment in the four-vessel transient occlusion model of 3 weeks Sprague-Dawley (SD) rats.

Method: Global cerebral ischemia was induced by four-vessel occlusion for 20 min using 3 weeks SD rat. Rats received TPM intraperitoneal injection immediately before and again after ischemia (50 mg/kg/dose), or vehicle for control. Neuronal cell loss in the hippocampal CA1 and CA3 were evaluated by thionin staining of section at 7 days later. We also evaluated the behavior of 8-week old rats following global cerebral ischemic injury with or without pretreatments of TPM using open field test and the Morris water maze test.

Results: Intraperitoneal pretreatment with TPM reduced the loss of neurons in the CA1 and CA3 subfields and subsequent cognitive impairments induced by global cerebral ischemia in young rats.

Conclusion: These results suggest that TPM treatment may be beneficial for global ischemic brain injury and related cognitive impairments in young rat and it may offer an effective means to decrease the incidence and severity of global cerebral ischemic brain injury in children.

p439
EXOGENOUS ERYTHROPOIETIN EXERTS OPPOSITE EFFECTS ON COGNITIVE DEFICITS AND ANXIETY IN EPILEPTIC RATS DEPENDING ON THE QUALITY OF LIVING ENVIRONMENT

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Purpose: Cognitive impairment and increased anxiety represent major problems in patients with epilepsy. Treatment of epilepsy with AED is not always adequate to eradicate these alterations. Therefore, the aim of our study was to determine whether erythropoietin (rEpo) exerts protective effects on cognitive function and anxiety in epileptic rats and whether this effect is potentiated by housing in the enriched environment provided in Marlau cages.

Method: Rats were subjected to lithium/pilocarpine-induced *status epilepticus* (Li/Pilo-SE) at weaning. rEpo (5000 IU/kg, i.p.) was administered on 5 consecutive days starting immediately after the cessation of SE. One day after SE, rats were reared either in standard (SH) or enriched (EH) housing. All behavioral tests were conducted on rats exhibiting behavioral spontaneous recurrent seizures (BSRS). Spatial learning and memory retention were evaluated using the Morris Water Maze (MWM) and anxiety-like behavior using the Elevated Plus Maze (EPM) and the Water Exploration Test (WET). Finally, rats were sacrificed for histological analysis.

Results: Rats subjected to Li/Pilo-SE at weaning developed BSRS 4 weeks later without obvious neurodegenerative processes and exhibited increased anxiety and deficits in spatial learning and memory. Treatment with rEpo exerted positive effects on anxiety and on learning and memory deficits in rats with BSRS reared in SH, while it exacerbated anxiety and generated memory impairments in rats with BSRS reared in enriched Marlau™ cages.

Conclusion: These findings suggest that determining the potential therapeutic effect of a molecule in epilepsy must take into consideration the quality of the living environment.

p440

TARGETING THE ARACHIDONIC ACID CASCADE IN THE AMYGDALA KINDLING MODEL OF TEMPORAL LOBE EPILEPSY

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Purpose: Recently, we suggested that targeting the arachidonic acid cascade helps to overcome pharmacoresistance. Whereas several rodent studies indicated that blocking the cascade exerts beneficial effects, others described aggravation of seizures. Therefore, translational development of respective add-on approaches requires further tolerability testing. The amygdala kindling model has a high predictive validity for both, anticonvulsant and proconvulsant effects, and was therefore considered as the optimal model to further explore the impact of compounds that target arachidonic acid signalling.

Method: Male NMRI mice were stimulated once daily via an implanted depth electrode until 10 generalized seizures were elicited. The COX-2 inhibitors celecoxib (7, 20, 30 mg/kg) and NS-398 (10, 30, 90 mg/kg) as well as the prostaglandin E2 EP1 receptor antagonist SC-51089 (3, 10, 30 mg/kg) were administered i.p. in fully kindled animals. Each drug experiment was preceded by a vehicle control experiment in the same group of animals.

Results: SC-51089 dose-dependently decreased the seizure severity, effects being significantly different from control data at 10 and 30 mg/kg with a pretreatment time of 60 min. There was no significant effect on the seizure threshold by SC-51089. The COX-2 inhibitors celecoxib and NS-398 did neither affect seizure thresholds nor seizure severity or duration.

Conclusion: The data argue against proconvulsant effects of different compounds targeting arachidonic acid signalling. Moreover, the results suggest that EP1 receptor antagonism in addition to potentiating antiepileptic drug efficacy based on control of P-glycoprotein expression at the blood–brain barrier, might also exert anticonvulsant effects itself.

p441

NR2B-CONTAINING N-METHYL-D-ASPARTATE (NMDA) RECEPTORS IN A RAT MODEL OF TEMPORAL LOBE EPILEPSY (TLE)

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Purpose: We investigated the changes in the Tyr^{1472} phosphorylation (P) of the NR2B subunit of the NMDA receptor in the hippocampus using a rat model of TLE. Since NR2B-P confers enhanced channel permeability to calcium, it may be implicated in the mechanism of hyperexcitability and excitotoxicity during epilepsy development. We also explored whether changes in NR2B-P were associated with glial expression of IL-1beta since this cytokine exerts proexcitatory effects via Src-mediated NR2B phosphorylation.

Method: Spontaneous recurrent seizures (SRS) were induced in Sprague-Dawley male adult rats following status epilepticus (SE) induced by electrical stimulation of CA3. NR2B subunit was analyzed by western blot in hippocampal homogenates following subcellular fractionation. IL-1beta and NR2B-P cellular expression was analyzed by immunohistochemistry.

Results: Increased NR2B-P was found 2 h (+231 ± 39%) and 18 h (+52 ± 9%) after SE onset, during epileptogenesis (+89 ± 19%), as well as 2 h (+73 ± 27%), but not 24 h, after SRS. NR2B-P was localized in the postsynaptic density, 2 h after SE onset or the last SRS. NR2B-P was instead present in a nonsynaptic compartment during epileptogenesis. Total NR2B levels were invariably decreased: NR2B reduction during SE was likely due to μ-calpain activation while neurodegeneration is likely to account for NR2B decrease during epileptogenesis and SRS. IL-1beta immunostaining was increased in glia while NR2B-P was expressed by neurons and microglia.

Conclusion: NR2B phosphorylation is increased in the stimulated hippocampus after an epileptogenic stimulus concomitant with IL-1beta, thus suggesting that these two factors contribute to increase neuronal network excitability and excitotoxicity during epilepsy development.

p442

COEXISTENCE OF TWO TYPES NONCONVULSIVE DISCHARGES IN ABSENT EPILEPSY PATIENTS AND GENETIC ABSENCE EPILEPSY WAG/RIJ RATS

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Purpose: Two types of nonconvulsive epilepsy discharges coexistence were described and analyzed in absence epilepsy patients and genetic animal model of absence epilepsy (WAG/Rij rats).

Method: Sixteen patients with childhood and juvenile absence epilepsy, males and females, of age 4–18 years old were investigated. For EEG registration standard scheme 10 × 20 of electrode placement was used. WAG/Rij rats, male and female were weight 200–250 g. Electrodes were placed in frontal, parietal and occipital areas with reference electrode above the cerebellum. The time-frequency analysis was performed by modified wavelet transform (Bosnyakova et al, Neurosci Methods, 2006; 154:80–88).

Results: Three from sixteen patients with typical generalized spike-wave discharges manifested discharges in occipital area appeared bilateral and unilateral. These data is compatible with the 1st (generalized) and 2nd (occipital) types discharges coexisted in about 1/3 of WAG/Rij rats. In patients just as in animals the occipital and generalized discharges were registered separately or ''coupled'' with occipital ones as the initial part of complex. Similar structure of two types discharges characteristics in patients and animals was revealed. Important finding was the opposite influence of some drugs to two types of discharges in WAG/Rij rats (Coenen et al, Epilepsy Res, 1995, 21: 89–94; Midzianovskaia et al, Brain Res, 2001, 911: 62–70) and the present investigation.

Conclusion: The analysis of two types of discharges in patients and in WAG/Rij rats revealed their similar characteristics. WAG/Rij rats proposed as a good model for the investigation of this type of brain pathology.

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NARINGIN PROTECTS KAINIC ACID INDUCED STATUS EPILEPTICUS IN RATS: EVIDENCE FOR AN ANTIOXIDANT, ANTIAPOPTOTIC, AND NEUROPROTECTIVE INTERVENTION

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Purpose: Bioflavonoids are being used as a neuroprotectants in the treatment of various neurological disorders including epilepsy. The effect of Naringin (4′,5,7-trihydroxyflavanone 7-rhamnoglucoside), a bioflavonoid, with potent antioxidant activity was studied against kainic acid (KA)-induced seizures, apoptosis, oxidative stress and on the expression of heat shock protein (HSP-72) in rat brain.

Method: The Naringin was administered for seven successive days at doses of 40 and 80 mg/kg/day i.p. On days 7th 30 min after the administration of last dose animals received kainic acid 10 mg/kg i.p. and observed for behavioral changes, incidence and latency of convulsions and mortality over four hours. The oxidative stress parameters- malondialdehyde (MDA) and reduced glutathione (GSH) and the expression of HSP-72 were evaluated. Immunohistochemistry and TUNEL assay were also carried to evaluate the effect of naringin against neuronal damage induced by kainic acid.

Results: Pretreatment with Naringin (40 and 80 mg/kg, i.p) significantly increased the latency of seizures as compared to the KA group. Naringin significantly prevented the increase in MDA levels and ameliorated the decrease in glutathione ($p < 0.001$). The expression of HSP-72 was reduced in the naringin treated rats as compared to the KA group. In addition, Naringin protected against neuronal damage and apoptosis in the hippocampus after KA administration. Naringin also improved cognitive deficit induced by KA, evidenced by increased latencies in passive avoidance task.

Conclusion: Naringin has therapeutic potential in suppressing KA-induced epileptogenesis in the brain, and these neuroprotective effects are due to its antioxidant and antiapoptotic property.

p444
SPREADING DEPRESSION AS A POTENTIAL MECHANISM OF SEIZURE TERMINATION: DATA FROM THE AUDIOGENIC KINDLING MODEL

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Purpose: Termination of seizures is suggested to depend on intrinsic anticonvulsive mechanisms. Here, we tested the hypothesis that spreading depression (SD), a wave of profound neuroglial depolarization, is involved in termination of audiogenic seizures (AS). These seizures triggered by sound in genetically prone rodents are driven by brainstem networks and manifests as explosive running which may be followed by clonic–tonic convulsions. With seizure repetition, the cortex is recruited into the AS network. This process named audiogenic kindling is characterized by appearance of an additional clonic convulsion and an epileptiform discharge in the cortex.

Method: Sound susceptible adult Wistar rats were subjected to repeated sound stimulation inducing minimal AS, a brief running episode. Changes in electrical activity of the cerebral cortex and the brainstem associated with repeated running seizures were recorded in awake freely moving animals.

Results: Abrupt termination of the audiogenic brainstem-mediated running seizure coincided with development of a large negative slow potential shift, a SD wave, in the rostral brainstem. In fully kindled rats, the running seizure was followed by severe forelimb clonus coupled with high-voltage cortical epileptiform discharge. The end of this forebrain-derived seizure was associated with triggering SD wave in the cortex.

Conclusion: The results show the close relationship between the end of audiogenic seizures and SD initiation. Spreading depression induces depolarization block of neuronal activity and may act as a mechanism of seizure termination.

p445
APNEAS ARE ASSOCIATED WITH IMPAIRED RESTING METABOLISM AND BRAINSTEM NORADRENERGIC PHENOTYPE IN RATS WITH SPONTANEOUS RECURRENT SEIZURES

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Purpose: Apneas may play a significant role in Sudden Unexpected Death in Epileptic Patients (SUDEP). Because brainstem noradrenergic neurons play a role in ventilation control, the aim of our study was to determine whether occurrence of apnea in rats with spontaneous recurrent seizures (SRS) was associated with altered brainstem noradrenergic system.

Method: SRS were developed in Sprague-Dawley rats about 2 weeks after pilocarpine-induced status epilepticus (SE). Metabolic rate was measured throughout 24 h at 2 and 4–8 weeks post-SE. Ventilatory reactivity was recorded in response to hypoxia and hypercapnia. Immunofluorescent labeling of tyrosine hydroxylase (TH) was performed 16 weeks post-SE on serial brainstem sections to detect (nor)adrenergic neurons.

Results: No metabolic rate dysfunction was found 2 weeks after SE. Apneas, detected by drastic and transient decreases in metabolic rate, were detected from 4 to 8 weeks post-SE in 30–50% of rats with SRS. Apneas were never detected in control rats; they were episodic (~7 times a day), lasted 7 ± 2 min, and were not explained by an impaired ventilatory reactivity to hypoxia and hypercapnia. In comparison with other rats with SRS, rats with apneas displayed a 46% decrease in resting metabolism and a reduced targeting of TH protein towards dendrites of brainstem noradrenergic neurons.

Conclusion: These findings suggest that a dysfunction of brainstem catecholamine system may induce ventilatory dysfunctions in epilepsy, associated with resting metabolism impairment. It may be possible that determination of resting metabolism in epileptic patients may be a relevant marker to detect elevated risks for SUDEP.

p446
IMPAIRED ANXIETY-TRAIT AND CA1 PYRAMIDAL CELL EXCITABILITY PRECEDE SPONTANEOUS RECURRENT SEIZURES AFTER INDUCTION OF STATUS EPILEPTICUS AT WEANING IN RATS: EFFECT OF ENVIRONMENTAL ENRICHMENT

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Purpose: Recent clinical investigations reported that psychopathology and cognitive dysfunction can precede the onset of seizures in children, and psychosocial factors were found to worsen these impairments. Anxiety and learning and memory deficits are increased in adult rats subjected to lithium pilocarpine-induced status epilepticus (Li/Pilo-SE) at weaning. In addition, environmental enrichment (EE) after Li/Pilo-SE preserved cognitive function. In these rats, spontaneous recurrent seizures (SRS) are observed 4 weeks post-SE. We thus investigated 2 weeks after Li/Pilo-SE whether impairment in anxiety and CA1 pyramidal cell excitability could be observed before SRS onset, and counteracted by EE.

Method: After induction of Li/Pilo-SE at weaning, rats were housed either in standard environment (SE) or in EE using the Marlau™ cage. Control rats were housed in SE. Two weeks after SE, anxiety was tested, and electrophysiological recordings were performed in CA1 pyramidal neurons using hippocampal slice preparations.

Results: Two weeks after SE, we observed: 1) an increase in anxiety-trait, 2) a decrease in spontaneous activity and excitability of CA1

pyramidal cells, and 3) an increase in GABAergic transmission at the collateral Schaeffer-CA1 neuron synapses. Housing in EE for 2 weeks post-SE had no effect on anxiety-trait.

Conclusion: Our findings provide evidence for the first time that psychopathology can occur before SRS in immature rats. Current studies are investigating whether: 1) long term potentiation (LTP), a cellular mechanism underlying learning in hippocampus, is altered before SRS onset, and 2) development of electrophysiological impairments in rats subjected to SE can be blocked by EE.

Poster session: Surgical treatment III
Wednesday 30th June 2010
13:30–14:30

p447
ANTIEPILEPTIC DRUGS MANAGEMENT AND LONG-TERM SEIZURE OUTCOME IN POSTSURGICAL MESIAL TEMPORAL LOBE EPILEPSY

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Purpose: To evaluate the routine AEDs management in an homogeneous population of mesial temporal lobe epilepsy (MTLE) postsurgery patients initially in Engel class I.

Method: Selection of MTLE patients in Engel class IA, 1 year after amygdalohippocampectomy. Data collected retrospectively according the clinical file and corroborated by a standardized phone interview. Variables studied: time of follow-up, Engel class at the end of the follow-up period, pre and postsurgical AEDs (number, dose, molecule change, time/reason for any change), seizures recurrence and corresponding Engel class changes and its relationship to AEDs adjustment.

Results: Sixty-eight patients were included with a mean-time of post surgery follow-up of 4.9 ± 3.0 years. Compared to presurgical medication, AEDs dose is currently lower in 31 (45.6%) patients. Among these, 10 (14.7%) achieved monotherapy and 19 (27.9%) are off medication. Mean time for starting reduction was 2.2 ± 1.6 years. Overall, AEDs reduction was attempted in 38 patients during this follow up period, 12 (31.6%) of which had seizure recurrence.

Conclusion: In our homogeneous MTLE population, the percentages of patients off AEDs and the recurrence rate after AEDs decrease was similar to previous studies including other epileptogenic zones. There was a significant variability in the timing for AEDs reduction, reflecting the absence of consensus on this subject. Prospective studies are necessary to evaluate risk factors for recurrence.

p448
LONG-TERM DEVELOPMENTS IN PRESURGICAL EVALUATION AND SURGICAL TREATMENT OF EPILEPSY AT ONE TERTIARY CENTER—PART I: PRESURGICAL EVALUATION

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Purpose: To assess changes over the period 1988–2009 in presurgical diagnostics at a major epilepsy center.

Method: We analyzed all patients studied up to a point when a definite decision about operability was made. Patients were classified according to the underlying epilepsy causes, mainly defined by morphological criteria (MRI and histopathology). Data were analyzed by linear regressions to determine significant increases/decreases ($p < 0.05$) over the observation period in a year-wise fashion together with correlation coefficients (R).

Results: Two thousand seven hundred forty patients were presurgically studied (+3.3/year, R = 0.56). 780 underwent intracranial electrode implantations (28.5%; −1.0%/year, R = −0.80, $p < 0.001$). Most frequent diagnoses were: mediotemporal lobe epilepsy with Ammon's horn sclerosis, N = 794, i.e. 29.0% (+0.7%/year, R = 0.50); nonlesional, N = 566/20.7% (change over time not significant [n.s.]); benign tumor, N = 436/15.9% (−0.9%/year; R = −0.81); focal cortical dysplasia, N = 225/8.2% (+0.4%/year, R = 0.77).

1766 patients were transferred for resective surgery, i.e., 64.5% (−1.5%/year, R = −0.85). Most frequent reasons for not proceeding to surgery were: patient decided against surgery or completion of diagnostics by means of intracranial studies (28.9%; +0.8%/year, R = 0.85); focus not identified (19.5%; +0.5%/yr, R = 0.74); multifocality (16.1%; +0.2%/year, R = 0.47); neurological/neuropsychological risk (11.3%; change n.s.). Discrepancies between presurgical MRI and histopathological diagnosis were found in 190/1724 patients (11.0%;−0.87%/year; R = −0.68).

Conclusion: Welcome developments are the increasing number of patients transferred for presurgical workup, the decreasing need of intracranial electrodes and MRI-histopathology-discrepancies. On the other hand, surgery rates are decreasing, probably due to the growing proportion of "difficult" patients. One indicator for this is that the proportion of nonlesional cases remains stable despite improving MRI sensitivity.

p449
PERSISTENT EPILEPTOGENICITY OF IRRADIATED HIPPOCAMPUS AFTER GAMMA-KNIFE RADIOSURGERY: A SEEG STUDY

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Purpose: Failure of Gamma-knife radiosurgery (GKS) in the treatment of temporal lobe epilepsy has mostly been related to misevaluation of the location of the epileptogenic zone. Alternatively, GKS-induced alterations of the neuronal networks may be insufficient to abolish the epileptic activity. However, whether the irradiated tissue may show persistent high degree of epileptogenicity has never been directly investigated in patients.

Method: Two patients suffering from disabling seizures 5 and 6 years after GKS were investigated with stereotactic intracerebral EEG recordings. GKS had targeted the mesial temporal lobe structures with a marginal dose of 24 Gy. In both patients, the epileptic temporal lobe was explored with eight electrodes including four that targeted the irradiated mesial temporal cortex.

Results: In both patients, the irradiated limbic cortex showed subcontinuous spike and wave rhythmic discharges which remained asymptomatic. Ictal discharges became symptomatic only after invading the nonirradiated temporal regions. Because of the subcontinuous discharges observed

doi: 10.1111/j.1528-1167.2010.02658.x

within the irradiated limbic cortex, one cannot conclude on the role of this epileptic activity in triggering the symptomatic seizures. Conversely, intracerebral EEG data provided evidence of seizure spread between the irradiated and the nonirradiated temporal regions at later stages of the ictal discharge. Both patients underwent anterior temporal lobectomy with an Engel class I outcome in one and class II in the other.

Conclusion: After GKS, the irradiated mesial temporal structures can demonstrate persistent high degree of epileptogenicity. Whether the poor seizure outcome of our two patients may be related to this persistent epileptic activity remains unclear.

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EPILEPSY SURGERY IN A TERTIARY CARE HOSPITAL: A DECADE OF EXPERIENCE

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Purpose: Thirty percent of epileptic patients have refractory epilepsy. When the epileptic focus is resectable, curative surgery can convert intractable epilepsy in seizure-free patients. In other cases palliative surgery can be considered. We analyze our surgical results, after 10 years of experience.

Method: Retrospective analysis of 145 operated patients with at least a year of follow up, from January 1998 until December 2008. Techniques performed were amigdalohippocampectomy with anterior temporal lobe resection and lesionectomy as curative procedures, and vagus nerve stimulation (VNS), callosotomy or hemispherotomy as palliative methods. Good prognosis was considered if Engel I was reached in curative techniques and ≥50% of reduction in seizure frequency in palliative techniques.

Results: One hundred forty-five patients were operated. 54 had an amigdalohippocampectomy, 42 suffered lesionectomy, 34 were implanted with a VNS, 11 underwent a callosotomy and 4 a hemispherotomy. 80%, 76%, 58%, 55% (64% patients improved ≥50% in drop-attacks) and 100% of patients had good prognosis respectively after 1 year of follow up. At last admission it was maintained in 76%, 70%, 48%, 64% and 75% of patients (with a mean of follow up of 61, 59, 37, 63 and 93 months). 7 patients needed reintervention and 2 people died (one with unknown cause and other in relation with seizures).

Conclusion: Our results agree with literature data. Good prognosis after curative surgery obliges to consider surgery as soon as diagnosis of refractory epilepsy with a resectable focus is made. For other cases, palliative surgery helps in the control of seizures.

p451
REOPERATIONS IN RESECTIVE EPILEPSY SURGERY: DATA FROM THE SWEDISH NATIONAL EPILEPSY SURGERY REGISTER 1990–2004

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Purpose: In some patients with continuing seizures after a first resective surgery for drug-resistant epilepsy, reoperation can be considered. In this study seizure outcome of reoperations in relation to resection type and pathology was analyzed.

Method: The Swedish National Epilepsy Register has national coverage and encompasses data on all patients operated in Sweden since 1990. In the present study we analyzed data for 1990–2004.

Results: Seven hundred eighty-three patients underwent resective epilepsy surgery 1990–2004 and a 2-year follow-up. 136 (17%) were reoperations: 76 temporal, 27 frontal, 16 parietooccipital, 7 multilobar or subtotal hemispherectomies and 10 complete hemispherectomies. In the whole group 36% became seizure-free and 16% had >75% reduction of seizure frequency. After hemispherectomy 80% became seizure-free and 20% had >75% reduction of seizure frequency. The multilobar and subtotal hemispherectomies had the worst outcome: 29% seizure-free and 14% with >75% reduction of seizure frequency. They also had the highest complication rate: 14% major complications compared to 3.8% in the whole group. In the subgroup with reoperation for lesions (low-grade astrocytomas, ganglioglioma/DNET and cavernomas, N = 37), 46% became seizure-free, and 22% had >75% reduction of seizure frequency.

Conclusion: Reoperation can be considered in selected patients after failure of the primary epilepsy surgery, with 35–40% expected seizure freedom. Reoperation for lesions seems to be rewarding. The hemispherectomy group must be considered as a subgroup, since some of these can be considered as staged procedures. The complication risk can be higher for reoperations, especially for extensive resections.

p452
TOOLS TO DEFINE THE EPILEPTOGENIC ZONE IN CRYPTOGENIC PARTIAL EPILEPSY NONINVASIVELY: CORRELATIONS BETWEEN FDG-PET, VOXEL-BASED MRI POSTPROCESSING, AND SCALP VIDEO-EEG RECORDINGS

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Purpose: Advanced neuroimaging techniques are increasingly employed in the presurgical management of refractory partial epilepsy. However, their diagnostic value in cases without abnormality identified by conventional MRI remains unclear. We investigated the topographic correlation between the functional deficit pattern obtained by FDG-PET, the cortical lesion detected by voxel-based MRI postprocessing and the epileptogenic zone hypothesized upon the scalp video-EEG recordings in cryptogenic partial epilepsy.

Method: We retrospectively analyzed a series of ten cryptogenic partial epilepsy cases. Interictal and ictal scalp video-EEG recordings were performed according to 10–20 system. The functional metabolism maps were acquired using (18)F-FDG PET scans and were overlaid onto a 3D-set of the patient's anatomic MRI scans. Voxel-based 3D MRI analysis was performed.

Results: The topography of electroclinically defined epileptogenic zone was neocortical temporal in three and extratemporal in seven patients. In eight patients it was concordant with the functional deficit pattern determined by FDG-PET. In two other cases PET abnormalities were widespread or outside the suggested epileptogenic zone. The MRI postprocessing detected abnormalities suggesting focal cortical dysplasia in two cases. Their topography correlated both with the PET pattern and the electroclinical epileptogenic focus.

Conclusion: Our data show the high rate of concordance between the functional deficit pattern in FDG-PET and the electroclinically hypothesized epileptogenic zone, suggesting PET as an important localizing technique in cryptogenic partial epilepsy. MRI postprocessing may increase

the yield of identified structural lesions, providing an additional tool for non invasive epileptogenic zone definition.

p453
EVALUATION OF OPERATED PATIENTS WITH MESIAL TEMPORAL SCLEROSIS

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Purpose: To investigate the general characteristics of operated patients with MTS, their surgical outcomes and the relationship between surgical outcomes and preoperative assesment.

Methods: Of the clinically and electrophysiologically TLE patients followed by the outpatient clinic of Epilepsy division of Neurology Department of Istanbul Medicine Faculty, Istanbul University, between 1999–2008, 54 operated patients, diagnosed MTS based on their cranial MRI and confirmed by pathological findings, are included. The seizure frequency and type are evaluated to define the outcome of the surgery according to Engel's classification. The association between these variables and surgical outcomeare statistically documented.

Results: Of the 54 patients (27M, 27F), mean age is 35.7 years, and mean age at seizure onset is 11.7 years. 32 patients have febrile seizures, 18 have family history of epilepsy. 46 patients out of 54 (85.2%) are classified as Class I at the first year follow up. Of the 20 patients, 14 (70%) are classified as Class I at the fifth year follow up. Family history of epilepsy is more common in Class I group (27.9%) than the other groups altogether (75%) ($p = 0.017$).

Conclusion: MTS has been associated with good surgical outcome. Our results are consistent with the previous studies which indicate good outcomes for epilepsy surgery. Since the number of patients classified as Class II and above is insufficient, the statistical analyses of their parameters appear insignificant. Further studies with large number of patients on surgical outcome in patients with MTS are needed to clarify the the preoperative assessment.

p454
VAGUS NERVE STIMULATION AND CHRONIC MIGRAINE

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Vagus nerve stimulation (VNS) proved its efficacy as a treatment for drug refractory epileptic seizures. During the past few years a potential therapeutic effect for depressive disorders and different chronic pain syndromes was described.

A few reports have been made of a pain relief in different kinds of headache (chronic tension headache, cluster headache, chronic migraine, posttraumatic headache). So far 9 patients with migraine have been described with different effect on the intensity and frequency of migraine attacks after a VNS initiation.

We present a 42-year-old female patient with posttraumatic epilepsy (complex partial seizures) with the history of migraine attacks prior to epilepsy related trauma. Her headaches were pulsative, right-sided, intense, worsened by light and physical activity, often associated with nausea, with the frequency of 2–3 attacks a week (MIDAS score about 50). An indication for the implantation of a VNS had been made after a 29 year long drug treatment of epilepsy. The patient noted improvement regarding headaches immediately: within a few days due to decrease in severity, while after 6 months even to the frequency of headaches (MIDAS score went to 2) followed by the improvement of the quality of life.

VNS proved beneficial to an antiepileptic and antinociceptive treatment. Although further trials should be made for VNS as a chronic headache therapy, in patients with drug refractory epilepsy and chronic pain syndromes it should be considered a therapy of choice much earlier in the course of the disease.

p455
INTRACRANIAL EEG MONITORING WITH SUBDURAL GRIDS IN REFRACTORY EPILEPSY: IMPLANTATION TECHNIQUE BY LINEAR CRANIOTOMY UNDER NEURONAVIGATION (''LETTER BOX'' TECHNIQUE), EXPERIENCE WITH 99 CONSECUTIVE GRIDS IN 43 CONSECUTIVE PATIENTS

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Purpose: To evaluate safety and effectiveness of implanting subdural grids (SG) by linear craniotomy under neuronavigation for intracranial electroencephalography (iEEG) in refractory epilepsy (RE).

Method: We report our first 43 consecutive patients who underwent SG implantation by linear craniotomy (from 2 to 55 y; F22). 99 SG (ADTECH) were implanted. For each patient, a preoperative MRI for neuronavigation (BrainLab, Germany) was performed followed by a postoperative MRI for localization control of the SG. A linear skin incision adapted to the SG and compatible with the possible following therapeutic surgery was carried out under neuronavigation. Then, one or two linear craniotomies (maximal length 3 cm, width 1 cm) with a bevel were performed (''letter box'' technique). The dura mater is then incised without opening the arachnoïde. One or two SG were then subdurally slipped through each linear craniotomy.

Results: 45 iEEG (twice in two patients) including bilateral SG in 17 (37.8%) added up 99 SG from 4 to 32 contacts. We used 1 to 4 SG for each patient. Two SG were slipped through the same linear craniotomy 23 times. No infection, no CSF leakage no neurological deficit, no permanent complication occurred. One transient peroperative venous subdural bleeding occurred during one SG slipping but stopped spontaneously. Three SG (3%) were not exactly localized as planned but without consequence for the iEEG analysis and did not require correction.

Conclusion: Implantation of SG through a linear craniotomy showed no permanent complication. This ''letter box'' technique appears highly useful and safe.

p456
INNSBRUCK EPILEPSY SURGERY PROGRAM (INES) 1999–2009: PROCEDURES AND OUTCOME

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Purpose: Epilepsy surgery is a well accepted, but still underutilized treatment method in drug resistant epilepsies. We present procedures and outcome of the Innsbruck Epilepsy Surgery Program, which started in 1999 as a collaboration of the Dpts of Neurology and Neurosurgery at the Innsbruck Medical University, Austria.

Method: One thousand two hundred forty-six patients (pt.) were admitted to the intensive video-monitoring unit (1–30 d). Forty-eight pt. had invasive EEG recording (35 subdural/dephtelectrodes, 13 foramen ovale electrodes). All pt. had MRT (1.5 Tesla), F18-FDG-PET, and neuropsychological testing. Interictal/ictal HMPAO-SPECT and WADA-test/fMRT for lateralization of speech dominance were performed when feasible. Follow up was done 1, 3, 6, and 12 month postoperatively, then annually.

Results: Two hundred eight pt. had surgery (105 f, mean 38 ± 11.8a; 172 TLE, 23 FLE, 8 PLE, 5 OLE). Seventy-six pt. had selective amygdalo-hippocampectomy, 48 anterior temporal standard resection, 8 modified standard-resection, 58 lesionectomy, 3 limited neocortical resection, 6 frontal lobe resection (9 other). Histopathology showed in 43% hippocampus sclerosis, 13% vascular malformations, 8% gliosis, 19% dysplasias, 10% tumors (7% others). After a mean follow-up of 5.5 years (N=202 FU>1a) outcome was Engel class I in 77% (cl. IA 52%; cl.II 12%; cl. III 9%; cl. IV 2%). Complications resulted in a NIII/NIV paresis in 5 cases; hemi-paresis in 3 cases; aphasia, hemihypesthesia, and hemianopsia in 2 cases; cerebellar syndrome, critical illness polyneuropathia and infection in 1 case each.

Conclusion: Epilepsy surgery can achieve a favorable outcome in refractory epilepsy patients, holding little risk of complications. An interdisciplinary approach is essential for a successful epilepsy program.

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CORTICAL RESPONSES TO SINGLE-PULSE ELECTRICAL STIMULATION UNDER GENERAL ANESTHESIA

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Purpose: At King's College Hospital (London), single pulse electrical stimulation (SPES) is a clinical part of the presurgical evaluation protocol for epilepsy in patients with intracranial recordings. Abnormal epileptiform responses after the stimulus (delayed responses – DRs) tend to occur in areas where seizure onset occurs, allowing interictal identification of epileptogenic cortex in refractory epilepsy. The main aim of this study was to investigate the validity of SPES in the under general anesthesia (GA) during the implantation procedure, in order to improve the positioning of intracranial electrodes.

Method: Nine patients with drug-resistant epilepsy evaluated with depth and/or subdural electrodes were studied. SPES (1msec duration pulses, 4–8 mA, 0.2 Hz) was performed during both the intraoperative electrode implantation under GA and during chronic telemetry recordings without GA. The two SPES recordings were compared in terms of the type of cortical responses produced by the stimulation and their electrode location.

Results: Of the 9 patients, 3 showed DRs in both conditions over the same electrode contacts and 2 showed no DRs in either condition. In 4 patients it was difficult to discriminate between spontaneous and stimulus related discharges because of profuse spiking during either or both conditions.

Conclusion: Under GA, delayed responses were reliably replicated and there were no false positive abnormal responses to SPES. The results support that SPES could be used during electrode implantation under GA to select implantation sites more likely to be related to seizure onset.

Poster session: Neuroimaging III
Wednesday 30th June 2010
13:30–14:30

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MRI ABNORMALITIES ASSOCIATED WITH VIGABATRIN TREATMENT – A LONGITUDINAL CASE STUDY

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Purpose: MRI abnormalities in basal ganglia, brain stem and cerebellum have recently been described in infants treated with vigabatrin (Pearl P et al. Epilepsia 2009; 50:184–194; Wheless JW et al. Epilepsia 2009;50:195–205). The abnormalities are considered to be asymptomatic and reversible, but there is no documented evolution of MRI changes at more than 2 points in time in the literature.

Method: We reviewed the medical records and MRI scans in 4 children showing the typical pattern of MRI abnormalities attributed to vigabatrin (age: 0.5–5 years; maximum osage: 95–139 mg/kg/d), who have been evaluated in our institution during the last 12 months.

Results: Two children had serial MRI scans due to other abnormalities, that allow us to document the course of MRI abnormalities starting with normal MRI before treatment and demonstrating the typical pattern after several months of therapy and its resolution with ongoing vigabatrin treatment. No specific clinical symptoms were noted. Interestingly, one child showed the typical pattern of abnormalities attributed to vigabatrin at an atypical age of 5 years, associated with hydrocephalus due to subependymal giant-cell astrocytomas.

Conclusion: MRI abnormalities associated with vigabatrin therapy in infants show a typical pattern without appreciable clinical symptoms. We longitudinally documented the course of these changes and their reversibility with ongoing vigabatrin treatment in two infants. A case of a 5-year-old boy with hydrocephalus raises the suspicion of a multifactorial etiology. The typical age-dependent appearance of the phenomenon might point to developmental processes of myelination as one potential cofactor to vigabatrin treatment.

p459
VOXEL-BASED OPTIMIZED MORPHOMETRY (VBM) IN THE IDENTIFICATION OF SUBTLE FOCAL CORTICAL DYSPLASIAS (FCDs) IN PATIENTS WITH REFRACTORY SEIZURES

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Purpose: Identification of subtle focal cortical dysplasias (FCDs) responsible for refractory seizures is difficult even with the latest magnetic resonance imaging (MRI) techniques and sequences. Detection of such FCDs will help the epileptologist to proceed with presurgical evaluation and surgery. Aim of the present study was to use voxel based morphometry to identify such subtle FCDs not well defined in a 1.5 T MRI.

Method: Sixteen patients with refractory seizures and subtle FCDs detected by T1W and 3D FLAIR MRI from September 2006 to September 2009 were chosen (mean age 34.6 ± 9.7 years; Male/Female-10/6; Temporal:extratemporal 13:3).15 normal controls (mean age 35.2 ± 11.2 years; Male: female-10:5) were also studied. MRI images

were acquired on a 1.5 T (Siemens, Magnetom, Avanto, Germany) system. T1W 3D-FLASH images with TR/TE/FOV/Flip angle of 11 s/4.94 s/23 cm/15°, matrix size 256 × 224, slice thickness of 1.5 mm and pixel spacing 0.89 mm were used. Data were analyzed using SPM-5 running MATLAB 6.1 version. Normalization, segmentation, smoothing and voxel-wise statistical analysis were done.

Results: By VBM, 13/16 of the lesions could be identified (80.6%) by scientists blinded to the MRI findings.6 of them underwent surgery who had concordant clinical and EEG correlate and is seizure-free at a mean follow-up of 1.5 years. Pathology revealed FCD Type I and II in 4 and 2 patients respectively. None of the controls had statistically significant gray-white differences by VBM.

Conclusion: VBM is a novel MRI technique to detect subtle FCDs accurately in patients with refractory seizures which may go undetected in routine MRI.

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TOWARD INVESTIGATING THE CAUSES OF MEMORY DIFFICULTIES IN TEMPORAL LOBE EPILEPSY: A STUDY USING THE NOVEL ALPHA5 $GABA_A$ RECEPTOR PET LIGAND [^{11}C]RO15 4513

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Purpose: Patients with temporal lobe epilepsy (TLE) generally have reduced GABAA receptors, best quantified for alpha1 subunits. However, alpha5 subunits are upregulated in animal models of epilepsy. Alpha5 inverse agonists are promnestic, and TLE patients often have poor memory performance. We investigated whether there were areas of abnormally increased alpha5 binding in TLE patients with normal MRI (nTLE) using the novel alpha5 PET tracer [11C]Ro15 4513, and correlated its binding with memory performance.

Method: Six controls and twelve nTLE patients were studied with [11C]Ro15 4513 PET, 3T MRI and the Adult Memory and Information Processing Battery (AMIPB). Volumes-of-distribution (VD) were quantified using spectral analysis and an arterial input function in selected anatomically defined areas, and VDs correlated with memory scores (Pearson). Two experienced neurologists blindly evaluated nTLE VD maps for asymmetries.

Results: On visual examination, increased VD was seen ipsilaterally to the epileptogenic focus in seven patients. AMIPB final recall scores for verbal material (out of 15) were 10.2 ± 4.2 (range 3–15) in controls and 8.6 ± 3.0 (range 3–12) in patients (p = 0.44). Visual scores (out of 9) were 8.5 ± 1.2 (range 5–9) in controls and 5.9 ± 4.5 (range −2 to 9) in patients (p = 0.19). None of the control's hippocampi but four of the patient's hippocampi had abnormal asymmetry indices. No significant correlation was found between memory scores and hippocampal VD in this small sample.

Conclusion: No major differences between ipsilateral and contralateral side in nTLE were found, and no strong correlations with the memory performance measures used here.

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ELECTRICAL SOURCE IMAGING FOR PRESURGICAL FOCUS LOCALIZATION IN EPILEPSY PATIENTS WITH NORMAL MRI

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Purpose: Patients with MR-negative focal epilepsy (MRN-E) have less favorable surgical outcomes (between 40–70%) compared to those in whom an MRI-lesion guides the site of surgical intervention (60–90%). Patients with extratemporal MRN-E have the worst outcome (around 50% chance of seizure freedom). We studied whether EEG source imaging (ESI) of interictal epileptic activity can contribute to the identification of the epileptic focus in patients with normal MRI.

Method: We carried out ESI in 10 operated patients with nonlesional MRI and a postsurgical follow-up of at least 1 year. Five of the 10 patients suffered from extratemporal lobe epilepsy. Evaluation comprized surface and intracranial EEG monitoring of ictal and interictal events, structural MRI, FDG PET, ictal and interictal perfusion SPECT scans. Eight of the 10 patients also underwent intracranial monitoring.

Results: ESI correctly localized the epileptic focus within the resection margins in 8 of 10 patients, 9 of whom experienced favorable postsurgical outcomes.

Conclusion: The results highlight the diagnostic value of ESI and encourage broadening its application to patients with MRN-E. If the surface EEG contains fairly localized spikes, ESI contributes to the presurgical decision process.

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COMBINED HIGH-FIELD MRI AND HISTOPATHOLOGICAL STUDY ON SPECIMENS FROM TEMPORAL LOBE EPILEPSY PATIENTS

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Purpose: We set out to investigate the cortical laminar pattern abnormalities observed in temporal lobe specimens obtained during surgery for intractable temporal lobe epilepsy with hippocampal sclerosis. Specifically, we attempted to correlate high-field ex vivo MR imaging and histopathological features.

Method: Fourteen specimens were studied. T_2-weighted MRI was performed immediately after surgery using a 7 Tesla Bruker BioSpec 70/30 spectrometer (78 × 78 × 700 micron^3 voxel size). Specimens were then fixated in paraformaldehyde for 48 h and embedded in agar. MRI was subsequently repeated, followed by histopathological (Black Gold myelin fiber staining) and immunohistochemical (NeuN neuronal staining) staining on the same sections chosen for MR imaging.

Results: While in fresh tissue, MRI did not discriminate the cortical layers, in fixed tissue supra- and subgranular regions can be distinguished, with a band of hyposignal corresponding to layer IV. A clear match was observed between the histological and the MRI sections. In particular, in specimens with cortical dysplasia, dislamination was similarly demonstrated by the MR images and by the histopathological sections. These correspondences were confirmed by profile analysis.

Conclusion: High resolution ex vivo MRI can reveal intracortical organization in normal and pathological areas. Comparisons between MRI, NeuN and Black Gold indicated that the T_2-signal differences are mainly

representative of fibers concentration, even though the hyposignal observed in layer IV is likely determined by both fibers and neuronal components.

Acknowledgments: supported by: Italian Ministry of Health, Fondazione Banca del Monte di Lombardia, Associazione Paolo Zorzi per le Neuroscienze and EU grant EPICURE, contract N° LSHM-CT-2006-0373315

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GROUP INDEPENDENT COMPONENT ANALYSIS (G-ICA) REVEALS DIFFERENCES IN NEUROFUNCTIONAL BASIS OF SEMANTIC PROCESSING BETWEEN HEALTHY CONTROLS AND EPILEPSY PATIENTS

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Purpose: To examine differences in neurofunctional basis of semantic processing between healthy controls (HC) and right (RE) or left hemispheric (LE) epilepsy patients using fMRI semantic/tone decision (SDTD) task and G-ICA.

Method: 49 HC, 30 RE and 27 LE received fMRI using 30'' on-off block design SDTD task (Szaflarski et al., 2008). G-ICA based on FastICA algorithm was compared with a random-effects GLM analysis of the same data set. Only semantic decision data are presented here.

Results: G-ICA detected several differences in language processing between groups not detected in the standard GLM analysis. HC: seven task-related ICA maps revealed BOLD signal changes in left inferior frontal gyrus (BA44/45), middle posterior temporal gyrus (BA39/22), angular gyrus/inferior parietal lobule (BA39/40), posterior cingulate (BA30), bilateral lingual gyrus (BA18/23), inferior frontal gyrus (L > R, BA47), parahippocampal gyrus (L > R, BA35/36) and anterior cingulate (BA32/24). Different task-related activations were observed in epilepsy patients. In particular, there were differences in the semantic memory encoding component (symmetric in HC, right-lateralized and co-occurring in LE and left-lateralized but occurring in the left prior to right medial temporal structures in RE) and phonological/semantic working memory module (HC – left-lateralized with frontal/temporal activations co-occurring; LE – left-lateralized but frontal and temporal signal changes occurring as part of sequential components; RE – similar to HC. Differences in other components were less striking.

Conclusion: Group ICA detected substantial differences in semantic language processing modules between HC, LE and RE patients. This confirms the negative effect of epilepsy on neurofunctional aspects of language processing.

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METABOLIC EVIDENCE FOR EPISODIC MEMORY PLASTICITY IN THE NONEPILEPTIC TEMPORAL LOBE OF PATIENTS WITH UNILATERAL MESIOTEMPORAL EPILEPSY

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Purpose: To characterize in patients with unilateral mesiotemporal lobe epilepsy (MTLE) the brain regions showing positive correlation between unilateral episodic memory performances estimated by intracarotid amobarbital test (IAT) and interictal cerebral metabolism measured by ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET).

Method: Resting FDG-PET was performed interictally in 26 patients with unilateral MTLE caused by hippocampal sclerosis (HS) (16 females, mean age: 36 years; 16 left HS). Using statistical parametric mapping (SPM8), IAT scores were used as covariates of interest in the patients' group to identify brain regions where metabolism showed positive correlation with IAT scores. Then, to better understand correlation analyses results, subtractive analyses comparing patients' brain metabolism with a group of 54 adults controls (27 females, mean age: 32 years) were performed, FDG-PET data of right HS patients being flipped.

Results: Positive correlations with left and right injection IAT scores were found in mesial and lateral temporal regions contralateral to the injected hemisphere ($P_{corrected} < 0.05$). Regression plots also showed that high IAT scores were mostly associated to high temporal metabolic level in the nonepileptic lobe. Subtractive analyses revealed that brain regions showing positive correlation between metabolism and IAT scores were hypometabolic in the epileptic lobe and hypermetabolic in the nonepileptic lobe ($P_{corrected} < 0.05$).

Conclusion: This study suggests that compensatory hypermetabolism in mesial and lateral temporal lobe occurs contralateral to HS. The positive correlation in these brain regions between IAT scores and metabolism supports the role of disease-induced plasticity mechanisms contralateral to HS, in relation with episodic memory processes.

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MODIFICATIONS IN LOCAL HEMODYNAMIC PRECEDES EPILEPTIC SPIKE: AN ANIMAL MODEL COMBINING SIMULTANEOUS ECoG AND NEAR INFRARED SPECTROSCOPY ANALYSIS

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Introduction: The mechanism that propels epileptic neurones to a freezing of synchronization resulting in tight coupling is still not completely understood. This complex prespike mechanism can be energy consuming and induce neurovascular coupling.

NIRS has the advantage, compared to fMRI, to have an excellent temporal resolution and to measure changes in both oxy-, deoxy- and total hemoglobin in tissues.

We evaluate combined EEG-NIRS recordings in rats, to get further insight in the relationship between spikes and the hemodynamism without restricting presumptions about the dynamics of the processes of spike development.

Methods: Acute experiments were performed on 9 anesthetized rats. 2 ECoG electrodes, 2 light sources and 2 detectors were inserted bilaterally. The epileptic spikes were induced by local application of bicuculline methiodide to the left cortex.

ECoG NIRS data were recorded simultaneously. The time of the spike peak was used for averaging ECoG and NIRS Data.

Results: It is shown that the hemodynamic changes precede the epileptic spike in all rats. The hemodynamic changes are characterized by a biphasic pattern. The ''initial dip'' in oxygenated (HbO) and total (HbT) hemoglobin occurred before the spike onset and was followed by postspike increasing in the HbO/HbT.

Conclusion: In accordance with results on fMRI (Gotman et al., 2006), we demonstrate, using NIRS, hemodynamic changes which precedes the onset of spike activity. We suggest that other structures (glial cells, non synchronized activities or low level synchronized activities) are likely to participate in this early hemodynamic modulation tightly associated with the mechanism of spike onset.

p466

HIPPOCAMPAL VOLUME IS REDUCED IN CHILDREN WITH OTHER FORMS OF CONVULSIVE STATUS EPILEPTICUS COMPARED TO CHILDREN WITH PROLONGED FEBRILE SEIZURES

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Aim: To investigate the relationship between convulsive status epilepticus (CSE), in particular prolonged febrile seizures (PFS) and hippocampal volume changes.

Methods: As part of an ongoing longitudinal prospective study of childhood CSE, children are enrolled from hospitals around London following an episode of CSE. They have MRI investigations and neuropsychology assessment at 1 month (mean 29 days, range 5–83) and 6 months (mean 180 days, range 124–280) post-CSE. Manual tracing of the hippocampi is used to measure the mean hippocampal volume on each scan.

Results: Fifty-five patients were analyzed. Mean age was 2.91 years (range 0.18–15.5). 27 had a PFS and 28 had CSE due to other etiologies. 27 patients had repeat scans at 6 months (13 PFS, 14 other CSE).

Univariate ANOVA showed a significant effect of age on hippocampal volume ($p = 0.002$). After adjusting for age, at 1 month patients with PFS had a 288 mm^3 ($p = 0.006$, 95%CI: 85–492 mm^3) larger mean hippocampal volume than patients with other CSE. This difference was maintained at 4 months with patients with PFS having 434 mm^3 ($p = 0.003$, 95%CI: 166–702 mm^3) larger hippocampi.

Conclusion: Psychological testing has shown that those with PFS perform better on tests of developmental ability than those with other CSE. Together with these findings this suggests that both functional and structural outcome post-CSE is relatively better in patients with PFS than in those with other CSE. This supports the view that etiology of CSE is the primary determinant of outcome.

p467

EFFECT OF EPILEPSY ON INTRACRANIAL VOLUME

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Purpose: To explore the developmental hypothesis of temporal lobe epilepsy (TLE) by examining differences in intracranical volume (ICV) between patients with TLE with and without evidence of hippocampal atrophy on MRI (pTLE and nTLE), patients with Juvenile Myoclonic Epilepsy (JME), and controls, using an automatic and reliable ICV measurement method.

Method: T_1-weighted MR images of 80 patients with TLE (60 pTLE, 20 nTLE), 29 patients with JME and 28 controls were available. ICV was measured with a Reverse Brain Mask (RBM) method (Keihaninejad S et al. submitted), using a brain mask in standard space, image registration and inverse transformations to warp this mask to each image in native space.

Results: ICV was significantly reduced (6.5%, $p < 0.05$) in patients with pTLE compared to healthy controls. There was no significant difference between pTLE patients with right and left seizure foci. ICVs of the nTLE group (1423 ± 150 ml) were between those of the pTLE group (1387 ± 128 ml) and controls (1483 ± 160 ml). There was no significant ICV change in the JME group ($p > 0.5$) and their ICV (1465 ± 140 ml) was close to controls.

Conclusion: ICV reduction in the pTLE group is likely to reflect brain damage during development, i.e., before the end of brain growth. Epilepsy as such (e.g. nTLE, with later onset) was not associated with reduced ICV. We found no evidence of ICV increases in JME. ICV may be insensitive to detect frontal grey matter increases previously described in JME (Woermann F et al. Brain 1999), or those increases could occur after cranial suture closure.

p468

DIAGNOSTIC UTILITY OF IMMEDIATE POSTICTAL MRI IN ACUTE SEIZURE DISORDERS

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Purpose: Even though MR is the most sought imaging modality, the clinical role of MRI in the management of acute seizure disorders (ASD) has not been well established. We investigated the diagnostic utility of MRI in the evaluation of the patients with ASD.

Method: One hundred forty-three (143) consecutive patients presented in the regional emergency center due to acute seizures were included. MRI findings obtained within 12 hours of the seizure onset were analyzed. The incidence and the patterns of MRI abnormality were described and the possible correlations with clinical profiles were explored.

Results: Abnormal MRI findings were detected in 103 patients with ASD (72%); nonrelevant abnormalities in 33 (23%) and significantly relevant findings in 70 (49%). Relevant abnormalities in T_2/FLAIR images were found in 70 (49%), mostly revealing remote symptomatic etiology. Abnormalities in diffusion weighted images (DWI) were seen in 19 (13%) patients; 14 status epilepticus (SE), 5 non-SE acute lesion. The patients with SE were more often accompanied by the relevant abnormality (18/21, 85%) as well as DWI abnormality (14/21, 67%). The patients with first onset or rare seizures, alcohol related seizure and younger age tend to have normal MRI. However, 15% (6/40) of patients who had normal MRI required in-hospital care due to recurrent seizures or other neurological dysfunctions.

Conclusion: This study implies that immediate postictal MRI provides somewhat limited guidance in ASD, other than revealing the presence of underlying focal etiology. DWI abnormality appears to represent the severity of seizure activity.

Poster session: Genetics II
Wednesday 30th June 2010
13:30–14:30

p469

NOVEL MUTATIONS IN EPM2A AND NHLRC1 WIDEN THE SPECTRUM OF LAFORA DISEASE

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Purpose: Lafora disease (LD) is an autosomal recessive form of progressive myoclonus epilepsy with onset in childhood or adolescence and with fatal outcome caused by mutations in two genes, EPM2A and NHLRC1. The aim of this study was to characterize the mutation spectrum in a cohort of unrelated patients with presumed LD.

Methods: Sequencing of the two genes and search for large rearrangements was performed in 46 unrelated patients with suspected LD, 33 originating from France and the others from different countries. Patients were classified in two groups according to the clinical presentation.

Results: Mutations of various types were found in EPM2A in 11 patients and in NHLRC1 in three patients. Mutations were found in 93% (14/15) patients with a classical clinical and EEG presentation of LD and in no patients with an atypical presentation. Eleven mutations were novel, including the first substitution in a donor splice site of EPM2A leading to the deletion of exon 2 at the RNA level. Four large deletions, including two deletions of exon 2 with different sizes and breakpoints, were found in *EPM2A*, corresponding to 20% of the alleles of this gene.

Conclusion: The mutation spectrum observed in our study challenge the classical view that *EPM2B*-LD is far more frequent than *EPM2A*-LD in the French population. Furthermore, we suggest that the relatively high frequency of LD on the European side of the Mediterranean basin may be due to the combination of several founder effects.

p470
NONPARANEOPLASTIC LIMBIC ENCEPHALITIS AND FAMILIAL MYOTONIA: A COMMON PHYSIOPATHOGENETIC BACKGROUND?

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Purpose: To describe a 25-year-old woman with autosomal dominant myotonia, nonparaneoplastic limbic encephalitis (LE) and celiac disease (CD).

Method: The proband was referred to us for daily temporal pharmacoresistant seizures and drastic weight loss at age 15, followed 5 years later by a severe memory impairment. Later the proband's father and brother were referred to us for a myotonic disorder since adolescence. Genealogic tree reconstruction did not disclose other family members reporting symptoms suggestive of myotonia. The proband and the other affected relatives underwent a full clinical, neurophysiological and immunological evaluation. Blood samples were collected for direct sequencing of CLCN1 gene.

Results: The proband underwent repeated neuropsychological evaluations, disclosing a severe memory impairment in immediate and delayed recall. Interictal EEG showed frequent epileptiform abnormalities over temporal regions. Brain MRI disclosed bilateral hippocampal hyperintensity in T_2-weighted sequences. Laboratory screening revealed autoimmune hypothyroidism, CD (confirmed by biopsy), oligoclonal bands and anti-GAD antibodies in CSF. No seizures were reported by the other affected relatives; their laboratory tests, including autoimmune screening, were negative, whereas neurological evaluation disclosed muscle hypertrophy and myotonia. The proband presented only a subclinical myotonia (elicited by the tongue percussion). Electromyography showed myotonic discharges without myopathic signs in all affected members. Genetic analysis disclosed a missense mutation (I290M) in heterozygosis, confirming the clinical hypothesis of Thomsen disease.

Conclusion: An ion channelopathy leading to central and muscle hyperexcitabilty as the pathogenesis of the association between autoimmune LE and autosomal dominant myotonia is intriguing, but a casual association cannot be excluded.

p471
GENOME-WIDE ANALYSIS OF STRUCTURAL GENOMIC VARIATIONS SUGGESTS NOVEL CANDIDATE GENES IN EARLY-ONSET ABSENCE EPILEPSY

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Purpose: The early-onset absence epilepsies (EOAE) are a rare subtype of the idiopathic generalized epilepsies (IGE) with onset of absence seizures before the age of 4 years. A genetic predisposition for EOAE has been suggested and mutations in GLUT1 account for a subset of cases. The underlying case still remains to be identified in the majority of patients. The role of structural genomic variants is increasingly recognized in various epilepsy subtypes and might also predispose to EOAE.

Method: Fifteen patients with EOAE were screened for structural genomic variations using the Affymetrix Genome-Wide Human SNP Array 6.0 and the Affymetrix Genotyping Console 3.0 algorithm. Identified structural genomic variants were compared to variants described in the Toronto Database of Genomic Variants.

Results: In 9 of 15 patients we found previously not described structural genomic variations encompassing possible candidate genes for epilepsy, including 2 deletions and 7 duplications. The two deletions encompass the BBOX1 and PIP genes, duplications span MCPH1, CACNA1B, CNTN4, CHRNB2, RPS6KA2, BRAF/MRPS33 and UNC13C. The age of onset in patients was 9–47 months (median 30 months).

Conclusion: We suggest that rare structural genomic variants contribute to the etiology of the early-onset absence epilepsies. Structural genomic variants identified in patients span known candidate genes for epilepsy and genes previously implicated in other neurodevelopmental disorders.

p472
THE VAL66MET BDNF GENE POLYMORPHISM IN GREEK CHILDREN WITH ROLANDIC EPILEPSY

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Purpose: Brain-derived neurotrophic factor (BDNF) is the most abundant neurotrophin in the CNS, where it plays a crucial role in the development of immature neurons and the survival and plasticity of mature nerve cells. The Val66Met polymorphism (rs6265) has been linked with anatomical and functional variation including an altered susceptibility to seizures. The aim of this study was to compare the frequency of the Val66Met polymorphism in children diagnosed with rolandic epilepsy and control individuals of similar age.

Method: Seventeen children with rolandic epilepsy, and 37 control children were genotyped for the BDNF Val66Met polymorphism, with an RFLP method, in this study. All participants were residents of northern Greece. Genotype and allele frequencies were statistically compared with the use of Fisher's Exact test.

Results: Carriers of the Met66 allele were overrepresented in rolandic epilepsy group (allele frequencies 29.4% compared to 18.9% among controls), but no statistically significant difference was detected. An apparent trend towards a risk effect of the Met66 allele was registered with respect to the rolandic epilepsy group (p = 0.081; OR = 2.976, 95% CI = 0.909–9.744).

Conclusion: The overall genotype and allele frequency distributions of the Val66Met polymorphism in Greek children are similar to the ones reported for other populations. The apparent risk effect of the Met66 allele with respect to rolandic epilepsy suggests that an extension of this study to a larger sample with the inclusion of intermediate phenotypes, such as EEG records, may be worth undertaking.

p473
PYRIDOXINE DEPENDENT EPILEPSY: NEW STRATEGIES FOR DIAGNOSIS AND THERAPY

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Pyridoxine dependent epilepsy (pyridoxine dependent seizures) is a rare autosomal recessive hereditary disorder causing a severe intractable epileptic seizures presenting in prenatal, neonatal or early infancy period.

Pyridoxine dependent epilepsy, caused by metabolic disturbance of pyridoxine, is associated with mutation in ALDH7A1 or ALDH4A1 gene. Similar condition, pyridoxal-phosphate dependent epilepsy (also called neonatal epileptic encephalopathy), is caused by mutation in PNPO gene. Pyridoxine dependent epilepsy is successfully treatable by high doses of pyridoxine. Neonatal epileptic encephalopathy is refractory to pyridoxine administration, however responses to treatment with pyridoxal-phosphate. The diagnosis of both pyridoxine dependent epilepsy and neonatal epileptic encephalopathy is based on biochemical and genetic examinations.

Authors present a group of 10 patients (age ranging from 3 days to 2 years; 5 male) who have been examined in Clinic of Child Neurology until May 2009.

Subjects were newborns and infants affected by intractable epilepsy with generalized tonic–clonic seizures (5 patients), infantile spasms (4 patients) and myoclonic seizures (1 patient).

In one of them (male; age 1 month) the mutation in ALDH7A1 gene specific for pyridoxine dependent epilepsy was found. We report a case of this infant affected by atypical form of pyridoxine dependent epilepsy.

p474
A CLINICAL AND GENETIC STUDY IN A MULTIPLEX FAMILY WITH DIVERSE EPILEPSY PHENOTYPES: FROM FS AND CAE TO PANAYIOTOPOULOS SYNDROME

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Purpose: To characterize the clinical features and molecular genetic basis of seizure susceptibility in a family with febrile seizures (FS), idiopathic generalized epilepsy and Panayiotopoulos syndrome (PS).

Method: Clinical, EEG and imaging data were collected by interviews and from medical records. Genome-wide linkage and fine-mapping analyses were performed with microsatellite markers and the nonparametric linkage (NPL) option of SimWalk2. Two genes, *CACNA1H* on the positive linkage region on chromosome 16pter and *SCN1A*, a previously reported candidate gene for PS and GEFS+, were sequenced.

Results: The pedigree included 11 affected subjects. Four patients presented with FS only, three with childhood absence epilepsy (CAE) alone and one with FS and CAE. One patient had FS and probable PS and another classical PS. One patient had FS and secondarily generalized tonic–clonic seizures. Inheritance pattern was compatible with multifactorial inheritance. In the genome wide scan two markers *D16S423* and *D22S274* generated a -log10 (p-value) NPL score of >1.5. After fine mapping, the highest NPL score was 2.85 at *D16S3072*. A novel missense alteration in *CACNA1H*, associated with the disease haplotype in one branch of the family was identified. Sequence analysis of *SCN1A* did not reveal a pathogenic alteration.

Conclusion: The family displays a complex seizure phenotype with FS, CAE and PS compatible with a multifactorial inheritance pattern. An alteration in *CACNA1H* may contribute to seizure susceptibility in one branch of the family. The molecular basis of the seizure phenotypes, including the significance of the novel *CACNA1H* sequence alteration, remains to be determined.

p475
BENIGN FAMILIAL EPILEPSIES WITH ONSET IN THE FIRST YEAR OF LIFE: A SPECTRUM OF POTASSIUM AND SODIUM CHANNELOPATHIES

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Purpose: To screen KCNQ2, KCNQ3, and SCN2A genes in families with benign epileptic syndromes with onset in the first year of life (BFNS, BFNIS, BFIS) and to perform a genotype-phenotype correlations.

Method: We analyzed by PCR and MLPA the KCNQ2, KCNQ3, and SCN2A genes in 161 subjects from 10 BFNS, 10 BFNIS, and 29 BFIS families. Clinical data were also collected to perform genotype-phenotype correlations.

Results: We identified mutations in one of the tested genes in 21 (42%) families. Twelve (57.1%) families had KCNQ2, 5 (23.8%) SCN2A, and one (4.4%) KCNQ3 mutations. In addition, three (14.3%) famiies with 20q deletions, including KCNQ2 and CHRNA4, were identified. Mutations were found in six (60%) BFNS (4 KCNQ2, 2 KCNQ2-CHRNA4 deletions), nine (90%) BFNIS (6 KCNQ2, 2 SCN2A, 1 KCNQ2-CHRNA4 deletion), and in six (20.1%) BFIS families (2 KCNQ2, 1 KCNQ3, 3 SCN2A). Seizures were focal with secondary generalization in 59.5% of the patients and tonic–clonic in 27.6%. Remission was constant in all cases but three. One subject developed rolandic seizures, one infantile spasms, and another one focal epilepsy with frontal and temporal seizures.

Conclusion: Benign familial epilepsies with onset in the first year of life include a spectrum of potassium and sodium channelopathies with onset in the first year of life. The approach of genetic testing should follow a unified protocol starting with mutational screening of KCNQ2, MLPA of KCNQ2-Q3, mutational screening of KCNQ3, and SCN2A.

p476
ARRAY-CGH IDENTIFIES GENOMIC REARRANGEMENTS IN PATIENTS WITH CRYPTOGENIC EPILEPSY

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Purpose: We performed an extensive search for the identification of genomic rearrangements in patients with cryptogenic epilepsy.

Methods: 215 patients with cryptogenic epilepsy were investigated by microarray-based comparative genomic hybridization (array-CGH). A "phenotype score" ranging from 0 to 10 was attributed to each patient. Subjects with a score ≥4 were excluded. Microrearrangements matching polymorphic copy number variations (CNVs) reported in the CNVs database were not further followed. Validation was performed by fluorescence in-situ hybridization or high-density array-CGH. Inherited rearrangements were tested in 200 controls by quantitative PCR. Multiple correspondence analysis explored associations among categorical variables. Hypergeometric distribution test was used to assess the recurrence of specific biological processes within the identified rearrangements.

Results: Genomic rearrangements occurred in twenty-one (9.8%) patients. No recurrent rearrangements were identified, except for the 22q13.32qter deletion. Eight of 21 rearrangements were inherited. Seven (33%) patients showed rearrangements that are associated with emerging microdeletion/microduplication syndromes. Genotype-phenotype correlations showed that higher phenotype score ($p = 0.003$), abnormal neuroimaging ($p = 0.01$), and mental retardation ($p = 0.04$) were more frequently associated with genomic rearrangements, particularly with deletions of de novo origin. Three novel single-gene rearrangements pinpointing novel candidate epilepsy genes (LRRTM4, EPHA7, KCNJ2), were identified. Bioinformatic analysis revealed that ion channel genes ($p = 2.3 \times 10^{-6}$) were significantly enriched within the identified rearrangements.

Conclusion: Our data show that genomic rearrangements may underlie cryptogenic epilepsy and that array-CGH is a valuable tool providing significant information for the diagnosis and genetic counselling in these common forms of epilepsy.

p477
MUTATIONS IN *KCNQ2* ARE ASSOCIATED WITH SEVERE NEONATAL EPILEPSY

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Purpose: Loss-of-function mutations in the voltage-gated potassium channels $K_v7.2$ and $K_v7.3$, encoded by the *KCNQ2* and *KCNQ3* genes respectively, are associated with benign familial neonatal seizures (BFNS), an autosomal dominant epilepsy syndrome of newborns characterized by a benign epilepsy phenotype and normal psychomotor development. However, in some BFNS families with a *KCNQ2* mutation patients occasionally have drug-resistant neonatal seizures and mental retardation.

Method: We analyzed 50 unrelated individuals with severe and intractable neonatal or early-infantile seizures for mutations in *KCNQ2* using direct sequencing.

Results: In three patients, we identified a de novo *KCNQ2* mutation predicting a missense mutation in $K_v7.2$ (p.G290D; p.M528V and p.R542W). None of these mutations has been associated with classical BFNS. Two patients had onset of tonic or myoclonic seizures at day 3 of life, in one patient tonic seizures started at the age of 4 weeks. In all of them EEG showed a burst suppression pattern at onset, with multifocal epileptic discharges later in evolution. One patient developed a spastic quadriplegia. All had moderate to severe mental retardation. We found no evidence for an additional second-site disease-causing mutation in *KCNQ3*, *KCNE1*, *KCNE2* and *AKAP5* in these patients.

Conclusion: We hereby confirm that mutations in *KCNQ2*, which are usually associated with benign epilepsy, also can be linked to severe and intractable epilepsy. In both severe and benign epilepsy the onset is in the neonatal period. Therefore, we postulate that screening of the *KCNQ2* gene is useful in all patients with a neonatal onset of epilepsy.

p478
PHOTOSENSITIVITY MIGHT BE PART OF THE WOLF-HIRSCHHORN SYNDROME!

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Purpose: Wolf-Hirschhorn syndrome (WHS), resulting from a 4p16.3 deletion, is characterized by typical facial appearance, growth retardation and mental retardation and almost always epilepsy. Although seizures

are frequently triggered by fever, there is no mentioning of seizures induced by visual stimuli or intermittent photic stimulation (IPS).

Method: In our patient (F, 5 years) the WHS diagnosis was confirmed by array CGH. A full diagnostic evaluation has been done. Before and after VPA treatment, video-polygraphic EEGs were performed with standardized IPS, according to the International Protocol.

Results: After several GTCSs triggered by fever, a nonconvulsive seizure occurred in front of the TV at age 5. Both abnormal EEG patterns described in WHS were recorded: diffuse slow waves with superimposed spikes and burst of posterior spikes. In addition, IPS between 9–25 Hz evoked consistently generalized discharges of atypical spike and waves of 1–3 s duration, with occipital onset. At 25 Hz she showed psychomotor arrest. After VPA, spontaneous generalization of discharges decreased markedly and the PhotoParoxismal Response disappeared.

Conclusion: This is the first report of WHS patient with well documented epileptic photosensitivity. We hypothesize that photosensitivity in WHS is probably much more common because of: 1) underreporting of provocative factors, 2) difficulty in discriminating spontaneous from IPS-evoked epileptic discharges, if no standardized IPS protocol is used, 3) presence of posterior epileptic EEG abnormalities, 4) clinical analogies with Dravet Syndrome.

Photosensitivity in chromosomal abnormalities is frequent and might be an additional important clue in identifying genes involved in photosensitivity and pathogenic mechanisms in epilepsy.

p479
EPILEPSY IN ADULT PATIENTS WITH DOWN SYNDROME

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Purpose: Epilepsy is reported to have a greater prevalence in subjects with Down syndrome (DS) than in general population, and at older ages the prevalence of epilepsy in this population ranges 46%. The aim of the present study is to describe the electroclinical characteristics of epilepsy in adult patients with DS followed at the Epilepsy Center, San Paolo Hospital in Milan.

Method: Twenty-three adult patients with DS (13 males, 10 females), with a mean age 45.2 years (range: 28–64 years), were followed at our Centre between January 1995 and November 2009.

Results: Mean age at epilepsy onset was 36 years (range: 6–60 years).

Ten out of 23 patients presented focal epilepsy, 9 showed a late-onset myoclonic epilepsy (LOMEDS). In 4 patients epilepsy was unclassified.

The EEG pattern was characterized by a progressive slowing of the background activity and a prevalence of paroxysmal activities over the fronto-temporal regions. In the patients diagnosed as LOMEDS the EEGs showed generalized polyspike-waves.

Five patients (20%) suffered from drug-resistant epilepsy and 3 subjects presented an epileptic status at the beginning or in the course of the disease.

Conclusion: Epilepsy in adult patients with DS shows peculiar electroclinical characteristics which should be early recognized, since as longevity of these patients is increasing, they could be encountered in clinical practice more frequently than currently acknowledged.

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ANOTHER LARGE FAMILY WITH INFANTILE CONVULSIONS AND CHOREO-ATHETOSIS (ICCA) WITH LINKAGE TO CHROMOSOME 16P12-Q12

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Purpose: ICCA is an autosomal dominant inheritable syndrome in which benign infantile convulsions and paroxysmal dyskinesias co-occur in the same family. Several families with linkage to chromosome 16p12–q12 have been described, but the responsible gene defect has not been identified yet. We describe another large three-generational Belgian family in which we confirmed linkage to the pericentromeric region of chromosome 16.

Method: We performed a clinical evaluation and genetic analysis in a four-generation family with 21 affected individuals with co-occurrence of benign infantile seizures and paroxysmal dyskinesias. Genotype analysis was performed with an in-house genome-wide mapping panel containing 425 autosomal microsatellite markers.

Results: Seven patients had a history of self-remitting seizures in the first year of life. Three of these seven patients had a single unprovoked tonic–clonic seizure or myoclonias later in life. One patient had frequent episodes compatible with chorea-athetosis since the age of 12 years. Eight additional patients were diagnosed with febrile seizures in childhood, although it remains unclear if indeed all events occurred with fever. Five patients of the first or second generation were diagnosed with not further specified epilepsy later in life. Linkage analysis showed conclusive linkage to chromosome 16p12–q12 with a maximal LOD score of 4.3 at marker D16S3080.

Conclusion: This study confirms linkage to chromosome 16p12–q12 in a large Belgian family with a phenotype compatible with ICCA. Identification of the responsible gene defect might provide a better insight in the common pathophysiology of epilepsy and paroxysmal dyskinesias.

p481
MDR1 GENE POLYMORPHISMS AND DRUG-RESISTANT EPILEPSY IN A PORTUGUESE POPULATION

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Purpose: One-third of epileptic patients develop drug-resistant epilepsy (DRE), a multifactorial process in which pharmacogenetic factors play a relevant role. The MDR1 drug efflux transporter is over-expressed in brain lesions from DRE patients. Several common polymorphisms of MDR1 have been identified. However, their effect on transporter function is subtle and complex, and discordant genetic associations with DRE have been reported.

Aim: To evaluate the association between MDR1 polymorphisms 1236 C > T, 3435 C > T and 2677 G > T, A and DRE in Portuguese patients.

Methods: A sequential cohort of 149 epileptic patients from the outpatient clinic at CHP, 112 of which with DRE, was compared with a cohort of 152 healthy individuals (HI). MDR1 genotyping was performed by Real Time PCR.

Results: The frequencies of the 1236 TT and 2677 TT genotypes were higher in the DRE cohort than in HI (23% vs. 11%, OR = 2.3 [1.2–4.6], p = 0.014 and 23% vs. 10%, OR = 2.6 [1.6–5.2], p = 0.006, respectively). The frequencies of the 1236 CT and 2677 CT genotypes were lower in drug-responsive patients than in HI (33% vs. 57%, OR = 0.33 [0.16–0.82], p = 0.012 and 35% vs. 54%, OR = 0.46 [0.21–0.97], p = 0.039, respectively). There were no differences in the frequencies of 3435 C > T.

Conclusion: The MDR1 1236T and 2677T alleles may be associated with a poor response to antiepileptic drugs in our patients, as previously reported for other populations [*Pharmacogenomics 2006;7:551–561*]. We could not replicate the association between DRE and 3435 C > T polymorphism.

Acknowledgements: Supported *by a BICE-Tecnifar Grant*

p482

A CANDIDATE GENE ASSOCIATION STUDY OF ANTIEPILEPTIC DRUG TOLERABILITY AND EFFICACY

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Purpose: It is widely acknowledged that individual response to antiepileptic drugs (AEDs) is influenced by genetic factors. However, most of the underlying genes and genetic variants remain unidentified to date. The purpose of this study is to examine the role of common variants in a number of candidate genes in the response to commonly prescribed AEDs.

Methods: We recruited 496 patients with epilepsy. For each patient, the following clinical data were recorded: 1) presence or absence of adverse drug reactions on carbamazepine, sodium valproate and phenytoin therapy, 2) efficacy of sodium valproate and 3) overall efficacy of AEDs with a major action on sodium channels. The replication cohort consisted of 817 patients with epilepsy. We genotyped 104 polymorphisms in the following candidate genes: *EPHX1,* GSR, *GSS, GSTA3, GSTA4, GSTA5, GSTM3, GSTM4, SCN1A, SCN2A, SCN3A*, *SCN8A, UGT1A6, UGT2B7, CYP2A6, CYP2C9* and *GSTM1*. We looked for statistically significant associations between these polymorphisms and efficacy and occurrence of adverse drug reactions to particular AEDs.

Results: We identified significant associations of *CYP2C9* variant alleles with presence of phenytoin adverse drug reactions ($p = 0.004$) and of *GSTM1* copy number variation with presence of carbamazepine adverse drug reactions ($p = 0.0093$). The latter association could not be confirmed in the replication study.

Conclusion: Our study is the first comprehensive candidate gene association study in epilepsy pharmacogenetics. Our results confirm the role of *CYP2C9* variants in phenytoin toxicity. No other definite associations were identified. Large-scale efforts are needed in order to unravel the genetic determinants of AED response.

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MUTATIONS IN NIPA1 MAY PREDISPOSE TO IDIOPATHIC GENERALIZED EPILEPSY

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Purpose: Idiopathic generalized epilepsies (IGEs) account for 30% of all epilepsies. Genetic factors play a predominant role in the etiology of IGEs, however the underlying genetic alterations remain largely unknown. Recently, a microdeletion at 15q11.2 has been shown to predispose to IGEs. The microdeletion contains at least 6 genes including NIPA1, which encodes a transmembrane magnesium transporter. Missense mutations in NIPA1 have been identified in 10 families with autosomal dominantly inherited spastic paraplegia (AD-HSP). In one of these families comorbid IGE was observed. This study aims to investigate the role of NIPA1 mutations in IGEs.

Method: We investigated DNA from one family with AD-HSP and comorbid IGE and from 47 patients with IGEs without HSP. All exons and exon-intron boundaries of NIPA1 were PCR amplified and sequenced using standard protocols and techniques.

Results: We found a missense mutation in NIPA1 in one patient from a family, cosegregating AD-HSP and IGE through three generations. This mutation is identical to the mutation previously identified in the HSP family with comorbid IGE. Furthermore, we identified a synonymous mutation in NIPA1 in a patient with juvenile myoclonic epilepsy without HSP. This mutation was not identified in DNA from 96 control subjects without epilepsy.

Conclusion: Our results indicate that mutations in NIPA1 might predispose to IGE. Relatively few epilepsy genes have been identified so far. The identification of mutations in NIPA1 as a possible genetic risk factor for IGE, may provide new insight into the complex genetic predisposition of common epilepsies.

Poster session: Psychiatry
Wednesday 30th June 2010
13:30–14:30

p484

ATTENTION DEFICIT HYPERACTIVITY DISORDER COMORBIDITY WITH EPILEPSY IN AN UNIVERSITY HOSPITAL PEDIATRIC CLINIC IN CHINA

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Purpose: To investigate the comorbidity of ADHD with epilepsy in a hospital based pediatric department in China.

Method: The sample included 192 consecutive children with epilepsy (124 boys and 68 girls), aged 6–15 years. The ages of epilepsy onset & at diagnosis, the epileptiform EEG discharges, the seizure types and epilepsy syndromes, and the antiepileptic treatment were recorded. The diagnostic assessment of ADHD was evaluated by semistructured clinical interview, ADHD parent Rating Scale scores and Conners' parent Rating Scale. The ANOVA and multiple linear regressions were used for data analysis.

Results: Among the 192 children, 84 had higher scores in ADHD parent Rating Scale detection, and 95 had higher scores in Conners' parent Rating Scale measurement. Eighty-one children were diagnosed with ADHD by clinical interviews in accordance with the diagnostic criteria of DSM-?. The prevalence of ADHD in this group of children with epilepsy is 42.2%. The comorbidity of ADHD are more common in some specific types of seizures or epileptic syndromes, such as generalizes tonic–clonic seizures, complex partial seizures, childhood absence epilepsy, and Lennox-Gastaut syndrome. Epileptiform discharges and antiepileptic medications were also significant associated factors.

Conclusion: ADHD occurred really frequently in epileptic children in China. The factors contributed to the increased risk for ADHD in this particular population included the chronic effects of seizures, the epileptiform EEG discharges, and the effects of antiepileptic drugs. The types of seizures or epileptic syndromes were also the risk factors of ADHD comorbidity.

p485
ELECTROENCEPHALOGRAPHY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVE DISORDER AND TREATMENT RESULTS WITH CENTRAL NERVOUS SYSTEM STIMULANTS

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Purpose: Attention deficit hyperactivity disorder (ADHD) is a syndrome characterized by inattention, impulsive disruptive behavior, impaired concentration, and motor restlessness. This study examined the relationships among electroencephalographic (EEG) findings, stimulant use, and seizure occurrence in children with ADHD.

Method: We retrospectively studied 308 children who visited our hospital because of ADHD since January 2001 to December 2005. We retrospectively analyzed age distribution, etiology, abnormalities of EEGs, the use of CNS stimulant. Among those children, EEGs was recorded in 84 patients.

Results: EEGs were performed in 84 children (72 males, 85.7%, 9.3 years of mean age; 12 females, 14.3%, 8.0 years of mean age) with ADHD. Nineteen patients (22.6%) demonstrated abnormalities, and 65 (77.4%) demonstrated normal EEGs. Stimulant therapy was applied to 59 of 84 patients (70.2%). Seizures occurred in one of 65 patients with a normal EEG (1.5%) and 3 of 19 treated patients with abnormal EEGs (15.7%).

Conclusion: These data suggest that ADHD patients with normal EEG have minor risk for seizure. In contrast, those with abnormal EEG have higher risk for seizure than patients with normal EEG.

p486
DETERMINANTS OF QUALITY OF LIFE IN PEOPLE WITH EPILEPSY

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Purpose: To find determinants of quality of life in people with epilepsy living in Belgrade, Serbia.

Method: We recruited in the study consecutive adults with epilepsy attending our outpatient department. Adult patients (age range 18–65 years) of normal intelligence and without any progressive neurological disease or psychiatric disorder were included in the study. They completed the following questionnaires: QUOLIE-31 Inventory (Serbian version), Beck's Depression Inventory, Beck's Anxiety Inventory, Symptom Check List – 90, Neurotoxicity Scale-II (Aldenkamp A.P. et al., 1995). Stepwise multiple regression analysis was performed to asses the predictive effects of some factors on QUOLIE-31 Inventory.

Results: Two hundred two patients completed the questionnaires. Their total score of QUOLIE-31 was 70.64 ± 17.74. Of sociodemographic factors studied (age, sex, education, employment), none demonstrated any significant influence on quality of life (Pearson's correlation coefficient r = 0.37). Clinical characteristics – seizure severity and etiology of epilepsy significantly predicted quality of life (R = 0.56) accounting for 30.9% of the variance. Depressive symptoms were significantly influential on quality of life (R = 0.84) accounting for 40.5% of the variance. Anxiety symptoms were significantly correlated with QUOLIE-31, accounting for 39% of the variance (R = 0.62). Cognitive effects of antiepileptic drugs, assessed by patient-based Neurotoxicity Scale-II significantly predicted QOL (R = 0.86) accounting for 2.4%.

Conclusion: As suggested by our findings, main determinants of quality of life in our sample of patients include seizure severity and etiology of epilepsy, depressive and anxiety symptoms, while neurotoxicity of antiepileptic drugs explained and in much smaller proportion of variance.

p487
A CASE OF CONTINUOUS ''SENSED PRESENCE'' RELATED TO SPIKE ACTIVITIES

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Purpose: ''Sensed presence'' is perception that another person exists on the side. It has been considered to be the right hemispheric equivalent to the left hemispheric sense of ''self.'' We report a patient with continuous ''sensed presence'' related to spike activities.

Method: A 70-year-old right-handed woman. She suffered from dysphemia and hallucination followed by the feeling of ''sensed presence.'' The symptom was described by the patient as follows: ''I have a feeling that a man stands behind me and he will follow me anywhere I would like to go. I feel very frightened by it.'' The symptom continued for several weeks. EEG and MEG revealed continuous spikes over the left temporal/occipital area. Her MRI findings showed previous left temporal subcortical hemorrhage.

Results: The patient experienced the continuous feeling of ''sensed presence'' with spike activities over the left hemisphere. Although the symptom remained despite trials with risperidone and quetiapine, the feeling resolved and EEG findings improved within a few weeks following the addition of carbamazepine.

Conclusion: The feeling of ''sensed presence,'' in our case, was considered to be closely related to the left temporal/occipital spike activities. As this phenomenon is often explained to be associated with the intrusion of right hemispheric processes into left hemispheric awareness, we suggest that the symptom was caused by transient relative domination of the right hemispheric function, rather than left hemisphere impairment by seizure activity.

p488
USE OF SHORT SCREENING TOOLS FOR ANXIETY AND DEPRESSION IN A NEUROLOGY OUTPATIENT SETTING

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Purpose: In people with epilepsy psychiatric comorbidities such as depression and anxiety are more common than in the general population. Treating psychiatric comorbidities has significant impact on improving quality of life. These comorbidities are often underdiagnosed. We set out to evaluate the use of short self-completed screening tools in a busy neurology outpatient clinic to identify anxiety and depression.

Method: A total of 122 consecutive patients (53% female, 66% White British, age range 16–89, mean 39.6) attending our epilepsy clinic completed five screening tools for anxiety and depression (NDDI-E; MDI; BDI-II; HADS; Revised Emotional Thermometers (rET)).

Results: For depression 44% scored positive on rET, 35% on NDDI-E (similar as in the American previous studies), and 43% on BDI-II. On the MDI 19% fulfil ICD-10 diagnostic criteria for depression. For anxiety 53% scored positive on rET and 48% on HADS. Sensitivities of all the tools are comparable (NDDI-E 96%, BDI 96%, rET 83%, HADS 70%).

Conclusion: Results suggest that brief self completed screening instruments (rET and NDDI-E) are useful to alert the clinician on psychiatric

comorbitidy. These results are also evaluating the NDDI-E in the local British multicultural population. Both tests are easily applicable in a busy neurology outpatient setting and do not require any complex scoring. However, it is important to recognise that these tests are not designed to diagnose such conditions. Further analysis of data is required to assess the sensitivity and specificity of these instruments and their overall usefulness in clinical practice.

p489
PSYCHIATRIC COMORBIDITY IN EPILEPSY

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Purpose: To evaluate the frequency of psychiatric disorders in patients with epilepsy, the significance of different factors for this comorbidity and the efficacy of antielileptic drugs (AEDs) on epilepsy and psychopathology.

Method: Twenty-four patients, 12 male, aged 29.9 ± 11.8 years, with psychiatric disorders diagnosed by psychiatrist (DSM-IV classification), out of 236 patients with epilepsy were included in prospective observational study. Variables as age, sex, epilepsy characteristic, neurological status, EEG and MRI data, mono/polytherapy and 6 month remission after correction of treatment were compared with these of 50 controls.

Results: Psychiatric disorders coexisted with epilepsy in 10.2% of patients (24 from 236) with the most frequent diagnosis depression - in 17, followed by anxiety and psychosis. Psychopathology significantly prevailed in patients with complex partial seizures (CPS), posttraumatic epilepsy, lack of long remission of seizures, polytherapy with AEDs, presence of interictal focal paroxysmal EEG activity, brain structural lesions, hippocampal atrophy in MRI. There were not significant differences with controls in the exploring variables like age, gender, duration of epilepsy, presence of neurological signs, frequency of partial or generalized seizures, localization and lateralization of epileptogenic focus. Efficacy of corrected antiepileptic therapy on epileptic seizures correlated with better prognosis for psychiatric syndromes.

Conclusion: Risk group for psychiatric disorders are patients with posttraumatic epilepsy, CPS without clear remission, focal epileptiform EEG activity, hippocampal atrophy and polytherapy. These patients need more consideration in AED selection and regular consultations with psychiatrist with assessment of level of depression. Successful treatment of epilepsy extends far beyond seizure control.

p490
EPILEPTIFORM ABNORMALITIES ON AWAKE AND SLEEP EEG IN ADHD CHILDREN WITHOUT HISTORY OF EPILEPSY

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There are some relationships between attention-deficit/hyperactivity disorder (ADHD), epilepsy, ADHD symptoms and interictal epileptiform activities (EA).

Purpose: This study investigated whether EEG recordings during sleep were useful in solving diagnostic difficulties at ADHD assessment. The relationships between EA obtained on awake and sleep EEGs and their clinical implications on assessment of ADHD patients without history of epilepsy were studied.

Method: Six hundred seven ADHD children (82.4% male), aged between 5–14 years, mean 9.4 + 2.5, who were diagnosed at our hospital between January 2000 and December 2005 were assessed. At least one routine digitized EEG during wakefulness was performed on 517 patients, 14 of them had previous history of epilepsy. EA on the EEG were registered in 27 (5.4%) patients without previous history of epilepsy and they were followed up for 3 years.

Results: 18 (66.6%) of 27 ADHD children performed also EEG recordings during sleep. EA were registered in 12 (66.6%) patients and 6 (33.3%) were without detected EA on the sleep EEG. Activation of EA during sleep in form of frequent EA were observed in 3 (25%), but the majority 9 (75%) of our 12 patients demonstrated no frequent EA on the sleep EEG recordings. Although 5 of 27 patients with EA on the routine awake EEG had some symptoms suspected for epileptic seizures, the diagnosis of epilepsy was not confirmed.

Conclusion: EEG recordings during sleep were useful in the diagnostic assessment of ADHD children with suspected epilepsy comorbidity and in the assessment of correlation between EA and ADHD symptoms.

p491
PSYCHOSOCIAL DETERMINANTS OF MATERNAL ANXIETY WITHIN THE FIRST YEAR AFTER DIAGNOSIS OF EPILEPSY IN CHILD

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Purpose: Authors evaluate the level of anxiety as a state and trait in mothers whose children were within the last year diagnosed with epilepsy and analyze the impact of psychosocial factors related.

Method: The study included 40 mothers (22 whose offspring (age 2–12) were patients of neurological outpatient clinic and 18 of children from diabetes outpatient clinic – comparative group). State Trait Anxiety Inventory and original questionnaire were applied, statistical significance was tested with the Fisher test.

Results: Anxiety as a trait is similar in mothers of children with epilepsy and control group (5.55 vs. 5.36). However, the level of anxiety as a state conditioned by situation is higher in mothers of children with epilepsy (7.32 vs. 6.33). 50% mothers of children diagnosed with epilepsy estimate their knowledge about disease as sufficient in relation to 94% mothers of children with diabetes. information's on acting in case of loss of consciousness as well as about the disease itself, mothers received mostly from the doctor. In case of families with children with epilepsy 18 (among 22) mothers stated that the child's disease changed positively the relations with partners.

Conclusion: The intensification of anxiety as a state within first year after diagnosis is higher in mother of children with epilepsy than diabetes. Authors suggest that professional psychological help for mothers of children with newly diagnosed epilepsy may be an important element of therapy and maintain the desired quality of life in children.

p492
STUDY OF EMOTIONAL-VOLITIONAL RECOVERY DYNAMICS IN CHILDREN WITH ATYPICAL FRONTAL ABSENCE

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A dynamics of mental state in 212 children (upon attainment of medicamental compensation) suffering from atypical frontal absence (AFA) has been studied. In 69 children (34 females and 35 males) no brain organic lesion has been revealed by MRI method (I group). Atypical frontal absence, accompanied by a diagnosed brain organic lesion symptoms (II group), has been revealed in 143 children (70 females and 73 males).

Purpose: To study impact of accompanying brain organic lesion on recovery dynamics of mental impairments, detected in children with am idiopathic frontal epilepsy.

Method: Neuropsychological tests.

Results: Attention deficit and hyperactivity disorder (ADHD) was twice more common in children of the I group ($p = 0.002$) in the course of the three years following complete cease of seizures, while in five years no significant difference of the condition was seen between both groups. Mental deviations, that were diagnosed as a severe psycho-organic syndrome with symptoms of despondency, sadness, moderate dysphoric periods, aggression, were also practically twice more common in children of the I group ($p = 0.001$). On the contrary to the I group children whose deviations remained stable in the course of the 5 years' rehabilitation process, in the II group children the deviations were twice less common: decrease from c 49 (34.3%) to 25 (17.5%).

Conclusion: An accompanying brain lesion in idiopathic frontal lobe epilepsy affects severity of mental deviations at the outset of rehabilitation process, but has no effect on rehabilitation quality.

Poster session: Drug therapy III
Wednesday 30th June 2010
13:30–14:30

p493
OUTCOME OF DISCONTINUATION OF ANTIEPILEPTIC THERAPY IN THREE YEARS FREE-OF-SEIZURE PATIENTS

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Purpose: To identify prognostic factors of relapse after withdrawal of antiepileptic medication in adult patients.

Method: We retrospectively examined clinical records of adult patients who attended the Epilepsy Outpatient Clinic of the Psychiatric Hospital of Thessaloniki, over a 5 year period. All patients were under monotherapy with antiepileptic drugs and gradually discontinued medication, over a period of six months, after a minimum of three years' free-of-seizures period. Patients were followed for at least one year after treatment discontinuation. Patients' records were evaluated in terms of age at disease onset, type of epilepsy, type of seizures, paroxysmal electroencephalographic findings, presence of CNS damage and mental retardation.

Results: Sixty-six adult patients (mean age: 43.15 ± 16.64, range: 18–80, M/F: 30/46) were included in the study. Forty patients (60.6%) exhibited seizures within 1 year following treatment discontinuation. These patients did not differ from patients who did not report seizure recurrence, in terms of gender, age at disease onset, type of epilepsy, namely, idiopathic or symptomatic, type of seizures, epileptic or focal findings in EEG, presence of CNS damage or mental retardation ($p > 0.05$). Results did not differ after stratification of patients according to age at disease onset (age at disease onset ≤40 years/>40 years, $p > 0.05$).

Conclusion: We hereby report an increased rate for epilepsy relapse following antiepileptic treatment discontinuation, compared to the existing literature.

p494
NEUROPSYCHOLOGICAL IMPAIRMENT IN MESIAL TEMPORAL LOBE EPILEPSY: CORRELATION WITH ICTAL FEATURES?

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Purpose: To identify and correlate neuropsychological deficits with atypical motor signs indicative of temporal ''plus'' epilepsies(T+) cases.

Method: We reviewed the ictal features (long-term video-EEG) and the neuropsychological examination (comprehensive-neuropsychological-assessment) of 42 patients with MTLE (diagnosis by structural MRI or histology). We had 26.2% patients with contraversive manifestations and 7.14% with ipsilateral tonic motor signs.

Results: Considering ''typical signs'' we observed a statistical correlation ($p < 0.05$) and a significant low performance in delayed visual recall in patients with postictal amnesia ($p < 0.05$) and similar results for several measures of language (Token test and tests of semantic memory) in cases with gestural automatisms ($p < 0.005$). Considering ''atypical signs'' we found a strong correlation between contraversive manifestations of the eyes or head and working memory tests, namely Trail Test and Stroop Test ($p < 0.02$), and a significant but not so robust correlation with learning parameters of memory tests ($p < 0.05$). These results indicate a frontal involvement/dysfunction in this subgroup of patients. As was described by other authors we observed a correlation between ipsilateral tonic motor signs and dysphoric behavior in the postictal phase.

Conclusion: Our findings seem to confirm that MTLE patients with ''typical-signs'' and ''atypical-signs'' have different neuropsychological profiles. While in the first group cognitive deficits were restricted to the temporal lobe, ''atypical-patients'' had a more extensive cognitive impairment including frontal dysfunction. These results corroborate the functional concept of temporal ''plus'' epilepsies.

p495
COMPARISON OF THE EFFICACY AND SAFETY OF ZONISAMIDE AND CARBAMAZEPINE AS MONOTHERAPY IN ADULTS WITH PARTIAL EPILEPSY: DESIGN AND CURRENT STATUS OF A PHASE III, DOUBLE-BLIND, RANDOMIZED, MULTICENTRE TRIAL AND LONG-TERM EXTENSION STUDY

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Purpose: To compare efficacy and safety of zonisamide (ZNS) and controlled-release carbamazepine (CBZ) monotherapy in adults with newly diagnosed partial epilepsy.

Method: This is an international Phase III, double-blind, randomized, noninferiority trial, with long-term, follow-on extension. A target of 582 adults, age 18–75 years, with untreated, newly diagnosed partial seizures (±secondary generalization) or generalized tonic–clonic seizures (in the absence of any trait of idiopathic generalized epilepsy) will be randomized 1:1 to ZNS 100 or CBZ 200 mg/day. After up-titration to 300 and 600 mg/day, respectively, patients enter 26–78-week flexible-dosing period (ZNS 200–500 mg/day; CBZ 400–1200 mg/day; according to response/tolerability). Once seizure-free for 26 weeks, patients enter 26-week maintenance phase, followed by open-ended, double-blind, extension period. For the initial trial, the primary end point is proportion of patients seizure-free for ≥26 weeks; secondary end points include proportion seizure-free for 52 weeks, time to start of 26- or 52-week seizure-free period, and time to withdrawal. For extension, the primary end point is retention; secondary end points include proportion seizure-free for ≥24 months and time to withdrawal. In both phases, safety assessments include: adverse events; clinical laboratory, physical and neurological evaluations; vital signs; concomitant medication(s). Changes in mood/attention, cognitive function and quality-of-life will also be measured.

Results: Recruitment began in May 2007, and all patients have been enrolled. Results should be available in 2012.

Conclusion: This study will provide important information on the comparative efficacy and safety of ZNS and CBZ monotherapy in adults with newly diagnosed partial epilepsy.

This study is supported by Eisai.

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A MULTICENTER COMPARATIVE TRIAL OF LOW AND HIGH DOSE ZONISAMIDE IN CHILDREN WITH NEWLY DIAGNOSED EPILEPSY AS MONOTHERAPY

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Purpose: To evaluate the efficacy and tolerability of zonisamide (ZNS) as monotherapy in children less than 16 years of age, using a dose-controlled study design.

Method: We conducted a multicenter, randomized, comparative trial in children with newly diagnosed epilepsy that was not being treated when randomized to low(3–4 mg/kg/day) or high(6–8 mg/kg/day) ZNS. The primary end point was seizure-free rate at 6 months; a secondary measure was the change from screening to the end of the maintenance phase in a combined analysis of standardized measures of cognition, behavior and quality of life.

Results: Out of 123 patients enrolled, 89 patients (49 low dosage, 40 high dosage) completed the study. Thirty-five (54.7%) patients on low dose group and 31 (52.5%) subjects on high dose group achieved 6 months of seizure freedom ($p = 0.665$). Perceptual Organization of the cognitive variables, Somatization, Anxiety/Depression and Aggression scores of the behavioral variables were significantly improved for both groups after treatment ($p < 0.05$). On comparing low with high dose, vocabulary subtest of the cognitive variables, Total Competence, Delinquent Behavior, Externalizing and Total Behavior problem on low dose showed significant improvements comparing with high dose ($p < 0.05$).

Conclusion: Low-dose and high-dose ZNS monotherapy demonstrate similar efficacy for treatment of newly diagnosed childhood epilepsy. As shown in this subset analysis, ZNS is effective and well tolerated as monotherapy in children. And, low dose ZNS monotherapy has similar efficacy in seizure control and more beneficial neurocognitive effects than high dose.

p497

EFFECTS OF RETIGABINE ON RATES OF SEIZURE-FREE DAYS AND PROPORTION OF SEIZURE-FREE PATIENTS IN ADULTS WITH REFRACTORY PARTIAL-ONSET SEIZURES

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Purpose: To evaluate the effects of retigabine, a first-in-class antiepileptic drug (AED) that reduces neuronal excitability by enhancing the activity of KCNQ (Kv7) potassium channels, on seizure-free rates in adults with refractory epilepsy in two Phase III studies.

Method: RESTORE 1 (NCT00232596) and RESTORE 2 (NCT00235755) were multicentre, randomized, double-blind, placebo-controlled Phase III trials in adults with ≥4 partial-onset seizures/28 days while receiving 1–3 AEDs, with/without vagus nerve stimulator. Patients randomized to retigabine or placebo t.i.d. underwent forced titration to 600 or 900 mg/day (RESTORE 2), or 1200 mg/day (RESTORE 1), followed by 12 weeks' maintenance. The percentage of seizure-free days (days without any seizures) and proportion of seizure-free patients were assessed.

Results: Of the intent-to-treat population, 256/305 and 471/538 patients entered the maintenance phase in RESTORE 1 (placebo = 137/152, 1200 mg/day = 119/153) and RESTORE 2 (placebo = 164/179, 600 mg/day = 158/181, 900 mg/day = 149/178), respectively. The median percentage of seizure-free days during maintenance was significantly greater with retigabine (RESTORE 1: placebo = 78%, 1200 mg/day = 87%, $p < 0.001$; RESTORE 2: placebo = 78%; 600 mg/day = 82%, $p = 0.003$; 900 mg/day = 85%, $p < 0.001$). A significantly greater proportion of patients were free from seizures during maintenance in RESTORE 1 (placebo = 2%, 1200 mg/day = 8%, $p = 0.027$), and numerically increased, although not significantly, in RESTORE 2 (placebo = 1%; 600 mg/day = 3%, p-value not available; 900 mg/day = 5%, $p = 0.091$). Most common adverse events were dizziness, somnolence, headache, fatigue and confusion.

Conclusion: Retigabine treatment is associated with an increase in seizure-free days and proportion of seizure-free patients during maintenance compared with placebo in adults with partial-onset seizures already receiving 1–3 AEDs. These results support the therapeutic usefulness of retigabine in refractory epilepsy.

p498

RISK FACTORS FOR RECURRENCE OF EPILEPTIC ATTACKS AFTER WITHDRAWAL OF ANTIEPILEPTIC THERAPY

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Purpose: To determine risk factors for the appearance of relapse attacks after suspending antiepileptic drugs (AED).

Method: A group of patients was examined who had the AE treatment stopped by advice and agreement with the doctor, or sometimes on the basis of self-initiative. The study includes patients who have repeated epileptic attacks. A detailed questionnaire has been completed, neurological examination has been done, EEG, MRI of the brain as well. Etiology is classified into symptomatic, idiopathic and cryptogenic.

Results: A group of 43 patients (from 16 to 75 years old) have been examined due to epileptic attacks after exclusion of the AE therapy. There were 20 male patients and 23 female ones. The largest number of the patients were 16 to 35 year old, i.e. 34 or 79% patients. Idiopathic epilepsy had 18 (42%) patients, 13 (30%) had cryptogenic, and 12 (28%) had a symptomatic one. A significantly large number of the patients received the recurrence of the attacks after the discontinuation of AE therapy in the period up to 2 years (91%) compared to the period after that. Pathological EEG results have been determined in 60% of the patients.

Conclusion: The most of the relapses of epileptic attacks after AE withdrawal occurs in the first 2 years which is consistent with the data from literature. Risk factor for recurrence of attacks is a pathological EEG. Considering the etiology of recurrence seizures, there was no significant difference in observed group.

Poster session: Drug therapy VI
Wednesday 30th June 2010
13:30–14:30

p499
BETA 1 NA+ CHANNEL SUBUNIT LOSS IMPAIRS THE EFFECTS OF CBZ BUT NOT LACOSAMIDE ON REPETITIVE FIRING VIA DIFFERENTIAL EFFECTS ON PERSISTENT NA+ CURRENTS

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Purpose: In chronic epilepsy, a substantial proportion of patients remain refractory to antiepileptic drugs (AEDs). Understanding of the mechanisms of pharmacoresistance requires a precise understanding of how AEDs interact with their targets, in many cases voltage-gated ion channels. Lacosamide (LCM) is a novel Na^+-channel acting AED that interacts primarily with slow inactivation of fast transient Na^+-channels. Given that loss of accessory Na^+ channel subunits is a feature of a number of neurological disorders including epilepsy, we examined the effects of LCM versus carbamazepine (CBZ) on the persistent Na^+-current (I_{NaP}) in the presence and absence of accessory subunits within the channel complex.

Method: Using patch-clamp recordings in intact hippocampal CA1 neurons of mice lacking the β_1 Na^+-channel subunit (*Scn1b*), I_{NaP} was recorded using slow voltage ramps.

Results: Application of 100 μM CBZ or 300 μM LCM reduced the maximal I_{NaP} conductance in both wild-type and control mice. Surprisingly, in *Scn1b* null mice CBZ induced a paradoxical increase of I_{NaP} conductance in the subthreshold voltage range, resulting in an ineffective block of repetitive firing in *Scn1b* null neurons; however, LCM maintained efficacy in blocking repetitive firing in β1-deficient mice. Modeling studies on a realistic CA1 neuron model indicate that the paradoxical increase of I_{NaP} by CBZ boosts the rate of interspike depolarization, resulting in a loss of CBZ efficacy.

Conclusion: These results suggest that novel anticonvulsant LCM maintains activity in the presence of impaired sodium channel beta subunit expression and thus may offer a better efficacy profile than CBZ in the treatment of epilepsy.

p500
LACOSAMIDE AS ADJUNCTIVE THERAPY IN PATIENTS WITH PARTIAL SEIZURES: CASE STUDY SERIES

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Purpose: To report early clinical experience with lacosamide (LCM) as adjunctive therapy in patients with focal epilepsy, with special assessment of nocturnal seizures.

Method: We retrospectively analyzed data from patients of four hospitals in Spain, collecting data on epidemiology, epilepsy characteristics, concomitant AEDs, reduction of seizure frequency, occurrence of seizures during sleep or wakefulness, and adverse events.

Results: 61 patients were included (mean age 38.3 years, 54% women). The average epilepsy duration was 26.2 years (range 1–67 years). All had focal epilepsy with monthly seizures (mean 9.7 seizures per month), with 43% of seizures occurring during sleep. All were taking other AEDs (mean 2.2 drugs per patient). LCM dose in 32 (52.5%) patients was 200 mg/day, 300 mg/day in 16, 400 mg/day in 9, and 500 mg/day in three. A total of 31 patients (51%) reported a greater than 50% reduction in seizure frequency, two of them were seizure-free for 6 months or longer. In 11 out of 31 cases with good response (37%) seizures occurred mainly during sleep. Twenty patients (33%) reported adverse effects (AE); the most common was dizziness, reported by 16 patients. However, only in eight patients (13%) the medication had to be withdrawn and none had serious AE.

Conclusion: The results of this study support the efficacy and tolerability of adjunctive lacosamide in patients with partial-onset seizures and suggest lacosamide may be an advantageous option in patients with seizures during sleep.

p501
AN INVESTIGATION OF THE EFFECT OF ESLICARBAZEPINE ACETATE ON CARDIAC REPOLARIZATION: A POOLED ANALYSIS OF OVER-READ ELECTROCARDIOGRAMS FROM THREE DOUBLE-BLIND PHASE III CLINICAL STUDIES

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Purpose: Evaluate the effects of eslicarbazepine acetate (ESL) on ECG parameters in patients with partial onset epilepsy during 3 Phase III studies of ESL at doses of 400, 800 and 1200 mg, as adjunct treatment to 1–3 other AEDs (OXC was not allowed).

Method: 12-lead ECGs were evaluated at screening, baseline, and Week 14 of the double-blind treatment period by a central vendor. A cardiologist over-read each ECG manually using handheld Vernier calipers on the original ECG paper tracing. Incidence of sponsor-defined potentially clinically significant (PCS) values was analyzed by treatment group, and mean changes from baseline were also calculated.

Results: Of the 5532 ECGs, 82% (n = 4541) were successfully overread. Mean changes from baseline to Week 14 for each ECG parameter were small, similar to those observed in the placebo group, and not clinically relevant in all treatment groups. The placebo and ESL groups had similar incidences for each postdose ECG abnormality and each PCS ECG abnormality. No patients in the active treatment groups had a QTc interval (QTc-B or QTc-F) that exceeded 500 ms.

Conclusion: In this pooled analysis of 3 Phase III studies, no clinically relevant ECG abnormalities were observed in association with ESL treatment. There was no relevant trend toward changes in heart rate or prolongation of ECG intervals. No clinically significant prolongations of the QTc intervals were seen in any patient despite ''real-use'' conditions with use of concomitant medications, including 1–3 AEDs.

Supported by BIAL- Portela & Co, SA.

p502
EFFICACY AND TOLERABILITY OF ORAL LACOSAMIDE AS ADJUNCTIVE THERAPY ON PEDIATRIC PATIENTS WITH PHARMACORESISTANT PARTIAL EPILEPSY

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Purpose: The aim of this study was to assess the efficacy and tolerability of Lacosamide (LCM) as adjunctive antiepileptic therapy on pediatric patients with pharmacoresistant partial epilepsy.

Method: Children and teens with intractable focal epilepsy receiving LCM as add-on therapy participated in the analysis. Data concerning diagnosis, seizure types, neuroimaging, past and concurrent antiepileptic drugs (AEDs), effects on seizure frequency, dose per kilo and side effects were analyzed.

Results: Eighteen patients with mean age 11 years 5 months (SD = 5 years 9 months) were enrolled. Fourteen of them were observed for at least 3 months (mean = 5 months, SD: 1.7 months) after LCM treatment initiation. All were receiving 1–3 other AEDs and had failed 3–16 AEDs in the past. LCM dose per kilo ranged between 2–8.8 mg/kg with mean value 5.17 mg/kg (SD = 2.08 mg/kg). After a 3 month observation period, 35.71% (n = 5) of patients reported a ≥50% reduction in seizure frequency. Two patients achieved seizure freedom while two other had a temporary good result for 2 and 3 months, respectively, but relapsed. Six patients (33.33%) out of 18 reported minor side effects. One patient presented with aplastic anemia and discontinued therapy even though this was considered unrelated to LCM.

Conclusion: LCM treatment on pediatric patients was found to be safe at doses up to 8.8 mg/kg/day without major adverse reactions. It was effective in controlling or reducing ≥50% of seizures in 14.28% (n = 2) and 35.71% respectively when used as adjunctive therapy on pediatric patients with pharmacoresistant partial epilepsy.

p503
RAPAMYCIN TREATMENT IMPROVED EPILEPSY STATUS IN TWO PATIENTS WITH TSC AND INTRACTABLE EPILEPSY

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Purpose: mTOR inhibitors has been proved beneficial in reducing the size of agiomyelolipomas (AML) and probably beneficial on reducing subependymal giant cell astrocytomas (SEGA) in TSC patients. We report two cases of definite TSC patients with intractable epilepsy in whom treatment with rapamycin targeting AMLs followed by substantial improvement of seizures.

Patients and method: Case A is a 7-year-old girl with a definite diagnosis of the TSC characterized by skin lesions, multiple cortical tubers, epilepsy, autistic behavior and renal and liver AMLs. In the past 11 antiepileptic medications were administered but patient continued with almost daily seizures. Rapamycin was started to control the increasing size of AMLs. Seizures decreased in frequency (once a week) and severity (mainly absences) 2 months after the initiation of treatment. Her behavior also improved. Case B is a 19-year-old female with a definite TSC characterized by skin lesions, cortical tubers, history of SEGA resection, renal and liver AMLs, lung lymphangiomyomatosis and intractable epilepsy with a bordeline cognitive level. Epilepsy started at the age of 9 with daily drop attacks intractable to 10 antiepileptic medications. Treatment with rapamycin was suggested for AMLs. Clinical improvement was noted 3 months after the initiation of treatment with almost complete cessation of drop attacks. Patient continues to have rare seizures mainly of focal type.

Conclusion: Rapamycin treatment improved seizure status in two patients with TSC. Accumulating evidence suggests that mTOR also participates in epileptogenesis and mTOR inhibition may represent a potential antiepileptogenic, especially in TSC patients.

p504
SEIZURE FREEDOM AND PATIENT RETENTION WITH ADJUNCTIVE ESLICARBAZEPINE ACETATE THERAPY IN ADULTS WITH REFRACTORY PARTIAL SEIZURES DURING THREE RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIALS WITH 1-YEAR, OPEN-LABEL EXTENSIONS

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Purpose: To evaluate seizure freedom and retention associated with adjunctive eslicarbazepine acetate (ESL) therapy in adults with refractory partial seizures.

Method: Seizure freedom was assessed in three Phase III trials (BIA-2093-301, -302, -303), and during 1-year open-label extensions. Retention was assessed during the 1-year extensions. Patients were randomized to 14 weeks' double-blind treatment (2 weeks' titration, 12 weeks' maintenance) with placebo (N = 290), or ESL 400 (N = 196), 800 (N = 284) and 1200 (N = 280) mg/day. Patients then entered open-label extensions, during which ESL was initiated at 800 mg/day and adjusted to 400–1200 mg/day, as required.

Results: In the individual Phase III trials, seizure freedom rates during the maintenance period were 1–2%, 3–5% and 4–8% for ESL 400, 800 and 1200 mg/day, respectively, versus 1–2% for placebo; in a combined analysis, the corresponding rates were 1.6%, 3.8% and 7.5% (4.5% overall) versus 2.5%, respectively. In 1-year extensions, seizure freedom during Weeks 1–4, 5–16, 17–28, 29–40 and 41–52 ranged from 8.7–12.5%, 4.6–12.0% and 5.8–17.8% in Studies 301, 302 and 303, respectively; overall seizure freedom rates were 3.8%, 2.5% and 2.6%, and retention rates were 76.1%, 68.6% and 77.3%, respectively.

Conclusion: During three Phase III trials, adjunctive ESL 800 and 1200 mg/day resulted in substantially higher seizure freedom rates than placebo. During 1-year extensions, favorable seizure freedom rates were maintained and retention was high, demonstrating ESL's effectiveness in this population.

These studies were supported by BIAL and the abstract by Eisai.

p505
BRIVARACETAM MODULATES NA^+ CURRENTS EXPRESSED IN A NEUROBLASTOMA CELL LINE: COMPARISON WITH CARBAMAZEPINE

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Purpose: Brivaracetam (BRV), currently in Phase III development for epilepsy, is a novel high-affinity synaptic vesicle protein 2A (SV2A) ligand that also displays inhibitory activity at neuronal voltage-dependent Na^+ channels. The purpose of this study was to compare the effects of BRV versus carbamazepine (CBZ) on the biophysical properties of the Na^+ current.

Methods: The effects of BRV and of CBZ, 1–100 μM, were studied under whole-cell patch-clamp on the biophysical properties of the endogenous voltage-activated Na^+ current expressed in N1E-115 mouse neuroblastoma cells.

Results: Similarly to CBZ, BRV induced a significant shift of the fast inactivation curve toward hyperpolarized potential values and did not affect the voltage-dependence of the activation and slow inactivation curves. In cells depolarized from -80 mV both drugs produced a dose-

dependent inhibition of the current. This inhibition, already significant at 1 μM, increased up to 30 ± 6% and 40 ± 6% with 100 μM BRV and CBZ, respectively. In contrast, when cells were held at −120 mV, BRV did not affect the current amplitude and CBZ induced <10% inhibition of the current. Interestingly, while 100 μM CBZ induced a consistent 30 Hz frequency-dependent facilitation of block, BRV only produced a weak effect on this parameter.

Conclusion: According to the Na^+ current properties investigated in this study, BRV perfused at therapeutic concentrations demonstrates effects on Na^+ currents comparable to those of CBZ but of a lower magnitude. In addition to its interaction with SV2A, the effects of BRV on Na^+ currents may contribute to its antiepileptic properties.

UCB sponsored.

p506
COMPARATIVE STUDY OF LACOSAMIDE WITH OTHER SODIUM CHANNEL BLOCKING ANTIEPILEPTIC DRUGS ON SODIUM CURRENT SLOW INACTIVATION

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Purpose: Lacosamide (LCM) differentiates from other classical voltage-gated sodium (Na_v) channel blocking antiepileptic drugs (AEDs) in that it specifically enhances slow inactivation of Na_v channels without affecting fast inactivation. This study provides for the first time a direct comparison of the effect of LCM with other AEDs on Na_v channel slow inactivation.

Method: In whole-cell patch-clamp, we compared the effects of LCM versus those of other Na_v channel blocking AEDs (carbamazepine, phenytoin, lamotrigine, zonisamide, rufinamide) on Na_v channel slow inactivation parameters. This study was performed in the N1E-115 mouse neuroblastoma cell line expressing native Na_v channels representative of central and peripheral nervous system Na_v isoforms.

Results: The electrophysiological results showed that compared to control, LCM produced a significant and very large hyperpolarizing V_{50} shift of the slow inactivation curve (ΔV_{50} = −33 ± 7 mV [mean ± SD] vs. ΔV_{50}control = −8 mV ± 7 mV) resulting in the enhancement of the fraction of unavailable Na_v channels at potentials near the membrane resting potential. This hyperpolarizing shift induced by LCM was not observed with other AEDs tested under the same experimental conditions. Carbamazepine and zonisamide did not affect Na_v current slow inactivation. Phenytoin, lamotrigine and rufinamide modified slow inactivation parameters differently from LCM.

Conclusion: The present study provides additional evidence of the unique mode of action of LCM compared to other Na_v channel blocking AEDs by demonstrating the selective enhancement of Na_v channel slow inactivation.

p507
ADJUNCTIVE BRIVARACETAM IN ADULTS WITH UNCONTROLLED FOCAL EPILEPSY: RESULTS FROM TWO RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIALS

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Purpose: To evaluate the efficacy, tolerability and safety of adjunctive brivaracetam (BRV) in adults (16–70 years) with partial-onset seizures (POS) uncontrolled on 1–2 AEDs.

Methods: Two prospective, confirmatory, multicenter, randomized, double-blind, placebo-controlled, parallel-group, fixed-dose studies (N01253/NCT00464269; N01252/NCT00490035). Patients experiencing ≥8 POS during the 8-week Prospective Baseline were randomized (1:1:1:1) to twice-daily BRV (mg/day); (N01253: BRV5, BRV20 or BRV50; N01252: BRV20, BRV50 or BRV100) or placebo without titration.

Results: Randomized/ITT population: 400/392 (N01253); 399/398 (N01252). Study N01253 achieved statistical significance on the primary efficacy end point, percent reduction over placebo in POS frequency/week during the 12-week Treatment Period for BRV50 (12.8%; p = 0.025). Study N01252 did not achieve statistical significance on the primary efficacy end point for BRV50 (6.5%; p = 0.261), however, statistical significance was achieved for BRV100 at the nominal 0.05 level (11.7%; p = 0.037). The 50% responder rates in POS frequency/week versus placebo (BRV/placebo) were statistically significantly higher for BRV50 (32.7/16.7%; p = 0.008; N01253) and BRV100 (36.0/20.0%; p = 0.023; N01252). Median percent reductions from baseline in POS frequency/week versus placebo (BRV/placebo) were statistically significantly higher for BRV50 (30.5/17.8%; p = 0.003; N01253) and BRV100 (32.5/17.0%; p = 0.004; N01252). BRV was well tolerated in both studies, with the majority of treatment-emergent adverse events being mild to moderate in intensity.

Conclusion: Adjunctive BRV (50 and 100 mg/day) was associated with a reduction in POS frequency/week during the 12-week Treatment Period. The primary efficacy end point was met in one of the two confirmatory studies. BRV, initiated without titration, was well-tolerated across all doses tested.

*Both authors contributed equally.

UCB-sponsored.

Poster session: Drug therapy IX
Wednesday 30th June 2010
13:30–14:30

p508
FREQUENCY DOMAIN PARAMETERS OF HEART RATE VARIABILITY IN PATIENTS WITH NEWLY DIAGNOSED EPILEPSY AND LAMOTRIGINE MONOTHERAPY

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Purpose: To assess the effect of lamotrigine (LTG) on selected frequency domain parameters of heart rate variability in patients with newly diagnosed localization related epilepsy.

Method: 15 consecutive adult patients with untreated, newly diagnosed localization related epilepsy having at least two well documented, unprovoked, clinically evaluated and classified partial seizures (with or without secondary generalization) and planned for LTG treatment was included in study. 24 h ambulatory ECG was performed before and 3 months after stabile treatment of LTG. Total power, power in the ultra low frequency range (ULF), in the very low frequency range (VLF), in the low frequency range (LF), and in the high frequency range (HF) were calculated. Paired t-test, Wilcoxon test of equivalent pairs and ANCOVA ware performed for alpha = 0.05

Results: When analyzing the full 24 h recordings, patients had significantly lower power ($p < 0.05$), LF ($p < 0.05$), VLF ($p < 0.05$) and HF

($p < 0.05$) parameters during treatment with LTG than before. However, when controlling for results of baseline measure as covariate we didn't find statistically significant effects of different LTG doses.

Conclusion: Our observations could highlight some effects of LTG on frequency domain measures of heart rate variability in newly diagnosed patients with epilepsy, but results must take in consideration many confounding factors. Supplementary studies with superior sample size are reasonable.

Keywords: Epilepsy, Heart rate variability, Lamotrigine

p509
CARDIAC REPOLARIZATION INDICES IN EPILEPSY PATIENTS

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Purpose: Epilepsy can a reason for sudden cardiac death. The Q-T interval has been used to identify potential abnormalities of ventricular repolarization.

Method: The aim of this study is to identify the Q-T ($QT_{max\ c}$, $QT_{min\ c}$, $QT_{dispersion}$) intervals of the epilepsy patients and compare these finding with the control group. Seventy-one patients with a mean age of 34.4 ± 12.4 (17–63) years, and 68 control subject with a mean age of 35.6 ± 8.7 (19–58) years were included in this study. Thirty-one of the patients were on carbamazepine, 26 of the patients were on valproate and 14 of the patients were on oxcarbazepine monotherapy. Q-T intervals were measured from 12-lead ECG. The average age of seizure onset was 18.6 ± 10.9 (1–50) years and disease duration was 12.2 ± 9.2 (1–36) years.

Results: There were statistical differences between two groups of $QT_{max\ c}$ (42.7 ± 3.0; 42.2 ± 2.8), $QT_{min\ c}$ (38.4 ± 2.6; 39.1 ± 2.4). But $QT_{dispersion}$ (4.1 ± 2.1; 3.0 ± 1.7; p: 0.001) of the patients were statistically longer then the control group. However there were no relation between QT_D and type of antiepileptic drugs and seizure frequency. On the other hand there was no correlation between QT_D and age of seizure onset (r: 0.15) and disease duration (r: 0.190).

Conclusion: The QT_D is clearly longer in epileptic patients. QT_D is a marker of ventricular repolarization. Repolarization abnormalities are associated with ventricular arrhythmias that may lead to ventricular fibrillation and sudden cardiac death.

p510
CASE REPORT: A RARE CASE OF SINUS BRADYCARDIA UNDER HIGH DOSE OF ORAL PULSE METHYLPREDNISOLONE IN AN INFANT WITH TUBEROUS SCLEROSIS AND HYPSARRHYTHMIA

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Purpose: Pulse methylprednisolone therapy in infants with hypsarrhythmia is done, if other antiepileptic drugs failed. Sinus bradycardia is a rare, usually not known side effect. The case of a 1 ½ year old girl with tuberous sclerosis and hypsarrhythmia is described who developed severe bradycardia.

Method: The epilepsy was unsuccessfully treated with phenobarbital, levetiracetam, and oxcarbazepine. For cortical dysplasia, lesionectomy of the left frontal lobe was done at an age of 10 months. The seizures persisted. Medication was extended with sulthiame, topiramate, and vigabatrin. Topiramate and vigabatrin led to seizure aggravation. Pulse methylprednisolone therapy was started because of tonic seizures and burst suppression pattern during sleep. Methylprednisolone, 20 mg/kg in the morning, was given for 3 days. After 4 days interruption, a next cycle followed.

Results: Under therapy with lamotrigine, levetiracetam, sulthiame, the first cycle of methylprednisolone had no side effects. The seizures markedly decreased, the EEG improved. At the end of the second cycle, the pulse diminished from 100–120/min to 60–80/min. The ECG showed sinus bradycardia (minimum 44/min at night). General health, blood pressure, electrolytes were normal. An echocardiography showed no rhabdomyomas. A Holter-ECG revealed a normalizing heart rate during the next days. Methylprednisolone therapy was stopped.

Conclusion: Corticoids are common drugs for hypsarrhythmia, given continuously or pulsating. Sinus bradycardia is a very rare side effect. In our case it was due to methylprednisolone. There are rare reports about bradycardia by corticoids, given intravenously, in higher dose. – One should attend to bradycardia due to oral pulse methylprednisolone for hypsarrhythmia.

p511
DOES LACOSAMIDE (VIMPAT) PROLONG THE PR INTERVAL OF PATIENTS WITH A VAGAL NERVE STIMULATOR (VNS)?

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Purpose: To investigate whether lacosamide causes clinically relevant prolongation of PR interval in patients with VNS.

Lacosamide is a newly available epilepsy drug indicated for add on treatment of partial seizures. Some patients with intractable epilepsy considered for lacosamide therapy will already have VNS implanted. VNS could theoretically worsen cardiac conduction, and lacosamide has also been shown to have a small effect on PR interval and is contraindicated in second and third degree heart block.

Method: A cohort of 7 adult patients for whom VNS had not proved sufficiently efficacious or had not maintained its efficacy were prescribed Lacosamide as adjunctive therapy, in addition to their usual antiepilepsy medication.

A standard ECG was recorded prior to commencement of treatment and repeated once a daily dose of 200 mg was reached (or maximum tolerated dose in one patient). The ECG findings were analyzed with particular reference to cardiac conduction parameters.

Results: All baseline ECGs showed normal cardiac conduction. The mean PR interval before treatment with Lacosamide was 153 ms (range 128–184 ms) and at a treatment dose of 200 mg daily the mean PR interval was166ms (range 132–215 ms). There were no other significant ECG changes.

The normal PR interval range is 120–200 ms.

Conclusion: In this small cohort of patients no clinically significant prolongation of the PR interval was demonstrated. Our data suggests that there is no increased risk of cardiac conduction problems in VNS-treated patients given lacosamide.

p512
EFFECTS OF LAMOTRIGIINE ON SELECTED TIME DOMAIN PARAMETERS OF HEART RATE VARIABILITY IN PATIENTS WITH NEWLY DIAGNOSED LOCALIZATION RELATED EPILEPSY

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Purpose: To assess the effect of lamotrigine (LTG) on selected time domain measures of heart rate variability in patients with newly diagnosed localization related epilepsy.

Method: Fifteen consecutive adult patients with untreated, newly diagnosed localization related epilepsy having at least two well documented, unprovoked, clinically evaluated and classified partial seizures (with or without secondary generalization) and planned for LTG treatment was included in study. 24 h ambulatory ECG was performed before and 3 months after stabile treatment of LTG. Standard deviation of all NN intervals (SDNN), standard deviation of the averages of NN intervals in all 5 min segments of the entire recording (SDANN), and the square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD) were calculated. Paired t-test, Wilcoxon test of equivalent pairs and ANCOVA ware performed for alpha = 0.05.

Results: When analyzing the full 24 h recordings, patients had significantly lower SDNN ($p < 0.05$), and SDANN ($p < 0.05$) parameters during treatment with LTG than before. However, when controlling for results of baseline measure as covariate we didn't find any statistically significant effects of different LTG doses.

Conclusion: Our observations could highlight some effects of LTG on time domain measures of heart rate variability in newly diagnosed patients with epilepsy, but results must take in consideration many confounding factors. Further studies with greater sample size are warranted.

Keywords: Lamotrigine, Epilepsy, Heart rate variability

p513
EVALUATION OF THE NEW QMS TOPIRAMATE IMMUNOASSAY ON THE OLYMPUS AU 640

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Purpose: Topiramate (TOPI), is a second generation antiepileptic drug (AED) which has a broad spectrum of clinical efficacy. The drug exhibits significant differences between individual patients in dose required to attain target plasma concentrations which make TOPI a good candidate for therapeutic drug management (TDM). Gas Chromatographic methods are reported for TDM of TOPI, and in addition a FPIA method was developed which could be run on a spare channel of an Abbott TDx analyzer. No other immunoassays have been commercialized until recently. The present work evaluates the first commercial batch of a new QMS TOPI immunoassay and compares its performance with the FPIA procedure.

Methods: One hundred thirty-five clinical samples submitted for TDM were analyzed on receipt by FPIA and the results reported. Residual specimen was deep-frozen (−25 °C) to await analysis by the QMS assay, run on an Olympus AU 640. Initially a 20 day between batch precision study was undertaken using supplied control sera, following which the stored clinical specimens were analyzed. The FPIA results were distributed across the TOPI range 0–32 mg/L. The methods were compared by regression and Bland-Altman plots.

Results: Interbatch precision for the controls (2.9, 9.9, 24 mg/L nominal) by QMS was between 2.5 and 5% CV. For patient samples, the correlation coefficient (r^2) for the comparison of QMS with FPIA was 0.98, the slope of the regression line was 1.005 and the *y*-intercept was 0.62.

Conclusion: The QMS immunoassay is precise, accurate, fast and easy to perform. It will enable local services for TDM of topiramate to be made more easily available since the assay can be installed onto a normal chemistry platform; also it avoids the use of specialized chromatographic procedures.

p514
SAFETY AND TOLERABILITY OF ADJUNCTIVE BRIVARACETAM IN ADULTS WITH UNCONTROLLED EPILEPSY: RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Purpose: Safety and tolerability of BRV at individualized tailored doses (20–150 mg/day) in adults (16–70 years) with partial-onset (POS) or primary generalized (PGS) seizures uncontrolled on 1–3 AEDs.

Method: Prospective, multicenter, randomized, double-blind, placebo-controlled, flexible-dose trial (N01254/NCT00504881). Patients with ≥4 POS or ≥4 days with PGS during 4-week Baseline Period were randomized (3:1) to BRV:placebo, initiated at 20 mg/day bid and increased at investigator's discretion up to 150 mg/day during 8-week Dose-Finding Period; followed by 8-week stable-dose Maintenance Period.

Results: Four hundred eighty patients randomized (359 BRV/121 placebo); mean age 35.9 years; 431 with POS (89.8%), 49 with PGS (10.2%). 90.0% BRV, 91.7% placebo-treated patients completed the study. Similar proportion of BRV and placebo-treated patients reported ≥1 TEAE (66.0/65.3%); majority mild to moderate. The overall incidence of TEAEs was higher during the Dose-Finding (BRV 56.0%/placebo 55.4%) than the Maintenance Period (BRV 36.8%/placebo 40.9%). The most frequent TEAEs were headache (BRV 14.2%/placebo 19.8%), somnolence (BRV 11.1%/placebo 4.1%), dizziness (BRV 8.6%/placebo 5.8%) and fatigue (BRV 7.8%/placebo 4.1%). Only 6.1% BRV and 5.0% placebo-treated patients discontinued study medication because of TEAEs. During 16-week Treatment Period, median percent reduction from baseline in POS frequency/week was 26.9% BRV/18.9% placebo ($p = 0.070$); 50% responder rates were 30.3% BRV/16.7% placebo ($p = 0.006$). The corresponding results for PGS days/week (exploratory analysis) were 42.6% BRV/20.7% placebo; 44.4% BRV/15.4% placebo.

Conclusion: When given at individualized tailored doses, BRV (20–150 mg/day) demonstrated a favorable safety and tolerability profile as add-on therapy in adults with uncontrolled partial or primary generalized epilepsy.

UCB-sponsored.

p515
ZONISAMIDE IN ADJUNCTIVE TREATMENT OF REFRACTORY EPILEPSY: MONOCENTRIC RETROSPECTIVE STUDY

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Purpose: The aim of the study was to assess the efficacy and tolerability of zonisamide in patients suffering from refractory epilepsy.

Method: We retrospectively analyzed 41, adult patients suffering mostly from refractory focal epilepsy and treated with zonisamide as adjunctive therapy for at least 12 months. One third of them had been treated by vagal nerve stimulation prior to the onset of zonisamide treatment. The primary end points were: 1-year retention rate, percentage seizure reduction and the incidence of adverse events.

Results: The retention rate at 12 months following the commencement of zonisamide treatment was 62%. The number of responding patients

([3]50% seizure reduction) at the above time was 50%. The number of patients completely seizure-free at the above time was 5.5%. Side effect was noticed in 25% of patients. We analyzed separately the efficacy of zonisamide in patients treated with vagal nerve stimulation.

Conclusion: Zonisamide is an effective and relatively well-tolerated option for the adjunctive treatment in adult patients with refractory epilepsy. The results are going to be updated.

p516
CANCER RISK IN PEOPLE WITH EPILEPSY USING VALPROATE-SODIUM

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Introduction: The antiepileptic drug, sodium-valproate has been shown to posses antitumor properties. We hypothesized that valproate has a cancer-protective effect in people with epilepsy.

Aim: To determine cancer risk in people with epilepsy using sodium-valproate.

Methods: Continuous data for 2997 subjects with epilepsy and a prescription for valproate between 01/01/1987 and 31/12/1992 and 11,922 unexposed subjects were provided by the General Practice Research Database, U.K. Hazard ratios for all cancers and individual cancers between the exposed and unexposed groups with smoking and alcohol consumption and age as covariates were calculated using the Cox proportional hazards method.

Results: A mild but nonsignificant excess of all cancers [hazard ratio (HR): 1.190 ($_{95\%}$CI: 0.966 to 1.467) (p = 0.10)], a significant excess of colon cancers [HR: 3.949 ($_{95\%}$CI: 1.968 to 7.922) (p = 0.001)] and a trend towards excess of prostate neoplasms [HR: 2.149 ($_{95\%}$CI: 0.921 to 5.016) (p = 0.08)] was noted in the exposed group. On the other hand, a trend towards reduced hazard ratios for breast carcinoma [HR: 0.404 ($_{95\%}$CI: 0.144 to 1.130) (p = 0.08)].

Conclusions: The lack of an inverse association between valproate use and hazard ratios for all cancers and several individual cancer sites does not lend support for a cancer-protective role for valproate. The trend towards an inverse association with breast carcinoma incidence and a significant association with colon cancer need further evaluation.

p517
PREGABALIN AS THE FIRST ADD-ON THERAPY OF PARTIAL EPILEPTIC ATTACKS AND ITS INFLUENCE UPON DEPRESSION, ANXIETY, COGNITIVE FUNCTIONS, LIFE QUALITY AND SLEEP DISTURBANCES IN THE SLOVAK REPUBLIC

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Purpose: To ensure safety and effect in outpatients suffering from partial epilepsy, who have been unsuccessfully treated with an antiepileptic drug (except of pregabalin). To determine the effect of pregabalin on anxiety, depression, cognitive functions, life quality and sleep disturbances in patients suffering from partial epileptic attacks.

Method: In interventional, prospective, multicentre, open label study the data from 256 patients suffering from partial epilepsy treated with pregabalin 150–600 mg/day. Patient's quality of life and influence of pregabalin on symptoms associated with epilepsy was assessed using HAM-A scale, HAM-D scale, MMSE, 10-item version of QOLIE scale and CGI-S scale. Efficacy, tolerability, compliance and safety was monitored throughout the study.

Results: Significant influence on efficacy, tolerability and compliance assessed by neurologists and also patients was found during 6-month follow-up. Favorable outcomes from scales (HAM-A, HAM-D, QOLIE, CGI-S, PGIC) showed positive effect from therapy. No negative influence on cognitive functions has been identified. Patients with partial epilepsy and comorbidities (anxiety, depression, sleep disturbances, etc…) showed significantly more profound benefit from therapy.

Conclusion: Being used as add-on therapy of partial epileptic seizures, pregabalin has proved good effectiveness and safety. We have documented not only its anticonvulsive effect but also its positive effect on anxiety, depression and sleep disturbances, and cognitive functions with have not been negatively influenced.

Poster session: Epilepsy syndromes in children and adults II
Wednesday 30th June 2010
13:30–14:30

p518
SERUM PROLACTIN LEVELS FOLLOWING SINGLE TEMPORAL EPILEPTIC SEIZURES

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Purpose: To explore value of serum prolactin (PRL) measurement `following single complex partial seizure.

Method: Forty-five patients with temporal seizures without secondary generalization and PRL level assessed within 10–15 min after event, were identified from a cohort of 71 patients with temporal epilepsy who had comprehensive presurgical assessment from 2006 to December 2009. In all cases interictal serum PRL levels at baseline and after the 54 seizures were compared and analyzed.

Results: Video-EEG monitoring confirmed 54 temporal seizures without generalized secondary tonic–clonic seizures. Serum PRL levels were elevated following almost all complex partial seizures. Marked PRL elevation, above three times or more of baseline was observed after 25 (46%) of 54 seizures, two times after 13 (24%) of 54 seizures and slight elevation after 13 (24%) of 54 seizures. PRL was decreased only after 3 (6%) of 54 seizures.

Conclusion: PRL is sensitive marker of single temporal lobe seizure without secondary generalization. During seizure-free intervals PRL should be measured when interpreting only slight elevation observed after considerable in number seizures.

p519
CLINICAL AND DIAGNOSTIC CORRELATION OF MESIAL TEMPORAL LOBE EPILEPSY

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Purpose: The objective of this study is to select the patients with MTLE, analyze the EEG, MRI, and clinical data and to give criteria which can help to confirm the existence of pathogenic and organic centers of lesion and analyze the factors related to degree of medical responsiveness.

Method: This study investigates the clinical course of 90 patients with MTLE. We analyzed MRI, EEG and clinical data of these patients: 45 patients with UHS, 5 patients with BHS, 20 patients with other temporal pathologies, 20 patients with MRI-negative picture. 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%). Oroalimentar automatisms were observed in 36% of patients, verbal automatisms in 22% of cases. Specific focal discharges were recorded in 59% of patients. 6% from HS (50) group were completely controlled with adequate therapy, 48% were intractable. The remaining 40% had their seizure reduced ($p < 0,045$).

Conclusion: Temporal pole signal changes and volumetric reduction were commonly found in this group of patients, both abnormalities appearing always ipsilateral to the HS. The age of seizure onset significantly younger in the intractable group, than in the well-controlled group, duration of disease and polytherapy are prognostic predictors for patients with TLE. Patients with a history of febrile convulsions or with epileptiform discharges in their EEG, had poorer seizure control, than those who did not.

p520
LONG-TERM SEIZURE OUTCOME IN ADULT PATIENTS WITH REFRACTORY EPILEPSY WHO WERE NOT CANDIDATES FOR SURGERY AFTER PRE-SURGICAL EVALUATION

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Purpose: To evaluate the long-term seizure outcome in adult patients with refractory epilepsy who were not eligible for surgery after video-EEG monitoring.

Methods: A special questionnaire was sent to 400 patients who underwent video-EEG monitoring between 2001 and 2007 in the Bethel Epilepsy Center. There were 154 patients who replied to the questionnaire, among them 63 males and 91 females. Temporal epilepsy was diagnosed in 57 patients, focal-epilepsy in 49, frontal in 21, posterior cortical in 18, multifocal in 7 and generalized epilepsy in 2 patients.

Results: Thirty-four patients (22.1%) reported a significant improvement in seizure control, 46 (29.9%) improved, 61 (39.6%) did not change, 10 (6.5%) deteriorated and 3 (1.9%) deteriorated significantly. Five patients reported seizure freedom for one year, 9 patients reported seizure freedom for 2 years and 13 patients reported seizure freedom for more than 2 years, 10 patients reported seizure remission, 3 of these 10 had AEDs withdrawn. In the long-term follow-up, 75% of the patients had AEDs changed either by adding new AEDs or by changing the AEDs prescribed to them prior to monitoring. Independent predictors of seizure freedom were age at epilepsy onset and the number of different seizure types a patient had.

Conclusion: A substantial number of patients with refractory epilepsy prior to video-EEG monitoring may improve over the years that follow. This may be the consequence of optimization in seizure control by revaluating the epilepsy syndrome and prescribing the appropriate medical treatment as well as the result of spontaneous fluctuations in the course of the disease.

p521
CAUSES OF MORTALITY IN 1921 PATIENTS WITH CHRONIC EPILEPSY DURING 12 YEARS

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Purpose: To determine frequency and causes of death among patients with chronic epilepsy treated in large outpatient clinic of a single neurologist during a 12-year period.

Method: Charts of patients with chronic epilepsy who had at least 2 visits separated by at least 6 months in outpatient clinic of DVS during 12 years were retrospectively reviewed. Frequency and causes of mortality were determined. For patients who missed their appointed visit telephone contacts with patient, family members or referring doctors were attempted.

Results: There were 1921 patients with chronic epilepsy during 12 years. Death was ascertained in 28 (1.46%) patients. Causes of death were brain tumor in 8, systemic carcinoma in 4, bacterial infection in 3, advanced multiple sclerosis in 2, complications of status epilepticus in 2, possible SUDEP in 1, and various causes in 8 patients. The last visit occurred during year 2009 in 643 (3 deaths; 0.46%), between 2008 and 2005 in 647 (15 deaths; 2.31%), between 2004 and 2001 in 444 (7 deaths; 1.58%), and between years 2000 and 1998 in 353 (3 deaths; 0.85%) patients. Nine patients were older than 50 years of age. Only in 3 out of 28 (10.7%) death was associated with seizures (2 with status epilepticus and 1 with possible SUDEP).

Conclusion: Although one-third of patients were not seen for more than 5 years, it appeared that mortality in patients with chronic epilepsy was low and usually associated with serious underlying disease.

p522
LENNOX-GASTAUT SYNDROME IN ADULTHOOD: A CROSS-SECTIONAL STUDY

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Purpose: To delineate characteristic features of Lennox-Gastaut Syndrome (LGS) in adulthood, and compare patients with classical age of onset (cLGS), defined as ≤6 years, to those with late-onset LGS (loLGS), defined as >6 years.

Method: We identified 151/5373 (2.8%) patients with LGS, treated at Innsbruck Medical University from 1975–2003. Information was collected on: sex, age at onset, seizure types, history of convulsive/nonconvulsive status epilepticus, family history, neurological status, etiology, seizure outcome, social status, EEG and brain imaging. Clinical characteristics of cLGS and loLGS patients were compared over a median follow-up of 17 (range 0–22) years.

Results: Ninety-nine of one hundred fifty-one (65.6%) patients (51M/48F) had cLGS, with mean ± SD onset at 2.2 ± 1.5 (median 2; range 0.5–6) years, and 52/151 (34.4%) patients (23M/29F) had loLGS, with mean ± SD onset at 12 ± 4 (median 12; range 6–28) years. Only 18/151 (11.9%) patients achieved seizure freedom during the year before last follow-up. For cLGS versus loLGS: symptomatic etiology was more common (70% vs. 50%; $p = 0.024$); social outcome, in terms of requirement for permanent care, was poorer (43% vs. 15%; $p < 0.001$); and patient independence was less common (4% vs. 13%; $p = 0.047$). No differences were found between groups regarding seizure types, family history, neurological status, treatment, seizure outcome, or EEG/brain imaging data.

Conclusion: Age at seizure onset was >6 years in approximately one third of LGS patients. Seizure outcome was generally unfavorable. Patients with cLGS were less well socially integrated than those with loLGS.

This abstract was supported by Eisai.

p523

IN 29.3% OF 65 PATIENTS THE PREVIOUS DIAGNOSIS OF A THERAPY-RESISTANT GENERALIZED EPILEPSY HAD TO BE REVISED—FOCAL SEIZURE ONSET COULD BE PROVED BY MEANS OF VIDEO-EEG AND MRI

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Purpose: Due to the facts that therapy-resistant generalized epilepsies (TRGE) are quite rare and focal epilepsies may mimic generalized epileptic syndroms, the aim of this study was to determine the percentage of so far unrecognized focal epilepsies in patients with the diagnosis of a TRGE.

Method: We evaluated the medical inpatient records of the last 6 years with the admission-diagnosis of a TRGE concerning the final diagnosis, seizure semiology, (video-)EEG, MRI, age of epilepsy onset, synopsis of antiepileptic medication and family history of epilepsies. Therapy resistance was defined as ongoing seizures despite of sufficient treatment with at least two antiepileptic drugs.

Results: Sixty-five patients (43 women, 22 men, age 18–74, median age 31) were included. In 19 patients (29.3%) diagnosis was revised and a focal seizure onset (FSO) was proved. No significant difference between the two groups with regard to median age of onset, median number of antiepileptic drugs prior to admission and family history of seizures was found.

In FSO-patients EEG exhibited focal abnormalities in 63% and exclusive generalized pathologies in 32% (vs. 17% and 59% in TRGE). MRI in FSO-patients showed relevant findings in 21% (two times focal cortical dysplasias, bilateral hippocampal sclerosis, bifrontal atrophy). 95% of the FSO-patients presented with generalized tonic–clonic seizures. Complex partial seizures (misinterpreted as absence-seizures) occured in 53%, unquestionable auras in 31%, tonic seizures in 21% (vs. 0%, 0%, 0% in TRGE).

Conclusion: Rate of false diagnosis in patients suspected to have a TRGE is high (29.3%). (Video-) EEG and MRI are helpful for differential diagnosis.

p524

LONG-TERM MORTALITY IN PEOPLE WITH EPILEPSY

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Purpose: It is generally accepted that the standardized mortality ratio (SMR) is increased in people with epilepsy, and is highest soon after diagnosis. Most studies of mortality in epilepsy have been retrospective hospital based. We estimated SMRs for a prospective community-based population up to 24 years after the initial suspicion of an epileptic seizure.

Method: The National General Practice Study of Epilepsy was established in 1984 to follow people in the community with newly suspected epileptic seizures. The study has followed 792 people whom we categorized as having definite or probable epileptic seizures, and 220 with febrile seizures, for up to 24 years.

Results: The overall SMR is significantly raised (2.2, 95% CI 2.0, 2.5) for people with definite or probable epilepsy. It is highest in people with neurological deficits present at birth, but also increased in those with acute symptomatic and remote symptomatic seizures. It is slightly but significantly raised (1.7, 95% CI 1.3, 2.1) in people with idiopathic or cryptogenic seizures, but not in people with febrile seizures.

SMRs decreased initially, but our data show that they are significantly increased in people with definite and probable epilepsy, and in those with idiopathic or cryptogenic seizures at 20–24 years after the initial seizure. The SMRs for those with definite epileptic seizures appear to be significantly raised overall in all age groups.

Conclusion: In this community based study, many people are in long-term remission. Nevertheless, the SMRs are significantly raised over 20 years later.

p525

EPILEPSY AND EEG ABNORMALITIES IN 104 CHILDREN WITH AUTISM SPECTRUM DISORDERS

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Relationship between epilepsy, autism and regression remains a complex and controversial subject. Some studies suggested that clinical and subclinical epilepsy may be a causative factor of regression in autism.

Retrospective study of children with autistic spectrum disorders, during a 16 year period (1993–2008). Age, sex, autistic regression, presence of epilepsy and EEG abnormalities were analyzed.

One hundred four children were found in the study period: 79M/25F. Age in first consultation was less than 24 months in 19 children; between 24 and 48 months in 54 children and more than 48 months in 31 children. Autistic regression was observed in 32.6% children (34/104). Epilepsy was observed in 12 (11.5% of total). We did not found significant difference between the group of children who regressed compared with the group who did not regressed, regarding the presence or absence of epilepsy. 59 children were investigated with sleep EEGs and in 12 epileptiform abnormalities were found. Once again, a significant difference in epileptiform activity in children who showed regression was not observed.

In our series, we did not find supportive evidence that epilepsy is a direct causal factor of regression in children with nonsyndromal autism. However, paroxysmal events in children with autistic spectrum disorders should be investigated with sleep EEG, as the prevalence of epilepsy in this group is higher. When epileptic EEG abnormalities are found during the investigation of a child with autistic features with or without regression and no history of seizures their significance remains unknown.

Poster session: Epilepsy syndromes in children and adults IV
Wednesday 30th June 2010
13:30–14:30

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EPILEPTIC SEIZURES WITH DISSOCIATIVE-LIKE BEHAVIOR

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Purpose: Bizarre behavior during prolonged epileptic aura may be misdiagnosed as psychogenic non–epileptic seizure (PNES). The aim of our study was to identify patients with dissociative-like behavior during aura and describe their clinical characteristics.

Method: Epilepsy patients whose behavior during aura was interpreted as dissociative-like were included into the study. Their clinical characteristics and seizure semiology were assessed.

Results: In series of 1175 consecutive patients examined since 1999 at video-EEG monitoring unit six patients with dissociative-like behavior during epileptic seizures were identified. All of them suffered from focal or multifocal epilepsy. Typical electroclinical characteristics of their seizures were as follows: They reported experience of their typical aura that

was lasting (minutes to tens of minutes). In that time there was no ictal EEG scalp pattern and the behavior of patient expressed typical signs of PNES - bizarre or violent movements, emotionally tuned vocalization, etc. This behavior was stereotypical in individual patients and finally evolved into another seizure type (complex partial or secondary generalized) with typical semiology and EEG ictal pattern.

Conclusion: Dissociative-like behavior during aura represents relatively rare condition in focal epilepsy patients. However, the correct diagnosis may not be always straightforward. We presume that this behavior pattern resulted from direct activation of autonomic centres or reflected patient's reaction to unpleasant feeling during aura. The correct diagnosis of epilepsy is based on video-EEG monitoring and seizure evolution confirming transition to obvious epileptic seizure.

p527
ELECTROENCEPHALOGRAPHIC MANIFESTATIONS AND THEIR PROGNOSTIC SIGNIFICANCE IN IDIOPATHIC CHILDHOOD OCCIPITAL EPILEPSY OF GASTAUT (ICOE-G)

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Purpose: To investigate the electroencephalographic (EEG) manifestations and their prognostic significance in ICOE-G.

Method: EEG and clinical analysis of ICOE-G manifesting with occipital seizures starting with elementary visual hallucinations (EVH). Patients were assessed from data collected over the last 33 years on children with onset of afebrile seizures between 1–16 years.

Results: Of 22 patients (prevalence around 1%) with at least one occipital seizure starting with EVH, 19 were classified as ICOE-G including 3 with clinically photosensitive occipital epilepsy. The remaining 3 patients with rolandic epilepsy (1) or Panayiotopoulos syndrome (2) were not included. Of 19 patients with ICOE-G only 4 had the classical occipital paroxysms—one in combination with generalized discharges, photoparoxysmal and spontaneous occipital spikes (OS). Five patients had photoparoxysmal OS alone (2) or in combination with spontaneous OS (1) or spontaneous OS and generalized discharges (2). Two patients had spontaneous OS—one in combination with C4, Cz, C3 spikes. Five patients had consistently normal EEGs while 3 had nonspecific (2) or generalized photoparoxysmal discharges (1). Only 4 patients had remission of seizures before the age of 17 years and 7 patients also developed other types of generalized seizures. Prognosis was not associated with a specific EEG pattern whether abnormal or normal.

Conclusion: The interictal EEG patterns of even this purest form of ICOE-G with EVH are much more diverse than it is generally reported. Furthermore, none of the EEG findings seem to correlate with the clinical outcome that in half cases is protracted beyond adolescence.

p528
PROGNOSTIC SIGNIFICANCE OF INITIAL EEG IN CHILDHOOD ABSENCE EPILEPSY

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Purpose: To investigate whether the initial EEG features allow to predict the prognosis in childhood absence epilepsy.

Method: We enrolled 21 newly diagnosed children with childhood absence epilepsy who were followed up more than 1 year. EEG features included 3 Hz spike and waves, OIRDA, photoparoxysmal response, fragments of generalized or focal epileptiform discharges. We evaluated the prognosis by seizure freedom and EEG normalization.

Results: There were 21 children (M 5, F16) with childhood absence epilepsy. Mean age of onset and duration of follow-up were 7.58 and 3.65 years. Twenty of 21 children (95.2%) became seizure-free at last follow up. Among EEG findings, shorter duration of 3 Hz spike and waves ($p = 0.01$) and absence of fragments of generalized epileptiform discharges ($p = 0.04$) were good prognostic factors for seizure control. OIRDA, photoparoxysmal response, and focal epileptiform discharges were not associated with prognosis for seizure control. For EEG normalization, the children with duration of 3 Hz spike and waves longer than 20 s ($p = 0.03$) or interval between start of hyperventilation and appearance of epileptiform discharges ($p = 0.04$) were good prognostic factors.

Conclusion: Shorter duration of 3 Hz spike and waves and absence of fragments of generalized epileptiform discharges are good prognostic factors for seizure control, while longer duration of 3 Hz spike and waves and interval between start of hyperventilation and appearance of epileptiform discharges are good prognostic factor for EEG normalization.

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ABSENCE SYNDROMES IN CHILDHOOD AND ADOLECENCE: CLINICAL COURSE AND EARLY RESPONSE TO TREATMENT

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Purpose: To follow the clinical course of children and adolecents with absence syndromes, estimate the percentage of patients entering remission with monotherapy or combination of antiepileptic drugs (AEDs) and identify prognostic factors of early remission.

Method: The study population consisted of 65 children, 34 girls and 31 boys, 3–14 years old (mean 6.94 years) with Childhood Absence Epilepsy (CAE) or Juvenile Absence Epilepsy (JAE) syndrome. All children received treatment with one or more AEDs. The patients were divided into three groups: 1) *with remission* (seizure-free for at least 1 year), 2) *with relapse* (recurrence of seizures after at least 1 year's remission) and 3) *without remission* (never seizure-free).

Results: Patients included in the study were followed up for a mean of 2.75 years. Sixty children were diagnosed with CAE and five with JAE. Among the group of children with CAE, 86.7% (N = 52/60) achieved remission, (80.8% with monotherapy and 19.2% with a combination of AEDs), 8.3% (N = 5/60) had a relapse and 5% (N = 3/60) never achieved remission. All children (N = 29/29) with seizure onset at the age of early school years (6–9 years) achieved remission, while children with seizure onset at preschool years (4–6 years) had a 70% remision, 22% relapse and 8% no remission at all.

Conclusion: The clinical course of absence syndromes in childhood and adolecence is benign, with over 85% of children achieving remission. Onset of seizures during the age of 6–9 years exhibits a more favorable response to treatment compared with seizure onset at the preschool years.

p530
ICTAL SPECT IN MYOCLONIC ABSENCE SEIZURES

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Purpose: Epilepsy with myoclonic absence (EMA) is a rare epileptic disorder characterized by the unique seizure type of myoclonic absence (MA). The pathophysiology of MA in patients with EMA is still unknown. This study aims to elucidate pathophysiological mechanisims implicated in MA using neuroimaging procedure.

Method: Two EMA patients (1 female (patient A), 1 male (patient B)) were evaluated. Age at the evaluation was 5 years (A) and 7 years (B), respectively. Each patient presented with more or less asymmetric features during MA. Patient A occasionally turned her head to left. Patient B constantly exhibited right predominant elevation of arms, head deviation to right, and right orofacial twitching. Such asymmetry was consistent from seizure to seizure in each patient. We perfomed ictal and interictal ^{99m}Tc-ECD single photon emission computed tomography (SPECT) and evaluated cerebral blood flow (CBF) change topographically during MA as compared to interictal state, by means of subtraction ictal SPECT coregistration to MRI (SISCOM) and brain easy analysis tool (BEAT).

Results: In patient A, CBF increased in left thalamus and right lenticular nucleus. In patient B, CBF increased in right thalamus, right lenticular nucleus and left precentral gyrus, and decreased in bilateral frontal lobes.

Conclusion: Involvement of motor cortex and basal ganglia may contribute to unique motor symptoms in MA, in addition to thalamocortical mechanism of absence seizure.

p531
SOMATIC COMPLAINTS IN PATIENTS WITH IDIOPATHIC EPILEPSIES OF CHILDHOOD ONSET

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Purpose: To investigate the prevalence of somatic complaints in patients with typical absence epilepsy or benign childhood epilepsy with centrotemporal spikes.

Method: The somatization scale from the SCL-90R questionnaire was administered to 42 patients (Mean age = 13.78 years, SD = 2.03), 26 of whom were boys, 19 with absence epilepsy. Items were rated using a Likert 5-point scale ranging from 1 (not true at all) to 5 (very true). Chi-square analysis was performed to test for differences in somatic complaints between the two epilepsy types, gender and family situation (parents married or divorced).

Results: Twenty patients complained of headaches, 5 of faintness/dizziness, 6 of lower back pains, 3 of nausea/upset stomach, 7 of sore muscles, 2 of trouble getting their breath, 11 of weakness in parts or their body and 2 of heavy feeling in their arms/ legs. There were no statistically significant differences in somatic complaints between the two epilepsy types. Only headaches ($x^2 = 9.29$, $p < 0.05$) and lower back pain ($x^2 = 8.47$, $p < 0.05$) appear to correlate with family situation and nausea/upset stomach with gender ($x^2 = 5.25$, $p < 0.05$).

Conclusion: Headaches and bodily weakness were the main somatic complaints within our patients; epilepsy type didn't correlate significantly with specific somatic complaints. Children of divorced parents reported more headaches and lower back pains; girls complained more frequently of nausea and upset stomach. These findings indicate that, in this group of epilepsy patients, characteristics such as family situation should be taken into account when somatic complaints are reported.

p532
MONOZYGOTIC TWINS WITH JUVENILE MYOCLONIC EPILEPSY - REMARKABLE SYNCHRONY OF BIOLOGICAL CLOCKS

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JME is classified as a distinct syndrome of the IGE. JME is characterized by myoclonic jerks on awakening, GTCSs and sometimes typical absences. The background EEG activity is usually normal, the typical ictal pattern is bilateral symmetric polyspike-wave complex with frontocentral accentuation.

The lack of obvious exogenous etiological factors and high concordance rate for monozygotic twins (0.7–1.0) suggest very high impact of genetics in the etiopathogenesis. 17–50% of the patients have positive family history.

In 20 monozygotic twin pairs reported by Berkovic et al. of whom at least 1 had IGE, 13 (65%) were clinically concordant.

The case: Two boys-twins: their mother suffered few GTCS during her adolescent age. Their development was normal. In the age of 13 years (2001) one boy suffered his first GTCS after awakening. When the emergency arrived, his brother fell into the same type of seizure. The time gap between the two seizres was less than 30 min. The EEG proved generalized PSW (accentuated by photic stimulation) and the CT was normal. The boys reported morning myoclonias of upper extremities even retrospectively before their GTCS. Valproate improved their clinical state promptly and the boys are seizure-free.

Recently, the DNA analysis proved the twins to be monozygotic.

Conclusion: We observed remarkable concordance in monozygotic twins with the JME not only in the diagnosis itself, but also in the seizure onset timing. The synchrony of biological clocks of the two boys was almost perfect. Their mother had first seizure also in similar age.

p533
HOW FREQUENT IS FATIGUE IN PATIENTS WITH EPILEPSY? A CLINICAL STUDY TO MEASURE ITS SEVERITY, IMPACT AND PHENOMENOLOGY

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Purpose: To validate the Fatigue Symptom Inventory-FSI, the Fatigue Assessment Instrument-FAI and the Fatigue Severity Scale-FSS) in people with epilepsy.

Method: This study was a cross-sectional study. We used concurrent validity. We applied the three selected questionnaires plus the Beck Depression Inventory (BDI) in 63 patients with epilepsy, 33 healthy patients and 52 patients with different neurological conditions. Reliability was assesed for the three questionaires. Pearson's correlations were used for the validation analysis. The reliability was asses also with Pearson's correlations. Cronbach's alpha was used to evaluate internal consistency.

Results: We studied 153 patients. The scores of the FSI in patients with epilepsy was 4.28 ± 1.36, in patients with other neurological conditions was 4.6 ± 1.5, and in healthy patients was 2.68 ± 1.16. The corresponding scores for the FAI were 3.99 ± 2.07, 4.5 ± 1.98 and 2.2 ± 1.28. For the FSS 4.5 ± 1.19, 4.46 ± 1.21, and 3.03 ± 1.08. The correlation between FSI and the BDI in patients with epilepsy was 0.48, for the FAI and the BDI was 0.53 and for the FSS and the BDI was 0.57, all of them were statistically significant ($p < 0.05$). The correlation scores in patients with epilepsy. (reliability analysis) were .81, .80 and .82 ($p < 0.05$) for the FSI, FAI and the FSS

Conclusion: Patients with epilepsy have significant higher scores of fatigue than healthy patients but comparable with other neurological conditions. The scores of the instruments explored in this study have and adequate correlation with the BDI. The selected questionnaires could potentially be used in studies of patients with epilepsy to measure fatigue.

p534
PROLONGED CORTICAL SILENT PERIOD (CSP) IN PATIENTS WITH GENERALIZED OR PARTIAL EPILEPSY

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Purpose: A lengthened CSP was found in untreated patients with idiopathic generalized epilepsy (IGE). However, normal CSP was reported in patients after a first-ever generalized seizure, and cryptogenic partial epilepsy (PE). In this study, we used transcranial magnetic stimulation (TMS) to investigate the difference of cortical excitability between patients and normal.

Method: Recruited 55 drug-naive patients with epilepsy and 32 normal subjects. Measured TMS parameters including resting motor threshold (RMT), motor evoked potential (MEP) amplitudes, cortical silent period (CSP), intracortical inhibition (ICI) and facilitation (ICF).

Results: In epilepsy patient and control groups, the CSP was lengthened linearly with increases of stimulus intensity in both hemispheres. In IGE patients, interhemispheric differences of CSP were not found ($p > 0.05$). However, the mean CSP was longer in IGE patients ($p < 0.05$). The mean CSP was significantly shorter in ipsilateral hemisphere to epileptic focus (IH) than that in contralateral one (CH) at 120% ($p = 0.028$) and 140% of RMT ($p = 0.003$). Mean CSP duration in CH was significantly longer at the stimulus intensities 120–150% of RMT and that in IH was longer only at 120% of RMT than that of normal ($p = 0.005$). Between PE and IGE patients, there were no significant differences of CSP. RMT, MEP, ICI, and ICF were not different among IGE, PE, and normal.

Conclusion: These suggest that the CSP may have a lateralizing value in partial epilepsy by shorter CSP in the epileptic hemisphere. Prolonged CSP in epilepsy patients compared to normal may indicate the abnormally increased interictal cortical inhibition in human epileptic brain.

p535
SEIZURES AND NEUROLOGICAL OUTCOME IN PATIENTS WITH CONGENITAL MELANOCYTIC NAEVI (CMN) AND CENTRAL NERVOUS SYSTEM (CNS) MELANOSIS

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Purpose: A congenital melanocytic naevus (CMN) may be associated with foci of melanocytes in the central nervous system (CNS) and associated with neurological symptoms or be asymptomatic. Study aims to Determine the seizure characteristics and outcome of patients with a CMN and CNS melanosis.

Method: Retrospective case note review.

Results: Twelve patients (6 male and 6 female) with a CMN and MRI showing CNS melanosis were identified. The age at referral was 6–91 months (median 14.5). Six (50%) had seizures. Age of seizure onset was 1–54 months (median 12 months). Seizures were focal in three and generalized in three. Four had only occasional seizures whilst one had 15 seizures/day. The number of antiepileptic drugs tried was 0–4 (median 2). Four had mild global developmental delay or learning difficulties. Three had behavioral problems and one had ADHD. 59% of patients had amygdala lesions. Other sites were the thalamus, hippocampus, temporal lobe, pons and cerebellum. Five of those with seizures had amygdala lesions. One male aged 14 years underwent a left temporal lobe resection with complete resolution of seizures at 1 year follow up. Histology confirmed cerebral melanosis.

Conclusion: 50% of those with CNS melanosis had a history of seizures with the amygdala being the most frequent site of melanosis. In the majority seizures were self limiting or controlled with medication. In one case with frequent seizures epilepsy surgery was successful.

Poster session: Social issues I
Wednesday 30th June 2010
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EPILEPSY NURSE SPECIALIST IN SWITZERLAND: THE DEVELOPMENT OF A NEW ROLE

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Purpose: Self-management education is recommended as standard care for patient with epilepsy in international guidelines (NICE). Goals are to empower the patients to cope with physical, emotional and psychosocial burden of the disease and to improve their self-esteem and quality of life. In order to develop a concept for an outpatient counselling program that introduces a Clinical Nurse Specialist in Epilepsy (CNSE) to pursue standard care literature has been reviewed.

Method: A literature search focused on content of self-management education programs as well as the role and competencies of the CNSE. Included were 11 scientific, six nonscientific articles and one guideline. Additionally, work shadowing with a CNSE in England completed the review.

Results: Content of self management education contain themes such as medication regimen, seizures, independency, information, general heath, lifestyle and safety. Core tasks of the CSNE included patient education and staff training. Diverse work models ranging from hospital based care to nurse-led clinics with independent prescription rights were described. CNSE nurses were known in some countries for up to 30 years and showed to improve for patients' knowledge/skills and quality of life.

Conclusion: Nurses with advanced level of practice have been shown to be beneficial for patients with epilepsy and their families. The reviewed literature as well as the practical experiences of a CNSE, were pivotal to develop a concept for ''Swiss'' CNSE. The findings on content can directly be applied to the Swiss health care system, whereas the scope of practice has to be adapted to Swiss regulations.

p537
INCIDENCE OF EPILEPSY IN ESKISEHIR, TURKEY AFTER 15 YEARS OF AGE

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Purpose: The aim of this study was to establish the incidence rate, incidence-related characteristics, and epidemiological profile of epilepsy in Eskisehir, Turkey.

Methods: Cases were prospectively recorded by utilizing multiple data sources, including case records obtained through the Hospital Informa-

tion System, files kept by family physicians, and files kept by private neurologists. Patients diagnosed with epilepsy, living in Eskisehir for more than one year between July 1, 2007 and June 30, 2008, and above the age of 15 years were included in the study.

Results: In total, 219 new cases were diagnosed with epilepsy. The adjusted incidence rate was 34.44 cases per 105 persons in males and 42.79 cases per 105 persons in females, for a total 38.07 cases per 105 persons. The incidence rates according to age were found to be greatest among the 15–19 year age group and the 70 ≥ age group. Among males, the age-specific incidence was higher in the elderly than among the younger age groups. Among females, the highest incidence rate was found in the 15–19 year age group. Cumulative incidence rates for all cases of epilepsy were 1.7% for ages 15–19 and 7.3% for ages 70 ≥. Partial seizures were observed more than generalized seizures after the age of 40. Unknown etiology accounted for 77.2% of the epilepsies. Stroke was the most common etiological cause of epilepsy among the symptomatic group.

Conclusion: The incidence rate of epilepsy in Eskisehir was comparable with the rates reported for developed countries.

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PAST AND PRESENT PUBLIC KNOWLEDGE AND ATTITUDES TOWARD EPILEPSY IN ITALY

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Purpose: A nationwide survey was performed in Italy to assess awareness and attitudes of the public about epilepsy.

Method: A telephone interview was conducted by a marketing research agency using a multistage clustered sample. A 19-question form was used investigating generic knowledge about epilepsy and familiarity with the disease, its clinical features, and attitudes towards its social and individual implications.

Results: Included were 819 women and 737 men aged 18 years or older. 93.4% declared they knew epilepsy, 56.6% knew a person with epilepsy, and 45.1% saw someone sizing. Only 29.2% gave an exact estimate of the prevalence of the disease. 50.4% were unaware of the causes, 56.1% indicated epilepsy a psychological/psychiatric disease, 36.5% a form of insanity, and 4.1% an evil spirit possession. Epilepsy was incurable according to 35.5%. Moderate-to-severe restrictions to driving, regular employment, military career, and leisure activities were suggested by 79.8, 57.0, 71.1, and 57.6%. Limitations included marriage and procreation for 46.2 and 38.7%. These findings are partly in keeping with other worldwide reports. Knowledge and attitudes changed with education, age and gender.

Conclusion: Awareness and attitudes towards epilepsy in Italy partly overlap those of other countries and vary according to population demographics and sociocultural characteristics.

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THE KNOWLEDGE OF AND ATTITUDES TOWARD EPILEPSY AMONGST UNIVERSITY STUDENTS

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Purpose: Several studies has suggested that measuring the knowledge and attitudes toward epilepsy in a society is a necessary initial step in ameliorating the understanding of and eliminating discrimination surrounding this condition, thus improving the quality of life of these individuals. The aim of the study was to explore the knowledge and attitudes toward epilepsy in students reading for a Bachelor of Education in Primary studies at the University of Malta.

Method: By using a descriptive design, a thirty eight-item self administered questionnaire was delivered to a convenience sample of 36 s and third year students.

Results: Moreover, the results showed that even though all the respondents claimed to know about epilepsy, there was significant deficits in terms of familiarity and specific knowledge. The majority of respondents (85%) considered epilepsy as a condition from which people rarely recover and which hinders employment eligibility. Responses to a series of attitude related questions and statements indicated that while most held favorable attitudes, 14% objected to a relative from marrying someone with epilepsy or would not disclose a relative's epilepsy. Three respondents were reluctant to teach a student with epilepsy. Furthermore, 55% believed that persons with epilepsy are more likely to have belligerent and antisocial traits. These responses were predominantly influenced by participants' previous experience with epilepsy in terms of seizures ($p < 0.05\%$).

Conclusion: These findings compare similar surveys in other countries concerning students' perceptions about epilepsy, and provide a useful starting point for future population-based surveys and educational campaigns in Malta.

p540
ENHANCING QUALITY, SAFETY AND EFFICIENCY OF EPILEPSY CARE IN IRELAND USING INFORMATION AND COMMUNICATIONS TECHNOLOGY

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Purpose: This study examined the structures and processes of epilepsy care in Ireland, to better understand the service, how it could be improved and how information and communications technology (ICT) such as an electronic patient record (EPR) could be utilized, to maximize quality, safety and efficiency of epilepsy care.

Method: Engagement via questionnaires, meetings, interviews and literature reviews with patients, patient representatives, general practitioners, hospital-based service providers, experts in healthcare services and health informatics were conducted. These interactions provided an analysis of the business of epilepsy care in Ireland and informed the requirements for an epilepsy EPR that is now in daily use supporting clinical care and research in the epilepsy service at Beaumont Hospital, Dublin.

Results: Preimplementation of the EPR, sharing and communication of patient information within and across healthcare agencies was limited by paper-based records. Postimplementation, the quality, availability and communication of information have improved and a service that is more responsive to patient needs is developing. More clinicians have access to the same information thus promoting a model of shared epilepsy care. Faster advice to the patient and their carers can be provided thus improving safety and continuity of care.

Enhanced referral and discharge processes have resulted from better understanding of structures and processes of epilepsy care; this has led to increased access to specialist epilepsy care.

Conclusion: The efficient use of ICT can improve quality, safety and efficiency of epilepsy care and therefore help provide a more valuable and effective service for the same resources.

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EPILEPSY CARE IN A RURAL AREA OF TOGO

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Purpose: To evaluate special aspects of epilepsy care and report characteristic patient histories influenced by traditional beliefs in a rural area in Togo.

Methods: We report a series of 58 epilepsy patients first seen in the health center Hôtel Dieu, Mome Katihoe, between 2004 and 2010. Included were patients in whom detailed medical history and clinical examination were obtained. Classification of seizures and epilepsy syndromes were based on these and additionally on EEG in 29/58 patients. Decisions about beginning of antiepileptic drug treatment and choice of drugs were based on these data, taking into account the availability of the choosen drug and the individual patient's conditions. During regular clinical visits a long term follow up over a term of 0.2–6 years was obtained.

Results: Of 58 patients 27 were male, mean age was 18.6 years, mean duration of epilepsy 9.3 years. 32.8% of patients had a positive family history of epilepsy. 75.9% had been treated by traditional healers before the first visit. 8.6% had sequela like burns. 43.1% of patients were impaired severely in their social participation. EEG was performed in 50% of patients and provided information for syndromatic classification in 36.2%. Mean seizure reduction after onset of treatment was 88%. 46.5% received PB, 37.9% other AED.

Conclusion: Traditional beliefs and customs delay onset of antiepileptic treatment and have a strong impact on outcome of epilepsy patients in Togo. Initiation of modern antiepileptic treatment is effective. EEG as additional diagnostic tool improves the reliability of syndrome classification significantly.

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TREATING EPILEPSY ON BOARD A TRAIN IN INDIA'S UNDERSERVED HINTERLANDS: CAN THIS BE A SUSTAINABLE AND SUCCESSFUL MODEL FOR EPILEPSY CARE DELIVERY IN INDIA?

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Purpose: A 70–80% treatment gap for epilepsy in India is largely due to a lack of awareness and a predominantly rural population which cannot access the largely urban health facilities. The purpose of this ongoing endeavor is to explore if epilepsy education and treatment can be successfully provided by a 'train-hospital' to the Indian villages. India has 6909 railway stations over a total route length of more than 63,327 kilometers.

Method: A 2–3 day epilepsy education and screening programme has been conducted at each of Lifeline Express's (train-hospital) destinations since June 2009. Villagers at each stop have been persuaded and incentivized to attend an epilepsy clinic on the train. A structured questionnaire has been developed, validated and pilot-run and is being used to explore epilepsy related knowledge, attitudes and practices across the country.

Results: To date, 693 PWE have been seen in 4 villages. There have been 310 females and 189 children. In this sample, 48% were drug naive and 17% were on irregular treatment. Nonavailability of medications(83%), financial hardships(58%), a belief that AEDs are ineffective (46%), lack of information about epilepsy(76%), prevalence of faith healing(76%) and ignorance about the importance of compliance (49%) were the main causes of the treatment gap. Significant differences between villages has been noted.

Conclusion: Use of the extensive railway network may be effective for spreading epilepsy awareness and narrowing treatment gap in India. This is an ongoing project being developed as a 'hub and spokes' programme enlisting medical/paramedical staff available in the rural community.

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EPILEPSY CARE IN IRELAND: A REGIONAL AUDIT OF GENERAL PRACTICE RECORDS

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Purpose: Epilepsy affects up to 40,000 individuals in Ireland. While concerns are frequently expressed internationally regarding the quality and consistency of epilepsy care little or no evidence specific to Ireland exists. This study examined the role played by Irish primary care clinicians in the provision of care to people with epilepsy (PWE).

Method: Two hundred fifteen general practitioners (GP) registered in the Mid-West region of Ireland were invited to participate in the study. A standard proforma was employed to collect and analyze the quantity and quality of epilepsy specific information in GP records of PWE.

Results: 60 (28%) GP practices consented to participation in the audit, 58 (27%) declined, 97 (45%) did not respond to the invitation. There was a paucity of specific information relating to epilepsy in patient records. For example, antiepilepsy drug history and epilepsy classification information required for good management was conspicuously absent. 13 (11%) GPs maintained a register for PWE while 7 (6%) ran a recall system. Many PWE were treated without any neurology specialist intervention. Documentation specific to counseling PWE regarding psychosocial issues was rare.

Conclusion: These findings suggest that primary care in Ireland does not have a strong role in epilepsy care. Given the drive to transform healthcare services and promote more integrated care, this requires attention. Continuity of care for PWE could be improved by establishing national shared care networks between healthcare sectors which is supported by the principles of effective chronic disease management. However this requires clear definition and establishment of roles and responsibilities.

Poster session: Social issues II
Wednesday 30th June 2010
13:30–14:30

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PUBLIC AWARENESS, ATTITUDES AND PRACTICE WITH RESPECT TO EPILEPSY IN THE KUMBO WEST HEALTH DISTRICT, NORTHWEST REGION, CAMEROON

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Purpose: This study was part of a series mandated by the Cameroon National Epilepsy Control Programme. It aimed at obtaining baseline data on public awareness, attitudes and practice towards epilepsy, to inform the development of an education programme on epilepsy for communities.

Method: We carried out a community-based study during which 401 nonepileptic adults in the Kumbo West Health District were interviewed using a 12-item questionnaire in English.

Results: Ninety-eight percent of respondents had heard about epilepsy, but only 10.2% had read on it. About 83% of participants knew someone with epilepsy while 78.1% had witnessed a seizure. About half (56%) of our informants would object to their child associating with PWE, much more 61.6% would object to their child marrying a person who sometimes has seizures. While 52.6% will offer equal employment to PWE, 56.9% thought there are jobs not suitable for PWE. Waste gas (32.4%) was the main mode of transmission, and foaming of the mouth (43%) was the most recognized sign of epilepsy. Many (53.1%) believed epilepsy could be cured and 77.1% of informants recommended modern medicine for treatment.

Conclusion: The relatively high awareness on epilepsy might reflect the importance of the problem in this area. False beliefs prevail and seem to be responsible for the high level of prejudice towards PWE. This prejudice rate is among the highest in the world. These findings confirm the urgent need for an education program which considers beliefs and value systems in the area, aimed at improving attitudes epilepsy.

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ASSESSMENT OF NEEDS OF PEOPLE WITH EPILEPSY, MEMBERS OF THE ASSOCIATION OF PARENTS WITH CHILDREN WITH EPILEPSY IN BULGARIA

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Purpose: The purpose of the study was to assess the unmet needs of the members of the Association of Parents with Children with Epilepsy (Bulgaria) regarding medical, psychological and social services.

Method: The study asked for the way the participants envisioned the role of the Association in provision of those services. The researchers used qualitative and quantitative data collection methods; 90 children and adults with epilepsy and their relatives participated in the study.

Results: The findings suggest that the most affected members of the Association see the organization as the major tool for facilitating access to services; for providing essential information about the medical treatment and most recent interventions in the field as well as for ensuring advocacy for seeking access to treatment in abroad. Adolescents need social contacts and information about intimate relationships. Relatives of people with epilepsy think that day care centers that offer individual casework would prevent placement of children with disability in institutions.

Conclusion: There is a tendency for unrealistic expectations towards the Association. This tendency can reflect the expectations for a total care inherited from the socialist years in Bulgaria.

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KNOWLEDGE, ATTITUDES AND PRACTICE WITH RESPECT TO EPILEPSY AMONG SECONDARY SCHOOL STUDENTS IN THE KUMBO WEST HEALTH DISTRICT - NORTHWEST REGION, CAMEROON

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Purpose: The main purpose of this study was to obtain baseline data on awareness and attitudes and practices with respect to epilepsy among secondary school students.

Method: We interviewed a total of 659 students from three randomly selected secondary schools in the Kumbo West Health District, using a 12-item questionnaire in English.

Results: About 94.7% had heard about epilepsy, 25.8% had read on the subject, 55.2% knew someone with epilepsy and 77.7% had witnessed a seizure. While 37.9% of students would object to association with people with epilepsy (PWE), 47.8% would object to marriage with PWE. About 77.2% would offer equal employment to PWE although 72.7% believed there were jobs not suitable for PWE. Up to 58% of our sample thought epilepsy is contagious and about 62.2% of them declared that epilepsy is curable. Respectively 65%, 9%, and 30% would recommend a medical doctor, a traditional healer and God's help for treatment of epilepsy. Independent determinants of attitudes were found to be: the belief that epilepsy is a form of insanity or is contagious, having witnessed a seizure, being female, being a Christian and having a higher level of education.

Conclusion: There was a high level of awareness on epilepsy and the negative attitudes observed among these students were better than those reported in the same community. The determinants of negative attitudes were found to be diversified, confirming our hypothesis of variation, and our data further suggest that the interplay between these factors may be more complex.

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A DOOR-TO-DOOR SURVEY TO ESTABLISH THE PREVALENCE, PHENOTYPE AND TREATMENT GAP FOR EPILEPSY IN A RURAL DISTRICT OF NORTHERN TANZANIA: INITIAL FINDINGS

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Purpose: Sparse clinical infrastructure and the stigma associated with epilepsy make estimates of prevalence in sub-Saharan Africa (SSA) difficult. We will determine the prevalence of epilepsy in an established disease surveillance site in northern Tanzania (Mswia e.a. In: INDEPTH Network, Population, Health, and Survival in INDEPTH Sites, International Development Research Centre: Ottowa, 2002; 151–158). We will report on the patterns of disease and provide an estimate of the treatment gap in this population.

Method: A door-to-door census of the district (population c.161,000) used a previously validated screening questionnaire to identify possible cases of epilepsy (Placencia e.a., Brain 1991;115:783–94). All people aged 6 and over responding positively will now be individually assessed to confirm a clinical diagnosis of epilepsy. All identified people with epilepsy (PWE) will be investigated by way of EEG and CT head scan and recruited into a case-control study to determine risk-factors for epilepsy in this population.

Results: In a pilot study the screening questionnaire effectively detected cases of epilepsy with a sensitivity of 100% (27 cases, 22 controls). A total of 733 people responded positively to screening at census, and initial clinical assessment of 226 adults (aged 15 and over) shows a positive predictive value of census screening of 78.3%. Clinical screening is expected to finish in early 2010.

Conclusion: This study will identify one of the largest cohorts of PWE to be studied in SSA to date, contributing to our understanding of epilepsy in this region and providing valuable data for use by local health services.

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SEIZURE IMPACT ON THE QUALITY OF LIFE OF SCHOOL-AGED CHILDREN IN DIFFERENT CULTURAL POPULATIONS IN THRACE REGION, GREECE

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Democritus University of Thrace, University Hospital, Alexandroupolis, Greece

Purpose: The aim of the study was to assess the self-estimated quality of life (se-QOL) of the school-aged epileptic children of the two communities (Christian, Muslims), to investigate if schoolmates were informed by the epileptic children itself and to determine the factors that could be correlated with these aspects.

Method: In this prospective study, we enrolled 62 children with epilepsy, 28 (45.2%) girls, 34 (54.8%) boys, aged 10.24 ± 3.29 (mean ± SD; range 6–18 years) who had answered to the subscale ''overall quality'' of the Quality of Life in Epilepsy Inventory-Greek version). Children and their parents were also evaluated by a semi-structured interview. Severity of the epilepsy measured with ''Illness Severity Index.'' Statistical analyses were performed using univariate analysis and multivariate logistic regression models.

Results: se-QOL score was correlated with seizure severity ($p = 0.040$) and seizure worry ($p = 0.008$). It was better in children from Christians families ($p = 0.043$) in which the problem was discussed more frequently. Schoolmates were informed more frequently among girls ($p = 0.012$) and children with generalized seizures ($p = 0.020$). In contrast, children older than 12, avoided discussing their disease with their peers ($p = 0.016$).

Conclusion: The majority of children did not discuss their disease in school. The se-QOL was better in children from Christian families. The fact that parents from Christian families discussed the problem with their children was perhaps the main reason for this difference. This observation may be useful designing information campaigns on the fight against misunderstanding of epilepsy in school-aged children.

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DIFFERENCES OF PUBLIC KNOWLEDGE, ATTITUDES, AND PRACTICE OF EPILEPSY BETWEEN PEOPLE IN METROPOLITAN AND URBAN AREA, KHON KAEN PROVINCE

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Purpose: Knowledge, attitudes, and practice of general population may affect social acceptance of people with epilepsy. The aim of this study is to evaluate the difference of public knowledge, attitude and practice towards epilepsy between people living in metropolitan and urban areas.

Method: Five hundred participants from each area of Khon Kaen province were randomly selected for face-to-face interviews. A survey concerning the knowledge, attitudes, and practices with respect to epilepsy was carried out during Jan and March 2008.

Results: Participants from metropolitan area were younger and had higher education level and income than participant from urban area. Regarding knowledge part, metropolitan group had known about epilepsy more than urban group (44.5% vs 29.2%, respectively). The numbers of participants who answered questions about definition, causes, types, and treatment of epilepsy correctly in metropolitan group were significantly higher than urban group ($p < 0.001$). In attitude aspect, metropolitan group would significantly allow their son or daughter to marry someone with epilepsy, hire persons with epilepsy, and not be hesitated to work with persons with epilepsy (p value 0.002, <0.001, and <0.001, respectively). Finally, metropolitan participants practiced more correctly than urban participants in view of first aids and status epilepticus (p value <0.001).

Conclusion: Participants in metropolitan area had better knowledge, attitude, and practice of epilepsy more than participants from urban area. Intervention to improve these factors should be focused more in urban community.

p550

IS THERE A DIFFERENCE IN MATERNAL STRESS BETWEEN MOTHERS WITH EPILEPSY AND MOTHERS WTHOUT EPILEPSY PRELIMINARY ANALYSIS?

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Purpose: Evidence suggests parental stress influences young children's development. The aim of the study is to examine self reported stress experienced by mothers with epilepsy with children aged <24 months. Comparisons are made to a control group of mothers without epilepsy with children aged <24 months.

Method: Maternal stress scores for competence, isolation, attachment, health, role restriction, depression, spouse scale and total parental domain were measured using the Parent Stress Index. Preliminary analysis regarding stress levels for the two groups are presented.

Results: Mothers with epilepsy (n = 143) differed significantly in comparison to mothers without epilepsy (n = 178) on the competence subscale, ($p = 0.003$) the isolation subscale ($p = 0.024$) and the overall parent domain ($p = 0.018$). Multiple regression analysis controlling for maternal age, maternal IQ, child's birth weight, and socioeconomic status did not find the presence of epilepsy to be predictive of decreased competence or increased isolation. Increased levels of isolation were found to be predicted by younger maternal age and the number of children and not maternal epilepsy.

Conclusion: Mothers with epilepsy reported increased feelings of isolation and decreased feelings of competence, the presence of maternal epilepsy was not the predictive factor. Knowledge and understanding of the stress experienced by mothers with epilepsy is useful for developing preconceptual counselling and post natal support for mothers with epilepsy. Encouragingly there are no reported significant differences for the depression or attachment subscales. Evidence indicates attachment acts as a positive influences on child development.

Research was sponsored by a research grant from Sanofi Aventis.

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SEXUAL DYSFUNCTION IN ADULT PATIENTS WITH EPILEPSY

Henning OJ, Nakken KO
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Purpose: Most patients do not spontaneously discuss sexual dysfunctions with their doctors, despite the fact that such problems are common

in people with epilepsy and may have a serious impact on their quality of life.

Method: 202 consecutive adult patients (108 inpatients, 94 outpatients) and their physicians received a questionnaire concerning the epilepsy, medication, side effects, sexual behavior, sexual function and quality of life. One hundred seventy-four patients (86%) completed the survey. Seven patients were excluded later.

Results: Sixteen percent of the patients had been asked sexually related questions during the consultation with their neurologist. In the questionnaire 68% reported sexual dysfunctions at any time, and 46% reported actual problems, most frequently reduced libido (26%), orgasmic dysfunction (16%), erectile dysfunction (9%) and dyspareunia (6%). The majority of patients stated that sex was very (17%) or quite (44%) important to them in order to feel content with daily life. No difference in sexual dysfunction was found regarding generalized versus localization related or temporal versus extra temporal epilepsy. Among patients with at least one seizure the last 12 month 47% reported sexual dysfunction, versus 39% among those being seizure-free. The antiepileptic drugs most often associated with sexual dysfunction were phenobarbital (71%), topiramate (68%) and carbamazepine (47%).

Conclusion: Among 167 adult patients treated at a tertial epilepsy centre, 46% reported ongoing sexual dysfunctions. Nevertheless, clinicians bring up sexual related matters only in 16% of the consultations. We found that phenobarbital, topiramate, carbamazepine and uncontrolled seizures were associated with an increased risk of sexual dysfunction.

Poster session: Social issues III
Wednesday 30th June 2010
13:30–14:30

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MORTALITY IN EPILEPSY: DATA OF 23 PATIENTS

Jung R
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Purpose: To investigate the extent and the causes of death and risk factors in patients with epilepsy.

Methods: We retrospectively studied the histories of patients with epilepsy who were treated at the Department of Neurology, Medical University of Vienna, between 1995 and 2009, and subsequently died. Demographic data, history of epilepsy, frequency of seizures, the results of comprehensive preoperative evaluations, type of operation, postoperative outcome, cause of death and age at time of death were systematically analyzed to assess the reasons for death and mortality risk factors in epilepsy patients compared to the sex- and age-matched general population.

Results: One thousand nine hundred sixty patients underwent Video-EEG-monitoring at the department of Neurology of the Medical University of Vienna. 23 patients (15 male) died. Six patients suffered from symptomatic epilepsy caused by an intracranial tumor. These patients died during chemotherapy or radiation. Nine Patients died during the seizure; in these patients, SUDEP was suspected to be the cause of death. One patient drowned in the bathtub, probably having a seizure. Two patients committed suicide. In 3 patients the cause of death could not be evaluated due to missing data. One patient died of mamma carcinoma and one patient died in a car accident.

Conclusion: Obviously mortality in epilepsy patients is increased compared to the general population. Most of the patients had been treated for an existing intracranial tumor. The data presented suggest that the increased mortality risk in patients with epilepsy is attributable in part to epilepsy itself, and is predominantly present at younger age.

p553
DIURNAL PATTERN OF FOCAL SEIZURES AND HEALTH RELATED QUALITY OF LIFE OF ADULTS WITH EPILEPSY

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Purpose: To study the relationship between the temporal pattern of focal seizures and the HRQOL of adults living with epilepsy. We hypothesized that patients with nocturnal seizures would have the highest HRQOL while those with no circadian pattern the lowest.

Method: Eighty-two adults (48 males, 34 females) with diagnosis of focal epilepsy filled out the 30-item Quality of Life in Epilepsy inventory (QOLIE-31), a measure of HRQOL, and indicated the diurnal pattern of their seizures. Sociodemographic and other illness data were also obtained.

Results: Twenty-two (26.8%) and 16 (19.5%) of the subjects had exclusively day time and nocturnal seizures respectively while 44 (53.7%) had no diurnal variation. They had a mean QOLIE-31 score of 76.4 ± 13.6, 74.5 ± 14.0 and 67.3 ± 16.8 respectively. QOLIE-31 score difference between the 3 groups approached significance ($F = 3.076$, $p = 0.057$). Post hoc test revealed a significantly higher mean score among patients with day time seizures than those without diurnal pattern ($p = 0.027$). When further stratified into those with diurnal variation and those without, the former had a significantly higher mean score (75.6 ± 13.6) than the latter (67.3 ± 16.8) ($p = 0.017$). There was also similar significant difference between the two groups in the seizure worry ($p = 0.004$), overall quality of life ($p = 0.013$) and social function ($p = 0.014$) subscales of the inventory.

Conclusion: Unpredictability of seizure timing relates negatively with HRQOL among adult Nigerian epilepsy patients.

p554
CAN SEIZURE RECOGNITION BE IMPROVED? AN EYE-MOTION STUDY

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Purpose: Epileptologists frequently get misleading data from eyewitnesses of seizures. The aim of this study was to understand seizure observation mechanisms of people with different experience on epilepsy and to train them to better describe epileptic seizures.

Method: Observers were grouped on the basis of their expertise level on epilepsy: 1) naive observers (without any experience on epilepsy), 2) pediatric residents, 3) nurses (working in Epilepsy Unit) and 4) experts (neurologists and assistants working in Video-EEG Unit). 5) reference data were collected from an epileptologist who has been watching ca. 5000 video-recorded seizures during the last 10 years. Twelve digital video-recorded seizure records were reviewed by all participants in three sessions. A modified set of the samples were also generated by highlighting each frame according to the fixation data of the reference. During seizure watching, eye motions and fixation times of all observers were recorded by a Tobii T120 Eye Tracking system. After watching a video clip, observers were asked to fill out a questionnaire containing seizure semiology data of seizures including motor, consciousness, autonomic and emotional aspects. A short description of each semiological aspect was described within the questionnaire.

Results: Quality of seizure assessment improved in all groups, especially among naive observers. Highlighted videos did not facilitate seizure observation. Eye fixation times were shorter for more experienced observers.

Conclusion: Seizure observation characteristics are different between experienced and inexperienced people. Reviewing seizures and a well-structured questionnaire might be a useful educational tool for naïve observers, e.g. parents and teachers.

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SIGNIFICANCE OF EEG FINDING IN ASSESSING FITNESS TO DRIVE IN SEIZURE-FREE EPILEPSY PATIENTS

Krijtova H, Tomasek M, Marusic P
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Purpose: Minimum requirements for fitness to drive in epilepsy patients should be harmonized within EU. Drivers/applicants can be declared fit to drive after a 1-year period free of seizures. EEG finding is not considered, although it may raise suspicion of ''subclinical'' seizures. The aim of our study was to assess – among a group of Czech neurologists – the significance attributed to various EEG abnormities.

Method: Model EEG findings in seizure-free epilepsy patients were presented to two groups of neurologists (N1 = 30, N2 = 21). Model situations included: normal finding, intermittent/continuous slow activity, focal spikes/sharp waves, generalized spike-wave (GSW) complexes lasting <1 s, or GSW lasting >3 s. Groups were asked for the opinion whether patient with individual EEG finding is fit to drive.

Results: The difference in assessment was not statistically different between both groups. When normal EEG or slow activity was present most respondents (90–98%) would permit patients to drive. In GSW lasting >3 s majority (92%) would not assess patient as fit to drive. In focal epileptiform discharges 47%, and in GSW <1 s 45% would permit patients to drive.

Conclusion: Majority of Czech neurologists still take EEG finding into consideration when assessing fitness to drive. Some types of abnormity (GSW >3 s) are probably taken as a marker of ''subclinical'' seizures, however, without requiring further video-EEG monitoring. Assessment of certain EEG abnormities is highly variable. Minimum requirements for fitness to drive should be harmonized not only within EU, but also within each Member State.

p556

LONG-TERM FOLLOW UP OF NONSURGICAL TEMPORAL LOBE EPILEPSY PATIENTS WITH MESIAL TEMPORAL SCLEROSIS

Kurita T, Sakurai K, Takeda Y, Koyama T
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Purpose: Epilepsy surgery can result in complete seizure remission rates of up to 80% in patients with mesial temporal sclerosis (MTS). However, some patients do not undergo surgery because of the various reasons including the bilateral focus or patient's refusal. We studied long-term clinical outcome and factors related to medical responsiveness in patients with MTS.

Methods: Subjects were selected among epilepsy patients actively followed up for >10 years at the Department of Psychiatry and Neurology, Hokkaido University Hospital. Inclusion criteria were as follows: 1) medical history and seizure semiology was consistent with that of temporal lobe epilepsy, 2) MTS was evident on MRI. 3) All the patients had not undergone surgical resection. We retrospectively reviewed the medical records and determined various clinical factors including seizure frequency and social adjustments.

Results: Forty-one subjects (male 13; mean age 53.1 ± 12.5) were available for analysis. Mean follow-up periods were 27.3 years. Twelve patients (29%) were seizure-free or had aura, while 22 (54%) had complex partial seizures more than once in a month. The latter group comprized a significantly higher rate of patients who had more than weekly seizures at the onset. Twelve patients had good social adjustments, including 13 patients making an independent life.

Conclusions: After long-term follow-up periods, almost 30% of TLE patients with MTS had a good outcome with anticonvulsants. Almost half of TLE patients with MTS got good social adjustments. Seizure frequency at the onset was the only factor which could predict the outcome.

p557

AUDIT OF ANALGESIC USE POSTICTALLY IN EPILEPSY IN ADULTS WITH AND WITHOUT LEARNING DISABILITY

Adadevoh CF[1], Nashef DL[2]
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Purpose: Pain occurs after seizures. There is little information on the use of postictal analgesia. Amongst those with learning disability, self administration may not be an option. We audited the use of analgesia postictally in those with and without learning disability.

Method: A questionnaire on pain and the use of postictal analgesia following generalized tonic–clonic and complex partial seizures was administered in unselected patients with epilepsy without and with learning difficulty. Carers provided information in the latter group. A validated seizure severity scale was also applied.

Results: Interviews were conducted in relation to 90 patients with epilepsy. Five were excluded from analysis due to seizure type. Of the remaining 85, 25 had learning disability and 60 did not. None of the learning disability group was reportedly given analgesia by their carers, even when as required medication was prescribed, while 35 of those without learning disability reported taking analgesia.

Conclusion: The audit highlights a potentially neglected area in the management of patients with epilepsy and learning disability and the need for more research in this area.

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THE PECULIARITIES OF PREGNANCY AND DELIVERY IN WOMEN WITH EPILEPSY AND ANTIEPILEPTIC DRUG THERAPY IN LITHUANIA

Valanciene I[1], Mameniskiene R[1], Jaskeviciene V[2], Budrys V[1]
[1]Vilnius University Santariskiu Hospital, Clinics of Neurology and Neurosurgery, Vilnius University, Faculty of Medicine, Vilnius, Lithuania, [2]Clinic of Neurosurgery, Kaunas Medical University, Kaunas, Lithuania

Purpose: To analyze pregnancy-related complications in women with AED, rate of fetal malformations; frequency of seizures during pregnancy.

Method: 146 pregnancies of women with epilepsy (mean age 25.7 ± 6.1 years) and AED treatment were prospectively evaluated according to EURAP (International Registry of Antiepileptic Drugs and Pregnancy) protocol, including data on AED therapy, seizure frequency, course of pregnancy and delivery, fetal malformations.

Results: Eighty-nine (61%) of women had 1st, 32 – 2nd, 13 – 3rd, 2 – 4th, 6 – 5th and 4 – 6th pregnancy. Seventeen had primary, 106 - secondary, 23 - high level of education. During pregnancy 101 (69.2%) used 1 AED, 36 (24.7%) - 2 and 9 (6.2%) - 3 AEDs. According etiology 33 (22.6%) had symptomatic, 41 - cryptogenic, 72 - idiopathic epilepsy. There were 4 premature terminations of pregnancy: 1 due to medical reasons, 1 spontaneous abortion and 2 interruptions of pregnancy (woman's willingness). 115 (78.8%) of women had natural delivery. Caesarean section performed in 22 (15.1%). 42 (28.8%) didn't experience seizures during first, 60 (41.1%) - second, and 82 (56.2%) - during third trimester of

pregnancy. One fetal malformation diagnosed for newborn of woman with VPA, another pregnancy was interrupted because of fetal malformations in woman on VPA and OXC. Overall incidence of malformation was 1.45%.

Conclusion: Most women with epilepsy and AED treatment do not have obstetric and delivery complications. Increase in seizure frequency during pregnancy is rare and more frequent in women treated with lamotrigine and oxcarbazepine. Our findings suggest that overall rate of malformations is relatively low.

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RISK COMMUNICATION IN THE PRECONCEPTION COUNSELING VISIT

Winterbottom JB, Jacoby A, Baker G
The University of Liverpool, Liverpool, United Kingdom

Purpose: Women with epilepsy preparing for pregnancy must balance individual seizure risk alongside general health risks. The risk of adverse pregnancy outcomes is communicated within preconception counselling visits, however, uncertainties remain. The relative risk of adverse pregnancy outcome secondary to in utero antiepileptic drug exposure is known for only a few commonly used antiepileptic drugs (AEDs), with little known about the safety of the newer AEDs or combination therapy. In addition, little is known about how women with epilepsy interpret risk information, or make decisions regarding future pregnancy plans.

Methods: This paper will present the findings from a qualitative study exploring how women with epilepsy perceive risk information and make personal decisions when preparing for pregnancy. The findings from 24 observed clinic visits and follow-up interviews with women with epilepsy, recruited from the NW of England, will be presented to illustrate the professional and patient factors influencing the risk communication discourse.

Results: Risk is presented both numerically and as narrative, to provide reassurance by the reframing of prior overestimations of risk, and the rationale to action health promotion advice. While communicating risk and uncertainty remains a challenge, the women's preconception counselling agenda is dependent on beliefs regarding the significance of pregnancy and seizure risk within the wider social context of health priorities, pregnancy intentions and general risk awareness.

Conclusion: The recognition of the social context of a woman's plans for pregnancy will be shown to be essential in interpreting poor treatment adherence on discovery of pregnancy.

Monday, 28.06.2010
07:30–09:00h
Hall 1 (Jupiter)
Satellite Symposium
Breakfast Symposium - Elekta
Clinical MEG in epilepsy

SHORT OVERVIEW OF MEG BASICS AND CLINICAL MEG INDICATIONS FOR EPILEPSY IN ADULTS

Stefan H (Germany)

CLINICAL MEG INDICATIONS FOR EPILEPSY IN CHILDREN

Van Bogaert P (Belgium)

Monday, 28.06.2010
07:30–09:00
Hall 2 (Roses)
Teaching Session
Seizure, arousal, or parasomnia? A road map into the borderlands

SEIZURE AND AROUSAL: EGG OR CHICKEN?

Kelemen A (Hungary)

Circuits involved in physiological sleep regulation generate pathological oscillations as well. Many interictal EEG abnormalities and seizures are activated by sleep and the arousal and vice versa. Often it is difficult to know what is first: the chicken or the egg. Sleep is structured by oscillations of different frequency ranges. Deltas and sleep spindles are continuous oscillation produced by the thalamo-cortical system. Stimulus-dependent phasic events are reflected in the cyclic alternating pattern (CAP). The interrelationship between epileptic phenomena and CAP/arousals is discussed. Two, reciprocally interrelated sleep-promoting and arousal inducing neuronal circuits control thalamo-cortical excitability, which networks' epileptic dysfunction is the substrate of the generalized spike-polyspike-wave and generalized repetitive fast discharge pattern related to in CAP A periods in IGE. During wake-sleep transitions the same dysfunctional thalamo-cortical oscillations might be the basis of absences and generalized tonic–clonic seizures on awakening. In JME patients arousal related phasic sleep events, especially anti awakening acting CAP A1 type of arousals may be the oscillations organizing the the epileptiform discharges, but not the seizures. In frontal lobe epilepsy, events with different degree of motor activity from pathological micro-awakenings to hypermotor seizures are associated with mainly CAP A1 arousals, but the interictal discharges may not. In temporal lobe epilepsy however, there was weak interrelation between the sleep phasic events and interictal discharges and seizures, although the spiking rate is sleep stage related and ictal onsets preceded arousals in nocturnal seizures. Examples for each of the above complex connections will be demonstrated.

SEIZURE, AROUSAL OR PARASOMNIA: HOW BEST TO RUIN A GOOD NIGHTS SLEEP

De Weerd A (The Netherlands)

SEIZURE, AROUSAL OR PARASOMNIA: IS THERE TRUTH IN DEPTH?

Nobili L (Italy)

Monday, 28.06.2010
07:30–09:00h
Hall 3 (Delphi)
Workshop
Epileptogenesis: mechanisms and prevention

EPIGENETIC FACTOR MEDIATE HCN1 CHANNELOPATHY

Bernard C (France)

Abnormal expression and function of ion channels may result in network derangements that characterize many neurological disorders. Looking for common regulatory pathways, we focused on the repressor REST/NRSF, and on its role in the hyperpolarization-activated (HCN) channelopathy in

experimental temporal lobe epilepsy (TLE), the most common epilepsy in adults. Nuclear NRSF was increased after seizures that lead to TLE, resulting in augmented binding of this repressor to the HCN type 1 (hcn1) subunit gene. Consequently, HCN1-mediated currents (Ih) were depressed in hippocampal CA1 pyramidal cell distal dendrites, and Ih-dependent resonance properties and temporal coding were compromized. Administration of ''decoy'' oligodeoxynucleotides comprising the NRSF DNA-binding sequence reduced NRSF binding to hcn1, prevented HCN1 downregulation and restored Ih to control levels. In vivo, blocking interaction of NRSF with target genes restored theta rhythm and attenuated the epileptic process, identifying NRSF-dependent regulatory mechanisms as novel therapeutic targets for epilepsy and related neurological disorders.

T-TYPE CALCIUM CHANNEL UPREGULATION AS A PROEPILEPTOGENIC FACTOR

Becker A (Germany)

Pronounced changes in intrinsic excitability have been observed in the pilocarpine-status epilepticus (SE) model of temporal lobe epilepsy (TLE), consisting of a conversion of regular firing to burst-firing hippocampal CA1 pyramidal neurons. This conversion likely plays a role in the transition from the interictal to the ictal state in TLE, because a subset of burst-firing neurons constitutes forerunners of epileptiform events observed in vitro. We have therefore investigated the cellular mechanisms of aberrant burst firing in detail. We found that the increased propensity for burst discharges in SE-experienced neurons is mainly due to functional up-regulation of T-type $Ca2^+$ currents. Real-time RT-PCR experiments showed that the increase in $Ca2^+$ currents is associated with transcriptional increase of the Cav3.2 but not Cav3.1 or Cav3.3 T-type $Ca2^+$ channel subunits. Patch-clamp experiments in SE-experienced CA1 pyramidal neurons from mice lacking ($Cav3.2^{-/-}$ mice) or having ($Cav3.2^{+/+}$ mice) Cav3.2 subunits, revealed that $Cav3.2^{-/-}$ mice do not express an increase in T-type $Ca2^+$ current density, as is found in $Cav3.2^{+/+}$ animals. These data confirm that increased expression of Cav3.2 subunits underlies the SE-induced up-regulation of T-type $Ca2^+$ currents. Further, we have analyzed $Cav3.2^{-/-}$ and littermate controls after pilocarpine induced-SE by telemetric EEG-/video-monitoring. We observed no significant differences in the severity of pilocarpine-induced SE between $Cav3.2^{-/-}$ and $Cav3.2^{+/+}$ mice. The frequency and severity of chronic seizures was significantly attenuated in chronic epileptic $Cav3.2^{-/-}$ versus $^{+/+}$ mice (n = 5 for both groups). Neuropathological sequelae of SE, such as segmental neuron loss and mossy fiber sprouting, were significantly reduced in $Cav3.2^{-/-}$ mice. These data indicate that the up-regulation of Cav3.2 after SE, and the associated dramatic changes in discharge behavior, may be important in the initiation of seizure activity. They further suggest that Cav3.2-dependent processes of intrinsic neuronal plasticity may contribute to neuronal cell death in chronic epilepsy. Supported by DFG SFB-TR3 and the German-Israeli Foundation.

PREVENTING EPILEPTOGENESIS: ANTIINFLAMMATORY STRATEGY

Vezzani AM (Italy)

Increasing evidence from experimental and clinical studies strongly supports the involvement of immune and inflammatory processes in the etiopathogenesis of seizures. Inflammatory responses, manifested as increased production of pro- and antiinflammatory cytokines and activation of downstream signaling mediators in the brain, are induced in response to neurotrauma, stroke, infection, febrile seizures, status epilepticus, which are events associated with a higher risk of developing epilepsy. Blood–brain barrier damage leads to increased neuronal excitability preceded by upregulation of inflammatory genes and proteins. Pronounced inflammatory processes have been described in epileptogenic brain tissue from clinical cases of drug-resistant epilepsies of different etiology. Pharmacological studies in experimental models, showed that specific inflammatory mediators such as proinflammatory cytokines, complement factors and prostaglandins, contribute to seizure onset and recurrence, and to seizure-associated cell loss and behavioral impairments. The use of transgenic mice with perturbed cytokine systems show that chronic overexpression of proinflammatory cytokines in brain can induce progressive neurological dysfunctions including spontaneous seizures. Recent findings in immature rats demonstrate that early life proinflammatory challenges can cause long-term changes in neuronal excitability resulting in lower seizure threshold and increased comorbidities in adulthood. Pharmacological attempts to block inflammation in brain to prevent seizures will be discussed with special emphasis to models of status epilepticus, prolonged febrile seizures, and infection.

PREVENTING EPILEPTOGENESIS: GROWTH FACTORS STRATEGY

Simonato M (Italy)

Monday, 28.06.2010
07:30–09:00h
Hall 4 (Nafsica)
How to do? Seizure Monitoring in the EMU Setting
How to do? Safety in the EMU

HOW TO PROVIDE A SAFE EMU ENVIRONMENT?

Canevini MP (Italy)

HOW TO SAFELY TAPER OR WITHDRAW AED TREATMENT FOR SEIZURE PROVOCATION

Claus S (Netherlands)

HOW TO PREVENT OR DEAL WITH SEIZURE RELATED ADVERSE EVENTS

Rubboli G (Italy)

Monday, 28.06.2010
07:30–09:00h
Hall 5 (Nefeli)
Teaching Session
Brain stimulation for epilepsy: current status and future prospects

VAGAL-NERVE STIMULATION: STATE-OF-THE-ART REVIEW

Selway R (United Kingdom)

TRANSCRANIAL MAGNETIC STIMULATION: DIAGNOSTIC AND THERAPEUTIC ASPECTS

Kimiskidis V (Greece)

EMERGING NEUROSTIMULATION PARADIGMS: DIRECT CORTICAL AND CLOSED-LOOP STIMULATION

Velis D (Netherlands)

Intracranial electrical stimulation for diagnostic purposes is commonly applied either directly on the cerebral cortex during awake craniotomy or

for functional mapping during invasive video/EEG telemetry studies, in which case current is passed through semipermanent subdural strip electrodes or grids. The paradigms used require an intensity level that may (2) cause afterdischarges on the running intracranial EEG record or (1) elicit a subjective sensation of a habitual aura or (3) elicit clinical semiology consistent with the function of the cortical area stimulated, whichever comes first. Patient safety requirements allow for current density charges up to 55 microcoulombs/cm^2/phase. Intracranial electrical stimulation for therapeutic purposes is a nondestructive, nonpharmacological alternative in refractory epilepsy. Targets for such paradigms are often deep-seated structures, most notably the subthalamic nucleus or selected thalamic nuclei, and, in some cases, the hippocampal formation. Intention-to-treat trials have recently been completed, based on high-frequency stimulation paradigms derived from deep brain stimulation in extrapyramidal disorders. The long-term effects, both advantageous and deleterious, of high- or low-frequency stimulation paradigms are as yet unknown. Neocortical areas may be targeted, as evidenced by a recently completed trial with a responsive neurostimulator, activated by potentially ictal discharges. However, none of these paradigms have been approved for routine use. Availability of a neurostimulator ''on demand'' has refocused attention on reliable seizure anticipation as well as seizure annihilation both for the purpose of so-called closed-loop intracranial electrical stimulation and for modulating the propensity of the brain to generate epileptic seizures in well-selected patients with difficult-to-treat epilepsy.

Monday, 28.06.2010
07:30–09:00h
Hall 6 (Marika)
Case Oriented Learning Session
Aging and comorbidity

EPILEPSY AND COMORBIDITY IN THE ELDERLY
Guekht A (Russian Federation)

CONTRIBUTION OF EEG IN ELDERLY PATIENTS WITH EPILEPSY AND OTHER COMORBIDITIES
Neufeld M (Israel)

NEUROIMAGING IN THE DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS OF EPILEPSY IN THE ELDERLY
Trinka E (Austria)

Monday, 28.06.2010
07:30–09:00h
Hall 7 (Colossus)
Teaching Session – Introduction to VIREPA
EEG in the diagnosis and treatment of epilepsy (supported by the ILAE Commission on Diagnostic Methods)

EEG IN THE DIAGNOSIS AND MANAGEMENT OF EPILEPSY: AN ORDERLY APPROACH
Van Emde Boas W (Netherlands)

PEDIATRIC EEG IN EPILEPSY: AGE DEPENDENT ISSUES
Plouin P (France)

Monday, 28.06.2010
09:00–11:00h
Hall 1 (Jupiter)
Chairs Symposium
The paradoxes of the paroxysms: seizure precipitating factors and underlying mechanisms

HOW DO BRAIN SYNCHRONIZATION MECHANISMS PROMOTE ICTOGENESIS?
Buzsaki G (United States)

THE DOUBLE FACE OF THE GABAergic SYSTEM IN SEIZURE ONSET
Avoli M (Canada)

GABA is the main inhibitory transmitter in the forebrain where it acts at both the ionotropic GABAA and the metabotropic GABAB receptors; GABAA 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 known that interfering with GABA receptor-mediated inhibition causes seizure activity. However, growing evidence indicates that GABAA 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 GABAA receptor depolarizations due to elevated internal Cl-; (2) glial and neuronal GABAA 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. In some of these experiments prolonged period of epileptiform synchrony that resemble electrographic seizures, are blocked by preventing GABA release by activating Ã¬-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 models of epileptiform discharge indicate that GABAA receptor-mediated mechanisms can also initiate and sustain ictal discharges.

SLEEP, AROUSAL AND SEIZURES
Nobili L (Italy)

IS IT A SUDDEN EVENT?
Navarro V (France)

Monday, 28.06.2010
11:30–13:00h
Hall 7 (Colossus)
Discussion Group
CEA — EU Symposium Funding of epilepsy research in Europe

NEED OF RESEARCH FUNDING: A VOICE OF THE PATIENT
Williams E (United Kingdom)

EU FUNDING INSTRUMENTS

Tosetti P (Belgium)

The aim of this presentation is to inform neuroscientists of the funding opportunities open within the 7th EU Framework programme for Research and Development (FP7). The talk will provide information (aim, description, rules) on some of the EU funding instruments of interest to the scientific community such as collaborative grants, individual ERC grants and Marie Curie fellowships.

INDUSTRY AS A PARTNER OF EU RESEARCH FUNDING FOR EPILEPSY

Salonen R (Finland)

Academia and pharmaceutical industry have successfully worked together in epilepsy research for tens of years and new therapies have emerged from these collaborations. Many of these medications are also used in other medical conditions (neuropathic pain, bipolar disorder, migraine, etc.) helping patients and making them successes also commercially. Animal models are fairly predictive of clinical efficacy and no clear bottlenecks exist in the development path. It would thus seem natural that the collaboration would bloom also in the future. The reality seems to be different. Industry is not often involved in the EU programs in epilepsy. The joint technology initiative between EU and industry, the Innovative Medicines Initiative has not had any calls related to epilepsy. This clearly reflects industry's lack of interest in this area as these calls are originally initiated from an Industry Consortium. Further, it is clear that many if not most of the large Pharma companies have dropped epilepsy from their core research agenda. From the epilepsy community point of view, these are alarming signs. Some of the reasons are scientific in nature: (1) for best efficacy, multiple modes of action are often needed. This is contrary to the current industry trend where single targets are preferred (2) the biggest unmet need is perceived to be in disease modification (antiepileptogenesis, neuroprotection). This is considered very challenging without suitable biomarkers (3) epilepsy is also problematic due to the need for separate indications across ages and seizure types (partial-pgtc, adult-peds, adjunctive-monotherapy), thus requiring expensive parallel development or a slower serial process. Other reasons include differences in global regulatory standards, challenges in recruiting clinical trials and overall commercial considerations and these will be discussed in the presentation. Personal suggestions for potential solutions will also be presented.

Monday, 28.06.2010
14:30–16:00h
Hall 1 (Jupiter)
Discussion Group
Generic products of antiepileptic drugs (AEDs): is it an issue?

UPDATE ON REGULATORY PROCESS IN APPROVING GENERIC PRODUCTS

Macheras P (Greece)

GENERIC AEDS: PRO

Johannessen S (Norway)

Antiepileptic drugs (AEDs) are not generally considered to be expensive, but due to the large number of prescriptions, the overall spending are high, and as the patent of the brand drugs runs out, there is a growing interest for generic drugs. There is substantial drug–budget saving possibilities by changing from the brand drugs to cheaper generic drugs. However, epilepsy calls for special caution, because most of the AEDs have a narrow therapeutic range that implies great care in dose adjustment to avoid loss of seizure control or risk for toxic adverse reactions. Epilepsy is characterized by uncertainty and unpredictability, and a worsened seizure control may have important consequences, for instance loss of driving license, problems with employment and independence. According to the FDA in the US a generic formulation is identical, or bioequivalent, to a brand name drug in dosage form, safety, strength, route of administration, quality, performance characteristics, and intended use. Thus there is no evidence that a bioequivalent generic product manufactured to meet its specifications could not be used interchangeably with a corresponding brand-name drug. The traditional acceptable confidence interval for bioequivalence for generic AEDs is 80–125%, but in some countries this has been narrowed (in Denmark to 90–111% for lamotrigine). This is also now in accordance with the new EMEA guidelines for narrow therapeutic index drugs. There are several recommendations regarding generic substitution. According to LICE, the Italian League, generic products may be used as initial monotherapy, when switching to alternative monotherapy, or as adjunctive therapy. Also in patients having incomplete seizure control with a brand product, switching to a generic product may be rational. Most importantly, patients should be informed about the criteria for approval of generic products and about the implications of the use of generic AEDs in order to consider the patients' opinion.

GENERIC AEDS: CON

Kraemer G (Switzerland)

GENERIC PRODUCTS OF AEDS: LET'S SEPARATE THE SCIENCE FROM THE POLITICS

Bialer M (Israel)

Most antiepileptic drugs (AEDs) are currently available as generic products, yet neurologists and patients are reluctant to switch to generics. Generic AEDs are regarded as bioequivalent to brand AEDs after meeting the average bioequivalence criteria and consequently, they are considered to be interchangeable with their respective brands without loss of efficacy and safety. According to the FDA the present bioequivalence requirements are already so rigorous and constrained that there is little possibility that generics meeting regulatory bioequivalence criteria could lead to therapeutic problems. The availability of generic AED products has raised the following concerns: (1) Do generic AEDs work as brand AEDs in terms of their efficacy, safety and quality? (2) Can generic AEDs be used as substitutions for brand AEDs? and (3) Can generic products of AEDs be used interchangeably? The common average bioequivalence analysis seems to address concern #1 but may not provide a complete adequate response to concerns # 2 & 3. Drug interchangeability can be classified as drug ''prescribability'' or drug ''switchability''. Drug ''prescribability'' is when are treated for the first time with either brand or generic AED. Drug ''switchability'' is related to the switch of a patient from a brand AED to a bioequivalent generic product of the same AED. Traditional average bioequivalence addresses the question of ''prescribability'' of a generic product, but does not assure the ''switchability'' between ''prescribable'' formulations.

Epilepsy is a single episode disease and prevention of seizure recurrence in controlled patients is essential, as even a single breakthrough seizure may have severe consequences, such as loss of driver's license, employment or injury. While the switch to generic AEDs is well tolerated by many patients and in general cost-effective, seizure control should not be sacrificed on the basis of cost alone, as the major end point in treating epilepsy with AEDs is seizure control without side effects. So is there a scientific rationale for the concerns about switching patients with epilepsy to bioequivalent generics? Recently Bialer & Midha discussed the assessment of bioequivalence of AED generic products and proposed a scaled-average bioequivalence approach where scaling of bioequivalence would be carried out based on brand lot-to-lot variance as an alternative to the conventional bioequivalence test as a mean to determine whether switching patients to generic formulations or vice-versa is a safe and effective therapeutic option. Meeting the proposed scaled-average bioequivalence requirements will ensure that when an individual patient is switched he/she will have similar fluctuations in plasma levels as those from lot-to-lot of the brand reference levels and thus should make these generic products will be safely switchable without changes in efficacy and safety outcomes.

References:
1. M. Bialer. Generic products of antiepileptic drugs (AEDs): Is it an issue? Epilepsia, 48:1825-1832, 2007.
2. M. Bialer, K. K. Midha. Generic products of antiepileptic drugs: A perspective on bioequivalence and interchangeability. Epilepsia, doi:10.1111/j.1528-1167.2010.02573x.

Monday, 28.06.2010
14:30–16:00h
Hall 2 (Roses)
The Michael Foundation Symposium
Pharmacoresistance and blood–brain-barrier: assessment of P-gp function from bench to bedside

P-GP OVEREXPRESSION VERSUS BBB DAMAGE IN THE EPILEPTIC BRAIN: IMPLICATIONS FOR PHARMACORESTISTENCE
Vezzani AM (Italy)

BLOOD–BRAIN BARRIER BREAKDOWN AND BRAIN DYSFUNCTION
Friedman A (Israel) 2007

INHIBITION OF P-GP: A NEW THERAPEUTIC CONCEPT?
Loescher W (Germany) 1993

IMAGING P-GP: FUNCTION IN EPILEPSY
Koepp MJ (United Kingdom) 2001

Monday, 28.06.2010
14:30–16:00h
Hall 3 (Delphi)
Discussion Group
Seizure prediction in epilepsy: from modeling to seizure prevention

FROM EEG SIGNALS RECORDED IN HUMAN PARTIAL EPILEPSIES TO DYNAMIC TRANSITIONS IN BRAIN ACTIVITY: INSIGHTS FROM COMPUTATIONAL MODELS
Wendling F (France)

A neurostimulation protocol has been recently proposed and tested in patients with temporal lobe epilepsy (Kalitzin et al., CN, 2005). It is based on (1) a low-intensity bipolar current injected using depth electrodes implanted in the hippocampus and (2) the computation of an index referred to as the ''phase clustering index'' (PCI) on recorded on EEG during monitoring. Results showed that this protocol could be efficient with respect to anticipating epileptic seizures. In order to gain some insights about the variations, in time, of the PCI values recorded during interictal-to-ictal periods, we used a computational modeling approach. First, we reproduced the stimulation effects in a macroscopic neurophysiologically-relevant model of the CA1 subfield in the hippocampus (Wendling et al., JCN, 2005). Second, we investigated how (1) changes in model parameters controlling the transition from the on-going EEG to ictal EEG (proictal state) are reflected on the properties of the simulated EEG output signals and (2) how the evolution of neuronal excitability can be monitored from EEG data. Simulations allowed us to explain why – and how – the PCI evolves with respect to impending seizures. In particular, a relationship between PCI values and underlying mechanisms related to the balance between excitatory and inhibitory processes in hippocampal circuits could be established in the model. This study, reported in (Suffczynski, PRE 2008), indicates that a stimulation paradigm combined with appropriate analytical tools may yield information about critical changes in the excitability of recorded neuronal networks during the transition to seizure.

RECENT ADVANCES IN SEIZURE PREDICTION
Feldwisch H (Germany)

In the last years, several methods for the prediction of epileptic seizures have been proposed, which are based on recordings of the electroencephalogram (EEG). By application of linear or nonlinear measures, preseizure changes have been reported in several studies, but prediction performances are hardly sufficient for clinical applications. Here, we present latest advances towards improved prediction performances. Our studies were based on the phase synchronization index, which measures the degree of interaction between pairs of recording sites. The evaluation was performed on long-term intracranial EEG recordings of patients that underwent presurgical diagnostics. We developed a novel method for a data-driven preselection of features that are suitable for means of seizure prediction. Since significant correlations between the proposed selection criterion and the predictive power of the features are found for 17 of 18 patients, it can be concluded that it represents an efficient way to identify features that contain on average a relatively high predictive performance. Additionally, we present an approach to optimize prediction methods to account for differences in day and night time. By adjusting alarm-generating thresholds to distinct levels for day and night, it allows an adaptation to the circadian cycle of the patient. Both methods constitute valuable means to increase the performance of prediction methods, which may lead to clinical applications thereof. This work was supported by the German Federal Ministry of Education and Research (BMBF grant 01GQ0420), the Excellence Initiative of the German Federal and State Governments, the European Union (Grant 211713), and the German Science Foundation (Ti 315/4-2).

CAN THE MICROELECTRODES RECORDINGS IMPROVE THE SEIZURE PREDICTION STRATEGIES?
Navarro V (France)

ELECTRICAL STIMULATION OF THE SEIZURE FOCUS
Boon P (Belgium)

Monday, 28.06.2010
14:30–16:00h
Hall 4 (Nafsica)
Discussion Group
Structural genomic variation in human seizure disorders: emerging themes in epilepsy genetics

LISTEN TO YOUR GENOME AND TALK TO YOUR PATIENTS: THE ARCHITECTURE OF THE HUMAN GENOME AND THE CHALLENGES OF PHENOTYPING
Helbig I (Germany)

Microdeletions and microduplications are increasingly recognized as risk factors for both common and rare epilepsy syndromes. While many of these genomic rearrangements are unique, a significant fraction of these

structural variants such as microdeletions at 15q13.3, 16p13.11, 15q11.2, 1q21.1 or 16p11.2 are recurrent. These loci share a particular genomic architecture and represent genomic hotspots. A relatively high recombination rate is thought to be due to flanking segmental duplications, which promote nonallelic homologous recombination. Collectively, genetic disorders due to rearrangements at these hotspots are referred to as genomic disorders. Many of the variants recently identified in common epilepsies have also been identified in a broad range of neurodevelopmental disorders including autism, intellectual disability and schizophrenia. The complex genomic duplication architecture at many of the loci implicated in neurodevelopmental disorders is the result of recent evolutionary hominid-specific duplications. This suggests that specific features of the human genomic architecture might help identify candidate regions for neurodevelopmental disorders including the epilepsies. In contrast to the traditional phenotype-based strategy, which has led to many of the breakthroughs in epilepsies genetics, the rareness and broad phenotypic spectrum of many microdeletions and microduplications currently requires a ''genotype-first'' strategy, by which recurrent variants can only be identified in large patient samples. Precise phenotyping, however, is virtually impossible in these large patients samples. With some of the structural genomic rearrangements becoming well-established genetic risk factors, the obvious and subtle phenotypic features of microdeletion and microduplication carriers will be main focus of future studies.

STATE OF THE ART: EPILEPSIES AS COMORBIDITIES IN CLASSICAL MICRODELETION SYNDROMES

Steensbjerre Moller R (Denmark)

The role of copy number variations (CNVs) in cognitive disorders is becoming increasingly evident, with at least 50 different recurrent microdeletions or microduplications known so far. Many of these CNVs predispose to a broad range of syndromes and neurodevelopmental disorders including epilepsy. Microdeletion/microduplication syndromes or genomic disorders are defined as a group of clinically recognisable disorders caused by a chromosomal alteration that might lead to complete loss or gain of a dosage sensitive gene(s) or alternatively disrupt the structural integrity of a gene. Disease-associated CNVs are now routinely being detected by the use of genome wide microarray platforms, which facilitates identification of new syndromes by a reverse phenotypic approach, in which the patients are characterized by overlapping CNVs before a common phenotype is defined. Epilepsy occurs as comorbidity in several microdeletion syndromes and the focus of this presentation will be on discussing both recurrent interstitial (e.g. 17q21) and terminal (e.g. 1p36) microdeletions associated with epilepsy.

AN UNDER RECOGNIZED SOURCE OF GENETIC MORBIDITY: MICRODELETIONS AND MICRODUPLICATIONS IN IDIOPATHIC EPILEPSY SYNDROMES

Zara F (Italy)

The structural variation of the human genome is commanding a great deal of attention as submicroscopic, genomic deletions and duplications constitute up to 15% of all mutations underlying human monogenic diseases. So far, the identification of CNVs underlying neurological diseases has been challenged by methodological limitations. However recent technology developments enable the efficient detection of novel disease-causing CNVs. The role of microrearrangments in the pathogenesis of epilepsy has been initially recognized for complex syndromic epileptic phenotypes, leading to the definition of novel clinical entities. More recently we and others showed that genomic microdeletions are also common in different monogenic forms of epilepsy such as Severe Myoclonic Epilepsy of Infancy, Lafora Disease and Benign Familial Neonatal Seizures. In addition genome-wide surveys of genomic disorders led to the detection of microdeletions and then the identification of the causative genes – STXBP1 and PCDH19 – for two epileptic encephalophaties. Hence, the detection of a pathogenic CNV in a single patient or family affected by a genetic disorder may represent a critical step toward the identification of a disease gene. The role of CNV have been also demonstrated in IGE as chromosome 15q13.3 deletion involving the acetylcholin receptor alpha7 subunit gene have been proved to be a risk factor in about 1% of patients with different forms of IGE. In a genome-wide array-CGH screening of 215 patients with cryptogenic epilepsy we identified 21 genomic rearrangements providing further evidence of the significant role of CNV in the etiology of epilepsy.

A GLIMPSE AT THE FUTURE: ANALYSIS OF GENOME-WIDE COPY NUMBER VARIATIONS IN LARGE DATASETS AND THE QUESTION OF PATHOGENICITY

De Kovel C (The Netherlands)

Some base-pair substitutions cause highly penetrant diseases, while others have smaller effects or no detectable effect at all; thus it is with copy number variants too. Now methods to detect CNVs in genome-wide SNP-typing data are developing, copy number variants with a role in multifactorial diseases are being identified. Odds ratios for these variants vary from 2 to >50, roughly corresponding to penetrances of 1–10%, and frequencies range up to about 10% of the patients. Though hundreds of genome-wide association analyses for SNPs have been performed by now, few genome-wide CNV-analyses have been published. While in theory SNP-data can be used for CNV-analysis, a number of technological and biostatistical challenges have to be overcome. An overview of possibilities and limitations will show what can be detected and what not (yet). Once a statistical overrepresentation of a copy number variant in a patient group has been established, the next task is to identify the gene or genes responsible for the disease susceptibility and to establish the mechanism by which the pathogenic effect is brought about. An interesting question is whether CNVs differ from other mutations, because multiple genes may be affected. It is, however, not easy to investigate the pathogenic effect of mutations that only increase susceptibility to a disease by a few percent on average. For example, some deletions may only cause haplo-insufficiency when there is an unusually high demand for the protein, because of additional unknown risk factors. This makes functional studies difficult. A review will be given of the first steps on the road towards understanding the effect of CNVs on multifactorial disorders.

Monday, 28.06.2010
14:30–16:00h
Hall 6 (Marika)
Discussion Group
Idiopathic childhood ''focal'' seizure susceptibility

CLINICAL ASPECTS AND GENETICS

Livingston J (United Kingdom)

EEG ASPECTS (INCLUDING MEG) AND RELEVANCE TO PATHOPHYSIOLOGY

Grosso S (Italy)

PRINCIPLES OF MANAGEMENT AND TREATMENT (ACUTE EARLY PHASE - FOLLOW-UP)

Covanis T (Greece)

PSYCHOSOCIAL ASPECTS, PARENTAL REACTIONS AND NEEDS

Valeta T (Greece)

Tuesday, 29.06.2010
07:30–09:00h
Hall 2 (Roses)
Case Oriented Learning Session
Pediatrics

CLINICAL CASE 1 (GENETICS)
Vigevano F (Italy)

CLINICAL CASE 2 (METABOLIC DISEASES)
Wolf N (Netherlands)

CLINICAL CASE 3 (SYNDROMIC APPROACH)
Bahi Buisson N (France)

Tuesday, 29.06.2010
07:30–09:00h
Hall 3 (Delphi)
Workshop
Are cognitive disturbances and epileptiform activity at night related?

COGNITIVE DISTURBANCES INCLUDING AUTISM IN PATIENTS WITH CONTINUOUS SPIKE-WAVE DURING SLOW SLEEP (CSWS)
Deonna T (Switzerland)

CSWS is now accepted as a nonspecific EEG abnormality during non-REM sleep that can be seen in idiopathic and symptomatic epilepsies of childhood and that appears and fluctuates during the active period of the disorder. The severity and duration (remission usually at or before adolescence) are extremely variable. It is considered as a manifestation of secondary bilateral synchrony related to a cortical spike focus. Since the increasing recognition of the role of various thalamic pathologies in this phenomenon, many more clinical reports have been recently published and have enriched the description and range/type of the correlative cognitive manifestations seen during the CSWS period. The late outcome of the various deficits encountered is also starting to appear in the literature. From another perspective, young children with developmental disorders with a documented regression (sometime within the autistic spectrum) have been extensively studied with sleep EEG (looking for CSWS) to find out whether part or some of their symptoms could be epilepsy-related, even in the absence of clinical epilepsy. These various sources of data will be reviewed in the presentation, in as much as provide new information on the type, change and evolution of the cognitive-behavioral manifestations with time and their relationship to the epilepsy-EEG variables.

NOCTURNAL EPILEPTIFORM ACTIVITY IN PATIENTS WITH ADHD
Silvestri R (Italy)

There is an increased risk of unprovoked seizures in ADHD children, especially for iADHD whereas benign centro-temporal seizures and related IEDs would prevail in hADHD. Potential pathogenetic factors include neurotrasmitters alterations, genetic, environmental and iatrogenic factors. A higher rate of cognitive dysfunction, language and learning disabilities is shared by ADHD and epilepsy. Also epileptiform EEG (IEDs) abnormalities occur more frequently in ADHD with a mean of 15% against a background incidence of 2–3% in normal school-aged children. Although rarely pursued during sleep, epileptic activity/abnormalities (EAS) is more frequent and severe during SWS even in children with no seizure history and none or sporadic IEDS while awake. Focal abnormalities, right sided or bilateral prevail over generalized ones, involving, in order, centro-temporal, frontal and parieto-temporal areas. They interfere with developing cognitive abilities and strongly relate to learning disability, contributing to attention impairment. Specific cognitive deterioration has been reported with severe IEDs even in the absence of clinical seizures, warranting specific AE treatment to ameliorate the cognitive domain. Informed therapeutic choices need to be cautions to avoid iatrogenic further damage from ''old'' or cognitive unfriendly drugs such as CBZ or TPM, whereas LEV, LTG and VPA hold favorable profiles. Also disorders of arousal (DOA) occur more frequently in ADHD children, representing a common dysmaturative factor expressing vulnerability to SWS fragmentation. A thorough differential diagnosis of nocturnal paroxysmal events is mandatory and a role for drugs acting as sleep stabilizers could prevent both seizures and/or other paroxysmal nocturnal events.

IS THE EPILEPTFORM ACTIVITY THE REASON FOR COGNITIVE IMPAIRMENT OR ONLY AN EPIPHENOMENON
Holmes G (United States)

Physiologically interictal spikes (IIS) are synchronous, paroxysmal depolarizations of neurons producing action potentials lasting a few hundred milliseconds. While IIS are one of the most important factors in the diagnosis of epilepsy, there is considerable evidence that IIS also contribute to cognitive dysfunction. It is known that IIS may cause transitory cognitive impairment and human studies have shown that IIS can cause impairments in reaction time, visual perception, verbal and spatial tasks and even driving behavior. In animal studies we have investigated the transient impact of focal IISs on the hippocampus, a structure crucial for learning and memory and yet highly prone to IISs in temporal lobe epilepsy. Bilateral hippocampal depth electrodes were implanted into rats, followed by intrahippocampal pilocarpine or saline infusion unilaterally. Rats that developed chronic spikes were trained in a hippocampal-dependent operant behavior task, delayed-match-to-sample. Depth-EEG was recorded during thousand of trials in many rats. Hippocampal spikes that occurred during memory retrieval strongly impaired performance. However, spikes that occurred during memory encoding or memory maintenance did not affect performance in those trials. Hippocampal spikes also affected response latency, adding approximately 0.48 s to the time taken to respond ($p < 0$ 0.001). During IIS there is a decreased likelihood of action potentials for up to 2 s compared to IIS free portions of the record. The responses to IIS are cell-dependent; IIS resulted in decreases in action potentials after the IIS in interneurons but not place cells. Hippocampal spikes seem most harmful if they occur when hippocampal function is critical, extending human studies showing that cortical spikes are most disruptive during active cortical functioning. The cumulative effects of spikes could therefore impact general cognitive functioning. These results strengthen the argument that suppression of IIS may improve memory and cognitive performance in patients with epilepsy.

TREATMENT OF COGNITIVE DISTURBANCES IN PATIENTS WITH CSWS
Eeg-Olofsson O (Sweden)

Continuous spike and waves during slow sleep (CSWS) consists of bilateral generalized but also focal 1.5–2.5 Hz spike and wave discharges strongly activated by non-REM sleep that fragment or disappear during REM sleep. It is a pure childhood manifestation and generally found between 2 and 14 years of age. This EEG pattern is also called ESES, electrical status epilepticus of slow sleep. Earlier studies on CSWS required a presence of this pattern in 85% of the sleep recording, but now a lower proportion is accepted. Morphologically it is similar to rolandic

discharges. CSWS is strongly associated with different seizure manifestations and with cognitive and language dysfunction. Depending on the basic disorder, CSWS shows a spontaneous resolution in the midteens, when also seizures remit, and when there is a stabilization or improvement of the neuropsychological manifestations. Thus, a maturational mechanism is apparent. CSWS is the typical electrographic pattern in some epileptic syndromes but can also be found in neuropsychological disorders as ADHD and autism spectrum disorders. It is compulsory in the syndrome Epilepsy with CSWS. It is not unusual in Landau–Kleffner syndrome and it has been reported in "benign" focal epilepsy syndromes, and in atypical benign partial epilepsy or pseudo–Lennox syndrome. All these syndromes have in common the negative influence of CSWS on the cognitive development. Patients with the mentioned disorders and the CSWS pattern may present focal motor seizures, and less frequently seizures as atypical absences, atonic or clonic events and generalized tonic–clonic seizures. Due to the seizure manifestations antiepileptic drug treatment has been advocated, and all available drugs have been used as monotherapy or in combination. Some children have responded to high dose steroids or to ACTH. Good results have been obtained by a combination of benzodiazepines and sodium valproate. In addition, drugs specifically directed to neuropsychological symptoms have been used. However, some of the AEDs as well as ACTH and steroids may aggravate neuropsychological symptoms, and a balancing using different drugs is important. Recently levetiracetam has been shown to have a positive effect on the EEG, the seizures, the behavior, and the cognition in patients with the mentioned syndromes and neuropsychological disorders. Levetiracetam may have side effects as aggressiveness and rage, which side effects have been treated with pyridoxine. In order to reveal the CSWS pattern, prolonged EEG recordings including sleep are necessary.

Tuesday, 29.06.2010
07:30–09:00h
Hall 4 (Nafsica)
How to do? Seizure Monitoring in the EMU Setting
How to do? How to observe and test patients and report seizures recorded in the EMU

SEIZURE OBSERVATION: DOS AND DON'TS
Gallmetzer P (Austria)

INTERACTION WITH THE PATIENT: DOS AND DON'TS
Fogarasi A (Hungary)

HOW TO REPORT THE SEIZURES RECORDED IN THE EPILEPSY MONITORING UNIT
Beniczky S (Denmark)

Tuesday, 29.06.2010
07:30–09:00h
Hall 5 (Nefeli)
Teaching Session
Interpretating video-EEG data in a surgical perspective

ANALYSIS OF INTERICTAL SCALP EEG DATA IN A SURGICAL PERSPECTIVE
Baumgartner C (Austria)

ICTAL AND POSTICTAL CLINICAL SIGNS THAT RELIABLY LATERALIZE AND LOCALIZE THE EPILEPTOGENIC ZONE
Rosenow F (Germany)

During the presurgical diagnosis of epilepsy the seizure semiology is routinely analyzed. If the subsequent operation leads to seizure freedom by definition, the epileptogenic zone has been removed of disconnected. This allows to reliably relate the observed seizure semiology to the brain region resected in this highly selected population. Over the last decades a large number of studies regarding the localizing and lateralising relevance of different ictal and postictal symptoms has been investigated. While the relative frequency of these symptoms varies from rare (e.g. ictal piloarection) to 40% (versive seizure prior to secondary generalization) the specificity for the side of seizure onset is usually between 70 and 95 and even 100%. Examples of such lateralizing signs are: unilateral clonus, unilateral ictal dystonia, postictal noes wiping, ictal nystagmus, unilateral visual aura). Other ictal symptoms are not lateralizing but localizing and may even be charcteristic of a certain pathology. Examples are olfactory aura (amygdalon or hippocampus, not infrequently involved by tumors or hippocampal sclerosis) or gelastic seizures (hypothylamic hamartomas). Keeping the caveat in mind, that all these data relate to the highly selected and therefore potentially atypical population of postoperatively seizure-free patients, this knowledge of high clinical relevance. Most of these ictal signs and symptoms can be observed by lay persons and can be asked for in the outpatient clinic. If they are present it can be assumed that the seizures are (1) epileptic rather than nonepileptic and (2) the patient has a focal rather than a generalized epilepsy syndrome, which in turn helps to guide further diagnostic procedures such as MRI and helps choosing the appropriate medical management.

Reference: 1. Rosenow F, Lüders H. Presurgical evaluation of epilepsy. Brain. 2001;124:1683-700.

SIGNIFICANCE OF THE FIRST ICTAL SCALP EEG CHANGES AND SEIZURE SPREAD PATTERNS
Tassi L (Italy)

PITFALLS AND CAVEATS OF VIDEO-EEG FINDINGS IN CHILDREN
Cross H (United Kingdom)

Video-EEG recordings have greatly enhanced our understanding of the epilepsies, especially in defining seizure types. More specifically, it aids in diagnosis, not only with regard to epileptic versus nonepileptic attacks but also of the underlying epilepsy syndrome, and in presurgical evaluation. However, there needs to be appropriate use, with recognition of its limitations, in order to maximize the yield of the procedure. A good room layout with video coverage and long cabling is imperative, with space for the child to play as well as sleep. Lighting is also important both by day and night, with possible use of different cameras. Only too often, in the heat of the event, carers may also stand in front of the child and block the view of the camera. Interpretation of the EEG alongside time locked video is the major advantage of the procedure. This will allow for determination as to whether changes in the EEG have clinical correlate (or vice-versa), or whether changes may be only movement artefact. It is important to determine that habitual events have been captured. This is particularly relevant when medication has been reduced, atypical attacks becoming unmasked. On reviewing data it is imperative for experienced personnel to be involved. The clinical manifestations of focal seizures in the very young differ from adolescents and adults. For example, complex automatisms in early life are unusual, presumably due to immaturity of distributed networks. Further, it may be extremely difficult to determine the state of awareness. Carers, nurses and technicians therefore need to

be aware of interaction required with the child at the time of any event. Manifestations that may or may not suggest lateralization of seizure onset also need to be interpreted with care. EEG changes at the time of an event need to be reviewed, bearing in mind possible timing in relation to clinical change, as well as any localization or lateralization. In surgical planning changes seen need to be interpreted in the context of other investigations, namely changes looked for consistent with the hypothesis of seizure onset. Ultimately much data is accumulated, with a requirement for systematic review by trained technicians, and ultimate interpretation by experienced epilepsy trained clinicians.

Tuesday, 29.06.2010
07:30–09:00h
Hall 6 (Marika)
Teaching Session – Introduction to VIREPA Genetics of epilepsy (supported by the ILAE Commission on Genetics)

GENETIC BASIS OF THE EPILEPSIES
Zara F (Italy)

PATHOGENESIS OF GENETIC EPILEPSIES
Lerche H (Germany)

Tuesday, 29.06.2010
07:30–09:00h
Hall 7 (Colossus)
Workshop
Infantile spasms: how to get rid of the catastrophy

MODELS OF INFANTILE SPASMS
Galanopoulou A (United States)

CAN THE EEG PREDICT THE OUTCOME?
Granata T (Italy)

Outcome of West Syndrome refers both to the short-term, that is cessation of spasms and the long-term, that is freedom from or recurrence of seizures and neurodevelopment. EEG in patients with WS is typically associated with hypsarrhythmia, whose characteristics may vary according to the age and etiology. The answer to the key question on the role of early EEG in predicting outcome may come from the observation of the interictal and ictal pattern at the onset, before any treatment was given, and from the EEG changes following treatment. At the onset of symptoms the presence of unilateral hypsarrhythmia or of a consistent focus of abnormalities suggests a severe epileptogenic potential, probably due to structural brain abnormalities thus prefiguring a poor outcome. Likewise, focal fast activity preceding the usually diffuse counterpart of spasm may suggest the presence of an underlying structural abnormality. Modification of EEG following treatment is another useful prognostic factor: the early disappearance of any EEG epileptic abnormalities, in patients with previous diffuse hypsarrhythmia, heralds a good prognosis, as in the case of cryptogenic infantile spasms. By contrast persistence of epileptic abnormalities or of subclinical ictal activity must suggest that infantile spasms are symptoms of an underlying disorder that requires careful investigation.

WHAT CAN WE LEARN FROM THE ARX MUTATION?
Noebels J (United States)

Infantile spasms syndrome (ISS) is a catastrophic pediatric epilepsy with motor spasms, persistent seizures, mental retardation, and in some cases, autism. One of its monogenic causes is a triplet repeat insertion mutation (c.304ins(GCG)7) on the X chromosome, expanding the first polyalanine tract of the interneuron-specific transcription factor ARX from 16 to 23 alanine codons. Null mutation of the Arx gene impairs GABA- and cholinergic interneuronal migration but results in a neonatal lethal phenotype. We developed the first viable genetic mouse model of ISS that spontaneously recapitulates salient phenotypic features of the human triplet-repeat expansion mutation. Arx (GCG)10+7 (''Arx Plus7'') pups display abnormal spasm-like myoclonus and other key EEG features, including multifocal spikes, electrodecremental episodes, and spontaneous seizures persisting into maturity. The neurobehavioral profile of Arx mutants was remarkable for lowered anxiety, impaired associative learning, and abnormal social interaction. Laminar decreases of Arx+ cortical interneurons and a selective reduction of calbindin-, but not parvalbumin- or calretinin-expressing interneurons in neocortical layers and hippocampus indicate that specific classes of synaptic inhibition are missing from the adult forebrain, providing a basis for the seizures and cognitive disorder. A significant reduction of calbindin, NPY-expressing and cholinergic interneurons in the mutant striatum suggest that dysinhibition within this network may contribute to the dyskinetic motor spasms. This genetic mouse model provides a basis to further selectively examine the abnormal patterns of disinhibition in ISS brain regions, and explore novel therapeutic strategies for reversing the interneuron migration defect underlying this catastrophic neurodevelopmental disorder.

HOW TO TREAT; EVIDENCE-BASED STUDIES
Lux A (United Kingdom)

Despite there being what feels like a myriad of treatments for infantile spasms that have been explored over the years, there is currently only a handful of treatments that are generally considered first-line. The most popular are forms of corticotropin (ACTH), oral corticosteroids, and vigabatrin. It is over fifty years since the hormonal treatments were introduced, but evidence suggests that they remain marginally more effective than other first-line treatment interventions, at least in terms of stopping the epileptic spasms. However, they are associated with significant side effects that make many physicians and families prefer other first-line treatment interventions. Vigabatrin, an inhibitor of GABA transaminase, was introduced twenty years ago and had become, for many physicians, the preferred first-line treatment when it was found be associated with significant risks of irreversible visual field deficits. This review of evidence, obtained mainly from randomized-controlled trials, considers these and other potential first-line treatments in the context of outcomes such as cessation of spasms, relapse of spasms, significant adverse events, and later neurodevelopment.

Tuesday, 29.06.2010
09:00–11:00h
Main Session
Hall 1 (Jupiter)
Advances in techniques to delineate the epileptogenic zone

HEMODYNAMIC CORRELATES OF EPILEPTIC ACTIVITY USING fMRI AND THEIR POTENTIAL CLINICAL ROLE
Lemieux L (United Kingdom)

Functional MRI is capable of revealing hemodynamic patterns correlated with epileptic discharges observed on EEG, providing unique

localizing information. We review the progress made over the last 10 years using EEG-correlated fMRI in patients with epilepsy, from block design-like spike-triggered fMRI to the modelling of continuously-recorded data, the use of source imaging technology to enhance detection and interpretation of the hemodynamic changes and data-driven analysis schemes. We will discuss the study of interictal and ictal epileptic activity and comparison of the results with invasive tests and postsurgical outcome.

SPECTROSCOPIC IMAGING IN PRESURGICAL EVALUATION OF EPILEPSY PATIENTS

Krsek P (Czech Republic)

Proton magnetic resonance spectroscopy (1H MRS) has proved to have a significant value in the evaluation of various types of epilepsy. It can help with the localization of epileptic lesions and provide an insight into the biophysical and biochemical processes related to epileptic seizures. Examination of patients with epilepsy using 1H MRS is focused on the observation of changes in N-acetylaspartate, creatine/phosphocreatine (Cr/PCr), cholines (Cho), glutamate (Glu), glutamine (Gln) and GABA signals and their correlation with the results of MR imaging and the other clinical methods. 1H MRS imaging (chemical shift imaging, CSI) is able to collect spectroscopic data from multiple adjacent voxels covering a large volume of brain tissue in a single measurement. It can be used for the lateralization of the epileptogenic zone in mesial temporal epilepsy as well as for the localization of the epileptogenic area outside temporal lobes. It was recently found to be valuable in the presurgical evaluation of patients without MRI-apparent lesions. We proved that 1H MRS could be more sensitive for the detection of discrete malformations of cortical development than conventional MRI. In the lecture, recent advances in 1H MRS methodology and its use in the evaluation and treatment of different types of epilepsy will be illustrated. Supported by Grants MZOFNM2005 and Kontakt Programme ME09042.

APPROACHES TO FOCUS LOCALIZATION USING MODERN PET TRACERS

Ryvlin P (France)

IDENTIFICATION OF SUPERFICIAL AND DEEP SOURCES OF EPILEPTIC ACTIVITY BY MAGNETOENCEPHALOGRAPHY

Ioannides A (Cyprus)

FROM SINGLE CELL RECORDINGS TO HIGH FREQUENCY OSCILLATIONS: NOVEL INDICATORS OF EPILEPTOGENICITY

Jacobs J (Germany)

Recently, high frequency oscillations (HFOs) between 80 and 500 Hz recorded from intracranial electrodes were recognized as novel markers of epileptogenicity. They can be divided into ripples (80–250 Hz) and fast ripples (250–500 Hz). HFOs most frequently occur in the seizure onset zone interictally and further increase during seizures. Preliminary studies reveal an association between removal of HFO generating tissue and good postsurgical outcome. Information gained from these oscillations is independent of other modalities such as spikes or lesional tissue changes. First studies analysing HFOs derived from recordings with microelectrodes. These revealed that HFOs are generated over small cortical areas. Nevertheless, later studies could record similar oscillations with standard macro electrodes during routine clinical monitoring. It is currently unclear whether different sized contacts can record specific types of HFOs and whether some electrodes types are best to delineate epileptogenic areas. Contradictory results are especially found in regard to the physiological or pathological value of HFOs of different frequencies. While microelectrode recordings clearly demonstrate that ripples are physiologic oscillations and fast ripples are correlated with epileptogenicity, this separation cannot be seen with macroelectrodes. There may also be significant differences between recordings in the mesial temporal lobe and neocortical areas. Single-cell recordings are the smallest scale recordings available in humans. Analysis of single cell spiking and multiunit activity interictally and prior to seizure may reveal patterns of ictogenesis and help to distinguish different epileptogenic areas as well as areas of propagation. This talk will present recent advances in the analysis of HFOs and single cell recordings. Their value in the presurgical evaluation and focus localization in patients with refractory epilepsy and unclear focus localization will be discussed.

Tuesday, 29.06.2010
09:00–11:00h
Hall 6 (Marika)
Main Session
AED development, selection and use relevant to gender and age

CLINICAL TRIALS OF AEDs: NEW EMEA GUIDELINES VERSUS CLINICAL NEEDS IN DIFFERENT AGE GROUPS

Baulac M (France)

TOWARD A SYNDROME-BASED AED SELECTION IN CHILDREN

Covanis T (Greece)

AED SELECTION AND USE IN WOMEN OF CHILDBEARING POTENTIAL

Morrow J (United Kingdom)

The choice of AED for a woman of childbearing potential encompasses a complex risk/benefit analysis. The benefits of seizure control must be carefully balanced against the risks to the individual (and to any unborn feotus) and is complicated further by the fact that individual risks are likely to change over time. While teratogenicity is of concern, it is only one of a number of factors in the prescribing of AEDs to women of childbearing potential. Other adverse effects, both short and long term, need to be considered. These include potential cosmetic changes, effects on cognition, effects on fertility, interactions with the oral contraceptive pill and the potential for longer term effects on bone health. In respect of teratogenic risk the large prospective pregnancy registers are now starting to provide a useful method of quantifying risk to the feotus, at least in terms of major structural defects but, there is ongoing interest and concern about minor (and dysmorphic) changes and neurodevelopmental delay. There is also a growing awareness that the use of certain antiepileptic drugs (some of which may be considered preferential because of a perceived low teratogenic risk) may prove more difficult to use during pregnancy than some of the traditional AEDs due to fluctuations in serum levels resulting in potential seizure breakthrough.

AED SELECTION AND USE IN THE ELDERLY: PHARMACODYNAMIC AND PHARMACOKINETIC CONSIDERATIONS

Perucca E (Italy)

IDIOSYNCRATIC ADVERSE EFFECTS: ARE THEY AGE-DEPENDENT AND IF SO WHY?

Pirmohamed M (United Kingdom)

Tuesday, 29.06.2010
Hall 1 (Jupiter)
14:30–16:00h
Special Symposium
The Neurobiology Symposium: Epilepsy, dementia, Alzheimer's disease and the temporal lobe

LINKS BETWEEN ALZHEIMER'S DISEASE/DEMENTIA AND EPILEPSY

Larner AJ (United Kingdom)

WHAT CAN ANIMAL MODELS OF ALZHEIMER'S DISEASE TEACH US ABOUT BRAIN EXCITABILITY

Tanila H (Finland)

Alzheimer's disease (AD) and epilepsy are traditionally considered totally separate disease entities, but epidemiological data actually indicate that AD patients have about 10-fold increased risk of developing seizures than age-matched controls. We and other colleagues working on AD mouse models carrying familial AD associated mutated forms of amyloid precursor protein (APP) and presenilin-1 have recently demonstrated that epileptic seizures are an essential part of the phenotype of this kind of mouse models. Furthermore, our data indicate that epileptic seizures are caused by the accumulating amyloid-beta protein and less likely by other direct consequences of the mutations. Thus we have a new interesting model of epilepsy caused by accumulation of excessive amount of physiological protein in the brain. There are several possible mechanisms whereby amyloid-beta protein can enhance brain excitability, including modulation of ion channels, interference with glutamate versus GABAergic neurotransmission, declined cell energy metabolism, and impaired astrocyte function rendering the neurons exposed to high extracellular glutamate or K^+ concentrations. If the seizures in APP transgenic mice are mediated by unconventional mechanisms, what would be the effect of conventional anticonvulsive drug treatment? AD patients with fragile cognitive abilities are a less favorable target group for antiepileptic medication, while undiagnosed temporal lobe seizures may underlie some symptoms that we considered typical of AD and may respond well to adequate drug therapy.

Tuesday, 29.06.2010
14:30–16:00h
Hall 2 (Roses)
Discussion Group
New insight into epilepsy management in children: proposed by the European Pediatric Neurology Society

EPILEPSY AS A PRESENTATION OF NEURO-METABOLIC DISORDERS

Wolf N (The Netherlands)

EPILEPSY AS A PRESENTATION OF AUTOIMMUNE DISEASES

Vincent A (United Kingdom)

GENETIC INSIGHTS TO EARLY ONSET EPILEPTIC ENCEPHALOPATHIES

Bahi Buisson N (France)

FOCAL EPILEPSIES WITH GENERALIZED MANIFESTATIONS

Cross H (United Kingdom)

The term ''focal'' within the new proposal for classification refers only to seizures, defined as ''seizures originating in one area of the brain.'' This is further qualified to indicate that seizures originate only within networks limited to one hemisphere, and in some cases there is more than one epileptogenic network, and more than one seizure type but each individual seizure type has a consistent site of onset. This is an important definition, especially for consideration of children for surgical management. However, it is not always so easy in the developing brain to specifically define a focal onset. Within the same classification electroclinical syndromes are maintained that are age related. During early development, rapid engagement of wider networks means that more generalized manifestations are seen despite apparent focal pathology eg infantile spasms the result of focal cortical dysplasia. The hypothesis that such spasms, on the whole associated with bilateral changes on EEG, originate from such focal pathology arises from (1) the fact that children may present with focal seizures, evolve into spasms and then subsequently return to focal seizures, and that (2) such may be alleviated by removal of that pathology. Later in the developmental process similar bilateral manifestations may be seen, interpreted as generalized despite unilateral pathology eg seizures from hemipolymicrogyria evolving into apparent generalized spike wave of slow sleep (ESES); discharges arising focally but rapidly propagating within and between hemispheres suggesting secondary bilateral synchrony. Even in the absence of a structural lesion such may be seen to be driven from one localized area in syndromes such as Landau Kleffner syndrome associated with ESES. The recognition that an apparent generalized clinical picture may arise from a more focal source is important, both for defining the relationship of the epileptic activity to any cognitive deterioration, as well as the awareness that some of these children may benefit considerably from surgical intervention.

Tuesday, 29.06.2010
14:30–16:00h
Hall 3 (Delphi)
Discussion Group
Clinical and basic concepts of IGE revisited

IS ABSENCE EPILEPSY TRULY GENERALIZED?

van Luijtelaar G (The Netherlands)

ARE ABSENCE AND LIMBIC SEIZURES MUTUALLY EXCLUSIVE?

Onat F (Turkey)

The coexistence of idiopathic generalized typical absence epilepsy and mesial temporal lobe epilepsy in the same patient is extremely rare. The

reason for this rare coexistence is poorly understood. Therefore, several studies have addressed a hypothesis of that there is a mutual cross-interaction in the circuits involved in mesial temporal lobe epilepsy and generalized absence epilepsy. A number of experiments in rats with genetically determined absence epilepsy have shown a resistance to secondary generalization of experimentally produced limbic seizures. In genetic absence epilepsy rats from Strasbourg (GAERS) and Wistar Albino Glaxo rats from Rijswijk (WAG/Rij), both well-validated genetic models of typical absence epilepsy, spike-and-wave discharges (SWDs) contributes to this resistance to experimental limbic epilepsy. The resistance to the secondary generalization of limbic seizures during amygdaloid kindling in GAERS increases with age as the SWDs on the EEG and the mechanisms underlying absence epilepsy matures. The evidence related to the effect of temporal lobe epilepsy on absence seizures suggests that the limbic seizures spread to areas involved in absence epilepsy mechanisms and modify their activity. These findings point to interactions between cortico-thalamo-cortical and limbic circuitry but do not show how and where the interactions occur. The connections of the thalamic reticular nucleus with limbic structures through the midline thalamic nuclei may be particularly relevant for understanding of the resistance to secondary generalized convulsive seizures in the absence epilepsy models or limbic seizure-induced changes in SWDs. Thus the first question of whether absence epilepsy has an antagonistic effect on temporal lobe epilepsy will be addressed in the first part of the talk and the second part will consider that whether limbic epilepsy has an antagonistic effect on absence seizures.

IDIOPATHIC ABSENCE AND SYMPTOMATIC FOCAL EPILEPSY SYNDROMES IN HUMANS; THE CLINICAL EVIDENCE

Elwes R (United Kingdom)

CHANNELOPATHIES AS A GENETIC CAUSE FOR EPILEPSY: THE RELATION TO IDIOPATHY

Avanzini G (Italy)

Tuesday, 29.06.2010
14:30–16:00h
Hall 4 (Nafsica)
Discussion Group
Valproic acid (VPA) an old and established antiepileptic drug that keeps surprising

THE ROLE OF HISTONE DEACETYLASE (HDAC) IN VPA EFFICACY AND TERATOGENICITY

Loescher W (Germany)

Valproate, a simple branched-chain fatty acid (2-propylpentanoic acid), is a broad-spectrum antiepileptic drug with well-established efficacy in both partial and generalized seizures. Valproate is also commonly prescribed for bipolar mood disorder and is a first-line prophylactic drug for migraine headache. After more than 40 years of clinical use, the mechanisms of action of valproate in epilepsy, bipolar disorder and migraine are still not fully understood. Various potential mechanisms of action have been described, including an increase of the inhibitory neurotransmitter GABA by increased GABA synthesis and/or decreased GABA degradation, modulation of voltage-dependent ion channels, and effects on cell signalling. Considering that about 2 weeks of daily valproate administration are required before its mood-stabilizing effect becomes significant, and that this effect persists well after valproate cessation, it has been assumed that the mechanism of action of valproate involves not only acute and short-term biochemical effects but also changes at the genomic level. Recent research suggests two mechanisms through which valproate can simultaneously affect the expression of multiple genes: the enhancement of AP-1 binding to DNA and the inhibition of histone deacetylases (HDACs). Histone acetylation has been shown to be an important regulatory mechanism, controlling the transcription of about 20% of the genome. Valproate-induced histone hyperacetylation by inhibition of HDAC has been demonstrated in vivo, and at clinically relevant concentrations. Inhibition of HDAC may explain the activating effect of valproate on GABA synthesis, at least part of its long-term antiepileptic effect (e.g., by increase of GABA), its neuroprotective effects, its antimanic effect, its anticancer effect, but also its teratogenic effect. However, two recent findings argue against a role of HDAC inhibition in valproate's antiepileptic activity. (1) analogues of valproate that do not inhibit HDAC still protect against chemically induced seizures in rodents; and (2) in contrast to valproate, inhibition of HDAC by a more selective inhibitor does not exert any long-term anticonvulsant effects. On the other hand, all inhibitors of HDAC have shown teratogenic effects similar to those described for valproate. In conclusion, influence of valproate at the genomic level provide novel insights into its therapeutic and adverse effects.

VPA AND COGNITIVE DECLINE: ADVERSE EFFECTS VERSUS THERAPEUTIC POTENTIAL IN ALZHEIMER'S DISEASE

Holmberg B (Sweden)

A REAPPRAISAL OF VPA DRUG INTERACTIONS AND, IMPLICATIONS FOR ITS USE IN NOVEL POTENTIAL INDICATIONS

Sills G (United Kingdom)

The clinical pharmacology of valproate (VPA) is complex and remains incompletely understood, despite more than 40 years' use in the treatment of epilepsy and more recent utility in both bipolar disorder and migraine. VPA exhibits high plasma protein binding, undergoes extensive metabolism by beta-oxidation and multiple UGT and CYP isoenzymes, and is a recognized hepatic enzyme inhibitor. These characteristics predispose VPA to interactions whenever it is employed in multiple drug regimens. The recent discovery of histone deacetylase inhibition with VPA opens up new therapeutic avenues in several disease areas, including cancer, HIV infection, schizophrenia and Alzheimer's disease. The propensity of VPA to precipitate drug-drug interactions should be considered when evaluating its potential as an adjunctive agent in these disorders. A handful of pharmacokinetic interactions between VPA and compounds used in the treatment of cancer (cisplatin), HIV infection (zidovudine), and schizophrenia (chlorpromazine, clozapine) have been reported. Many more are predicted but have yet to be formally investigated. There also exists the potential for pharmacodynamic interactions, particularly in respect of hepatotoxicity. Interactions with VPA are likely to be noteworthy in any new indication but they should not be viewed as a barrier to the investigation of its possible therapeutic benefit. An understanding of the clinical pharmacology of VPA and the agents with which it is likely to be coadministered is essential in order to ensure that potentially useful clinical effects in new disease areas are not undermined by something as simple and predictable as drug-drug interactions.

HOW CAN WE DEVELOP A SUCCESSFUL SECOND GENERATION TO VPA DRUG?

Bialer M (Israel)

Valproic acid (VPA) is one of the four major antiepileptic drugs (AEDs). Although in anticonvulsant animal models VPA is the least potent of the established AEDs, in patients Two VPA amide derivatives, valrocemide and valnoctamide are currently in phase II clinical trials for epilepsy and bipolar disorder, respectively. 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, its hepatotoxicity results from biotransformation into hepatotoxic metabolites with a terminal double bond 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) better potency than VPA in epilepsy and other CNS disorders while retaining broad-spectrum antiepileptic activity; (2) lack of teratogenicity and hepatotoxicity; (3) lack of weight gain. These characteristics will endow such a VPA derivative a promising potential to become a second generation to VPA drugs. 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 VPA anticonvulsant and CNS-activity, while avoiding its teratogenicity and hepatotoxicity. 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. The leading aliphatic VPA amide derivatives that emerged from our studies were valrocemide, valnoctamide (racemate and individual stereoisomers) and the enantiomers of propylisopropylacetamide (PID), (R)-PID and (S)-PID. These compounds were more potent than VPA in a wide range of animal models for epilepsy and 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), α-fluoro-TMCD, α-chloro-TMCD, N-methyl-TMCD (MTMCD) and 2,2,3,3-tetramethyl-cyclopropanecarbonyl urea (TMC-Urea), possess two quaternary carbons in the β-positions to the carbonyl and hence cannot be biotransformed into hepatotoxic metabolites with a terminal double bond. MTMCDand TMC-Urea were found to be broad-spectrum anticonvulsants. Furthermore they are nonteratogenic and most probably nonhepatotoxic. In rats (po) α-Cl-TMCD had an MES-ED_{50} of 97mg/kg and a scMet-ED_{50} of 27mg/kg. α-F-TMCD was 120 times more potent than VPA in the rat-scMet test (ED_{50} = 6mg/kg) and had a protective index (PI = TD_{50}/ED_{50}) of 20. In the 6 Hz psychomotor mouse model α-F-TMCD had ED_{50} values of 57mg/kg (32 mA) and 59mg/kg (44 mA) and in the hippocampal-kindled-rat and in the pilocarpine-induced-status rat models its ED_{50} values were 30mg/kg and 23mg/kg, respectively. In conclusion, valrocemide, valnoctamide and its stereoisomers, PID enantiomers, α-F-TMCD, α-Cl-TMCD, MTMCD and TMC-Urea, are CNS-active amide derivatives of VPA that are more potent than VPA, due to their lipophilicity, better brain permeability and metabolic stability. Their broad spectrum and potent anticonvulsant and CNS activity, along with their lack of teratogenicity (animal models), high safety margin and favorable pharmacokinetic profile, make these compounds attractive candidates to become new, successful second generation to VPA drugs.

Tuesday, 29.06.2010
14:30–16:00h
Hall 5 (Nefeli)
Discussion Group
New developments in K^+-channel involvement in epilepsy

AXONAL KCNQ-CHANNELS REGULATE NEURONAL EXCITABILITY AND SYNAPTIC TRANSMISSION

Storm J (Norway)

ATYPICAL GATING OF KCNQ-CHANNELS IN BNFC

Taglialatela M (Italy)

CRITICAL REDUCTION OF SK-CHANNELS IN A MODEL OF TLE

Kirschstein T (Germany)

Action potentials in hippocampal CA1 pyramidal neurons are followed by a prominent after-hyperpolarization (AHP) whose medium component is thought to be generated by small-conductance $Ca2^+$-activated K^+ channels (SK channels). Neuronal excitability is increased in epilepsy, and the AHP in turn is fundamentally involved in regulation of cellular excitability. Hence, we investigated the involvement of the SK channel-mediated AHP in controlling cell and network excitability in the pilocarpine model of temporal lobe epilepsy (TLE). Both acutely isolated CA1 pyramidal cells and isolated hippocampal slices were investigated in terms of the impact of SK channel-mediated AHP on hyperexcitability. Our findings show that pilocarpine-treated chronically epileptic rats exhibit significantly reduced SK channel-mediated hyperpolarizing outward current which was accompanied by a significant decrease in the somatic AHP. Paradoxically, SK channel inhibition had a substantially greater impact in exacerbating epileptic activity induced by decreased $Mg2^+$ in hippocampal slices from pilocarpine-treated rats suggesting that network excitability critically depended on SK channel-mediated AHP in the diseased animal. Additional real-time RT-PCR and semiquantitative Western blot experiments revealed that both the SK2 channel transcript and protein were significantly down-regulated in the epileptic CA1 region. We conclude that SK2 channels are down-regulated in chronic TLE underlying the impaired SK channel function in CA1 pyramidal cells, and a further reduction of the remaining critical mass of SK channels results in an acute network decompensation.

K^+-BUFFERING VIA KIR CHANNELS IS REDUCED IN SEIZURE-INDUCED BLOOD–BRAIN BARRIER DISRUPTION

Friedman A (Israel)

Tuesday, 29.06.2010
14:30–16:00h
Hall 6 (Marika)
Workshop
Mapping brain functions using intracranial electrodes

WHAT EVOKED POTENTIALS TELL US ON THE FUNCTIONAL ANATOMY AND CONNECTIVITY OF THE HUMAN BRAIN?

Brazdil M (Czech Republic)

Information processing in the human brain is generally based on two fundamental principles – functional specialization and functional integration. Functional specialization refers to the existence of specialized neurons and brain areas, which are organized into distinct neuronal populations grouped together to form segregated cortical areas. Functional integration refers to the interactions among multiple specialized neuronal populations, and how these interactions depend upon the context. Functional integration is mediated by functional or effective connectivity. Functional connectivity is defined as correlations between spatially remote neurophysiological events; effective connectivity refers to the influence that one neuronal system exerts over another. Both functional specialization and connectivity can be investigated across several magnitude scales – celular, neuronal populations, and large-scale systems. Intracerebral macro-EEG recordings, performed in epilepsy surgery candidates, provide us with unique direct measures of neuronal population activity. Detailed analysis of recorded local field potentials fundamentally contributes to the study of both functional anatomy and connectivity at the mesoscopic scale. Simple averaging of the depth EEG signals has been repeatedly used in the last two decades to study various cognitive functions (attention, memory, consciousness, error processing, etc.) using intracerebral event-related potentials (ERPs). Multiple sources of different ERPs have been identified within cortical and subcortical structures,

which has importantly complemented our knowledge on functional human brain anatomy arising from neuroimaging studies. In contrast the role of ERPs for understanding of functional or effective connectivity seems to be limited. Instead, advanced mathematical methods of signal analysis are used, including measures of phase synchrony, cross-correlation or computing the directed transfer function. The study was supported by MÅ MT Ã^R Research Program no. MSM0021622404.

DYNAMIC SPECTRAL IMAGING AS AN ONLINE EXPLORATORY TOOL OF BRAIN FUNCTIONS

Lachaux JP (France)

DO MICRO-RECORDINGS ADD ANYTHING NEW TO WHAT CAN BE DONE USING MACRO-ELECTRODES?

Fried I (Israel)

Tuesday, 29.06.2010
14:30–16:00h
Hall 7 (Colossus)
Discussion Group

IMAGING THE CONNECTIONS OF THE ELOQUENT BRAIN AND EPILEPTOGENIC FOCI
IMAGING VISUAL PATHWAYS IN TEMPORAL LOBE EPILEPSY SURGERY

Nilsson D (Sweden)

Background: Injury to the optic radiation (OR), resulting in a visual field defect (VFD) is common after temporal lobe resection (TLR) for temporal lobe epilepsy (TLE). Tractography generates virtual maps of white matter tracts from information on the directionality and magnitude of water diffusion motion provided by diffusion tensor imaging (DTI).

Methods: TG was used to visualize the OR in TLE patients before and after surgery. The anatomical accuracy of the two main TG algorithms was compared. A review of studies using TG of the OR in TLE patients was performed. Results: TG can assess the anatomical location of the OR and the interindividual variability in the anterior extent of the OR in both normal controls and in temporal lobe epilepsy patients. Energy minimization techniques for TG were more accurate than line propagation techniques but also more time-consuming. A correlation between postoperative VFD and TG of the OR has been reported and suggests that the method's validity is good.

Discussion: TG can visualize the anatomical location of the OR preoperatively in TLE patients and estimate the risk of developing a VFD. If used intraoperatively TG may guide the epilepsy surgeon to avoid injury to the OR and thus reduce the risk of a postoperative VFD. Limitations of TG include DTI artifacts, insufficient validation and subjectivity in selection of seed points. The optimal technique for performing TG remains to be determined.

CONNECTIVITY OF LANGUAGE AND MEMORY CIRCUITS IN TEMPORAL LOBE EPILEPSY

Yogarajah M (United Kingdom)

IDENTIFYING THE CONNECTIVITY OF THE EPILEPTOGENIC ZONE

Vulliemoz S (Switzerland)

Tractography, based on diffusion tensor magnetic resonance imaging, has recently emerged as a powerful noninvasive tool to map white matter tracts and study the structural connectivity of the brain in vivo. Different strategies can be applied to study the propagation of interictal and ictal epileptic activity along structural tracts mapped by tractography. Seeding from noninvasive or invasive localization of the epileptic focus allows mapping all connections from the seeding region. Alternatively, the tracking can be restricted with masks or waypoints/end points based on individual anatomic and neurophysiologic characteristics, for instance using two seeds in regions corresponding to seizure onset and seizure propagation. We showed that qualitative analysis of tracts by comparing the spatial extent of the tracts in individual patients versus controls helps to identify patients specific tracts, while quantitative tract measures including mean fractional anisotropy, mean diffusivity and tract volume can show different tract properties in patients versus controls. Individual patterns of structural connectivity can then be correlated to functional connectivity estimated by EEG, MEG, functional MRI to better identify individual or syndrome-specific patterns of propagation in the epileptic brain. This could have great implications for epilepsy surgery, by helping to tailor ''disconnection surgery'' when the seizure onset zone cannot be resected.

THE FUTURE APPLICATIONS OF TRACTOGRAPHY TO DEFINING THE RELATIONSHIP OF ELOQUENT AND EPILEPTOGENIC CORTEX AND TO PLANNING SURGERY

Duncan J (United Kingdom)

Tractography has the potential to visualize white matter tracts that are critical to cerebral functions and interruption of which will cause deficits. To date, most attention has been paid to the corticospinal tract, optic radiation and arcuate fasciculus. At present the spatial resolution of in vivo tractography is of the order of 2 mm, and work is in progress to determine how this may be improved within a reasonable image acquisition time. The coregistration of tractography results with T_1-weighted scans that show anatomical detail needs to take into account the different anatomical distortions of the T_1-weighted and Diffusion Tensor sequences. The integration of tractography data with surgical neuro-navigation software presents challenges. After a craniotomy, the physical distortion of cerebral anatomy means that preoperative tractography will not represent the current position of eloquent tracts. Approaches being introduced are to acquire intraoperative T_1-weighted scans and to realign the preoperative tractography to this. A further approach is to acquire intraoperative Diffusion Tensor Imaging and to derive tractography from these data. A practical limitation is that the time taken is currently excessive to be carried out intraoperatively.

Wednesday, 30.06.2010
07:30–09:00h
Hall 2 (Roses)
Teaching Session
Pediatric epilepsy surgery in practice: the U-task experience

A CASE OF CATASTROPHIC EPILEPSY TREATED BY HEMISPHEROTOMY

Braun K (Netherlands)

A CASE OF LESIONAL TEMPORAL LOBE EPILEPSY TREATED BY LESIONECTOMY ON THE BASIS OF VIDEO-EEG MONITORING DATA ONLY

Strobl K (Germany)

A CASE OF LESIONAL EXTRATEMPORAL EPILEPSY TREATED AFTER INVASIVE MONITORING

Tassi L (Italy)

A CASE OF AN MRI-NEGATIVE PATIENT STUDIED BY STEREO-EEG

Ryvlin P (France)

Wednesday, 30.06.2010
07:30–09:00h
Hall 3 (Delphi)
Teaching Session
MRI postprocessing in epilepsy

OVERVIEW OF MRI POSTPROCESSING TECHNIQUES IN THE PRESURGICAL EVALUATION OF EPILEPSY PATIENTS

Huppertz HJ (Switzerland)

Using the example case of a former patient as a guiding line, the talk gives an overview of several novel methods of computer-assisted MRI postprocessing and their clinical application in the noninvasive and invasive presurgical evaluation of epilepsy patients. Morphometric MRI analysis is a voxel-based method which applies SPM5 algorithms to a T_1-weighted volume data set and compares the resulting feature maps to a normal database. The method facilitates the detection and delineation of subtle focal cortical dysplasia and other cortical malformations by highlighting structural alterations like thickening of the cortical ribbon, blurring of the grey-white matter junction, and abnormal gyration. Automatic curvilinear reformatting of 3D MRI data calculates serial convex planes in different depths from the cortical surface. The method improves the display of the gyral structure, permits a precise localization of lesions, and helps to identify subtle abnormalities difficult to detect in planar slices. Preoperative planning of subdural electrode implantation for invasive EEG recordings by means of realistic 3D representation of electrode contacts is a novel method which allows calculating electrode positions on the convexity of the individual cortical surface in correct spatial proportions with respect to brain size. Thereby, it permits rapid and exact determination of optimal electrode positions and supports planning and execution of electrode implantation. After implantation, the localization of subdural electrodes is determined by an automated fast method for volume rendering of 3D MRI at the level of the implanted subdural electrodes. The results of all presented methods can be integrated into neuronavigation to support final lesion resection. In conclusion a variety of MRI postprocessing methods may aid in the presurgical management of medically refractory epilepsy patients.

DIAGNOSTIC VALUE OF MORPHOMETRIC MRI ANALYSIS IN CLINICAL AND PRECLINICAL SETTINGS

Wellmer J (Germany)

AUTOMATIC DETECTION AND QUANTIFICATION OF HIPPOCAMPAL PATHOLOGY ON MRI—RESULTS AND CLINICAL APPLICATIONS

Hammers A (United Kingdom)

Focal MRI changes amenable to surgery, most importantly hippocampal sclerosis (combined hippocampal atrophy (HA) and increased T_2/FLAIR signal), are missed in up to 86% of cases on routine radiological evaluation, particularly outside epilepsy centers (von Oertzen J et al. JNNP 2002). This often prevents or delays adequate therapeutic management. Even with optimal reporting, no abnormalities are found in a quarter of patients with focal epilepsies. Manual quantification of HA on T_1-weighted images is time-consuming and not scalable. Some automatic volumetry techniques are robust enough to be used for automatic detection of HA, notably region-growing techniques with probabilistic atlas initialization (Chupin M et al. Neuroimage 2009) and multiatlas propagations with decision fusion (Hammers A et al. Neuroimage 2007). Such techniques can achieve 100% sensitivity in detecting HA (necessary for a screening technique) while maintaining excellent specificity. Voxel-based regional image similarity measures have also achieved excellent results (Duchesne S et al. 2006) in HA and TLE with normal MRI (TLE-N). Recently, we have successfully combined improved multiatlas label-propagation volumetry (Heckemann RA et al. Neuroimage 2010) and machine learning techniques to replicate 100% accuracy in the detection of HA. In addition, we achieved over 90% accuracy in distinguishing TLE-N patients from controls based on T_1-weighted MRI alone, and the algorithm correctly lateralized the epileptogenic side in 19/20 TLE-N patients (94%; Keihaninejad S et al. ISBI 2010, ECE 2010). Automated and reliable whole-brain segmentation and structure selection can show and quantify known structural abnormalities in TLE with HA. In addition, previously unknown structural differences in TLE-N patients compared with healthy controls and patients with HA have been detected. The techniques await validation on multicentre data, extension to patients with epilepsy other than TLE, and routine clinical application at the individual patient level.

DIFFUSION-BASED MRI AND TRACTOGRAPHY IN EPILEPSY

Yogarajah M (United Kingdom)

Wednesday, 30.06.2010
07:30–09:00h
Hall 4 (Nafsica)
How to do? Seizure Monitoring in the EMU Setting
How to do? Digital video/EEG seizure monitoring: how to get more bang for your buck

DIGITAL VIDEO-EEG DATA ACQUISITION: THE INS AND OUTS OF IT

Velis D (The Netherlands)

CHOICE OF MONTAGES: THE LONG AND SHORT OF IT

Beniczky S (Denmark)

EFFICIENT SPIKE DETECTION: THE TRICKS OF THE TRADE

Larsson PG (Norway)

Wednesday, 30.06.2010
07:30–09:00h
Hall 5 (Nefeli)
Teaching Session – Introduction to VIREPA
EUREPA session: Neuroimaging: supported by the ILAE Commission on Diagnostic Methods

ROLE OF NEUROIMAGING IN PRESURGICAL EVALUATION IN ADULTS
Marusic P (Czech Republic)

WHY, WHEN AND HOW TO PERFORM PET AND SPECT IN A CHILD WITH FOCAL EPILEPSY?
Chiron C (France)

Wednesday, 30.06.2010
07:30–09:00h
Hall 7 (Colossus)
Case Oriented Learning Session
EUREPA session: Epilepsy surgery

CLINICAL CASE 1
Kahane P (France)

CLINICAL CASE 2
Stefan H (Germany)

CLINICAL CASE 3
Francione S (Italy)

Wednesday, 30.06.2010
09:00–11:00h
Hall 1 (Jupiter)
Main Session

CHALLENGING THE CONCEPT OF IDIOPATHIC EPILEPSIES
CLINICAL EEG (ICTAL – INTERICTAL) EVIDENCE
Guerrini R (Italy)

EVIDENCE FROM ANALYSIS OF CLINICAL SEIZURES AND INTERICTAL FINDINGS WITH ADVANCED NEUROPHYSIOLOGICAL AND NEUROIMAGING TECHNIQUES
Kimiskidis V (Greece)

MECHANISMS OF THEIR DEPENDENCE ON AROUSAL LEVEL
Halasz P (Hungary)

Recent developments challenged the hitherto prevailing epilepsy classification concept. Focal epilesies proved to be not focal, generalized epilepsies not generalized. In the same time more and more evidences support that epilepsy should be concipiated better as network and system epilepsies. In the present talk we provide evidences that sleep activation of spike – wave discharges of IGE are associated with micro-arousal dependent delta/K-complex bouts (CAP A1 periods, or paradoxical ''antiarousals'') of light NREM sleep (mainly on descending slope of first cycles). This activation could be connected with the dynamic momentum of triggering the burst-firing sleep working mode of the thalamo-cortical system. These data will be interpreted as supporting the idea that substrate of IGE is the epileptic distorsion of the thalamo-cortical part of sleep system.

IN SEARCH OF A SATISFACTORY TERMINOLOGY (TAXONOMIC IMPLICATIONS)
Wolf P (Denmark)

Wednesday, 30.06.2010
09:00–11:00h
Hall 6 (Marika)
Main Session
Predicting epileptogenesis: how far are we from reaching the goal?

PREDICTORS AND BIOMARKERS, DEFINITIONS AND GENERAL CONCEPTS
Shorvon S (United Kingdom)

The use of biomarkers have become a prominent feature of recent work in a several neurological disorders (including MS, Alzheimer's and other neurodegenerative diseases). However, in clinical epilepsy, their application is currently extremely limited. In this talk, the definitions of 'biomarkers' and 'risk factors' will be considered and their differences emphasized. Major reasons for the lack of biomarkers include the diversity of causes and forms of epilepsy, the importance of exogenous factors in its clinical presentation. Hughlings Jackson felt that the mechanism of epilepsy had the same final common path, whatever the initiating cause and this concept remains largely valid, and the search for biomarkers in epilepsy should perhaps be best focused on these final mechanisms. An appraisal of the current clinical risk factors will be undertaken, and include aspects of biography, clinical history genetic traits, EEG and imaging features. The value of these factors in predicting the occurrence of epilepsy or its prognosis will be discussed. A decade ago, it was thought that pharmacogenomic markers for predicting drug resistance would be in routine use in clinical epilepsy, and this was a field in which biomarkers were predicted to have a major role (so-called 'personalized' drug therapy). However, despite large funding, progress has been disappointing and the possible reasons for the failure of this field of study to make any impact in clinical epileptology will be discussed as a paradigm for the challenge of clinical application in this field.

NEUROBIOLOGICAL MARKERS OF EPILEPTOGENESIS
Pitkanen A (Finland)

PRACTICAL BENEFITS OF PREDICTING EPILEPTOGENESIS: WHEN AND HOW BIOMARKERS CAN BE HELPFUL
Engel J (United States)

BIOLOGICAL AND CLINICAL PREDICTORS OF PHARMACORESISTANCE
Shiller Y (Israel)

Wednesday, 30.06.2010
14:30–16:00h
Hall 1 (Jupiter)
Discussion Group
Pediatric epilepsy surgery: state of the art on special syndromes

RASMUSSEN'S ENCEPHALITIS

Bien C (Germany)

Rasmussen's encephalitis (RE) is an inflammatory unihemispheric brain disorder. Its two clinical key facets are the progressive tissue and function loss and the epilepsy, often in form of epilepsia partialis continua. For both, treatment options are available. Whereas the antiseizure effect of antiepileptic drugs is usually limited, hemispherectomy in one of its modern variants offers a very high chance of seizure freedom at low complication rates. The operation, however, has the price of irreversible loss of functions located in the affected hemisphere. For prevention or slowing down of tissue and function loss, long-term immunotherapy can be effective. It does, however, mostly not improve the epilepsy. In practical terms, hemispherectomy should be considered and presurgical evaluation therefore be performed in all patients with pharmacoresistant and handicapping seizures due to RE. The key aims are: (1) To corroborate the unilateral nature of the disease (by MRI and video-EEG); (2) prediction of postoperative functional outcome in comparison to the actual presentation regarding language, motor, and visual function (visual field). Finally the expected benefits (very high chance of getting seizure-free and tapering the antiepileptic drugs) and the expected functional changes need to be individually weighted and thoroughly discussed with the patient and its family. In this situation, unequivocal treatment proposals can be readily made for many patients. A dilemma may emerge only in those with severe epilepsy but still preserved hemispheric function. In our experience, the two most frequent sources of therapeutic disappointment can readily be avoided: (1) Ambiguity regarding the therapeutic aims of a given intervention, and (2) underuse of treatment options including that of timely hemispherectomy.

HYPOTHALAMIC HAMARTOMAS

Delalande O (France)

Hypothalamic hamartomas (HH), require surgical treatment in patients presenting with refractory epilepsy.

We report on a single-center series of 51 patients who underwent surgery between January 1997 and April 2007. They experienced several types of seizure (gelastic, tonic, partial, atonic, generalized tonic–clonic, dacrystic, infantile spasm, mental retardation, behavioral and endocrinological abnormalities. Seventy-nine interventions were carried out. Every patient with the exception of the first underwent hamartoma's disconnection (pterional approach: 6 cases, endoscopy: 15 cases, both: 11 cases). Endoscopic approach was performed with a frameless stereotactic system in order to enhance feasibility and efficacy of the disconnecting procedure.

Surgery-related neurological complications occurred in 3 cases, 2 hemiparesis and one meningitis, all following a pterional microsurgical approach. Furthermore, 1 patient developed panhypopituitarism, 3 patients presented a hyperphagia and 1 patient a transitory central insipid diabetes, 3 had variable memory deficit.

All patients but 2 showed recovery or considerable improvement of their epilepsy (Engel I: 69%; II: 6%; III: 21%, IV: 4%); mean follow up: 3.2 years). According to our proposed classification of sessile HH into four types, the best candidates for endoscopic disconnection are type II and type III HHs. In the present series, patients affected by type II HH became seizure-free in 79% of the cases and improved in the remaining 21%, those presenting type III HH recovered in 65% of the cases and improved in 35%. Neuropsychological tests showed improvement in many cases.

Data from our series demonstrates that frameless stereotactic endoscopic disconnection should be considered as the treatment of choice in the presence of favorable anatomical conditions.

STURGE–WEBER SYNDROME

Arzimanoglou A (France)

TUBEROUS SCLEROSIS

Van Nieuwenhuizen O (The Netherlands)

A diagnosis of tuberous sclerosis complex (TSC) confronts patients, caregivers, and their clinicians with a high risk of intractable epilepsy and mental retardation. Although tuber load and genotype are related to cognitive outcome to a certain extent, early onset of seizures has been proven the only independent risk factor of cognitive deficits. Epilepsy surgery for medically refractory seizures is a well-accepted treatment option. Until now, there are still uncertainties about which TSC patients are good surgical candidates. Given the complexity of epilepsy in patients with TSC and its precarious prognosis, different surgical strategies, sometimes including invasive investigations, are justified. Standardized presurgical evaluation is not available in TSC patients. To date, multimodal approach, including magnetic source imaging, subtraction SPECT, [11C] methyl-L-tryptophan ([11C] AMT) PET, or invasive recordings with subdural and depth electrodes, has been reported of surplus value in the identification of the epileptogenic zone, but final resection zones have to be tailored by intraoperative electrocorticography. Postsurgical shift of epileptogenicity to other tuberal regions is feared, but a systematic review of the literature provided circumstantial evidence that the presence of multiple seizure types, multifocal lesions on imaging, and multifocal EEG abnormalities are not associated with seizure recurrence. In selected series surgery has been proven successful in 75% of the patients (Engel classification 1 and 2). Although seizure freedom may be an unrealistic aim in patients with severe cognitive disability, the chance of substantial seizure reduction renders surgery a compelling option, and therefore epilepsy surgery should be considered in all multidrug-resistant TSC patients.

Wednesday, 30.06.2010
14:30–16:00h
Hall 2 (Roses)
Discussion Group
Epileptic networks and lesions

EPILEPTIC NETWORKS

van Luijtelaar G (The Netherlands)

LESION DETECTION BY MRI POSTPROCESSING

Huppertz HJ (Switzerland)

In spite of continual technical advances in MRI epileptogenic lesions are still detected in less than half of patients with focal epilepsy. Computer-assisted MRI postprocessing methods may assist conventional visual analysis and increase the sensitivity for subtle lesions. The talk gives an overview of several novel techniques and their clinical application. Morphometric MRI analysis based on SPM5 algorithms facilitates the detection of subtle focal cortical dysplasia and other cortical malformations by highlighting structural alterations like thickening of the cortical ribbon, blurring of the grey-white matter junction, and abnormal gyration. Automatic curvilinear reformatting of 3D MRI data calculates serial convex planes in different depths from the cortical surface. The method improves the display of the gyral structure, permits a precise localization of lesions, and helps to identify subtle abnormalities difficult to detect in planar slices. Simple skull-stripping and subsequent 3D visualization of the cerebral surface allow to detect deviations from the normal sulcal pattern thereby giving additional hints to local malformations of cortical development. Automated voxel-based analysis of whole brain FLAIR as proposed by N. Focke et al. identifies lesional signal alterations by normalizing FLAIR intensities and comparing the rescaled images to a normal database. In a further development a regional analysis based on probabilistic hippocampal masks allows to quantify FLAIR signal alterations in temporo-mesial regions. Voxel-based volumetric MRI analysis based on a probabilistic brain atlas is a fully automated method for the detection and quantification of volume changes and atrophy of the whole brain and various cerebral substructures. The pattern of atrophy may point to certain neurodegenerative diseases (also those presenting with epileptic seizures) whereas longitudinal studies permit monitoring of dis-

ease progression and potential therapy effects. In conclusion MRI post-processing may assist lesion detection by extracting image properties which are not readily accessible by pure visual analysis.

HIGH FREQUENCY OSCILLATIONS (HFO) AND EPILEPTIC ACTIVITY

Rampp S (Germany)

The detection of epileptiform discharges in electro- and magnetoencephalography recordings (EEG/MEG) is a crucial part in diagnosing and presurgical evaluation of epilepsy. In recent years, the existence of oscillations in frequency bands >60–80 Hz (ripple activity) has been demonstrated in the animal and human brain. It was demonstrated that these high frequency oscillations (HFO) are highly associated to epileptic networks. Analysis of HFO provides valuable information for localization of epileptic networks and understanding of their dynamics. While initial research concentrated on the investigation of basic mechanisms, clinical applications, especially the diagnostic value beyond the information yielded by well-known patterns such as epileptic transients, are becoming more important and are on the brink of entering routine diagnostics. In addition, concepts of noninvasive HOF detection and analysis have emerged, which show first successful results. The presentation will thus give an overview of recent findings using invasive and noninvasive methods, as well as clinical applications.

NETWORKS AND SURGICAL TREATMENT

Chauvel P (France)

Wednesday, 30.06.2010
14:30–16:00h
Hall 3 (Delphi)
Discussion Group
Controversies in IGE

SYNDROMES IN DEVELOPMENT AND DECLINE

Hirsch E (France)

SYNDROMES IN DEVELOPMENT AND DECLINE

Walker M (United Kingdom)

PEDIATRIC AND ADULT EPILEPTOLOGY VANTAGE POINTS OF IGES: HOW DIFFERENT ARE THEY AND HOW CAN THEY MERGE?

Dulac O (France)

PEDIATRIC AND ADULT EPILEPTOLOGY VANTAGE POINTS OF IGES: HOW DIFFERENT ARE THEY AND HOW CAN THEY MERGE?

Agathonikou A (Greece)

Wednesday, 30.06.2010
14:30–16:00h
Hall 5 (Nefeli)
Workshop
Neurobiology of memory dysfunction in temporal lobe epilepsies

FUNCTIONAL AND ANATOMICAL ORGANIZATION OF MEMORY FORMATION IN THE TEMPORAL LOBE

Grunwald T (Switzerland)

Converging evidence from numerous lesional, functional imaging and electrophysiological studies has implicated the human hippocampal system with both the encoding for and the retrieval from episodic (declarative) memory. Invasive recordings from the medial temporal lobes of epilepsy patients undergoing invasive evaluations for possible resective surgery have shown that the human hippocampus proper and rhinal cortex contribute especially to the processing of stimulus novelty: ''New'' but not ''old'' verbal stimuli elicit event-related (cognitive) N400-like potentials within the rhinal cortex whose amplitudes correlate with the neuronal density of pyramidal cells within the hippocampal CA1-region. Likewise rare and unexpected but not frequent and expected stimuli elicit hippocampal P300-like potentials that correlate with the density of granule cells within the dentate gyrus. Meanwhile both potentials have been shown to correlate with encoding for declarative memory. Thus both (ento)rhinal cortex and hippocampus proper contribute to successful memory formation. However, both regions of the medial temporal lobe contribute differentially to recall and recognition: While the (ento)rhinal cortex contributes to familiarity-based recognition processes independent of a person's awareness of an event's history the hippocampus proper is instead involved especially during conscious recollection.

HIPPOCAMPAL GRANULE BUT NOT PYRAMIDAL CELL LOSS PREDICTS MEMORY IMPAIRMENT IN TLE PATIENTS

Pauli E (Germany)

THE DIVERSE REGENERATIVE CAPACITY OF THE HUMAN HIPPOCAMPUS AND ITS IMPACT ON MEMORY FORMATION IN TLE PATIENTS

Blümcke I (Germany)

Ample evidence points to the dentate gyrus as anatomical region for persistent neurogenesis in the adult mammalian brain. This has been confirmed in a variety of animal models under physiological as well as pathophysiological conditions. Notwithstanding, similar experiments are difficult to perform in humans. In rodent hippocampus, the neurogenic plasticity has been shown to directly translate into memory processing, whereas the physiologic role of hippocampal stem cells in the human hippocampus remains to be determined. The contribution of neurogenic plasticity in the development of drug-resistant temporal lobe epilepsy (TLE) is another controversial issue to be clarified. In vitro experiments using neural hippocampal stem cells obtained from epilepsy surgery offer an unique opportunity to approach these enigmas. Adult human hippocampal stem cells can be isolated from surgical tissue, proliferated in vitro and cell culture protocols allow neuronal differentiation in up to 80% of cell progenies in vitro. Our own studies revealed an ambiguous regenerative capacity in patients suffering from chronic drug-resistant TLE. Adult human neural stem cells with a high proliferation in vitro (HPC) were also capable of neuronal differentiation. A low proliferation capacity (LPC) of human hippocampal stem cells was associated with failure of neuronal differentiation in vitro. This is reflected by reduced numbers of dentate granule cells immunoreactive for Doublecortin, brain derived neurotrophic factor and cdk5 in the LPC group in vivo. There was no correlation between the regenerative capacity and seizure history in our cohort of TLE patients. In contrast, a remarkable association was found between the proliferation capacity of hippocampal stem cells in vitro and each patient's preoperative memory performance. In conclusion, surgical specimens obtained from TLE patients represent an important tool to study mechanisms of stem cell recruitment, proliferation and differentiation in the human brain. Our results further suggest that encoding new memories is related to the regenerative capacity of the hippocampus also in the human brain.

NEUROBIOLOGY OF ADULT HIPPOCAMPAL NEUROGENESIS UNDER PHYSIOLOGICAL AND PATHOPHYSIOLOGICAL CONDITIONS

Kuhn HG (Sweden)

Wednesday, 30.06.2010
14:30–16:00h
Hall 6 (Marika)
Discussion Group
Photosensitivity: from focal abnormality to generalized seizures

LINKS BETWEEN PHOTOSENSITIVITY AND IDIOPATHIC GENERALIZED EPILEPSY

Stephani U (Germany)

Photosensitivity (photoparoxysmal reaction, PPR) is paradigmatic for exogenous – endogenous interactions in the brain: Light (in EEG laboratories standardized intermittent flash light – photic – stimulation, IPS) or contrast rich patterns provoke PPR in a predisposed brain. PPR is defined as an epileptiform activity detectable in the EEG being observed as spike or poly spike wave locally over the posterior parts of the brain and/or generalized (grading acc. to Waltz et al. 1992). As an endophenotype (1) PPR is (causally) associated with IGE (prevalence of PPR in IGE: about 50%/90%, in idiopathic focal epilepsy –IFE- up to 25%; Wolf et al. 1986; Lu et al. 2008), (2) PPR is heritable (compatible with an autosomal dominant trait), (3) PPR represents a pathogenetic part of IGE (possible provocation of seizures by IPS), (4) PPR genetics seem to be less complex than IGE itself, (5) PPR segregate partly in families with multiple IGE affecteds, (6) PPR is not common in the general population (prevalence: 1,4–7,6% healthy children and adolescents), (7) PPR is more easily (objectively) measurable than most other IGE associated laboratory parameters. The age of maximum expression is the 1st and 2nd decade of life. PPR may also be found in photosensitive epilepsy, migraine, syncope and other disturbances. Photosensitivy as an EEG trait by itself is not a proof of epilepsy diagnosis and should not be mixed with the diagnosis of photosensitive epilepsy.

PHOTOSENSITIVITY AS A FOCAL EPILEPTIC PHENOMENON

Siniatchkin M (Germany)

There is a number of evidences for a focal nature of the photoparoxysmal response (PPR). EEG source analysis demonstrated a focal occipital generator of PPR which led to a rapid generalization of epileptic activity. Studies on transcranial magnetic stimulation, visual evoked potentials and psychophysical experiments (i.e., motion aftereffect) revealed a significant increase of occipital cortical excitability in patients with PPR. The excitability of the motor cortex at rest was normal even in patients with PPR propagating to frontal cortical areas. Studies of functional MR imaging demonstrated a significant increase of cerebral blood flow in the parietal cortex as well as in the premotor cortex. The parietal activation, which could be observed few seconds before PPR, corresponded well with an increase in phase clustering index of gamma oscillations – a feature of synchronization – preceding the PPR described in a MEG study. Neuroimaging studies did not show thalamic involvement during generalized, presumably interictal PPR. It seems likely that PPR primarily is a cortical phenomenon which starts in the occipital cortex and propagates to the frontal cortex. An accidental recording of a photically induced tonic–clonic seizure in a MR scanner in a patient with idiopathic generalized epilepsy revealed a gradual increase in cerebral blood flow during the photic stimulation in the occipital cortex. This build-up of occipital neuronal activity, which was accompanied by a constant thalamic activation, resulted in a seizure. Although the PPR belongs to the primary generalized epileptic activity and is often associated with idiopathic generalized epilepsies, this phenomenon starts locally and represents an example of a generalized phenomenon with a focal origin.

HOW TO PROVOKE THE GENERALIZED PHOTOPAROXYSMAL RESPONSE IN PHOTOSENSITIVE SUBJECTS?

Parra J (Spain)

We live surrounded by visual stimuli that could potentially trigger seizures in susceptible people. We can identify persons at risk by performing an intermittent photic stimulation (IPS) procedure, eliciting photoparoxysmal responses (PPRs) within the safe environment of the EEG lab. Beyond providing valuable information for the classification of the epileptic disorder, IPS should be aimed at quantifying the risk for seizures on an individual basis and, likewise, at educating patients to avoid these potential hazards. Unfortunately the methods to perform IPS differ greatly among different centers. Apart from technical factors, such as the characteristics of the stimulator, the frequencies used, the sequence in which they are presented and testing for PPRs at different eye conditions (eyes open, closed, or during eye closure) are essential factors for an accurate interpretation of the results. Identifying whether a patient is sensitive to light intensity changes or to the wavelength of the stimuli (color), has important consequences regarding the use of an individualized non-pharmacological treatment, like sunglasses. However, this procedure is technically very demanding and only available at highly specialized centers. Even though a significant proportion of photosensitive patients are sensitive to geometric patterns, its testing is frequently omitted, misdiagnosing those subjects who are more sensitive to patterns than to flashing lights. Testing videogames or different television sets might be especially relevant for some patients to recognize their risk in their own environment. Other factors that may trigger visually induced seizures such as fixation-off sensitivity or eyelid myoclonias must be properly characterized.

HOW TO PREVENT THE LOCAL INCREASE OF CORTICAL EXCITABILITY IN PHOTOSENSITIVE SUBJECTS?

Kasteleijn-Nolst Trenité D (The Netherlands)

Wednesday, 30.06.2010
14:30–16:00h
Hall 7 (Colossus)
Discussion Group
Interpreting ictal semiology: localizing automatisms or emergence of inborn behaviors?

GESTURAL AND ORAL AUTOMATISMS

Ozkara C (Turkey)

THE SPECTRUM OF COMPLEX MOTOR BEHAVIORS

Gardella E (Italy)

The analysis of ictal semiology is an essential component of the presurgical evaluation process, representing an important instrument to go back to the anatomic structures involved from ictal discharge. Nevertheless, is well known as some of the ictal manifestations do not reflect a focal cortical activation, but rather the effect of an ictal releasing mechanism. Moreover, the clinical patterns of a large number of ictal behaviors and their specific cortical-subcortical correlate have not been outlined yet.

Despite the relative homogeneity in the descriptions of complex motor behaviors with hyperkinetic (HK) features, we observed a significant interindividual heterogeneity of the clinical manifestations. Consequently, we performed a clinical and kinematic study of this kind of ictal complex motor behaviors, in order to characterize the features of different clinical subgroup of HK behaviors. Afterword, a study of clinical-EEG/SEEG correlations has been developed in order to try to discriminate: (1) which of the complex automatisms have a cortical representation and in which relationship with the involved cerebral structure; (2) which of them are due to a subcortical disinhibition as a result of the activation of topographically defined cortical structures and (3) which of the complex automatisms are due to a disinhibition ob subcortical networks without a clear relationship with specific cortical areas. These patterns should not be taken into account in the future developments of presurgical investigations.

AGE-DEPENDENT SEIZURE SEMIOLOGY

Holthausen H (Germany)

AN ETHOLOGICAL PERSPECTIVE OF ICTAL AUTOMATISMS AS FIXED ACTION PATTERNS

Tassinari CA (Italy)

Wednesday, 30.06.2010
16:30-18:00h
Hall 3 (Delphi)
Workshop
The multiple challenges of insular epilepsy

SEIZURES ORIGINATING IN THE INSULA: THE GREAT ELECTROCLINICAL MIMICKER

Ryvlin P (France)

INVASIVE INVESTIGATION OF THE INSULA: METHODOLOGY AND RESULTS FROM STIMULATION

Kahane P (France)

SURGICAL APPROACHES TO INSULAR EPILEPSY

Bouthillier A (Canada)

Purpose: The insular region has long been neglected in the investigation and treatment of refractory epilepsy. Furthermore, surgery in the insular region is rarely performed because of the risk of injury to the opercula (especially on the dominant side for language), the arteries transiting on the surface of the insula and the deep structures such as the basal ganglia and the internal capsule. Also, the complex surface anatomy and high functionality of the three adjacent lobes often require high density electrode coverage to localize seizure origin and brain functions. We present two methods of intracranial implantation for the investigation of suspected insular and perisylvian epilepsy that combines depth and subdural electrodes to capitalize on the singular advantages of each technique. We also describe the surgical technique and results of insulectomy.

Methods: The first method of intracranial implantation (Type 1) consisted in a craniotomy, insertion of insular electrodes after micro-dissection of the Sylvian fissure, orthogonal implantation of medial temporal structures with neuronavigation and coverage of the adjacent lobes with subdural electrodes. The second method (Type 2, or Yale-Grenoble type) consisted of MRI-stereotactic frame-guided depth electrode implantation into the insula and the hippocampus using sagittal axes, and insertion of subdural electrodes through burr holes to cover the three adjacent lobes. Insulectomy was either performed selectively, or combined with partial resection of an adjacent lobe. It was either done subpial or after micro-opening of the Sylvian fissure.

Results: Since 2004, twenty patients had an intracranial study sampling the insula among other regions. Sixteen patients were implanted using the first method which allowed a mean of 4, 5, 20, 15 and 42 contacts/patient to be positioned into/over the insular, medial temporal, neocortical temporal, parietal and frontal areas respectively. The second method (four patients) allowed a mean of 8, 7, 16, 6 and 9 contacts/patient to sample the same areas, respectively. Insular seizures were recorded in seven patients. Cortical mapping of functions (language and/or motor) were achieved in most patients when needed. Transient neurological deficits occurred in four patients. Eleven patients had an insulectomy: a selective resection was done in one patient, and the others had the resection combined with partial removal of an adjacent lobe (temporal and/or frontal and/or parietal). Three patients had the surgery performed on the dominant side for language. All patients had excellent results (Engel class I). However, one patient needed completion of treatment with radiosurgery to achieve that result. Transient neurological deficits occurred in five patients.

Conclusions: The opened technique of implantation (Type 1) is more invasive, but provides better neocortical sampling for seizure and function localization. It is designed for unilateral studies and when performed on the dominant side for language. The combined Yale-Grenoble implantation (Type 2) is less invasive, but provides less neocortical coverage. It is ideal when performed bilaterally and when high density cortical sampling is not crucial. Both techniques can be safely used to investigate complex insular/perisylvian refractory epilepsy. Surgical insulectomy is a safe procedure and can lead to excellent results.

Wednesday, 30.06.2010
16:30-18:00h
Hall 4 (Nafsica)
Workshop
Absence seizures and absence epilepsies across the ages: electroclinical correlation

ABSENCE SEIZURES AND SYNDROMES VARIABILITY UNDER AGE OF 3 YEARS OLD

Stephani U (Germany)

The early-onset absence epilepsy (EOAE) starting before the age of 4 or 3 years constitutes a rare and heterogenous subgroup of the idiopathic generalized epilepsies (IGE). First described by Beaumanoir (1976) EOAE may have more complex phenotypes than childhood absence epilepsy (CAE) with additional seizure types (esp. generalized tonic–clonic seizures; Doose, 1994), movement disorders (e.g. dystonia; Guerrini et al., 2002), intellectual and behavioral impairment and complicated treatment response. In about 12% of cases EOAE is caused by a metabolic condition, i.e. Glut-1 deficiency (Roulet-Perez et al., 2008; Suls, et al., 2009) with mutations of SLC2A1 gene for the respective glucose transporter. The seizure semiology of these patients is different from those of classical GLUT1-deficiency, but treatment with ketogenic diet improves the epilepsy. Recently Muhle et al (2010, submitted) described a boy with absence seizures starting at the age of nine months with both parents being affected by CAE. A 212 kb duplication in 1q21.3 was identified in the proband and his father, encompassing the gene CHRNB2 coding for the $\hat{I}^2$-2 subunit of the nicotinergic acetylcholine receptor and the gene ADAR coding for adenosine deaminase, an enzyme responsible for RNA editing. Examples of cases with EOAE will be demonstrated including their EEG patterns. Additional to EOAE absence seizures with generalized spike and waves in EEG are seen also in myoclonic astatic epilepsy.

ABSENCE SEIZURES AND SYNDROMES VARIABILITY IN CHILDHOOD AND ADOLESCENCE

Giannakodimos S (Greece)

ABSENCE SEIZURES AND SYNDROMES VARIABILITY IN ADULTS

Genton P (France)

Classical absence epilepsy syndromes have been described in children and adolescents, but both their prevalence and incidence remain high in adults. Although many experience continuation of absences with onset in earlier age classes, or have an unclear age of onset, it is clear that the clinical presentations and the practical problems are different in adults. The variability of absences seizures and epilepsies is such that the concept of a continuum, or even of a common biological basis, seems unrealistic. In adults with absences, there are several uncommon, but recognizable late-onset situations that should be recognized as syndromes: phantom absences and absence status epilepsy may overlap («phantom seizures» may remain fully unnoticed, the typical clinical presentation being one of recurrent episodes of absence status). In elderly patients, usually in an acute context (e.g., abrupt withdrawal of chronic benzodiazepine treatment), isolated episodes of absence status may occur, often with misleading clinical presentation. Absences related to photosensitivity are particularly prevalent in adults, and self-stimulation may persist. When absences persist beyond childhood/adolescence in one of the more classical settings, a change in symptomatology may occur: increased duration, occurrence of absence status, even exacerbation of absences in later life. It it worth to mention here cases of eyelid myoclonias with absences that persist unchanged, except for the more common occurrence of GTCS, in adults and even in the elderly. In spite of all the recent progress in functional neuroimaging and molecular biology, diagnosis and adequate management still rely mostly on electroclinical correlations. In adults, the EEG presentation, especially interictally, may be misleading, and mistaken therapeutic choices may further complicate diagnosis and management.

Wednesday, 30.06.2010
16:30-18:00h
Hall 6 (Marika)
Teaching Session
Frontal lobe seizures: from basic mechanisms to semiology and therapeutic approach

FRONTAL LOBE: SEIZURES SEMIOLOGY AND SEIZURES ORIGIN

Chauvel P (France)

FRONTAL LOBE SEIZURES AND SLEEP BEHAVIOR EVENTS

Manni R (Italy)

Differential diagnosis between NFLE seizures and behavior sleep events (NREM and REM parasomnias) may be difficult due to semiological similarities between the manifestations of the two disorders and the poor informative value of interictal and even ictal surface EEG in NFLE. Clusters of symptoms peculiar to each disorder have been identified, the main distinctive clinical features of NFLE being several per night attacks of brief duration, with stereotyped motor patterns, often including tonic/dystonic posturing. A standardized scale, so called FLEP scale, has been proposed to distinguish, on clinical grounds, NFLE from NREM arousal parasomnias and REM sleep behavior disorder. However sensitivity and specificity values less than those found in the scale's validation study and inadequacy of some items of the scale have been found in testing FLEP scale in a sample of outpatients' sleep and epilepsy unit for diagnostic assessment of nocturnal motor-behavioral episodes. Even though video-polysomnographic monitoring is still thought to be the best procedure to distinguish NFLE from Parasomnias, the potential role of Video records only, is under investigation. A diagnostic decision tree has been proposed, the most basic clinical features supportive of parasomnias diagnosis being interactive behavior, failure to wake after event, and indistinct offset. The possible comorbidity of NFLE seizures and parasomnias, namely NREM arousal parasomnias, complicates the differential diagnosis of these two disorders and gave rise to hypotheses about a potential sharing of pathophysiologic mechanisms mainly involving the arousal system.

FRONTAL LOBE SEIZURES: THERAPEUTIC APPROACHES

Elger C (Germany)

Wednesday, 30.06.2010
16:30-18:00h
Hall 7 (Colossus)
Workshop
Endogenous anticonvulsive mechanisms activated by seizures

TONIC INHIBITION IN EPILEPSY: THE BRAIN FIGHTS BACK

Walker M (United Kingdom)

DYNAMIC EXPRESSION OF NEUROPEPTIDES AS ENDOGENOUS ANTIEPILEPTIC PRINCIPLE

Sperk G (Austria)

Neuropeptides are often stored and released together with classical neurotransmitters and are considered as neurotransmitters or – modulators. In experimental epilepsy in animals and in human temporal lobe epilepsy (TLE) expression of some neuropeptides is dramatically altered. Thus, neuropeptide Y, somatostatin, neurokinin B or galanin are overexpressed in the rodent models of epilepsy, whereas dynorphin becomes highly expressed in granule cells of TLE patients. There is now converging evidence that e.g., neuropeptide Y acting on its Y2 receptors may contribute to seizure termination in the animal models and in human TLE patients, overexpression of dynorphin mRNA is related seizures prior to surgery. Recently, the use of viral vectors leading overexpression of neuropeptide Y or galanin has been shown to cause prominent anticonvulsant effects and inhibition of epileptogenesis.

THE ENDOGENOUS CANABINOID SYSTEM IN SEIZURE PROTECTION AND ITS IMPAIRMENT IN SEIZURE GENERATION

Magloczky Z (Hungary)

NEUROGENSIS AND PLASTICITY: DO THEY REDUCE EXITABILITY?

Kokaia M (Sweden)

Neurogenesis in animal and human brain continues through adulthood and is modified by various factors, including seizures. Increased numbers if neurons are born after seizures, and functional integration of the

neurons born in epileptic environment is altered compared to normal conditions. How this altered synaptic integration of newborn cells affects excitability in epileptic animals? Our studies and those from other groups indicate that there may not a simple answer, and outcome may depend on specific characteristics of the pathological environment in which the cells are born, as well as on the particular model of seizures and epilepsy used. Inflammation could be one of the major environmental factors affecting the functional integration of newborn cells into the epileptic circuitry.

Thursday, 01.07.2010
07:30–09:00h
Hall 2 (Roses)
Workshop
Patients management in epilepsy surgery failure

WHAT IS AN EPILEPSY SURGICAL FAILURE IN ADULTS?

Steinhoff B (Germany)

In principle, epilepsy surgery aims at postoperative freedom of seizures without increased surgery-related morbidity. Surgery has failed if this is not achieved. Over the last decades the percentage of surgical failures according to this definition has not changed considerably. However we are nowadays better aware of good and worse candidates and therefore able to inform patients and relatives about the realistic prognosis much more precisely. However, due to the growing experience more and more patients are considered to be potential surgical candidates whose prognosis is not ideal or even whose devastating situation may require palliative approaches or resective curative surgery that accepts surgery-related deficits. Examples for both clinical situations are provided. In this latter more complex context patients just with worthwhile improvement may be successes if their quality of life improves significantly. After having overcome the more or less unnecessary methodological comparison between drug treatment and epilepsy surgery and having approached a philosophy of both possibilities being complimentary, there are certainly patients who may be regarded as failures shortly after an operation but still become winners by modified drug treatment since the intractibility of their epilepsy has been resolved. Finally, even seizure-free patients may be sometimes losers if their social and personal situation is extremely destabilized by the dramatic impact of superficially successful surgery.

WHAT IS AN EPILEPSY SURGICAL FAILURE IN CHILDREN?

Van Nieuwenhuizen O (Netherlands)

Antiepileptic drug treatment provides seizure freedom in 80% of children with epilepsy. Twenty percent remains with insufficient control of seizures or unbearable side-effects of medication. For these children, other treatment modes have to be sought, such as epilepsy surgery, ketogenic diet and vagus nerve stimulation. Regarding epilepsy surgery, aim is to achieve seizure freedom (SF) in carefully selected cases. Is this aim gained? Children are different from adults: underlying etiologies are much more heterogeneous. In a survey ('92-'02) of the Dutch pediatric epilepsy surgery program (1) 2 years after operation SF occurred in 70%, >90% seizure reduction in 18%, >50% in 6% and no improvement in 6%. After follow-up of 4.5 years, 17% showed recurrence after initial seizure freedom; at 7.5 years follow-up this percentage had increased to 21%. Considerable differences are found between different operations (2): after temporal resection SF in 58–78% (same as in adults) and after neocortical resections 59–70% (60–91% for temporal and 54–66% for extratemporal resections). Association between length of follow-up and poorer outcome may be related to multiple factors (3) (i) completeness of resection, (ii) AED withdrawal after operation, (iii) increasing pharmacoresistance over time and (iv) development of new seizure foci. Higher rates of SF were found in operations performed after 1980 reflecting greater skilfulness.

References: 1. Van Oijen et al, Eur J Ped Neurol 2006;10:114. 2. Spencer Lancet Neurol 2008;7:525. 3. Téllez-Zenteno et al, Brain 2005;128:1188.

PHARMACOLOGICAL AND VAGAL NERVE STIMULATION IN EPILEPSY SURGERY FAILURE

Hirsh E (France)

REOPERATION IN EPILEPSY SURGERY FAILURE

Francione S (Italy)

Thursday, 01.07.2010
07:30–09:00h
Hall 3 (Delphi)
Teaching Session

NEW FINDINGS FROM EPILEPSY GENOMICS: IMPLICATIONS FOR CLINICAL PRACTICE AND RESEARCH GENOMICS AND BASIC MECHANISMS: NEW DIRECTIONS

LeGuern E (France)

GENOMICS: EXPLORING THE FUNCTIONAL CONSEQUENCES IN HUMANS

Sisodiya S (United Kingdom)

GENOMICS: IMPLICATIONS FOR CLINICAL PRACTICE

Guerrini R (Italy)

Thursday, 01.07.2010
07:30–09:00h
Hall 4 (Nafsica)
How to do? Seizure Monitoring in the EMU Setting
How to do? How to work with infants, children and parents in the EMU

HOW TO WORK WITH INFANTS AND CHILDREN IN THE EMU

Pressler R (United Kingdom)

HOW TO DO INVASIVE MONITORING IN INFANTS AND CHILDREN

Fohlen M (France)

HOW TO WORK WITH PARENTS IN THE EMU
Polster T (Germany)

Thursday, 01.07.2010
07:30–09:00h
Hall 5 (Nefeli)
Case Oriented Learning Session
Classification and/or differential diagnosis

CLINICAL CASE 1
Ozkara C (Turkey)

CLINICAL CASE 2
Kelemen A (Hungary)

CLINICAL CASE 3
Van Emde Boas W (The Netherlands)

Thursday, 01.07.2010
07:30–09:00h
Hall 6 (Marika)
Teaching Session – Introduction to VIREPA EUREPA Session: Clinical pharmacology and pharmacotherapy (supported by the ILAE Commission on Therapeutic Strategies)

CRITICAL INTERPRETATION OF AED TRIALS IN EPILEPSY
Perucca E (Italy)

DRUG TREATMENT OF RESISTANT EPILEPSY
French J (United States)

Thursday, 01.07.2010
09:00–11:00h
Hall 1 (Jupiter)
Special Symposium
The symposium of excellence in epileptology

ROAD TO REFRACTORY EPILEPSY
Brodie M (United Kingdom)

NEURONAL MIGRATION DISORDERS AND EPILEPSY: ANTIEPILEPTIC DRUGS CAN BE ADVERSE AGENTS
Represa A (France)

Neuronal migration is one of the critical steps of the CNS construction. Once generated in the germinal layers immature neurons start to migrate to reach their target fields. Genetic and environmental factors are key players modulating neuronal migration. Data obtained in my laboratory regarding the influence of neurotransmitters, antiepileptic drugs and cytoskeleton-linked proteins in cell migration will be documented. Disruptions of neuronal migration constitutes a broad spectrum of developmental disorders characterized by gross structural alterations, abnormally located cell clusters, or subtle rearrangements of cellular patterning and architecture in the cerebral cortex. They can result from either genetic disruptions (affecting for example cytoskeleton proteins) or exposure to adverse drugs (e.g., AED acting on GABA) during the embryonic life. Cortical migration disorders are frequent cause of severe epilepsy in childhood but the physiopathological basis for these conditions remains poorly elucidated: how malformed networks of neurons may contribute to pathophysiological development in an otherwise normal brain is currently not known. We recently investigated a model of subcortical band heterotopia (doublecortex) induced by in utero inactivation of DCX gene and provided evidences to suggest that migration disorders produce major alterations not only in neurons that fail to migrate but also in their programmed target areas. Our data suggest that this duality play a major role in cortical dysfunction of DCX brains. These changes have important consequences for cortical function and are likely to be involved on the neurological manifestations linked to this type of disorders. As suggested many years ago, seizures beget seizures and contribute to the evolution of the epileptic condition itself. Our institute recently discovered that seizures convert the antiepileptic actions of phenobarbital, the drug of first intention to treat infantile epilepsies, to proepileptic ones by down regulating KCC2 and enhancing GABA excitation, thus providing a rationale for the observation many times reported that Phenobarbital often aggravates seizures at early developmental stages.

LONG-TERM ANTIEPILEPTIC DRUG THERAPY CONTRIBUTES TO ACCELERATION OF ATHEROSCLEROSIS
Chuang YC (Taiwan, Republic of China)

Thursday, 01.07.2010
11:30–13:00h
Hall 3 (Delphi)
Discussion Group
The boundary between focal and generalized idiopathic pediatric epilepsies

GENERALIZED ASPECTS IN IDIOPATHIC FOCAL EPILEPSIES
Fusco L (Italy)

Idiopathic focal epilepsies in infancy, i.e. rolandic epilepsy and Panyiotopoulos syndrome, share several clinical and EEG characteristics with idiopathic generalized epilepsies. From a clinical point of view, children with both syndromes might have, other than orofacial or autonomic seizures, generalized febrile convulsion in early childhood or sporadic generalized seizures later on, during adolescence. From EEG point of view focal epileptiform abnormalities may be associated with more diffuse epileptiform discharges and with a later generalized photoparoxysmal response. Moreover, in both syndromes, the shifting of clinical manifestation, as well as of epileptiform abnormalities on the EEG, from one side to the other, suggests that the generator, although focal, is not stable and possibly entails the involvement of multiple circuits more than a clear-cut focal cerebral region.

FOCAL ASPECTS IN IDIOPATHIC GENERALIZED EPILEPSIES
Ferrie C (United Kingdom)

A dichotomy of focal and generalized epileptic seizures and epilepsy syndromes has been fundamental to epilepsy classifications. Distinguishing focal from generalized seizures is an early part of the diagnostic process and is usually relatively easy. However, there are traps that may lead to an erroneous diagnosis of a focal rather than a generalized seizure and both focal and generalized forms of epilepsy may coexist. The idiopathic generalized epilepsies (IGEs) are characterized by typical absence seizures (TAS), myoclonic seizures (MS) and GTCS. Usual manifestations of all three can be misinterpreted as indicating focal seizures. This is often because the clinician is unfamiliar with the expected manifestations of TAS (e.g. automatisms); exceptionally TAS may be manifested with experiential phenomena. MS demonstrated on video-EEG to be generalized may be perceived as or reported to be focal. However, video-EEG shows a minority of MS have significant asymmetries. Video-EEG suggests focal features and asymmetries in GTCS of IGE are relatively common. Sequences of seizures are characteristic of some IGE, e.g. showers of MS or TAS may precede GTCS in juvenile myoclonic epilepsy (JME). These can lead to suspicion of spreading focal seizures. Versive seizures with initial forced head (±eye)-turning is commonly considered to indicate focal onset. Cycling seizures may be a variant. Both are reported in IGEs. Focal EEG abnormalities in JME are widely reported. Less well known is their development in childhood-onset absence epilepsies. Their recognition is important to avoid misdiagnosis. It is hypothesized that they may indicate focal cortical pathology, particularly microdysgenesis, or the development of localized, self-sustaining cortical hyperexcitability. Occasional patients are reported with distinct seizures types suggesting the coexistence of focal and generalized epilepsies. These include patients with evidence of both symptomatic focal seizures, successfully treated surgically, and IGE. Even more intriguing is the apparent coexistence of idiopathic focal and generalized seizure disorders, suggesting the dichotomy between focal and generalized seizures in the idiopathic epilepsies is not absolute.

THE CONCEPT OF AGE-DEPENDENT HYPEXCITABILITY

Moshe SL (United States)

HOW OUR THERAPEUTIC APPROACH WILL CHANGE?

Genton P (France)

The classification of seizures and epilepsies into generalized and focal types has been justified mostly on practical consequences in terms of assessment and treatment. Recent insights into the mechanisms of seizure origin and propagation, and into molecular mechanisms of the epilepsies, have rendered such distinctions obsolete – up to a point, i.e., in terms of therapeutic choices. Against a large, discontinuous spectrum of epilepsy syndromes, we can use a nearly equally large and discontinuous spectrum of antiepileptic drugs (AEDs). The mechanisms of action of AEDs are only partially predictive of their clinical efficiency and effectiveness. A major feature of modern therapeutics is the recognition of potentially aggravating effects of AEDs in either predictable circumstances (e.g., increased myoclonic jerks on carbamazepine in juvenile myoclonic epilepsy), or as a surprise (e.g., the aggravating effect of topiramate in some patients with focal epilepsy). The effects of AEDs cannot be fully predicted in terms of generalized versus focal seizure or epilepsy type. Epilepsies with multiple seizure types (as in the Doose syndrome) or with undetermined seizures (as in Dravet syndrome), are specially challenging. There is little evidence to show that treatment is anything beyond purely symptomatic and has any effect on the long-term prognosis. The paradigms we can refer to in clinical practice remain thus theoretically simple: – in terms of therapeutic strategy, the need for anticonvulsant treatment is greatly determined by the syndromic diagnosis (the second major determinant being the patient's individual circumstances) : amount and duration of treatment can be planned in advance, and adjusted along the way. – In terms of drug choice, we can still rely on broad categories, but exceptions to classical pharmacosensitivity may be the rule in some settings. Due to the absence of fully reliable and predictable effects of AEDs in the various forms of idiopathic epilepsies, we should refrain from being dogmatic and obstinate and accept clinical evidence even if it is contrary to our expectations.

Thursday, 01.07.2010
11:30–13:00h
Hall 4 (Nafsica)
Discussion Group

ACUTE SYMPTOMATIC SEIZURES: RISK FACTORS OR SYMPTOM OF EPILEPSY?
BASIC MECHANISMS OF ACUTE SYMPTOMATIC SEIZURES

de Curtis M (Italy)

ACUTE SYMPTOMATIC SEIZURES AND UNDERLYING BRAIN INJURY: EPIDEMIOLOGICAL CRITERIA FOR CAUSATION

Sander JW (United Kingdom)

ACUTE SYMPTOMATIC SEIZURES: RISK FACTORS FOR EPILEPSY?

Beghi E (Italy)

Acute symptomatic seizures are defined as seizures occurring at the time of a systemic insult or in close temporal association with a documented brain insult. Acute symptomatic seizures must be distinguished from unprovoked seizures, i.e., seizures occurring in the absence of a potentially responsible clinical condition (idiopathic/cryptogenic seizures) or seizure caused by a static CNS injury (remote symptomatic seizures) in several important aspects. First, unlike epilepsy, the proximate cause of these seizures is clearly identifiable. The close temporal sequence makes causality likely for conditions such as uremia, head injury, anoxia, or stroke, which all immediately precede or are concurrent with the seizure. Biologic plausibility also supports causality when there is an acute disruption of brain integrity or of metabolic homeostasis in association with the insult. In many cases, there is also a dose effect with more severe injury leading to a higher risk of seizures. Second, unlike epilepsy, acute symptomatic seizures are not necessarily characterized by a tendency for recurrence unless there is recurrence of the underlying acute causal condition. Third, although acute symptomatic seizures are an undisputable risk factor for epilepsy, they cannot be included in the definition of epilepsy, which should be still intended as the occurrence of two or more unprovoked seizures. However, acute symptomatic seizures are reported more frequently in patients with stroke or traumatic brain injury accompanied by unprovoked seizures. In addition, over a 10-year period, individuals with a first acute symptomatic seizure are less likely to experience a subsequent unprovoked seizure compared with individuals with a first unprovoked seizure but more likely to present an unprovoked seizure compared to those with no antecedent seizures. Finally, acute symptomatic status epilepticus (SE) increases the risk for subsequent unprovoked seizures compared with brief acute symptomatic seizures. Among patients with SE, the risk of unprovoked seizure varies according to the underlying cause. The increased risk for unprovoked seizure after SE compared with shorter seizures may be due to SE being a marker for severity of injury, damage caused by SE, or a biological substrate associated with the tendency to experience SE.

IS THE CONCEPT OF ACUTE SYMPTOMATIC SEIZURES VALID?

Guerrini R (Italy)

Thursday, 01.07.2010
11:30–13:00h
Hall 6 (Marika)
Discussion Group
Recent advances in SUDEP

UPDATE ON INCIDENCE AND RISK FACTORS

Nashef L (United Kingdom)

SUDEP MECHANISMS: LESSONS FROM EXPERIMENTAL STUDIES

Koehling R (Germany)

Already early investigations by Hoff and Green (1936) suggested that cortical activity influences autonomic functions, inducing de- or increases in mean arterial pressure. Consequently, in several epilepsy models, a coactivation of subcortical regions could be demonstrated, i.e. thalamic nuclei, central grey, pontine regions and the medulla with its autonomic centres. For the analysis of SUDEP, several in vivo animal models were developed, such as systemic or intracerebroventricular application of PTZ or penicillin (generalized/focal seizures), systemic lidocaine application, hypothalamic/mesencephalic penicillin injection and systemic infusion of bicucullin, as well as kainate and kindling models of temporal lobe epilepsy (TLE) in rats. While some of these models do not mirror the clinical situation very well, in particular PTZ and penicillin models as well as the TLE models are suited to mimic the human situation. In these models it could be shown that during seizures both sympathetic / parasympathetic postganglionic variability of discharge frequency rises dramatically. Concomitantly, in particular changes in mean arterial pressure, and less so in heart rate could be observed. An observation common to all investigationsis a phasic activation of both sympathetic and parasympathetic systems. Particularly in recent reports (kindling, kainate in rats), besides hypertension, bradyarrythmia and cardiac dilation was seen to be the precipitating factor in ensuing seizure-associated death. Another, less well investigated factor can be central apnea/hypoventilation, as demonstrated in sheep. A closer analysis of the relation between autonomic activity and electrographic one reveals that these appear to be tighly locked, with highest risk of death in so called unstable lock-step interaction, whereby the discharge rate in autonomic fibers becomes unpredictable. Autonomic instability may be chronic, since baroreflexes were shown to be disturbed in kindled animals even during seizure-free intervals. In summary, the observations to-date suggest an instability of autonomic response to be instrumental in SUDEP, while mechanisms and risk factors are still being debated.

SUDEP MECHANISMS: INSIGHTS FROM MORTEMUS

Ryvlin P (France)

WHAT NEXT? PROPOSAL FOR A PROSPECTIVE EUROPEAN STUDY (MORTEMUS II)

Tomson T (Sweden)

The incidence of sudden unexpected/unexplained death in epilepsy (SUDEP) varies widely within the epilepsy population, from 0.09 to 0.35/1,000 person-years among incident cases to 6.3–9.3/1,000 person-years in epilepsy surgery candidates with refractory epilepsy. Case-control studies have identified risk factors for SUDEP such as high frequency of generalized tonic–clonic seizures, long duration of epilepsy and polytherapy with antiepileptic drugs, all indices of chronic refractory epilepsy. However, a critical remaining question is what distinguishes the refractory epilepsy patient who will die in SUDEP from the one who does not. Although some risk factors have been identified we are still lacking methods to predict the risk. The MORTEMUS project was primarily designed to assess the risk of SUDEP in the epilepsy monitoring unit and to analyze SUDEP mechanisms. However, during this project, 150 epilepsy centers were identified with active monitoring units. All together these centers monitored approximately 10,000 patients per year. Half of these were epilepsy surgery candidates, i.e., high risk patients for SUDEP. We intend to discuss the possibility to establish a prospective collaborative study across Europe including these centres. Detailed data from the presurgical work up will be collected and patients followed up to identify future SUDEP cases. The objective would be to better understand risk factors among patients with refractory epilepsy and to possibly identify predictors.