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Poster Sessions

Poster session: Adult epileptology I
Monday, 29 August 2011

p055
WHAT REALLY MATTERS TO PEOPLE WITH EPILEPSY IN 2011? A PAN-EUROPEAN PATIENT SURVEY

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Purpose: To conduct a pan-European survey amongst people with epilepsy to define issues of importance in their daily lives, correlated with duration of epilepsy, age, as well as other characteristics. Questions allowed challenges to traditional assumptions of therapy goals.

Method: We collaborated with The International Bureau for Epilepsy (IBE) to develop an easy-to-complete Web-based survey, distributed through the IBE's country chapter websites and by e-mail. The predominantly multiple-choice questionnaire was available in 12 different languages. Questions primarily focused on personal experiences of the specific impact of epilepsy, individual management, and on which aspects actually mattered most to them. Issues raised provided opportunities for patients to consider their personal needs and goals in contrast to traditional assumptions of therapeutic goals (doctor's point of view). All survey responses were deidentified and collated on a central database for analysis. The scope of the survey allowed for multiple sub-analyses including demographical stratifications.

Results: Preliminary results of the first round of the survey will be presented.

Conclusion: The survey findings will provide an insight to the real needs and challenges of people with epilepsy and may play a part in shaping future management strategies.

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p056
SUDDEN UNEXPECTED DEATH IN EPILEPSY (SUDEP) SAFETY CHECKLIST : A WAY OF QUANTIFYING AND DESCRIBING A PATIENT'S RISK OF SUDEP USING A PRACTICAL CLINICAL CHECKLIST ON A SINGLE SHEET

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Purpose: It is estimated that SUDEP causes about 500 deaths each year in the UK (0.001% of those with epilepsy). The risk of dying due to epilepsy and especially due to SUDEP is low but when it happens it is traumatic for all involved. Each individual with epilepsy has their own level of risk of SUDEP hinging on the presence and absence of well recognized risk factors.

We aim to present a clinical visual checklist to capture risks factors for SUDEP as evidenced by a detailed review of the current literature.

Method: We conducted a careful analysis of the current evidence base via a medline search using the search terms in various permutation and combinations: SUDEP, sudden death in epilepsy, death, epilepsy, risk factors, checklist.

Results: We divided the identified possible and probable risk factors into very low, low medium and high risk using the Australian risk mapping system for safety checklists AS4360. A simple tick box design facilitates at a glance profile of an individual's risk and the overall severity of risk on a particular date.

Conclusions: We have synthesized the available evidence into an easy reference checklist which can be quickly completed during a clinic. Once gathered the checklist can be used to prioritise clinical activity based on mortality risk. The checklist becomes a baseline from which to compare future progress or deterioration. One of the main uses of the checklist can be in discussing risk objectively on a sensitive rare event with patients, families and carers.

p057
CLINICAL PROFILES, PROGNOSIS, AND MANAGEMENT OUTCOMES OF PATIENTS WITH STATUS EPILEPTICUS (SE) AND PREDICTIVE FACTORS FOR REFRACTORY CONVULSIVE SE: A 7-YEAR RETROSPECTIVE STUDY

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Purpose: The study aims to characterize the demographics of status epilepticus (SE) patients, determine prognostic factors for survival, and identify predictive factors for developing refractory convulsive SE (RCSE).

Method: This is a retrospective study, involving 67 patients admitted for SE at our institution from January 2003 to September 2010. Clinical profiles, presentation and laboratory results were obtained from chart reviews. Prognostic factors for survival were determined using logistic regression. Predictive factors for developing RCSE were identified using stepwise regression analysis.

Results: About 52.2% of the patients had first-onset seizures progressing into SE. Half of the events (50.7%, N = 34) were caused by primary seizure disorder. Mortality rate of SE is 19.4%. About 16% (N = 11) of the patients with SE were classified as RCSE. Six RCSE cases were diagnosed with viral CNS infections. Two variables were associated with RCSE ($p < 0.05$), first onset seizures ($p = 0.017$), and abnormal cranial imaging ($p = 0.006$). Sensitivity of first onset seizures and abnormal cranial imaging, as predictive factors for developing RCSE is 81.82%, and specificity of both variables is 52.7 and 63.4% respectively. An

88.91% probability of RCSE occurrence was noted if first-onset seizures and abnormal cranial imaging are both present.

Conclusion: This study identified two predictive factors for developing RCSE, abnormal cranial imaging and first-onset seizures. Presence of both variables can predict occurrence of RCSE with a relatively high sensitivity rate. It is important to identify patients who are at risk for developing SE to reduce the probability of progression into RSE, and prevent long-term deleterious complications.

p058
THE MANAGEMENT OF REFRACTORY STATUS EPILEPTICUS IN ADULTS IN THE UK: THE CALL FOR A STANDARDIZED CARE PROTOCOL

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Introduction: Status epilepticus (SE) is a life-threatening neurological emergency with patients presenting in a protracted epileptic crisis. Suboptimal management is associated with high morbidity and mortality. Continuous EEG monitoring is regarded as essential by NICE in the management of refractory status epilepticus (RSE).

Purpose and Methods: We conducted a national audit to determine current clinical practice in the management of RSE amongst adults in Intensive Care Units (ICU) in 55 randomly selected UK NHS Trusts and a literature review of the management of RSE.

Results: While 29 (56%of responders) had a protocol available in ICU for early stages of SE just eight trusts had specific guidelines if RSE occurred. Only 14 trusts involve neurologists at any stage of management and just 11 (20%) have access to continuous EEG monitoring.

Conclusion and Discussion: This study identifies considerable variability in the management of SE in ICU's across the UK. A minority of ICU units have a protocol for RSE or access to continuous EEG monitoring despite it being considered essential for management. The evidence base for interventions in RSE is extremely limited. However, we propose that all ICU's should develop a standard protocol, in consultation with local neurologists, incorporating the management of refractory SE. Alongside both early neurological referral and universal patient access to continuous EEG monitoring, this achievable strategy would be a major step towards optimizing care the management of SE.

p059
NONCONVULSIVE STATUS EPILEPTICUS (NCSE) AND NONCONVULSIVE SEIZURES (NCS) IN CRITICAL CARE UNITS: DETERMINATION OF RELATED FACTORS

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Purpose: Determine the frequency of both NCS as NCSE in intensive care unit and intermediate care unit and factors related to their triggering.

Method: Case–control study. Residents were asked to indicate a routine electroencephalogram (EEG) to every patient with impaired consciousness of undetermined cause and after suffering a convulsive status. Patients in which epileptiform activity was found (cases) were compared with those without these abnormalities (controls) in relation to neurological history and their current condition.

Results: Between May 2009 and April 2010 87 EEG were requested to 60 patients. In 16 (27%) we found NCS pattern. In 7 (12%) there was a pattern of nonconvulsive status. The initial diagnosis in these patients was: convulsive status (1), central nervous system (CNS) tumor (1), moderate Trauma Brain Injury (1), hydrocephalus with shunt malfunction (2), ventriculitis (2). In 69% the etiology of epileptiform activity was attributed to a secondary cause and the remaining 31% to prior epilepsy. Forteen patients had focal EEG pattern and two generalized. Ninety-four percent of those with crisis were in treatment with an antiepileptic drug. Factors significantly associated with crisis were: CNS malformations $p = 0.005$ OR = 7.77.95% CI (1.87–32.36), $p = 0.012$ prior epilepsy. OR = 9.55, 95% CI = (1.63–55.98), prior CNS infection $p = 0.001$ and CNS surgery $p = 0.001$ The same factors were associated with SENC.

Conclusion: Given these findings we believe EEG should be incorporated in all patients with this factors who enter to critical care units.

p060
COST OF EPILEPSY CARE AMONG ADULT NIGERIANS MANAGED IN A UNIVERSITY HOSPITAL

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Purpose: Epilepsy is a major public health disorder that causes enormous burden on individual and family. Nearly 80% of people with epilepsy (PWE) reside in developing countries where there is a wide treatment gap, widespread poverty, illiteracy, inefficient and unevenly distributed health care system and social stigma. The aim of this study is to estimate direct and indirect cost of outpatient care of epilepsy in Nigeria.

Method: A cross-sectional observational study of PWE managed at neurology clinic of University of Ilorin Teaching Hospital in Ilorin middle belt Nigeria between January 2010 and December 2010. Patients included were those who had attended clinic more than twice.

Results: A total of 69 patients were enrolled into the study with mean age of 35 ± 18 years and 52% were female. Close to 23% were students, of which 32% had only secondary education and 43% are gainfully employed. About 13% had a comorbid condition and 12% had a least one family member living with epilepsy. Patients average clinic attendance was 6 per year with 51% came accompanied by a relative. The average distance travelled to clinic was 20 km and average waiting for consultation was 4 h. Majority (80%) were on single antiepileptic drug (AED). Direct medical cost per year was #2,090,100.00 ($13,934.00), of which highest contributor was AED #1,429,389.48 ($9529.26). AED accounted for 68% of total cost burden. Cost of transportation was #433,920.00 ($2892.80) and that for routine investigations was #226,800 ($1512.10). It was difficult to estimate indirect cost in monetary terms.

Conclusion: Epilepsy is associated with significant economic burden in resource scarce countries like Nigeria. Direct costs in patients with epilepsy will be underestimated if only epilepsy-related costs are considered. There might be need for attending physicians to scale up use of low cost AED drugs to minimize cost of care.

p061
TOBACCO HABIT IN NOCTURNAL FRONTAL LOBE EPILEPSY (NFLE)

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Purpose: The beneficial effect of nicotine administration was reported in patients with autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) with mutation of neuronal nicotinic acetylcoline receptor (nAChR). Our study aimed to verify whether there is a higher frequency of tobacco use among NFLE patients and their relatives compared to a healthy control group

Method: The following groups have been included: NFLE patients with video-EEG recording of at least one hypermotor/asymmetric tonic

seizure or two paroxysmal arousals; relatives of patients with NFLE: at least seven members of the proband family; control subjects: matched with probands for age, sex, education and geographic origin; relatives of control subjects: at least seven members of the control family.

Results: We interviewed 434 individuals with a questionnaire regarding tobacco use. Thirty-three patients with NFLE, 182 relatives of probands, 31 healthy controls and 188 relatives of controls. The frequency of tobacco use did not differ in the two groups: NFLE group (48.8%) vs control group (43.4%)($p = 0.289$).

Conclusion: We didn't find a significant difference in the distribution of tobacco use among NFLE patients and their relatives respect to the control group. Our finding could be due to the fact that none of our patients have any of the known mutation of nAChR. Alternatively the genetic model of ADNFLE is not representative of the whole NFLE population. Genetic and environmental mechanisms other than the known mutations may be implicated in the pathogenesis of NFLE in most cases making NFLE a multifactorial polygenic disease.

p062
CAPTURING THE PATIENT'S EXPERIENCE OF EPILEPSY: A REVIEW OF PATIENT INTERVIEW DATA, LITERATURE, AND EXPERT OPINION TO IDENTIFY ASPECTS OF SEIZURE SEVERITY

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Purpose: Epilepsy has many signs, symptoms, and impacts which are best assessed by the patient. Patient reported outcome (PRO) epilepsy instruments traditionally capture distal concepts of the seizure experience, such as health-related quality of life. The goals of this work were to: (1) identify aspects of seizure severity; (2) evaluate existing PRO epilepsy instruments.

Methods: Literature review, qualitative interviews with 25 patients with epilepsy to capture patients' seizure experience, interviews with four epilepsy experts elucidating clinical perspective, and available PRO instrument evaluation.

Results: Seizure severity was not consistently defined or applied. Literature, patients, and experts identified seizure severity as a complex concept best assessed from the patient's perspective. Three aspects of seizure severity were identified and supported by literature, experts, and patients: symptoms, seizure duration, and frequency. Symptoms included loss of consciousness, injury/bodily harm, muscle/body pain, exhaustion, headache, confusion, awareness, memory loss/impairment. Duration was characterized as part of seizure severity, and defined as the total time from onset of a seizure to recovery. Frequency included seizure number, pattern, and timing. The PRO epilepsy instruments were evaluated according to expectations in the FDA PRO guidance; existing instruments did not capture all specific aspects of seizure severity as defined by the patients, and lacked documentation of content validity or definition of measurement concept.

Conclusions: There is a need for PRO epilepsy instruments that capture the patients' experience and are developed according to regulatory expectations. This work is a starting point for development of a new PRO instrument measuring seizure duration (UCB Sponsored).

p063
NONCONVULSIVE STATUS EPILEPTICUS: VALUE OF A BENZODIAZEPINE TRIAL FOR PREDICTING OUTCOMES

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Purpose: Managing nonconvulsive status epilepticus (NCSE) poses many challenges that would benefit from reliable, early measures to predict patient outcomes. Here we evaluate clinical and electroencephalographic (EEG) responses to an acute antiepileptic drug (AED) trial for predicting outcomes in patients presenting with suspected NCSE.

Method: We analyzed all patients referred to our Neurology Service with suspected NCSE assessed by a standard acute intravenous (IV) benzodiazepine (BDZ) protocol. We correlated patients' clinical and EEG responses to the BDZ trial with their subsequent outcomes, including survival, recovery of consciousness, and functional status at hospital discharge.

Results: With an acute IV BDZ protocol trial. A favorable clinical response with improvement in consciousness was observed in 22 patients (35%), while 40 (65%) were clinical nonresponders. All of the positive clinical responders (100%) survived, recovered consciousness, and exhibited good functional outcomes. In contrast, outcomes were significantly poorer ($p < 0.001$) for the clinical nonresponders; only 14 (35%) recovered consciousness and 22 (55%) survived, with 59% of those survivors demonstrating poor functional outcomes. EEG improvement with BDZs also predicted better outcome, but it was less robust than the clinical response, with better subsequent recovery of consciousness ($p < 0.05$), but not functional outcome or survival.

Conclusion: This study demonstrates that a clinical and, to a lesser degree, EEG response to an acute trial of IV BDZs are predictive of subsequent outcome in patients with suspected NCSE, and warrant further consideration and investigation for assessing and managing such patients.

p064
VITAMIN D STATUS IN AN OUT-CLINIC PATIENT POPULATION OF A TERTIARY REFERRAL EPILEPSY-CENTER

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Purpose: People with epilepsy (PWE) have a two to sixfold increased risk for bone fracture. About 40% of fractures are osteoporosis-related. Vitamin D plays a major role in bone homeostasis. Vitamin D deficiency not only leads to fragility fractures but is also associated with fatigue, muscle-weakness and bone-pain. In a prospective study we investigated hypovitaminosis-D and its risk factors.

Method: 25-hydroxyvitaminD_3 (vit-D), calcium, phosphorus, alkaline-phosphatase serum-concentrations were measured in 150 consecutive out-clinic patients, who underwent vena-puncture for therapeutic-drug-monitoring. This selection is characterized by: Age 6–72 years, mean 19, 55% under 18 years; 78 males, 72 females; 24% of non-Dutch origin. AED-use: 1–4 (mean 1.9). Seizure-free >6 months: 42%; 37% had serious developmental, psychomotor or psychiatric disorders. Definitions: vitamin D-deficiency: vit-D < 30 nM; Insufficiency ≥30 and <50 nM. Hypocalcemia: children <2.10 and adults <2.14 mM.

Results: No differences were seen for age or sex. Vit-D levels were clearly lowered in nonnative compared to native PWE (30.7 versus 53.9 nM). In nonnatives, vit-D deficiency was established in 58%, insufficiency in 25%, in natives 16% and 34% respectively. Vit-D deficiency was not strongly related to the use of enzyme-inducing AEDs (30.3% vs. 20.6% for noninducing AEDs). A higher risk for vit-D deficiencies was seen in patients with persisting seizures and/or developmental and psychiatric disorders. Two patients had vit-D deficiency and hypocalcemia.

Conclusion: Vitamin D-deficiency/insufficiency is very common in patients with chronic epilepsy in all age groups. Nonnative patients and PWE with developmental/motor/psychiatric problems and/or intractability are especially at risk. Enzyme-inducing AED use was no significant risk factor.

Poster session: Adult epileptology II
Monday, 29 August 2011

p065
DO CALCIFIED LESIONS REQUIRE LONGER DURATION OF TREATMENT?

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Purpose: Neurocysticercosis (NCC) is one of the common causes of seizures in India. CT brain scan shows cysts in different stages and most of them respond well to antiepileptic drugs (AED), albendazole and steroids. The exact duration of antiepileptic drug treatment is not known. We have seen some patients who respond well to antiepileptic drugs and their AED tapering becomes difficult if they have calcified lesions on their CT brain scan.

Method: In the last 3 years we have seen eight patients at our out patient clinic with seizures and calcified granulomas on their CTS can brain. Five patients were woman three were men. Age varied from 17 to 55 years, their seizures were controlled well with antiepileptic drugs. EEGs were normal. Routine blood and urine examinations were normal.

Results: After seizure-free period of 2 years when we tried to taper AEDs gradually over a period of 3 months all of them had shown recurrence of their seizures within 6 months. There is no change in their clinical status and their neuro imaging from previous ones. Their EEGs were normal. No other cause for their seizures was found.

Conclusion: We conclude calcific lesions (NCC) may require longer duration of treatment with AEDs.

p066
EPILEPSY PATIENTS RESPONDING TO A KETOGENIC DIET: MUTATIONS IN *SLC2A*, CODING FOR THE GLUCOSE TRANSPORTER TYPE 1 (GLUT1)?

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Purpose: The glucose transporter type 1 (GLUT1) delivers the most important energy carrier of the brain across the blood–brain -barrier. In the early nineties, the first genetic defect of *SLC2A1,* coding for GLUT1, has been described, known as Glut1 deficiency syndrome (GLUT1-DS). GLUT1-DS is characterized by early infantile seizures, developmental delay, microcephaly and ataxia. Recently, the clinical picture of Glut1 defects and the pathophysiological knowledge about the disease has been significantly enlarged. A special form of transient movement disorders, paroxysmal exercise-induced dyskinesia (PED) and absence epilepsy, particularly with an early-onset (EOAE), can be based on a Glut1 defect. Despite the rarity of these diseases, the GLUT1 syndromes are of high clinical interest since a very effective therapy, the ketogenic diet, can improve or reverse symptoms, in particular if it can be started as early as possible. Additionally, the ketogenic diet can be very effective as an add-on therapy in patients with different forms of severe pharmacoresistant epilepsies.

Method: We tested the hypothesis if patients responding well to a ketogenic diet might have an underlying mutation in the gene *SLC2A1*. Patients with different forms of severe lesional and nonlesional epilepsies were sequenced in *SLC2A1* including the intron-exon boundaries.

Results: In 16 patients screened, a mutation in *SLC2A1* could not be detected.

Conclusion: The response to a ketogenic diet in severe lesional and nonlesional epilepsy is not based on the presence of an *SLC2A1* mutation, but patients with early-onset absence epilepsy (EOAE) or other forms of idiopathic generalized (IGE) epilepsies less responding to a first line antiepileptic drug should be screened in *SLC2A1*.

p067
THE EFFECT OF VITAMIN B SUPPLEMENTATION ON HOMOCYSTEINE IN PATIENTS WITH EPILEPSY TREATED WITH CARBAMAZEPINE OR VALPROIC ACID

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Purpose: Antiepileptic drug (AED) therapy is associated with an increase of plasma total homocysteine (p-tHcy) level. Hyperhomocysteinemia (hHcy) is an independent cardiovascular and cerebrovascular risk factor. The aim of the study was to investigate effect of AEDs on p-tHcy, serum folic acid (s-FA) and vitamin B12 status in adults patients with epilepsy and the influence of vitamin B supplementation on these parameters.

Method: Eighty-one patients (age range: 18–65 years, mean age 39.6 ± 14.3): 51 with chronic epilepsy (G1), 30 with newly diagnosed epilepsy (G2) receiving carbamazepine (CBZ) or valproic acid (VPA) and 13 sex- and age-matched controls were enrolled in the study. In all groups p-tHcy, vitamin B12 and folic acid levels were measured at baseline and after 1 year of vitamin B supplementation (G1) and before and after 1 year of VPA or CBZ therapy (G2).

Results: Hyperhomocysteinemia (p-tHcy ≥12 μM) was found in 20 G1 patients (39.2%): 16 (57.1%) receiving CBZ and 4 (17.4%) receiving VPA ($p = 0.001$). Hyperhomocysteinemia was diagnosed in only 4 G2 patients (13.3%). At the beginning of the study mean p-tHcy level was significantly higher in G2 than G1 and control group ($p = 0.0001$ and $p = 0.02$ respectively). There were no significant differences in s-FA and vitamin B12 levels between G1 and G2 patients or controls. In G1 s-FA and vitamin B12 levels in CBZ group were lower than VPA group. After 1 year of vitamin supplementation p-tHcy level significantly decreased in G1 CBZ group ($p = 0.00002$) and increased in both G2 groups after 1 year therapy. s-FA level significantly increased in both G1 groups ($p = 0.00005$) and decreased in G2 receiving VPA ($p = 0.0001$). Vitamin B12 level significantly increased only in G1 VPA group ($p = 0.0001$).

Conclusion: AEDs rather, not a disease, play a major role in the early development of hyperhomocysteinemia in epileptic patients. Adding folate and vitamin B12 to everyday AED therapy is safe and inexpensive way of reducing the risk of hyperhomocysteinemia.

p068
THE EVOLUTION OF VISUAL FIELD LOSS IN INDIVIDUALS WHO CONTINUE VIGABATRIN THERAPY OVER A 10-YEAR PERIOD

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Purpose: Vigabatrin associated visual field loss (VAVFL) occurs in around 45% of exposed individuals. It is generally accepted that, once established, VAVFL is stable and does not progress with continued VGB exposure. However, most studies have followed individuals for short observation periods. The aim of this study was to assess the evolution of VAVFL in individuals continuing VGB therapy over a 10-year period.

Method: Fourteen individuals were included in the study. Visual fields were assessed using Goldmann perimetry over a 10-year period. All visual field results were analyzed and quantified retrospectively by one investigator.

Results: One hundred seventy-four visual fields from fourteen individuals were available for analysis. The average follow-up period was 128 months between the first examination (Time 1) and the most recent examination (Time 2). The prevalence of VAVFL increased from 64% at Time 1–93% at Time 2. The visual field size was significantly smaller at Time two compared to Time 1. All individuals showed a trend for decreasing visual field size with increasing cumulative vigabatrin-exposure. There was a high degree of variability in visual field size between successive test sessions.

Conclusion: VAVFL progresses with continued vigabatrin exposure over a 10-year period. Progression may be small and difficult to detect because of the high degree of variability in visual field size between test sessions. New techniques are needed to monitor the effects of vigabatrin retinotoxicity in individuals who continue vigabatrin therapy.

p069
TERATOGENIC EFFECT OF ANTIEPILEPTIC DRUGS ON EPILEPSY PATIENTS

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It's know that lots of antiepileptic drugs (AED) have teratogenic potencies. The risk of teratogenity is much higher at patients on AED treatment then without AED patients and control subject. The prevelance of major malformation is 4–6% and minor malformation is 1.25–11.5 % on epileptic patients babies.

This study involved 45 female, from outpatients epilepsy clinic since 2000 years. The mean age of patients was 32 ± 6.5 (21–44) years, disease duration was 9.49 ± 7.4 (1–34) years and mean number of pregnancy was 1.9 ± 1.3 (1–6). The neurologic examination was normal and only three of patient's radiologic imaging revealed patologic results. According to seizure type 62.2 % (N = 28) of the patients have partial epilepsy, 37.8% (N = 17) of them have primary generalized epilepsy. Of the patients 91.1 % were on monotheraphy (N = 41; carbamazepine (CBZ): 19, valproate (VPA): 16, lamotrigine (LTG): 4, levetiracetam: 1, oxcarbazepine (OXC): 1) and 8.9 % were on (N = 4; CBZ + VPA: 2, OXC + LTG: 2) polytheraphy.

In terms of pregnancy 53.3 % (N = 24) of the patients were nullipara and 46.7% (21) of them were multipara (two pregnancies: 10; three pregnancies: 6; five pregnancies: 4; and six pregnancies: 1 of the patients 31.1 % (N = 14) of them have had problem with pregnancies. Four of the patients were on VPA, six of them were CBZ, two of them were LTG and two of them on polytheraphy (CBZ + VPA). According to AED, the babies whom mother was on VPA have had intrauterin growth retardation, multiorgan abnormaliteis and cardiac defect, CBZ group have had IUGR (2), spontaneous abortus (3), stillborn (1); CBZ + VPA group have had ASD (1) and spontaneous abortus (1).

Teratogenic effect or malformation rates with AED have considerably have been found higher. That is why the patient who is on AED treatment should be folllowed up by gynaecolgy and neurology expert properly and the patients must be informed about the risk of teratogenic results.

p070
SELF-KNOWLEDGE OF MEDICAL HISTORY AND QUALITY OF LIFE OF THE PATIENTS WITH SEIZURES BEFORE NONINVASIVE VIDEO- EEG EXAMINATION IN ADULTS IN UNIVERSITY HOSPITAL OSTRAVA, CZECH REPUBLIC-3 MONTHS PROSPECTIVE STUDY

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Purpose: Noninvasive video- EEG is the basic method of diferencial diagnosis of seizures. Due to unconsciousness in most of the cases while having seizures we were interested in self-knowledge of the seizures and the quality of life before video EEG examination was established. We plan to repeat the questionnarie in 1 year time to verify the change in life of the patient with focus on effect of the recommended procedures and treatment.

Method: We have screened prospectively 42 patients in 3 months period in year 2010. We have used questionnaries of Epilepsy Centre Prague-Motol (2003)- 54 questions of medical history, seizures and health status and 11 questions of quality of life. All patients answered the questions by themselves during video EEG examination before final diagnosis was established.

Results: We have examined 42 patients, 20 men and 21 women. Questions 1–25 focus on history, symptoms and known semiology of the seizure. Question 26–29 is interested in school and psychomotor progress in childhood, question 30–35 focuses on possibly known origine of the seizure and comorbidities, question 38–41 is based on possibly dependance od drugs, nicotine and alcohol, 42–45 asks about working possibilities. Quality of life data are correlated with type of seizures and treatment effectivity. Data are transfered into electronic format using Micrososft Excel and statistical program Stata v.10. For analysis is used basic descriptive statistics- for quantitative data (mean average, standard deviation, modus, median) and for qualitative data absolute and relative number, modus. For testing of statistic hypothesis parametric tests for quantitative data with normal distribution (*t*-test, ANOVA) and nonparametric tests (chi-square test, Fisher's exact test, *U*-test etc.) at 5% level of significance.

Conclusion: Seizures have deep effect on general health status of the subject. The patient has overall wide knowledge of the character of the seizure although uncousciousness is mostly present. Listening to the subject's experience in comparison with video EEG result leads to the most possible diagnosis with proper treatment recommendation. Stabilization of health status after 1 year is expected.

p071
COMPLICATIONS OF MANAGEMENT OF NEWLY DIAGNOSED EPILEPSY IN ELDERLY IN CLINICAL PRACTICE

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Purpose: The incidence of epilepsy is disproportionately high in patients over 60 years of age. We develop this study to know clinical characteristics and type of treatment, as well as neurological and systemic complications or comorbidities that have been displaying.

Method: We reviewed clinical record of patients with newly diagnosed epilepsy between 2008 and 2010 older than 60 years. We excluded patients that were not followed in the outpatient clinic at least 6 month.

Results: We found 25 patients (male 11, female 14), mean of age at the time of the diagnosis 68.3. If we consider etiology: cryptogenic (unknown cause) 16%, secondary 84% (cerebrovascular disease 60%). According to the type of seizure 76% was of focal onset and 24% generalized tonic–clonic. With respect to antiepileptic drugs 92% of patients was in monotherapy, but 24% had need change treatment, in all the cases by adverse events, and in one of them by ineffective. With respect to control seizures, 92% was seizure-free. They presented polypharmacy in 96% of the cases. They had need to go emergency department 80% of patients. In the follow up, 28% presented systemic complications, 32% neurological complications, 12% deceased.

Conclusion: The treatment of epilepsy in elderly has particularities different from other ages. We conclude that despite the seizures responded well, in almost one quarter of patients have needed to modify

the antiepileptic drug by adverse events. Most of them presents polypharmacy and frequently has or develops systemic or neurological comorbidity that makes its treatment more complex.

p072

PLURONIC P85 ENHANCES THE DELIVERY OF PHENYTOIN TO THE BRAIN VERSUS VERAPAMIL IN VIVO STUDY

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Purpose: The overexpression of P-glycoprotein in the blood–brain barrier (BBB) capillary endothelium may be one of the mechanisms of pharmacoresistant epilepsy. Meanwhile Pluronic P85 had been shown to enhance drug transport across BBB in vitro models and in vivo. So the goal of this work was to examine the effect of Pluronic P85 on the traditional anti-epileptic drug phenytoin in brain, liver and kidney distribution and to find out whether Pluronic P85 could CNS-targeted deliver the phenytoin compared with verapamil.

Method: Phenytoin dissolved in 0.1%, 1% and 10% Pluronic P85 phosphate buffered solution was injected to the rats via intravenous, 35 mg/kg. And verapamil was started 30 min before systemic administration of phenytoin. Dialysates and blood samples (30, 60, 120, 180, 240 and 300 min postdose) were collected, and after termination of the experiment, major organs such as the liver and kidney were removed for tissues distribution study.

Results: Pluronic P85, evoked a dose-dependent effect on phenytoin brain distribution, significantly increased the extracellular fluid concentrations of phenytoin in brain after systemic administration, compared with verapamil. And there were not increase of phenytoin distribution in liver and kidney in Pluronic P85 groups, while the accumulation of phenytoin in liver had a significantly increase in verapamil group, compared with control group.

Conclusion: Pluronic P85 can enhance the distribution of phenytoin in brain, and use of Pluronic P85 as CNS delivery systems for AEDs like phenytoin may constitute an interesting novel approach for treatment of pharmacoresistant epilepsy.

p073

PREVENTIVE EFFECTS OF CALCIUM CHANNEL BLOCKER ON THE DEVELOPMENT OF DELIRIUM TREMENS IN ALCOHOL WITHDRAWAL SEIZURE PATIENTS

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Purpose: An increase of calcium influx during alcohol withdrawal state may contribute to neuronal hyperexitability, which causes delirium tremens (DT). Some investigators have found calcium channel blockers effects in prevention of DT in experimental animals. Therefore we evaluated the preventive effects of calcium channel blocker (nimodipine) and benzodiazepine (chlordiazepoxide) on the development of DT in alcohol withdrawal seizure (AWS) patients.

Method: A total 59 patients with AWS were divided into three groups according to the management nimodipine-treated, chlordiazepoxide-treated, and control (no specific medication) groups. We compared the incidence rates of DT in the three groups.

Results: Total incidence rate of DT was 30.5% (18 of 59 patients). There were six DTs of 18 patients (33.5%) in nimodipine-treated group, 4 of 21 patients (22.5%) in chlordiazepoxide-treated group, and 8 of 20 patients (44.0%) in control.

Conclusion: The control group (44.0%) showed the highest incidence rate of DT. And nimodipine-treated (33.5%) and chlordiazepoxide-treated group (22.5%) were followed. However, this result failed to demonstrated statistically significant differences due to small numbers size.

p074

REDUCING RISKS: HAVE THE CHANGING ANTI-EPILEPTIC DRUG PRESCRIBING HABITS, IN PREGNANCY, RESULTED IN AN IMPROVEMENT IN PREGNANCY OUTCOMES BETWEEN 1995 AND 2010

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Purpose: The risk of major congenital malformations (MCM) with in utero exposure to valproate used in monotherapy (6.2%; 95% CI 4.1–7.8) or in polytherapy (7.8%; 95%CI 5.6–10.7) has previously been shown to be greater than the risk due to exposure to carbamazepine (2.6%; 95%CI 1.9–3.5) or lamotrigine (2.3%; 95%CI 1.6–3.2). (Morrow JI, et al. J Neurol Neurosurg Psychiatry 2006; 77:193–198) The awareness of this association has increased over the past 10–15 years. This current study sought to assess the impact on prescribing habits and on MCM rate.

Method: An analysis of the UK Epilepsy and Pregnancy register, which now encompasses more than 8000 registrations, allows for review of prescribing habits and for calculation of MCM rates from 1995 to 2010.

Results: There was no change in the ratio of monotherapy, polytherapy and no drug exposures, but sodium valproate prescription fell from 31.2 to 23.25% of monotherapy exposures during the study period. This was associated with a trend towards reducing MCM in the pregnancies of women with epilepsy from 4.3% (95% CI 3.5–5.4%) to 3.2% (95%CI 2.6–3.9%).

Conclusion: The MCM rate has fallen by approximately a quarter during the study period, this equates to 26 less children born with MCM per annum. Given the spectrum of MCMs seen with valproate and their cost to the Health Service this may represent an extrapolated direct health cost saving in the order of £2–3 million per annum in the UK.

p075

SHORT-TERM PREDICTIVE FACTORS OUTCOME IN PATIENT WITH WITHDRAWAL OF ANTIEPILEPTIC DRUGS

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Purpose: The right time for withdrawal of antiepileptic drugs is still unknown. Because unwanted adverse effects, teratogenicity, driving privileges, employment, psychological impact on well-being state, many studies suggest withdrawal of antiepileptic drugs after two or three seizure-free years in many patients. Our objectives were to analyze the short term outcome in patients with withdrawal of medication and to identify possible predictive factors for relapse.

Method: We reviewed the clinical findings and laboratory data of 256 patients with epilepsy hospitalized in our neurological service for primary diagnoses between 2005 and 2007 and a 2 years follow-up in outpatient's service after withdrawal of medication. All patient received CT or

MRI scan (no mesial temporal sclerosis case was included), EEG, studies, biochemical and hematological investigation.

Results: One hundred forty-eight patients with idiopathic seizure and 108 with symptomatic and possible symptomatic seizure, were analyzed by: ILAE classification, comorbidity, age, number of antiepileptic drugs, neurological abnormalities, EEG, and the moment of relapse onset. The risk of seizure recurrence following drug withdrawal was higher in symptomatic group especially in poststroke patients (32% vs. 10 % idiopathic), multiple epileptic drugs (28 % vs. 10%), 1 year versus 2 years of withdrawal (42 % vs. 15%), partial versus generalized seizure (43% vs. 25%), older age (55% in patient >50 years old), coexistence of brain ischemic disease, no correlation with persistence of EEG abnormalities.

Conclusion: We identified some risk factors for higher seizure recurrence, but the decision regarding drugs withdrawal must be individual, patient drivin.

p076
COGNITIVE AND BEHAVIORAL ADVERSE EFFECTS OF TOPIRAMATE USED AS ADD-ON TREATMENT OF REFRACTORY EPILEPSY IN PATIENTS WITH MILD TO MODERATE MENTAL RETARDATION: PROSPECTIVE STUDY

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Purpose: This prospective study was conducted to assess the cognitive and behavioral adverse reactions following treatment with topiramate in adults with refractory epilepsy and mental retardation.

Method: Our study group comprised 35 adult patients, 25 males and 10 females, aged 18–55 years, affected by partial and secondary generalized refractory cryptogenic/symptomatic epilepsy and mild (20) to moderate mental retardation. They were given Topiramate up to 200 mg as add-on therapy to their baseline treatment with VAL, PB, CBZ or LTG. The caregivers of each patient were administered special questionnaires – Scales of Independent Behavior and Holmfrid Quality of Life inventory- at baseline, 3, 6 and 12 months after the beginning of treatment.

Results: After a 3-month follow up, cognitive dysfunction and behavioral adverse reactions (psychomotor slowing, confusion, decreased alertness, dysexecutive syndrome, space disorientation and word finding difficulties) were detected in three patients and in another three patients after a 6-month follow up. After 12 months of follow up global cognitive worsening associated with significantly impaired quality of life persisted in six patients in spite of excellent seizure control and topiramate was discontinued.

Conclusion: In our study the use of low doses of slowly titrated topiramate in adults with refractory epilepsy and mild to moderate mental retardation was associated with 17% rate of serious cognitive and behavioral adverse reactions after 12 month of follow up, especially in patients comedicated with phenobarbital and valproate.

p077
LACOSAMIDE: LONG-TERM SAFETY IN PARTIAL-ONSET SEIZURES

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Purpose: Long-term safety of the antiepileptic drug (AED) lacosamide was evaluated in an open-label extension trial SP926 (NCT00655486).

Method: Eligible participants were enrolled from IV infusion trial SP925 (NCT00655551). Investigators could adjust lacosamide oral tablet (100–800 mg/day) and/or concomitant AED dosage to optimize treatment. Safety assessments included adverse events (AEs), ECGs and clinical laboratory data.

Results: Of the 97 enrolled patients, 58.8% and 38.1% had >12- and >18-months of lacosamide exposure, respectively. The median modal lacosamide dose was 500 mg/day. TEAEs (incidence ≥15%) included dizziness (44.3%), diplopia (17.5%), and vomiting (16.5%); most were mild/moderate in intensity. Only one serious AEs (SAEs) occurred in >1 patient (convulsion, n = 2). One patient discontinued due to SAEs (arrhythmia supraventricular and atrial fibrillation) and continued commercial lacosamide after treatment of the SAEs. One TEAE led to discontinuation in >1 patient (dizziness, n = 3). Median clinical laboratory values remained within normal range; changes from Baseline were not of clinical relevance. Small increases in mean PR interval and QRS duration were consistent with the known lacosamide safety profile and did not vary with lacosamide exposure.

Conclusion: Safety evaluations indicate long-term lacosamide administration (100–800 mg/day) is generally well tolerated as adjunctive treatment for patients with partial-onset seizures.

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p078
LONG-TERM SAFETY AND EFFICACY OF THE RNS SYSTEM FOR ADJUNCTIVE TREATMENT OF MEDICALLY INTRACTABLE PARTIAL ONSET SEIZURES IN ADULTS

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Purpose: The RNS System (NeuroPace, Inc.) is an investigational device that includes a cranially implanted programmable responsive neurostimulator connected to depth and/or subdural leads, a programmer, a patient remote monitor and a Web-based interactive database. Long-term effects on seizure frequency and safety were assessed in subjects with medically intractable partial onset seizures participating in the RNS System studies.

Method: Subjects were 18–70 years of age, had >3 disabling partial seizures/month and had failed >2 AEDs. After a 3 month baseline, the neurostimulator and leads were implanted and the neurostimulator was programmed to detect epileptiform activity. After a 12-week blinded period during which 97/191 subjects in a randomized Pivotal study and 51/65 subjects in a Feasibility study received responsive stimulation, all subjects could receive stimulation in an open label period until 2 years post-implant. Subjects could then enter an ongoing 7 year, open label trial to assess % change in disabling seizures and the responder rate (RR = % subjects with ≥50% reduction in seizures), as well as overall rate and type of adverse events (AEs).

Results: Two hundred fifty-six subjects were implanted: mean age 34.0 years, mean duration of epilepsy 19.6 years, mean number of AEDs 2.9, and median seizure frequency 10.2 seizures/28 days. At 2 years postimplant, the median % change in seizures and the RR was −38.9 and 44.8, at 3 years was −49.3 and 49.5, and at 4 years was −52.5 and 54.2, respectively. There were no serious unanticipated device-related AEs and there was no increase in the rate of specific AEs or over-all AEs over time.

Conclusion: Seizure frequency was reduced long-term in subjects treated with the RNS System and the seizure response continued to improve over time. Adverse event rates were stable, supporting the long term safety of responsive stimulation. Responsive cortical stimulation for treatment of medically intractable partial onset seizures in adults appears to have a favorable long-term safety and efficacy outcome.

p079

VALPROATE DOSE IS AN INDEPENDENT RISK FACTOR FOR AUTISM SPECTRUM DISORDER: EVIDENCE FROM PROSPECTIVE ASSESSMENTS IN THE AUSTRALIAN BRAIN, COGNITION AND ANTIEPILEPTIC DRUGS STUDY

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Purpose: This study aimed to systematically evaluate autism spectrum disorder traits in a sample of prospectively recruited children exposed to antiepileptic drugs (AEDs) during pregnancy. Previous research has raised the possibility of elevated autism risk through retrospective pregnancy records or diagnoses outside of study protocols.

Method: Children of mothers who took AEDs during pregnancy were recruited via the Australian Pregnancy Register, which provided prospectively obtained data on epilepsy, pregnancy and lifestyle factors. Children with major malformations or epilepsy were excluded and all assessments were conducted blind to drug exposure status. Assessment of austism spectrum traits was performed with the Conners Autism Rating Scale (CARS) by trained clinical research staff. We report data on 103 exposed children aged 6–8 years.

Results: Eleven children exceeded the CARS threshold (10.7%). Of these, 2/26 were exposed to valproate monotherapy (7.7%), 2/32 to carbamazepine monotherapy (6.3%) and 7/15 to polytherapy with valproate (46.7%). No child exposed to polytherapy without valproate (N = 19) exceeded the CARS threshold. There was a significant relationship between first trimester valproate dose and CARS scores ($r = 0.56$, $p < 0.05$).

Conclusion: We present the first prospective, systematic screening of autism after foetal AED exposure. Our data demonstrate a higher rate of autism traits than previously reported or in the general population. This was particularly with valproate polytherapy, which in our sample may reflect the higher doses in that group. The dose-response relationship highlights a need for ongoing prospective studies of child outcomes in low-dose valproate pregnancies so that informed decisions may be made by women and their treating doctors. Taken together with the emerging literature on the cognitive impairments associated with foetal AED exposure, this study points to the need for clinical review of exposed children in early childhood.

p080

ASSOCIATION BETWEEN CARBAMAZEPINE-INDUCED SEVERE CUTANEOUS ADVERSE AND HLA-B*1502 ALLELE IN HAN PEOPLE OF CHINA

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Purpose: This study aims to explore the association between HLA-B*1502 allele and carbamazepine-induced cutaneous adverse reactions in Han Chinese of China mainland, and to find the genetic marker that can predict carbamazepine-induced cutaneous adverse reactions.

Method: HLA-B*1502 allele genotyping was performed by PCR-SSP. A total of 48 patients from unrelated families were developed cutaneous adverse reaction within 12 weeks after taking carbamazepine (CBZ). They were classified into two groups according to Roujeau's diagnostic criteria 3. One group was diagnosed Stevens-Johnson syndrome (nine cases) or toxic epidermal necrolysis (two cases); the mean recipient age was 32.00 ± 16.81. The other group was maculopapular eruption (MPE) defined as erythematous exanthem without blistering, pustulation, mucosal or systemic involvement, including 54 patients (35 men and 19 women); the mean recipient age was 32.23 ± 19.85. Meanwhile, 100 patients (45 men and 55 women) of CBZ tolerance were invested, who took CBZ at least 3 months without adverse effects; the mean age was 29.57 ± 16.22. Healthy individuals comprised subjects who had not taken CBZ and had no history of drug induced cutaneous adverse reactions. In healthy individuals group (60 men and 40 women), the mean age was 38.08 ± 13.60. The study was performed in accordance with the Declaration of Helsinki and its amendments and the document of informed consent was obtained from all subjects.

Results: The frequency of HLA-B*1502 allele among SJS/TEN patients (90.9%) is significantly higher than HLA-B*1502 allele among carbamazepine-tolerant controls (15%, $p < 0.01$) and healthy individuals (17.07%, $p < 0.01$). But the frequency between MPE patients and carbamazepine-tolerant controls (34.78% vs. 15%, $p = 0.069$), did not have any significant difference.

Conclusion: The data showed that HLA-B*1502 allele is strongly associated with carbamazepine-induced SJS/TEN but not MPE in Han Chinese of China mainland.

Poster session: Adult epileptology III
Monday, 29 August 2011

p081

PAROXYSMAL MOVEMENT DISORDER AND EPILEPTIC SEIZURES ASSOCIATED WITH ANTI-VGKC ANTIBODY ENCEPHALITIS

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Purpose: To describe an unusual, newly recognized pattern of movement disorder, dementia and epileptic seizures associated with antibodies to voltage-gated potassium channels antibodies (VGKC-Abs).

Method: We reviewed the history, clinical examination, brain MRI, brain ^{18}F-FDG-PET, CSF analysis, and video-EEG of abnormal movements and seizures of a patient with high levels of VGKC-Abs.

Results: A 79-year-old man developed frequent (10–20/h), short left hemibody dystonic episodes, responsive to carbamazepine. Brain MRI T_2-weighted images showed periventricular and right putaminal hyperintensities.

Six months after, he developed rapidly progressive cognitive disorders. At this moment, dystonic episodes were present both in the left and in the right hemibody, with unchanged EEG during episodes. During each episode, tonic contraction began in one hemibody, spread to the other hemibody and then back to the first hemibody. Consciousness was preserved during episodes. FDG brain PET showed bilateral mesial temporal and basal ganglia hypermetabolism. CSF was normal.

Eight months after dystonia onset, he went in partial status epilepticus with EEG showing rhythmic discharges beginning in the left posterior part of the brain. This status was refractory to several intravenous AED and finally stopped with the administration of phenytoin and high doses methylprednisolone. VGKC-Abs were strongly positive (4379 pm; N < 100 pM). The patient died from septic shock. The full postmortem examination did not show any neoplasia.

Video-EEG will be presented.

Conclusion: We believe our patient first presented with paroxysmal dyskinesia secondary to antibody-mediated basal ganglia hyperactivation, then dementia and partial status epilepticus.

p082
PROPOSAL TO STUDY THE IMMUNE-MEDIATED EPILEPSIES IN ADULTS

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Purpose: The clinical spectrum of the autoimmune encephalopathies (AIE) usually includes, but rarely presents only or mainly, by epilepsy. Since the several phenotypes of these immune-mediated epilepsies (IMEs) remain largely unknown, we intend to contribute for their better characterization.

Method: Prospective, multicentric, 2 years long, study.

Results: Protocol for studying IMEs: I- Inclusion criteria: (1) patients ≥16 years aged; (2) difficult control, or catastrophic presentation, of focal de novo epilepsies; (3) unexpected recurrent or de novo status epilepticus; (4) focal epilepsies associated with systemic and/or neurological symptoms suggesting an autoimmune dysfunction, or belonging to a well defined AIE; (5) normal, or disclosing a lesion with no obvious cause for the event, high resolution brain MRI; II- Study protocol: (1) serum or serum plus CSF antineuronal (ANNA1, ANNA2, PCA1, CRMP5, Ma2, amphiphysin, GAD, NMDA, AMPA, GABAb, LGI1) and non- antineuronal (antithyroid; others, if appropriate) antibody screening; (2) CSF cytochemical and oligoclonal bands search; (3) scalp sleep EEG and video-EEG monitoring (if appropriate); (4) search of systemic neoplasia in all cases; (5) standardized immunomodulatory sequential treatment protocol with corticosteroids, intravenous immunoglobulin, plasma exchange and/or cyclophosphamide.

Conclusion: With this protocol, we aim to establish the prevalence, clinical spectrum, best treatment, and predictive factors for the IME outcome. We invite all the centres to participate in this study. The desirable, but difficult to achieve, goal of antibodies search centralization, and standardization of the immunomodulated therapy can be limitations but no impediments to its accomplishment.

p083
LIMBIC ENCEPHALITIS ASSOCIATED WITH FOUR AUTOANTIBODIES (ANTI VGKC, AMPA, GAD, IA2)

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Introduction: Limbic encephalitis is a neurological syndrome that may present in association with cancer, infection, or as an isolate clinical condition often accompanying autoimmune disorders.

Observation: We describe a 43-year-old women without any particular history; presented with acute temporal lobe seizure and cognitive impairment (bradypsychia and anterograde amnesia).

Temporal seizures were recorded by video-EEG. Brain MRI showed bilateral hippocampal sclerosis and FDG- PET showed hypermetabolism in both medial temporal lobes.

Additional evaluation revealed no evidence of neoplasia or central nervous system infection. Significant high titers of anti-VGKC, anti-AMPA, anti-GAD and anti IA2 antibodies were present in the serum and cerebrospinal fluid.

Intravenous immunoglobulin infusion was initiated and continued monthly. Association with antiepileptic drugs resulted in improvement of cognitive impairment and disappearance of seizures.

Discussion: The association between acute encephalopathy and the presence of circulating autoantibodies has been recognized over the past for decades. These disorders have been categorized as poor-prognosis paraneoplastic encephalitis associated with antibodies targeting intracellular antigens. In the last years a new variety of autoantibodies (directed against membrane antigen) have been identified with new neurological disorders which are less often associated to neoplasia and carry a better prognosis.

Nevertheless, the underlying trigger for the immune-mediated process and the role of these auto antibodies in the pathogenesis of limbic encephalitis remain to be clarified.

Conclusion: We report an unusual observation of limbic encephalitis associated with four autoantibodies targeting both intracellular and cell membrane antigens. Early and intensive treatment resulted in recovery of neurological condition and seizure remission.

p084
PARTIAL EPILEPTIC SEIZURES IN STROKE PATIENTS

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Purpose: Different epileptic seizures are very often present during the evolution of stroke. The purpose of our study was to following the partial epileptic seizures developed in stroke patients and found does the early treatment could improving the prognosis in stroke patients.

Method: We studied 88 stroke patients, 64 females, 24 males, age range 45–85. All patients were observed using standard protocol: laboratory, neurological examinations, electroencephalography (EEG), brain CT and/or MR.

Results: Partial epileptic seizures were present in 45 patients (26 during hospitalization and 19 after more than 1 year of stroke). Eight patients had hemorrhagic stroke and 37 ischemic stroke. Among patients with hemorrhagic stroke early seizures were present in 3 (37.5%) patients. Among the patients with ischemic stroke early seizures were present in 23 (62.1%) patients. The most common localizations of brain lesions were cortical and frontal. Patients with early seizures had a better prognosis and smaller frequency of repetition seizures against the patients with late seizures. Three patients become worse with generalized epilepsy and bad prognosis. Motor manifestation of seizures were present frequently than sensitive.

Conclusion: Early seizures, ischemic stroke and frontal/cortical localizations of brain lesions are more frequent in evolution of stroke. Early treatment is very important to improving the prognosis in stroke patients.

p085
LIMBIC ENCEPHALITIS WITH ANTIBODIES TO VOLTAGE-GATED POTASSIUM CHANNEL COMPLEX: PHENOTYPING THE SUBFORMS WITH LGI1 AND CASPR-2 ANTIBODIES

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Purpose: Limbic encephalitis with antibodies (abs) to voltage-gated potassium channel complex (VGKC-LE) is a known form of autoimmune

encephalitis. Recently two proteins associated with this complex could be identified as specific ab-targets: leucine-rich, glioma inactivated protein 1 (LGI1) and contactin-associated protein-2 (CASPR-2). Identification of these ab-subforms was hypothesized as a clue to explain the diversity of the syndrome. The aim of this study was to subdivide the formerly identified VGKC-LE patients at our centre into these subgroups and to evaluate their proportion, comparative phenotypes and clinical courses.

Methods: All VGKC-LE patients, identified between 2002 and 2010 at our centre, with available serum and CSF samples for retest were included. The study was approved by the local ethics committee. All samples were retested for abs to VGKC, LGI1 and CASPR-2 by indirect immunofluorescence. Clinical and paraclinical data were obtained from the patient records.

Results: Seventeen VGKC-LE patients were identified: ten (53 %) were positive for LGI1-abs, 3 (16 %) were positive for CASPR-2-abs, 4 (21 %) could not be classified furthermore. None of the VGKC-LE patients had a tumor. Comparing the three VGKC-subgroups there were no differences in clinical characteristics. All patients received immunotherapy with intravenous methylprednisolone (MP) pulses as standard therapy. Seventy-six percent of VGKC-LE patients were seizure-free at follow-up (20 months, range 3–70). No relapses were seen in our study cohort. Outcome parameters were similar in the VGKC-subgroups. Only MRI features at outcome were different: all hippocampal scleroses developed under immunotherapy (N = 7) were seen in the LGI1 ab group ($p = 0.02$).

Conclusion: VGKC-LE has a good prognosis with a proportion of 76% with good recovery and is assumed to be a mostly nonparaneoplastic monophasic condition. Majority of the VGKC-LE patients can be subdivided in LE associated with LGI1-abs (53%). The fact that only patients with LGI1-abs developed hippocampal sclerosis leads to the presumption that standard immunotherapy with MP pulses is not sufficiently effective in this subgroup and early escalation of therapy could improve outcome.

p086
CLINICAL SPECTRUM OF POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME

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Purpose: To retrospectively identify patients with posterior reversible encephalopathy syndrome (PRES) with a characteristic clinical presentation and neuroimaging abnormalities and summarize the diagnosis and treatment strategy.

Method: Retrospectively analyze associated comorbid medical conditions, presenting clinical symptoms, diagnostic test results (magnetic resonance imaging, electroencephalography, and lumbar puncture), and time to clinical recovery in patients with PRES.

Results: Nine patients with PRES (eight females and one male) were identified with a mean age of 46.3 years. Comorbid conditions included hypertension, eclampsia, teroid therapy, cirrhosis and systemic lupus erythematosus. Presenting symptoms included headache, vomiting, seizures, altered mental status, visual impairment, and psychiatric symptoms or visual hallucination. Mean peak systolic blood pressure at presentation was 161.7 mm Hg. Clinical symptoms resolved after a mean of 5.3 days in most patients. Atypical neuroimaging features included frontal, temporal, cerebellum, brainstem, thalamus and basal ganglia involvement in most patients, unilateral lesions or hemorrhage were not found. Electroencephalogram demonstrated slow wave activity.

Conclusion: Clinical recovery occurred in most patients within 1 week. MRI is the golden standard of diagnosing this entity. Atypical neuroimaging features were frequent. Early diagnosis and proper treatment is essential in the management of PRES.

p087
EPILEPSY IN CELIAC DISEASE: NOT JUST A MATTER OF CALCIFICATIONS

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Purpose: To describe the clinical, neuroradiological and neurophysiological features of epileptic patients (pts) with celiac disease (CD), comparing cases with and without cerebral calcifications.

Method: We selected eight consecutive epileptic patients (seven females) with a diagnosis of CD confirmed by duodenal biopsy, attending our Epilepsy Center from 1991 to 2009. On the basis of brain CT scan, we identified a group of pts with CEC (ie. CD, epilepsy and cerebral calcifications) and a group without brain calcifications.

Results: Mean age at epilepsy onset and at CD diagnosis was respectively of 12.85 and 22.7 years. Most cases presented a focal epilepsy with temporal (2 pts) or occipital (2 pts) seizure onset; two had focal epilepsy without a clear localization of seizure onset. Our cohort included a case with progressive myoclonic epilepsy (PME) and one with limbic encephalitis (LE) with high anti-GAD antibodies titres. Interictal EEG showed clear focal epileptic abnormalities in four pts, generalized discharges in three cases and unspecific abnormalities in one. Brain CT scan revealed posterior calcifications in half the pts. Brain MR highlighted a mild cerebral and cerebellar atrophy in the patient with PME. Pts with CEC presented a normal neurological examination, focal EEG abnormalities and a good response to gluten free diet in half of the cases. One of them underwent surgery with excision of the calcific area, without any clinical improvement. The group without cerebral calcifications was more heterogeneous, including pts with good prognosis and pts with a more complex clinical picture (PME and LE) and poor outcome.

Conclusion: Our study suggests that different pathological mechanisms could be involved in the association of CD and epilepsy. Cases characterized by a diffuse neurological impairment and the absence of brain calcifications should be differentiated from CEC syndrome, a specific entity where epilepsy is often confined to the occipital lobe. Moreover our data minimise the role of calcifications in epileptogenesis and indicate that CD should be included in the screening for PME etiology.

p088
EARLY POSTSTROKE EPILEPTIC SEIZURES

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Background: Stroke is the most common identified etiology of epileptic seizures and symptomatic epilepsy in the elderly population. Early seizures after stroke are defined as those occurring within 7–14 days after acute stroke.

Purpose: The aim of the study is to assess the rate and predictive factors for early seizures in patients with acute stroke.

Patients and Methods: One hundred thirty patients with ischemic or hemorrhagic first-ever stroke admitted at our Service from March to December 2010 were included in the study. Patients with SAH, cerebral vein thrombosis and history of seizures were excluded from the study. All the patients underwent brain CT scan or MRI. Our study focused on analyzing the following variables: age, gender, severity of symptoms at admission (using the Modified Rankin Scale dichotomized in 0–2 and 3–5), stroke types and location.

Results: Ischemic stroke was diagnosed in 94 (72.4%) patients and hemorrhagic stroke in 36 (27.6%) patients divided in 76 (58.5%) males and 54 (41.5%) females and mean age 68 SD ± 12 years. Early epileptic seizures were diagnosed in 10 patients (7.6%). Seizures were significantly more frequent in patients with hemorrhagic stroke 11.1% (4/36) than in those with ischemic stroke 6.4% (6/94). Overall incidence of early epileptic seizure was 7.6% (10/130). Most seizures (70%) were simple partial or partial with secondary generalization while 20% were primary generalized tonic–clonic seizures. Modified Rankin scale >3 (OR 2.9) was an independent risk factor for poststroke epileptic seizures. Cortical involvement was found in 81% of the patients.

Conclusions: Independent predictive factors for early seizure development in patients with acute stroke included: Lobar hemorrhagy, stroke disability and cortical involvement in the neuroimaging studies.

p089
EPILEPSY AND MULTIPLE SCLEROSIS: THE INITIAL PRESENTATION, COURSE AND CAUSALITY

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Purpose: To study the relationship between epilepsy and multiple sclerosis (MS) in regard to the initial presentation, course and causality of both diseases.

Method: Electronic database of patients in outpatient clinic of one of the authors (DVS) was searched for subjects suffering both epilepsy and MS during 10-year period (2001–2010). Patients with psychogenic nonepileptic (99), acute symptomatic (52) and isolated spontaneous seizures (16 patients) were excluded. There were 1919 patients treated for epilepsy and 14 (0.73%) had both epilepsy and MS (according to modified McDonald's diagnostic criteria).

Results: The median age of eight female and seven male patients was 36 (22–57) years. In 5/14 patients epilepsy started 2–15 (median 6) years after clinical onset of MS. In those patients, no other cause of epilepsy except cortical or juxtacortical lesions of MS were found. In the remaining 9/14 patients epilepsy preceded clinical appearance of MS by 1–29 (median: 8) years. Cortical and juxtacortical MS lesions were the best etiological explanation for epilepsy in 5, and other diseases (cavernoma, AV malformation, idiopathic generalized epilepsy, and perinatal injury) were the cause of epilepsy in the remaining four patients. The course of epilepsy (five pharmacoresistant, nine pharmacosensitive) and MS (five clinically isolated syndrome, six relapsing-remitting, three secondary progressive) were randomly distributed over the two groups. Psychosis (2), dementia (2), allergy to lamotrigine (2), and suicidality (1) were main comorbidities.

Conclusion: In busy outpatient epilepsy clinic MS is rare but significant cause of epilepsy. In considerable number of patients epilepsy could precede MS for many years.

p090
PARTIAL EPILEPSY AND BRAIN TUMORS

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Purpose: Of the study was to analyze the clinical data of patients diagnosed as brain tumors companioned with partial epilepsy.

Method: Methodology of the study was developed using clinical anamnesis, histories and diagnostic methods EEG, CT; NMR for the 6 years period of time. Data were analyzed using statistical parameters: structure, prevalence, mean and standard deviation. Value of the results was tested with: *t*-test and X^2-test.

Results: In the investigation were involved 15933 patients hospitalized in Neurological Clinic, 1725 of them with prevalence of 10.8% were diagnosed as epilepsy, and 175 cases or 1.09% of them were diagnosed as brain tumor, 75 of them or 42.86% were associated with epilepsy seizure with significance $p > 0.05$.

In overall, as partial epilepsy seizure, focal senso motoric seizures were dominant at 510 cases with prevalence of 46.0%. Focal seizures with complex crises were present at 123 cases with prevalence of 11.1%.

Epilepsy cases with known etiology, epileptogenic tumors participate with 75 cases or 6.8%. Structure of the participation of the types of epileptic seizures is different to the epileptogenic brain tumors in compare with overall epilepsy cases. Focal seizures senzo motoric are present at 40 patients with prevalence of 53.3%, and focal seizures as complex crises are present with prevalence of 20.0%.

Mean age of all brain tumors is 41.6 years old.

Partial onset of epilepsy has to be for about 60% of adult epilepsy.

Conclusion: Data indicates a strong correlation between partial epilepsy and brain tumors.

Poster session: Adult epileptology IV
Monday, 29 August 2011

p091
EPILEPSIES IN THE ELDERLY: ETIOLOGY, SEIZURES AND COMORBIDITIES

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Purpose: The prevalence and incidence of epilepsies in elderly is high. However, only few studies compared etiology and seizure semiology of epilepsies dependent on the age at onset of epilepsy.

Method: Our prospective, multicenter, cross-sectional study investigated etiology, seizure semiology, postictal symptoms and comorbidities in the following groups were recruited from five centers: Group A: 79 elders with late onset of epilepsy (age ≥ 65 year, age at onset ≥65 year) Group B: 67 elders with established epilepsy (age ≥65 year, age at onset ≤50 year) Group C: 56 younger adults with epilepsy (age ≤50 year).

Results: Epilepsies in group A were significantly more often focal (A:96.2%, B: 85.1%, C:69.6%; $p = 0.002$) and symptomatic (A:70.9%, B:40.3% C:50.0%; $p < 0.001$); cerebrovascular diseases (A:36.7%, B:1.5%, C:3.6%) and tumors (A:11.4%, B:7.5%, C:12.5%) were the main causes. In group A, simple partial seizures were less often (A: 48.1%, B: 64.2%, C: 46.4%, $p = 0.002$) and secondarily generalized seizures more often (A: 46.8%, B: 28.4%, C: 33.9%; $p = 0.005$) reported, especially compared to group B.

Postictal confusion (A: 45.6%, B: 25.4%, C: 19.6%; $p = 0.003$) and Todd's paresis (A: 19%, B: 3.0%, C: 1.8%, $p < 0.001$) occurred more frequently in group A, postictal symptoms lasted longer compared to group B. Comorbidities, especially hypertension, were more frequent in group A.

Conclusion: Etiology, postictal conditions, and comorbidities clearly depend on age of the patients and age of onset of epilepsy. Intensive

research is required because of the upcoming demographic changes, especially in western countries.

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p092

A COMPUTERIZED ALGORITHM FOR COMMUNICATING TREATMENT PROGRESS AND OFFERING CHOICE TO PATIENTS AND CARERS ACROSS EIGHT MAJOR DOMAINS IN THE EPILEPSY MANAGEMENT OF THE LEARNING DISABLED POPULATION

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Purpose: In epilepsy management the therapeutic goal is seizure freedom, but this is not always achievable. This is more so in the learning disability (LD) population. In the LD population improvements in quality of life, overall safety and access to the community via optimizing treatment might be more cherished than being successful in abolishing seizures. We have identified eight aspects of treatment response that are clinically and holistically important. As there might be cognitive complexity in understanding this as verbal information we have developed a visual communication tool to maximize comprehension.

A computer binary algorithm allows the information to be captured swiftly during a clinic and an instant personalized single screen graphic is produced with visual display to facilitate information sharing and decision making. The display is responsive to compare changes between appointments across a period of time and helps in treatment decisions.

Method: The dimensions:

1. Number of AEDs.
2. Presence of seizure life threatening issues such as clusters, cyanosis etc.
3. Uality of life indicators including side effects of AEDs.
4. Surgical intervention, e.g., VNS.
5. Seizure severity.
6. Seizure frequency.
7. Syndromal diagnosis.
8. Use of rescue medication.

Patient and carer involvement in the further development of the algorithm will concentrate on making the information accessible and meaningful.

Results: The eight-item binary algorithm of the above factors is displayed on a computerized eight spoke wheel diagram.

Conclusion: The algorithm is being used in community epilepsy clinics for the learning disabled population as an aid to communication.

p093

STUDY ON CLINICAL AND EEG FEATURES IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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Purpose: The aim of the study was to evaluate the correlation between clinical and EEG data in patients with temporal lobe epilepsy.

Method: We enrolled in the study 25 patients (10 men and 15 women) aged between 17 and 55 years who fulfilled the inclusion criteria: diagnosis of complex partial seizures of the temporal lobe without secondary generalization, at least one seizure in the day of admission in the study and stable dose of antiepileptic therapy 2 months prior to the study. The EEG recordings were made in standard conditions using bipolar derivations. We performed to each patient one EEG after the seizure and then another two in the following 3 days.

Results: The first EEG performed after the seizure revealed unilateral epileptic focus in 14 cases and bilateral in 11 cases. The EEG varied from 1 day to another in 13 cases: the epileptic focus migrated on the same side from anterior to posterior temporal derivations in five cases and on contralateral side in eight cases. Regarding the correlation between EEG and clinical data, we found three cases with different types of aura and only one focus on EEG, four cases with one type of seizure and two foci on EEG and five cases with different type of seizures and one focus on EEG.

Conclusion: The temporal lobe epilepsy is often characterized by polymorphism both in EEG and clinical aspects.

p094

DIAGNOSTIC CHALLENGES OF DE NOVO EPILEPSY IN ELDERLY. A 2 YEAR PROSPECTIVE STUDY

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Purpose: Epilepsy is a common neurological disorder in later life. The annual incidence of epilepsy in people between 65 and 69 years old is 85.9/100.000 and 135/100.000 for those aged older then 80 years. Epilepsy in elderly has been often unrecognized and misdiagnosed. Most of the published data come from cases and retrospective studies. Here, we conducted a 2-year prospective study including all inpatients, aged 65 years or older, admitted in our neurological division, in whom we diagnosed a de novo epileptic disorder. We then compared clinical features of this sample with an age-matched population admitted for a ''brain attack'' (i.e., acute focal or generalized brain dysfunction), focusing on diagnostic challenges.

Method: Twenty-four elderly patients (six males, 18 females, mean age: 77.7 years) with a de novo diagnosis of epilepsy were included in this study.

A population of 352 patients, age-matched, admitted in our neurological division over the same time window for a generic diagnosis of ''brain attack,'' was selected for statistical purposes.

Statistical analysis (ANCOVA) was performed on age, gender, vascular risk factors, CT scan results, EEG findings, neurological admission diagnosis (from emergency units) in the two samples selected.

Results: Statistical analysis showed that epilepsy represents about 9% of all brain attacks observed in elderly and is more frequently misdiagnosed in the emergency unit compared to other causes of acute brain dysfunction; comorbidities and neuroradiologic findings appeared similar in the two sample populations; EEG appeared to have the highest specificity and sensitivity in the differentiation between the two sample populations studied.

Conclusion: The present study represents, to our knowledge, the first prospective study on clinical and electrophysiological features in elderly with a de novo diagnosis of epilepsy. It provides clinical and EEG data which might improve the sensitivity and specificity of diagnosis of epilepsy in old people with ''brain attacks.'' Our results confirm the necessity of an expert neurological care in the evaluation of these patients particularly on admission at emergency.

p095

PREDICTORS OF 5-YEAR REMISSION IN FOCAL EPILEPSY OF UNKNOWN CAUSE

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Purpose: To study prognosis and prognostic predictors in patients with FEUC.

Method: Two thousand eighty-three patients with FEUC were consecutively seen from 1987 to 2010 in two Epilepsy Centers (Reggio Calabria and Catanzaro, Italy). Nine hundred nine were excluded because of insufficient data, psychogenic seizures, absence of neuroimaging or presence of brain lesions on MRI. The following variables were considered: age, gender, age at onset, family history of epilepsy or febrile seizures (FS), perinatal factors, history of FS, history of status epilepticus, type of seizures, presumed lobar localization, EEG, type of recruitment (incident or prevalent case). Survival curves were generated with Kaplan–Meier method and compared with log-rank test. The end point was cumulative time-dependent chance of 5-year remission. Independent predictors of remission were tested by multivariate analysis (Cox proportional hazards function models).

Results: One thousand one hundred seventy-four patients were followed for 1019.4 person-years. One hundred five cases presented 5-yr remission. The cumulative probability of remission was 9% at 5 years, and 14, 18, and 21% at 10, 20, and 30 years. At univariate analysis, factors predicting remission included female gender, older age at onset, family history of epilepsy, drop attacks, and presumed lobar localization.

Independent predictors of remission were older age at onset (Hazard Ratio, HR for each increasing year 1.001; 95% confidence interval, CI 1.000–1.002), family history of epilepsy (HR 1.6; 95% 1.1- 2.4), seizures with loss of consciousness (HR 1.7; 95% CI 1.1–2.6), secondarily generalized seizures (HR 1.6; 95% CI 1.0–2.5), drop-attacks (HR 0.2; 95% CI 0.0–0.8), parietal epilepsy (HR 3.2; 95% CI 1.4–7.1), occipital epilepsy (HR 1.8; 95% CI 1.1–3.2), and being an incident case (HR 2.9; 95% CI 1.84.6). In incident cases, independent prognostic predictors were loss of consciousness and occipital epilepsy.

Conclusion: One-fifth of cases with FEUC attain 5-yr remission during follow-up. Older age at onset, family history of epilepsy, seizure type, and lobar localization are independent prognostic predictors. However, only lobar localization and seizures with loss of consciousness are favorable prognostic predictors in incident cases.

p096

THE PROGNOSIS OF FOCAL EPILEPSIES IN ADULT PATIENTS FOLLOWED AT TWO ITALIAN EPILEPSY CENTERS: THE EFFICACY OF ''NEW'' ANTIEPILEPTIC DRUGS

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Purpose: To verify the course of epilepsy and to the risk factors possibly correlated to the prognosis in patients with focal epilepsies; to evaluate the response to subsequently tested antiepileptic drugs (AEDs), and the efficacy of ''new'' AEDs.

Method: We selected 1155 patients affected by focal epilepsies. Their data were analyzed by the univariate and multivariate logistic regression.

Results: Seizure freedom was achieved in 553 cases (47.9%), with the first tested AED in 235 patients (25.3%), with the second in 137 patients (11.9%), with the third in 97 (8.4%) and with the fourth or further AED in 86 (7.4%). Familiarity for febrile convulsions, remote acute seizures, psychiatric pathology, epileptiform interictal EEG abnormalities and identified etiology significantly correlated with persistence of seizures ($p < 0.001$, $p < 0.032$, $p < 0.026$, $p < 0.001$, $p < 0.005$). The interim analysis of the data at the day of this report shows 141 seizure-free patients (25.5% of the seizure-free cases) which were treated with a ''new'' AED.

Conclusion: The percentage of seizure-free patients after the first or second AED is lower than the one reported in the literature; this result can be attributed to the patients selection at a tertiary center. On the contrary, the percentage of seizure freedom achieved after three or more pharmacological attempts was not negligible. The use of ''new'' AEDs was quite common (43.7%) and their contribution to reach seizure freedom was remarkable (i.e. 25.4% of the seizure-free patients were treated with a ''new'' AED).

p097

GELASTIC SEIZURES WITHOUT HYPOTHALAMIC HAMARTOMA

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Purpose: Gelastic epilepsy is a well recognized epilepsy syndrome, and is associated in almost all cases with the presence of a hypothalamic hamartoma. However, the epileptologist should be alert to alternative causes for such presentations. We present two cases from our service of gelastic seizures in the absence of hypothalamic hamartoma.

Method: We reviewed the clinical features in both cases. Both patients were male and right-handed. The duration of epilepsy was similar in both cases, with onset in late adolescence. In both cases, epilepsy was refractory to treatment with antiepileptic medications. Clinical examination was unremarkable in both men. Both patients were investigated with video EEG monitoring and imaging to localize a seizure focus.

Results: Video EEG monitoring in both cases suggested a right frontal focus for seizure onset. MRI in one patient revealed a right frontal mass lesion, and in the other, a right frontal cortical dysplasia. There was no evidence of a hypothalamic lesion in either case. After discussion, both cases were felt to be suitable for neurosurgical intervention.

Conclusion: Gelastic epilepsy without hypothalamic hamartoma is rare, but some cases reported have had a right frontal focus for seizure onset. Causes reported in such cases have included tumors and cortical dysplasia. Many of the cases reported have had a good response to surgical intervention. In gelastic epilepsy, the clinician should be aware of causes other than hypothalamic hamartomata. Investigations should be directed towards confirming a seizure focus with a view to offering surgical intervention.

p098

ANTI-LGI1 ANTIBODIES IN A PATIENT WITH SHORT TONIC SEIZURES COMBINED WITH SPEECH ARREST AND ANXIETY

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Purpose: During the last years it has been established that epileptic seizures can be associated with antibodies against ion channels and neurotransmitter receptors. The whole clinical spectrum of these conditions and the relationship between immunotypes and phenotypes, however, remain unknown. Our case expands the phenotype of immunopathies with anti-LGI1 antibodies.

Method: Case report. A 63-years-old man developed seizures with initial sensations of anxiety and tightness in the chest followed by speech arrest and a feeling of weakness in the right arm and right leg occurring many times during a day. Video EEG monitoring including surface EMG disclosed short tonic seizures involving all extremities pronounced on the right side with a maximum duration of one second suggestive of SMA and extrapyramidal involvement, respectively. Interictal EEG showed intermittent slowing over the temporal region of both hemispheres. MRI disclosed only some microvascular lesions. Treatment with OXC, LEV, PGN, PHT did not suppress the seizures completely. After detection of anti-LGI1 antibodies in serum treatment with intravenous immunglobulines, corticosteroids and azathioprine stopped the seizures completely,

but the further course was complicated by a mild mania and pulmonary embolism. No tumor was found in an extended screening. After cessation of seizures neuropsychological testing disclosed impairment of executive functions and anterograde verbal and nonverbal memory.

Conclusion: Our case resembles the patients described by Irani et al. (Ann Neurol. 2010 Oct 28. doi: 10.1002/ana.22307). In newly diagnosed patients with epilepsy an immunological etiology should be looked for especially if seizures are not controlled with AEDs.

p099

INSOMNIA IN EPILEPSY PATIENTS. CLINICAL AND POLYSOMNOGRAPHIC CHARACTERISTICS

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Purpose: Patients with epilepsy have multiple sleep problems, including insomnia. Mood disorders are a significant comorbidity in epilepsy. There is a high prevalence of insomnia in patients with mood disorders. The clinical and polysomnographic (PSG) characteristics of patients with epilepsy and insomnia have not been described.

Method: The medical records of all patients seen at Sleep Disorders Center affiliated to a Epilepsy Center were reviewed over a 6 months period. All adults with epilepsy presenting with insomnia were selected. These patients were matched with consecutive patients presenting with insomnia and no epilepsy (controls).

Results: Seventeen adult patients with epilepsy met inclusion criteria. Among epilepsy patients, 76.1% were women, the mean age was 40.7 years and 58.8 % had partial seizures. Difficulties to fall asleep was present in 88.2% patients with epilepsy vs. 81.2% of controls, and 68.2% of epilepsy patients had troubles staying sleep vs. 82.4 of controls (there was no statistically significant differences). At time of presentation 52.9% of patients were using a sleep medication vs. 64.7% of controls. Sleep medication was used in the past by 76.5% of patients and 88.5% of controls. Zolpidem was the most common sleep medication prescribed among patients and controls (64.7 % and 76.5%, respectively) followed by melatonin (41.2 % and 41.2%, respectively). These results were not statistically significant. Patients with epilepsy had a statistically significant higher percentage of depression compared to controls (52.9% vs. 17.6%, $p = 0.028$). PSG showed a mean sleep efficiency of 69.0% with a mean sleep latency of 48.8 min among epilepsy patients. These results did not differ from controls. Sleep disordered breathing was present in 47.0 % of patients and 29.4% of controls.

Conclusions: Adult patients with epilepsy and insomnia have a higher prevalence of depression compared to controls. There is a high percentage of use of sleep medications among these patients and zolpidem is the most common medication used. The clinical and PSG characteristic did not differ when compared with controls.

p100

APPLICATION OF NEW ILAE AXIS CLASSIFICATION TO CLASSIFY PATIENTS: A STUDY FROM TERTIARY CARE EPILEPSY CLINIC IN SOUTH INDIA

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Purpose: To clarify the clinical validity of the new axis scheme in patients with epilepsy.

Method: Retrospective analysis of clinical, EEG and imaging data was performed in 2257 patients with epilepsy. All patients were classified as per the new ILAE diagnostic scheme into three axes.

Results: *Axis 1*: 2257 patients had total of 4076 epileptic phenomena, 3108 (76.3%) were motor manifestations, amongst which GTC was commonest (47.7%) followed by tonic motor (25.3%) automotor (13.6%) and myoclonic (13.4%). Aura was present in 506 (12.4%) cases. Absence seizures were present in 357 (8.6%). Fifty-five (1.4%) had epileptic spasms. 1.2% phenomena could not be classified. *Axis 2:* 1498 (66.4%) had focal seizures with or without bilateral evolution or impairment of consciousness. 616 (27.3%) had generalized seizures, 55 (2.4%) had epileptic spasms. Eighty-eight (3.9%) cases could not classified. *Axis 3:* The most frequent category included ''Epilepsies attributed to and organized by structural-metabolic causes'' (30%). Specific electroclinical syndrome was identified in 26.6% of patients, mainly juvenile myoclonic epilepsy (12.7%), followed by epilepsy with GTCS alone (7.9%). 3.9% had infancy and childhood onset electroclinical syndromes. 9.5% had MTLE with HS. 16 % were classified as probably symptomatic focal epilepsy (16%). 1.6% patients could not be ascribed to any syndrome. 14.5% could not be categorized because of poor follow-up.

Conclusion: Axis 1 can document the ictal clinical manifestations without EEG information. There is duplication between the terms in axis 1 and axis 2. In axis 3, patients with generalized seizures, but who do not conform to the known idiopathic generalized epilepsy syndromes could not be categorized. Epilepsies of unknown cause require clarification. Advanced neuroimaging, metabolic and genetic studies will decrease the proportion of unclassified patients.

p101

NOCTURNAL FRONTAL LOBE EPILEPSY AND PARASOMNIAS DIFFERENTIAL DIAGNOSIS: A PROSPECTIVE STUDY OF 48 PATIENTS

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Purpose: To identify critical clinical and instrumental features for nocturnal frontal lobe seizures (NFLS) and parasomnias differential diagnosis. In fact the standard criteria for nocturnal episodes are unreliable, as in the case of several parasomnias (Vignatelli et al., J Neurol 2005; 252:71–17), or are still lacking, as in the case of NFLS (Tinuper et al., Sleep Med Rev 2007; 11:255–267).

Method: We studied all subjects with suspected NFLS or parasomnias, referred to the Sleep Center and Epilepsy Center of our department during the last 3 years. For every patient a diagnosis was made, based on the results of anamnestic, clinical and instrumental (EEG, home-video and video-EEG polysomnography, VEPSG) data. After at least 6 months follow-up, all patients were reevaluated through a questionnaire that was inclusive of the Frontal Lobe Epilepsy and Parasomnias Scale (FLEP scale) (Derry et al., Arch Neurol 2006; 63: 705–709) telephonically administered by a neurologist blinded to the initial diagnosis.

Results: Forty-eight patients were enrolled and after the first evaluation they received the following diagnosis: NFLS (50%), parasomnias (23%), uncertain diagnosis (despite of the episodes recording, 27%). After the follow-up period and the new evaluation, the most cases with uncertain diagnosis remained uncertain.

Conclusion: (1) VEPSG that, even it is considered the ''gold standard'' diagnostic test, is not a satisfactory diagnostic tool, as in 27 % of our cases does not allow to make diagnosis; (2) the FLEP scale has poor sensibility and specificity; (3) a follow-up period often does not significantly improve the diagnostic possibility.

p102

CLINICAL AND NEUROPHYSIOLOGICAL ANALYSIS OF ADULTS PATIENTS WITH EPILEPTIC SEIZURES ONLY DURING SLEEP

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Purpose: We selected patients (P) with epileptic seizures only during sleep. We studied clinical, EEG, subjective quality and architecture of nocturnal sleep.

Methods: Each patient was examined on Video-EEG Unit from 18 to 8 h. We reviewed awake and sleep EEG, basal and paroxistic interictal activity (PIA). To quantify PIA was made an index to compare awake/sleep period. Hypnogram was made for each P. We measure proximal corporal temperature along 12 h of continuous recording with a superficial sensor. Each P. completed a 1-week sleep diary and answer Pittsburgh Scale evaluating subjective quality of sleep.

Results: We studied 16 P; the mean age was 34 years (17–61). Male/Female relation was 3:1. 87.5% P had focal epilepsy, being most frequent temporal lobe epilepsy, 62.5% P presented drug resistant epilepsy. More frequent DAEs were CBZ, PB, TPM y LTG. Most of patients presented two to three times PIA index during slow sleep compare with wake period. No one presented PIA during REM sleep. In 50% of P hypnogram presented superficial and fragmented sleep; in this population the 78% P showed increase of PIA index. The temperature showed expected oscillations on a 12 h cycle. The subjective sleep quality was normal for all P.

Conclusion: There was male, temporal lobe epilepsy and drug resistant P predominance. We observed a significant increase of PIA during slow sleep, this finding correlated with alteration of architecture of nocturnal sleep. No P reported alteration of subjective sleep quality.

p103
RURAL EPILEPSY CLINIC: OUTREACH PROGRAM

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Aim: To improve rural compliance and overall health through holistic care.

Methodology: With help from the village Head, leaflets announcing the camp were pasted on trees. A neurologist, general practitioner, special educator, psychologist and support group members volunteer at these camps. Twenty-four camps were held from 18–11-07 to 13.02.11. Five basic AEDs: phenobarbitone, phenytoin, carbamazepine, sodium valproate, clobazam, and paracetemol syrup have been distributed. Three hundred twenty-two patients attended these camps, of which 228 had epilepsy. Average attendance at first three camps was 41 and 92 for last three camps. For research purpose only those persons who have had 50% attendance and have attended a minimum of three clinics have been taken (N83).

Conclusions: Proper documentation, regular follow-up, group talks, counseling, educational and vocational guidance, improved compliance and seizure control. A comparison of data 6 months prior to clinic versus last 6 months of treatment revealed that 48% of research group had attained 6 months seizure freedom (of which two had successful surgeries). The rest had a 91% average decrease in seizures.

There is a shift in thinking in rural areas, with people coming forward to be investigated and treated: 59% had done EEG/CT/MRI. Thirty percent had a treatment gap of an average of 12 years. Nonaffordability, nonavailability of medication, long distances to travel, medicine not helping and side effects were reasons given for irregular compliance. Verbal reports suggest that patients seek medical help but do not realize the importance of continuing medication for 2–3 years after seizure freedom.

Poster session: Adult epileptology V
Monday, 29 August 2011

p104
SLEEPINESS DURING DAY AND SLEEP DISTURBANCES IN A POPULATION OF EPILEPTIC PATIENTS: A CASE–CONTROL STUDY

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Purpose: Several studies evaluated the prevalence of EDS (excessive daytime sleepiness) and sleep disturbances in epileptics, focusing ob possible causes of sonnolence but data are controversial. The aim of the present study is to evaluate the prevalence of EDS and some sleep disturbances in a population of epileptic subjects assuming no more than two AEDs.

Methods: Seventy-nine consecutive patients were recruited prospectively among those referred to epilepsy centre of the department of experimental biomedicine and clinical neurosciences of university of Palermo that were recruited among medical staff, high school and university students. Questionaire validated to evaluate EDS, insomnia, RLS and OSAS were used and 21 patients and eight controls undertook polymesam. Among patients 58% was suffering of focal epilepsy, and 41% from generalized epilepsy; 68.3% were on monotherapy and 30% had a refractory epilepsy. Among epileptic patients, 30% had EDS while OSAS was prevalent among males (85%) with focal epilepsy and with mean age of 50.7 years.

Results: No significant differences were found between epileptics and controls concerning EDS frequency ($p = 0.669$), prevalence of specific sleep disturbances such as insomnia ($p = 0.538$), RLS ($p = 0.888$), presence of OSAS in polymesam ($p = 0.316$), severity of OSAS. Sonnolence in epileptics seems to correlate to high risk for OSAS ($p = 0.0027$) and high frequency of OSAS ($p = 0.0024$).

Conclusions: Our preliminary results do not indicate a greater frequency of EDS in epileptic patients compared to controls, nor a difference among specific sleep disturbances according to previous studies. Also greater frequency of OSAS in adult males with focal epilepsy is in agree with literature data.

Further data are necessary to recognize the causes of EDS in epileptic patients and the prevalence of some specific sleep disturbances but only OSAS as a sleep disturbance seems to be associated with EDS. This disturbance should be evaluated as a diagnostic routine in epileptic patients in order to optimize the therapy.

p105
HOW FAR DO PATIENTS TRAVEL FOR PROLONGED AMBULATORY ELECTROENCEPHALOGRAPHY AND DOES IT HELP?

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Purpose: To demonstrate the large geographical region where prolonged ambulatory electroencephalogram (AEEG) services are delivered by a tertiary referral centre in NSW, Australia and to assess the impact of this test on diagnosis.

Method: We retrospectively reviewed data of 400 patients who underwent prolonged AEEG from January 2007 to June 2010. Postcodes were extracted from patient records and kilometers travelled were plotted on a map according to metropolitan, rural and statewide regions. We also compared the provisional diagnosis of each patient to the final diagnosis.

The percentage of normal prolonged AEEG recordings with and without reported events were also documented.

Results: Patients were referred from 193 postal regions and distances travelled by road ranged from 1 to 3.950 kms. Flight distances were up to 1.970 kms. Patients also travelled from interstate and overseas.

Of the 400 patients tested, a provisional diagnosis of epilepsy was confirmed in 136 (34%) patients. Epilepsy was excluded in 110 (27.5%) patients with no recorded events as well as another 69 (17.25%) patients with recorded events that were not epileptic. In the remaining 63 (15.7%) patients prolonged AEEG was used to diagnose nonepileptic medical conditions. In only 22 (5.5%) patients prolonged AEEG did not offer a clear diagnosis after testing.

Conclusion: Prolonged AEEG recordings can service a population that is widely geographically dispersed. Prolonged AEEG testing has proved to be highly effective as the test was noncontributory in only 5.5% of the 400 patients tested.

p106
TONIC EYE DEVIATION DUE TO HYPERGLYCEMIA-INDUCED FOCAL SEIZURES: CASE REPORT

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Purpose: We present a case of hyperglycemia-induced focal seizure presenting as episodic conjugate eye deviation.

Method: A 51-year-old male attended our out patient department with the complaint of intermittent both eyes deviate to right side. Limbs convulsion did not happen. Each episode lasted a few seconds and disappeared without any discomfort or fatigue. He did not have any aura before the episode and responded well to the environment throughout the attack. The patient had several episodes per hour during the day. The history had cardiac arrhythmia and diabetic mellitus for years but not on regular treatment. He also had a vague history of stroke and left no sequel. Neurological examination revealed normal extraocular and limbs movement. Intermittent eyeballs deviate to right side with clear consciousness during interviewing. After admission for further evaluation, the blood sugar was 528 mg/dl. Electrocardiogram (ECG) showed persistent atrial fibrillation. Brain MRI showed one enhanced lesion in the left prefrontal area which was compatible with a recent infarction, several nonenhanced low intensity lesions in bilateral middle cerebral artery region. Unfortunately, emergent electroencephologram (EEG) was not available.

Results: His condition was diagnosed as simple partial seizure with the presentation of conjugate eye deviation to right side. It was suspected to be elicited by hyperglycemia but not the recent cerebral infarction. He was treated with insulin and intravenous fluids. No anticonvulsant was given. The episode ceased after blood sugar returned to normal range a few days later. The EEG did not show any epileptic activity.

Conclusion: In the presence of hyperglycemia gamma aminobutyric acid (GABA) metabolism increased and the levels of this important inhibitory neurotransmitter may be depressed resulting in a reduction of seizure threshold. Focal seizures associated with hyperglycemia are refractory to anticonvulsant treatment and respond best to insulin and rehydration. A thorough history and systematic evaluation of any eye movement disorder is essential for accurate anatomical localization, etiological diagnosis and management.

p107
ALTERATION OF GLOBAL WORKSPACE (GW) DURING LOSS OF CONSCIOUSNESS: A STUDY OF PARIETAL SEIZURES

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Purpose: According to the global workspace (GW) theory, conscious processing results from a coherent neuronal activity between widely distributed brain regions including frontoparietal associative cortices. Alteration of consciousness (AOC) in epileptic seizures is a major negative prognostic factor. Recently, we have shown that AOC during temporal lobe seizures is correlated to nonlinear increases of neural synchrony within distant cortico-cortical and cortico-thalamic networks. Excessive synchrony seemed to prevent this distributed network to encode for conscious representations. Whether such mechanisms are involved in AOC occurring during extratemporal seizures is unknown. This study investigates the relationship between changes in synchrony and AOC intensity during parietal lobe seizures.

Method: Eleven patients with well defined parietal seizures were selected. Three seizures in each patient were analyzed. Video Stereotactic-EEG (SEEG) recordings were reviewed and AOC intensity was scored using an eight criteria scale (CSS, Arthuis et al., Brain 2009 132 (Pt 8): 2091–101). Changes in synchrony between six regions explored in each patient were studied using nonlinear regression method (Guye et al., Brain. 2006 July;129 (Pt 7):1917–28) during four different periods: whole seizure, onset, mid part and end of the seizure.

Results: Seizures were divided into three groups according to AOC intensity. Preliminary results showed that low values of correlations between regions involved in GW (parietal associative cortex, frontal lobe) were observed in seizures without important AOC. In contrast, abnormal synchronization in such cortices correlated with AOC in parietal seizures.

Conclusion: Finally, we propose that during seizures with loss of consciousness, information cannot be processed within the GW because structures that are the most important for its activity are oversynchronized (in time and space).

p108
AN OBSERVATIONAL LONGITUDINAL STUDY ON LATE SEIZURES IN NEUROSURGICAL PATIENTS

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Purpose: Seizures are a frequent complication in patients who undergo neurosurgery, and can complicate the postoperative course. Evidence on the prophylactic anticonvulsant therapy after craniotomy is still lacking. Conventional antiepileptic drugs (AEDs) have been widely studied and there is limited evidence of their prophylactic or antiepileptogenic effect. Studies with newer AEDs are still lacking, although interest is increasing (Sirven et al., Mayo Clin Proc. 2004; 79 (12):1489–94) (Temkin et al., J Neurosurg. 1999; 91 (4):593–600).

Method: A 48-month observational longitudinal study was undertaken in patients receiving supratentorial neurosurgical interventions and routinely treated with a prophylactic antiepileptic therapy, to evaluate onset of late seizures (i.e. after 1 month from the procedure) and effects of antiepileptic therapy.

Results: A total of 101 people undergoing a craniotomy were enrolled. Before the neurosurgical procedure, seizures occurred in 34% of patients. During the observation, 46 people (46%) presented late seizures; among them 22 subjects had had seizures before surgery, nine had presented early seizures (i.e., within 1 month). No statistical differences in late seizures incidence were observed in people who took conventional antiepileptic drugs compared to whom took newer AEDs at baseline (1 month after craniotomy). Adverse events were mainly associated with phenytoin intake.

Conclusion: In our cohort late seizures had a relevant incidence. Future studies are needed to answer unsolved questions about possible strategies

to prevent postoperative seizures. It is actually advisable to manage antiepileptic and prophylactic therapy on individual factors, considering risks and benefits in each situation.

p109

LOCALIZER AND LATERALIZING VALUE OF UNILATERAL FACIAL MOTOR MANIFESTATION (UFMM) IN FOCAL EPILEPSY, USING VIDEO ELECTROENCEPHALOGRAPHY AND/OR DIRECT CORTICAL STIMULATION

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Purpose: To evaluate the localizer and lateralizing value of unilateral facial motor manifestations (UFMM) in spontaneous seizures, as well as in UFMM obtained by direct cortical stimulation (DCS).

Method: We analyzed 83 seizures from 27 patients who presented UFMM during video electroencephalography, and eight patients who presented UFMM during DCS. We correlated the localization and lateralization of the hypothesis of the epileptogenic zone (HEZ) and the zone of DCS that produced UFMM, with the time of presentation of the UFMM.

Results: Population under study consisted of 35 patients, 13 male and 22 female. Patients with seizures in VEEG had the following HEZ: 11 patients frontal lobe (FL), nine patients central region (CR), three patients posterior region (PR), three patients temporal lobe (TL). UFMM were ipsilateral to the HEZ in five seizures from the FL, in three seizures from the CR, and in four seizures from the PR. We did not find UFMM ipsilateral to the HEZ among the seizures from the TL. Latency of UFMM was long (beyond 10 s) in 80% of seizures ipsilateral to the HEZ, and early in 55.2% of seizures contralateral to the HEZ in the LF; early in the 66.6% of seizures ipsilateral to the HEZ and in 54.5% of seizures contralateral to the HEZ in the CR; long in 100% of seizures ipsilateral to the HEZ and in 100% of seizures contralateral to the HEZ in the PR; early in 80% of seizures contralateral to the HEZ in the TL. UFMM produced by DCS in two patients were ipsilateral, secondary to DCS in the temporal basal area and in the opercular motor area.

Conclusion: UFMM could be originated away from the ICR, with ipsilateral or contralateral origin.

p110

THE EFFECT OF THE MODIFIED ATKINS DIET FOR ADULTS WITH INTRACTABLE EPILEPSY

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Introduction: Approximately 30% of patients with epilepsy have refractor epilepsy. The use of dietary therapy treatment for epilepsy is technologically simple. However, the ketogenic diet is rarely offered to adults. The modified Atkins diet induces ketosis, but without fluid, calorie, or protein restriction, nor the requirement for fasting, food weighing, or hospitalization. We hypothesized that the modified Atkins diet would be also an effective therapy for adults with intractable epilepsy, as defined as a failure to respond to at least two anticonvulsant medications.

Material and methods: In a controlled clinical trial, we compared the efficacy, tolerability, and effects of modified atkin's diet in adult with refractory epilepsy. The primary outcome was at least 50% decrease in seizure frequency after 2 months of therapy; the secondary outcome was effects of weight loss on seizure frequency.

Results: The mean change of seizure frequencies in case and control groups was 2.5 ± 2.4 and 0.5 ± 1.3 respectively and the difference between two groups was statistically significant ($p < 0.001$). An interesting and surprising finding was that a decreased body mass index (BMI) correlated with seizure reduction.

Conclusion: The results of this study and comparison with other investigations showed that the modified Atkins diet have a positive effect for reduce of seizure in adults epileptic patients and probably we can apply this diet in epileptic patients for control and reduce of seizure. In addition, weight loss may provide added benefits for patients with epilepsy and comorbid obesity.

p111

APPLICATION OF PROPOSED CONSENSUS DEFINITION OF DRUG RESISTANT EPILEPSY IN CLINICAL PRACTICE

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Purpose: The International League Against Epilepsy appointed a Task Force to formulate a consensus definition of drug resistant epilepsy. We have conducted a study to apply it to outpatients of our hospital.

Methods: We reviewed one hundred consecutive patients with epilepsy on our database, we excluded patients with <1 year of follow up and patients with only one seizure.

Results: Level 1 for categorizing of treatment outcome, we described the above mentioned category in the last visit. With respect to seizure control: Category 1, seizure-free (65%); Category 2, treatment failure (20%); Category 3, undetermined (15%). Each category is subdivided into A (no), B (yes), C (undetermined) based on outcome with respect to adverse events: 1A (56%), 1B (8%), 1C (1%), 2A (17%), 2B (3%), 2C (0%), 3A (11%), 3B (1%), 3C (3%).

For Level 2 classification of drug responsiveness of epilepsy, we obtained the following data: drug responsive (65%), drug resistant (12%), undefined (23 %). Considering the pharmacological treatment, 66% was in monotherapy and 34% in combination: Drug responsive (54% and 11%), drug resistance (0% and 12%), undefined (12% and 11%) respectively.

Conclusions: The study has allowed us to be trained in the use of this definition. This identifies not only a group of drug responsive and drug resistance but another subgroup classified undefined, and considers that epilepsy is a situation that can change. We need to put into practise its use which can be difficult in some situations, and secure future prospective studies.

p112

STATE OF AUTONOMIC NERVOUS SYSTEM (ANS) IN MESIAL TEMPORAL EPILEPSY PATIENTS

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Purpose: Assessment of tonus, reactivity and homeostatic potential of ANS activity, functional condition of catecholamines system and possible meaning of their changes in epileptogenesis.

Method: One hundred two patients with mesial temporal epilepsy age of 18–45 and 17 healthy persons (HP) of the same age were investigated. Test MMPI was used. Tonus ANS was estimated according to clinical data. Reactivity of ANS was studied: changes of heart rate, systolic/diastolic BP after injection of fixed adrenaline dose and Danigni–Aschner test. Homeostatic potential of ANS activity was investigated by use of ortho-clinostatic test. Also we defined quantity

of adrenaline (A), noradrenaline (NA) and their precursors (L-DOPA) in four daily urine parts.

Results: MMPI test revealed typical increase on the1st, 2nd, 3rd, and 8th scales. Sings of autonomic dysfunction were shown in 102 (92.2%) patients. Excretion of A was decreased 1.5 times, NA, two times. Adrenalin test revealed in patients quality of answer: increase of BP by different addition of both systolic and diastolic one, just as in HP by rise of systolic and decrease of diastolic one; increase of A excretion was not enough (3.6 ± 1.0 vs. 9.2 ± 1.3 ng/min, $p < 0.05$). Danigni-Aschner test evoked decrease heat rate instead of its increase. Insulin test also evoked only 1.3 ± 0.5 vs. 5.2 ± 0.4 ng/min ($p < 0.001$) increase A excretion ($p < 0.001$). Some positive and negative correlations were fined.

Conclusion: Revealed data show the presence of AVS denervated hypersensitivity, exhaustion of provision of homeostatic mechanisms organism action, insufficiency of NA mechanism of counteraction to epileptogenesis.

p113
PRELIMINARY OBSERVATIONS ON AN AMBULATORY INTRACRANIAL EEG (IEEG) EPILEPSY MANAGEMENT SYSTEM

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Purpose: A multicenter clinical feasibility study was initiated to evaluate the safety and efficacy of an implantable epilepsy management system designed to predict seizure likelihood and quantify seizures in adults with medically refractory complex partial seizures.

Method: Ten adult subjects were implanted with the system at three clinical sites. Subjects had 2–12 disabling partial onset seizures/month; an identifiable seizure focus; and no history of psychogenic seizures. Postsurgery, subjects entered a data collection phase to train an algorithm for identifying periods of high, moderate, and low seizure likelihood. If the algorithm met performance criteria, subjects entered the advisory phase and received advisories regarding seizure likelihood. Primary safety evaluation is assessed 4 months post-implant.

Results: The system collected high quality, continuous iEEG records for all subjects. One serious complication followed implantation of the device; a subdural seroma related to previous resective surgery that was successfully treated. The device has otherwise been well tolerated. The iEEG data enabled quantification of clinical/subclinical seizure activity. Key observations include significant disparity between patient reported seizures and those captured by the device. The data has resulted in management changes for two subjects with a marked decrease in seizures for one patient. Eight subjects have completed the data collection phase with six meeting algorithm performance criteria and entering the advisory phase.

Conclusion: We have demonstrated that ambulatory iEEG monitoring is safe and that data acquisition meets expectations. Preliminary results suggest the system provides clinically useful information and the majority of study subjects met criteria for enabling seizure advisories.

p114
DETECTION OF EPILEPTIC SEIZURES BY PATTERN RECOGNITION FROM WIRELESS ACCELEROMETER DATA

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Purpose: Many persons with drug-resistant epilepsy are not aware of all seizures. This is a problem both in the evaluation of treatments (e.g. new antiepileptic drugs or epilepsy surgery) and for legal purposes (e.g. driving licenses). We have developed a system for automatic logging of seizures based on custom wireless inertial motion sensors and pattern recognition algorithms. This system provides a quantitative and objective seizure count and may aid physicians in the evaluation of treatments.

Method: Motion data has been recorded using wireless acceleration sensors mounted on three locations on persons with epilepsy who have undergone seizure monitoring at Sahlgrenska University Hospital. The dataset includes 38 patients and covers over 130 days and 200 seizures. EEG recordings have been used as reference to provide accurate seizure timing information.

Results: The wireless sensors have been well received, with very few patients experiencing discomfort. Different approaches to the machine learning problem have been investigated, resulting in a signal processing system which uses both short-term seizure-unique motion features as well as longer term seizure progression information. In patients with generalized tonic–clonic seizures it is common to see 100% sensitivity with no false positives, and for patients with focal seizures the sensitivity typically reaches 90%–95% with only 15–20% false positives (relative to the total number of positives).

Conclusion: Automatic logging of different kinds of epileptic seizures based solely on motion data has shown to be a reliable technique. Small wireless sensors that can be mounted, e.g., in clothing also provide a much less obtrusive alternative than systems that rely on EEG data. This automatic seizure logging system may become a useful tool in the evaluation of epilepsy treatments.

p115
COGNITIVE MODULATION OF EPILEPTIFORM EEG DISCHARGES IN PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY

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Purpose: Previous studies suggested that cognitive tasks (CTs) modulate (provoke or inhibit) the epileptiform EEG discharge (ED) in patients with juvenile myoclonic epilepsy (JME). Their inhibitory effect was found to be especially frequent (64–90%). These studies arbitrarily defined modulation as a 100% increase or 50% decrease of the ED compared with baseline which may not sufficiently distinguish from spontaneous fluctuations. These findings therefore needed corroboration using more rigorous statistics.

Method: Fifty-six patients with JME underwent video-EEG recordings including 50-min. baseline, sleep, hyperventilation (HV), intermittent photic stimulation (IPS) and CTs (praxis, reading and writing).

To account for spontaneous fluctuations of the ED, we divided the baseline period in 5-min. epochs and calculated the 95% confidence interval for the baseline ED rate in each patient. Modulation was assumed when the number of EDs during any 5-min. test period was outside the 95% confidence interval.

Results: Using the earlier methodological approach, our results were similar to previous publications: EDs during CTs were reduced in 93% of the patients and increased in 25%. However, when spontaneous fluctuations were accounted for, inhibition was found in 26% of the patients and provocation in 18%. HV and sleep were more provocative than CTs (HV: 23%; sleep: 22%). IPS had provocative effect in 9%. We observed inhibitory effects also for HV (4%), IPS (4%) and sleep (14%).

Conclusion: Spontaneous fluctuations of ED account for most of the previously described inhibitory effect of the CTs on ED. CTs were slightly less provocative than the nonspecific conditions HV and sleep.

p116
INHIBITORY EFFECT OF OLFACTORY STIMULI IN REFRACTORY MESIAL TEMPORAL LOBE EPILEPSY PATIENTS: A PILOT STUDY

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Purpose: Synchronization and desynchronization of cortical activity play a basic role in seizure susceptibility. EEG synchronization forms the main underlying basis for the generation of seizures (ictogenesis) whereas desynchronization counteracts it. Olfactory areas are connected to regions where seizures develop in mesial temporal lobe epilepsy (MTLE) and neuronal activity generated by olfaction could influence the spread of synchronous activity underlying seizures. Our purpose is to confirm with quantitative methods earlier findings that olfactory stimuli can modify epileptiform discharge (ED) in the EEG.

Method: Twenty patients diagnosed with refractory MTLE were submitted to Video – EEG recordings including 15-min. awake baseline, two hyperventilation phases (HV) and olfactory stimulation with ylang-ylang essential oil odorant solution at 10%. To account for natural fluctuations of the ED we divided the baseline period in 3-min epochs and calculated the 95% confidence interval for the baseline ED per epoch in each patient.

Results: Using this protocol, 6 (30.0%) of the tested patients showed modulation of ED (reduction in four and increase in 2) with olfactory stimuli whereas 7 (35.0%) patients had activation of ED with HV. No seizure occurred during the olfactory stimulation.

Conclusion: We evidenced that the olfactory system may be involved in ictogenic circuitry, and both desynchronization and synchronization in the ictogenic network underlying MTLE may have occurred through the olfactory stimulation. Beyond the contribution to our understanding of ictogenesis in human epilepsies, detection of inhibitory factors may be useful for the development of therapeutic approaches for patients with refractory epilepsy.

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Monday, 29 August 2011

p117
INTENSE OLFACTORY STIMULATION BLOCKS SEIZURES IN AN EXPERIMENTAL MODEL OF EPILEPSY

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Purpose: An olfactory stimulus prevents seizures in epileptic patients [Efron R, Brain 1956; 79 (2):267–81] while toluene (TOL) inhalation suppress seizures in amygdala electrical kindled rats [Ebert U et al., Neuroscience Letters 2000; 287:199–202]. In Wistar Audiogenic Rat (WAR strain) a loud sound (110 dB) triggers brainstem-dependent audiogenic seizures. Audiogenic kindling (AK) activates first the brainstem and subsequently recruits the forebrain, evidenced as limbic seizures [Garcia-Cairasco et al Epilepsy Res. 1996; 26 (1):177–92]. Thus, we aimed to evaluate if TOL would interfere with WAR seizures after AK.

Methods: Twenty-four male WAR (250–350 g) underwent AK, consisting of two acoustic stimuli (AS)/day/10 days. Each rat inhaled for 15 s 0.9% saline (SAL) or TOL, 20 or 60 s before the 21st AS. The seizure severity was classified for each AS using brainstem (ISc) and limbic (IL) seizure scores. The 20th and 21st indexes were compared to each AS index (Student *t*-test) (University Ethics Committee; protocol 172/2010).

Results: The SAL ISc (n = 6) ranged from 2 to 7 in the 20th and 0–7 at 21st AS. The 21st ISc was lower than the 1st, 2nd, 3rd, 7th and 20th indexes ($p < 0.05$). The TOL 60 s ISc (n = 9) ranged from 0 to 7 in 20th and 21st AS, without differences with the previous indexes ($p > 0.05$). The TOL 20 s ISc (n = 9) ranged from two to eight in the 20th and was zero (6/9 rats) or below 3 (3/9) at 21st AS. The 21st ISc was lower than the 20 previous indexes ($p < 0.05$). The SAL IL ranged from 0 to 3 in the 20th and 0–2 at 21st AS, without difference with the previous indexes. The TOL 60 s IL ranged from 0 to 4 in the 20th (6/9) and 0–3 at 21st AS (3/9), also without difference. The TOL 20 s IL ranged from 2 to 3 in the 20th (6/9) and was 3 (2/9) at 21st AS, with difference between the 21st and 19th IL ($p < 0.05$).

Conclusions: TOL decreased the ISc and IL, especially when inhaled 20 s before the AS.

p118
THE ANTIEPILEPTIC DRUGS CARBAMAZEPINE, PHENYTOIN AND LAMOTRIGINE DISPLAY NO SELECTIVITY VERSUS NAV1.1 AND NAV1.2 CHANNELS

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Among ion channels, NaV1.1 is the most involved in inherited epilepsies, with about 600 different mutations identified so far in severe myoclonic epilepsy of infancy (SMEI) patients. As shown recently, NaV1.1 has a prominent role in inhibitory interneuron action potential firing and the severity of clinical symptoms of NaV1.1-linked epilepsies are correlated to the amplitude of NaV1.1 loss of function (Martin et al., 2010). Some of the most prescribed antiepileptic drugs (AEDs) are known to target sodium channels. Therefore, it was of high interest to know if these AEDs display any selectivity between NaV1.1 and NaV1.2, this latter channel being the archetypal neuronal Na channel, strongly expressed in hippocampal pyramidal cells. In this whole-cell patch-clamp study, we report on the inhibitory effect of 3 Na channel blocking AEDs (e.g. carbamazepine, phenytoin and lamotrigine) at human NaV1.1 and NaV1.2 channels, stably expressed in HEK cells. All three compounds displayed a voltage-dependent blockade of NaV1.1 and NaV1.2 channels, with almost no effect at hyperpolarized voltages. At voltages close to the half inactivation, the maximal inhibition achieved was $-73 \pm 4\%$, $-61 \pm 4\%$ and $-51 \pm 7\%$ at NaV1.1 and $-64 \pm 6\%$, $-42 \pm 3\%$ and -37 ± 5 % at NaV1.2, for carbamazepine (300 μM), phenytoin (100 μM) and lamotrigine (100 μM), respectively.

When considering their use-dependent inhibitory effects, these compounds displayed similar properties at NaV1.1 and NaV1.2.

Our findings demonstrate that these important AEDs do not discriminate between NaV1.1 and NaV1.2, probably explaining why pro-convulsant effects are seen at high dosages. One could infer that new Na channel blocking molecules inactive at NaV1.1 should be safer and more efficient AEDs.

References: Martin MS, Dutt K, Papale LA, Dube CM, Dutton SB, de HG, Shankar A, Tufik S, Meisler MH, Baram TZ, Goldin AL, Escayg A (2010) Altered function of the SCN1A voltage-gated sodium channel leads to gamma-aminobutyric acid-ergic (GABAergic) interneuron abnormalities. J Biol Chem 285:9823–9834.

p119

ADENOSINE RECEPTORS A_1 AND A_{2A} MODULATE THE OCCURRENCE OF FAST RIPPLES IN THE DENTATE GYRUS AND HIPPOCAMPAL CA3 AREA

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Purpose: Fast ripples (FR) are associated with interictal and ictal activity in human epileptic patients and in animal models of epilepsy. We sought to characterize how the endogenous antiepileptic adenosine modulates FR.

Method: We recorded field activity in the DG and in CA3 in hippocampal slices from control and kindled Wistar rats. FR occurred spontaneously or were induced by applying high frequency stimulation over the perforant path. We assessed the effect of the activation and blockade of the adenosine A_1 and A_{2A} receptors on the frequency of appearance and power of the FR.

Results: Kindled rats have a higher probability of showing FR than control rats in the DG and in CA3. Adenosine (100 μm) completely suppressed the FR in the DG and in CA3 in five out of eight control and in three out of eight kindled rats. In the rest of the slices, a frequency reduction of ca. 20% in control and in kindled rats was observed. Adding an A_{2A}R antagonist reduced further the frequency by 60% in control but not in kindled rats. Interestingly, adenosine reduced FR amplitude in CA3 but not in DG and this effect was again more evident in control (37%) than in kindled rats (9%).

Conclusion: Adenosine inhibits the occurrence of FR oscillations in the DG and CA3 primarily through A_1Rs and its effects are more evident in control than in epileptic rats. The inhibitory effect of adenosine is potentiated by the blockade of A_{2A}Rs.

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p120

OPTOGENETIC INHIBITION OF EPILEPTIC ACTIVITY

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A new generation of optical probes, the light-sensitive ion-channels, channelrhodopsin-2 (ChR2) and halorhodopsin (NpHR), allow bidirectional modulation of electrical signals with high temporal resolution. These characteristics make optical inhibition a potentially advantageous new antiepileptic treatment strategy that relies on optical activation of neurons to interrupt seizures.

Purpose: In this study we investigated the therapeutic potential of light-activated inhibition in the tetanus toxin rodent model of focal epilepsy, which is characterized by recurrent bursts of high frequency activity.

Method: Six-week old male Sprague-Dawley rats were stereotactically injected into the right motor cortex with 17.5 ng tetanus toxin in 500 nl high-titre lentivirus carrying NpHR tagged with EYFP under the CaMKIIa promoter. Control animals were injected with virus alone. An optical cannula and EEG electrodes were subsequently implanted above the injection site. Telemetric recordings were continuously recorded from the first postoperative day. For optogenetic studies, the freely moving animals were connected to a 561 nm laser via an optical fibre and stimulated on and off in 20 s intervals for sessions of 1000 s duration. At the end of the experiments, brains were stained for immunofluorescence.

Results: Halorhodopsin expression in the cortex was robust, targeted to principal neurons and persisted for over 2 months with no signs of cytotoxicity or apoptosis. In vivo experiments showed a reduction in high frequency activity on EEG during the 1000-second periods that the laser was pulsed on and off. No EEG changes were detected in control animals injected with a GFP virus alone.

Conclusion: Halorhodopsin is reliably expressed in rat motor cortex, without clinical signs of dysfunction in the live animal. Preliminary results indicate that optical inhibition of epileptic discharges represents an exciting new strategy to be pursued in models of epilepsy, and which may eventually translate into a viable treatment alternative for human disease.

p121

P-GLYCOPROTEIN REGULATION IN ISOLATED HUMAN BRAIN CAPILLARIES

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Purpose: Pharmacoresistance poses a multifactorial problem in epilepsy therapy. Increased expression of the efflux transporter P-glycoprotein at the blood–brain barrier is discussed as one factor limiting brain penetration of antiepileptic drugs (AEDs). The aim of this study was to determine signaling factors that regulate P-glycoprotein in human brain capillaries. We tested whether targeting of candidate signaling factors prevents glutamate-associated up-regulation of P-glycoprotein.

Methods: Transport activity of P-Glycoprotein was studied using the fluorescent P-glycoprotein substrate NBD-CSA. Brain capillaries were isolated from tissue dissected during epilepsy surgery. For preexperiments capillaries were isolated from pig brains. The luminal fluorescence intensity was analyzed by confocal microscopy.

Results: Human brain capillaries exposed to glutamate showed significantly higher luminal fluorescence compared to control. Inhibition of the glutamate-induced endothelial signaling pathway by celecoxib significantly reduced luminal NBD-CSA accumulation. Aiming to identify further targets for prevention of P-glycoprotein up-regulation we tested whether the signaling cascade can be blocked using an antagonist of the glycine-binding site of the NMDA receptor (L-701,324). In both, pig and human capillaries L-701,324 prevented the glutamate-induced up-regulation of P-glycoprotein activity.

Conclusion: The findings argue against any species differences in the signaling factors regulating P-glycoprotein in the epileptic brain. Moreover, the results suggest that targeting COX-2 or the NMDA receptor glycine-binding site might offer novel approaches to control P-glycoprotein expression, improve AED brain penetration and response in patients.

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p122

A COMMON GABAERGIC SIGNALING DEFECT IN HUMAN EPILEPTIC LESIONS

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Purpose: Postoperative tissues obtained from drug resistant focal epilepsies allow direct studies of networks and signaling underlying epileptic activities. We compared lesions responsible for pharmacoresistant seizures such as hippocampal sclerosis and lesions associated with pharmacosensitive epilepsies, like gliomas.

Method: Slices of mesial human temporal lobe tissue containing the subiculum and of neocortical tissues surrounding low grade gliomas were prepared after surgery. Field potentials and unit activity were recorded with extracellular electrodes. Intracellular recordings were performed with sharp electrodes.

Results: In vitro postoperative tissue of both types displays epileptic activity. They synchronized a 5–10/5 mm region in all three layers of the subiculum and were characterized by embedded multiple networks. In the peritumoral neocortex, interictal-like events were recorded in superficial layers and appeared to synchronize cortical columns but did not spread laterally more than 1 mm. Both activities were suppressed by both glutamatergic AMPA antagonists and by the blockade of $GABA_A$ receptors. Depolarizing responses to GABA were involved in both activities since interictal discharges were blocked by bumetanide (10 μM), a selective antagonist of the chloride loading cotransporter NKCC1. They were confirmed in intracellular records, which showed that more pyramidal cells were depolarized by GABA in the tumoral neocortex (60%) than in the subiculum of sclerotic temporal lobe (20%).

Conclusion: These data show that tissue from epileptic patients with distinct etiology, severity and disease duration share a defect in Cl-homeostasis and so in GABAergic signaling. This defect may be a promising therapeutic avenue.

p123
ROLE OF GABA-B RECEPTORS IN TERMINATION OF CORTICAL SEIZURES IN IMMATURE RATS

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Purpose: Recently we published data on marked prolongation of cortical epileptic afterdischarges (ADs) by GABA-B receptor antagonist CGP35348 in developing rats (Mareš, Epilepsy Res. 92: 125–133, 2010). To know if it is a general action of GABA-B receptor antagonists we studied the action of another antagonist – CGP46381 – on CxADs and postictal refractoriness.

Method: Rats 12, 18 and 25 days old with implanted electrodes were used. First series of experiments was formed by six suprathreshold stimulations with 10-min intervals. CGP46381 (3 or 10 mg/kg i.p.) was injected after the first ADs. Second series was focused on postictal refractoriness. Two stimulations were applied with 1-min interval, then CGP46381 was injected and 10 min later the double stimulation was repeated. Individual age and dose groups were formed by 8–10 animals.

Results: CGP46381 prolonged ADs in a dose-dependent manner in all age groups in the first experiment. The second experiment demonstrated that 1 min after ADs it is impossible to elicit another AD in 25-day-old rats. This refractoriness was partly suppressed by CGP46381 (short ADs were elicited). The 12-day-old group does not exhibit postictal refractoriness, administration of CGP46381 augmented all ADs in these rats.

Positive modulator of GABA-B receptors CGP7930 did not significantly influence postictal refractoriness in 25-day-old rats. It tended to suppress second ADs in 12-day-old animals.

Conclusion: GABA-B receptors are at least partially responsible for termination of cortical afterdischarges and for postictal refractoriness.

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p124
ALTERATIONS IN SHAKER-RELATED K^+ CHANNEL EXPRESSION CONTRIBUTE TO EPILEPTOGENESIS AND CHRONIC EPILEPSY

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Purpose: To determine whether Shaker-related K^+ channel expression is altered during epileptogenesis and chronic epilepsy.

Method: Seizures were induced in male Sprague Dawley rats using perforant path stimulation (PPS) or kainic acid (KA) administration. Expression of hippocampal $Kv_{1.1}$ and $Kv_{1.2}$ subunits was mapped using immunohistochemistry and Western blotting 1, 7 and >21 days post-status epilepticus (SE).

Procedures were carried out under the Animals (Scientific Procedures) Act 1986 and subject to local ethical approval.

Results: $Kv_{1.1}$ expression colocalized with the axonal protein tau. An initial increase in $Kv_{1.1}$ expression in CA subfields, though not in the dentate gyrus (DG) was observed in samples from PPS animals 1 day post SE. At 7 and 21 days, there was significantly reduced expression in all subfields. Loss of $Kv_{1.1}$ was associated with increased subunit phosphorylation. Reduced hippocampal $Kv_{1.1}$ expression was also observed >21 days after KA administration.

Interestingly, expression of leucine-rich, glioma inactivated 1 (LGI1) – a secreted glycoprotein involved in $Kv_{1.1}$ trafficking and which inhibits inactivation of Kv channels – was down-regulated in a similar time frame in the epileptic DG.

$Kv_{1.2}$ expression was unaltered.

Conclusion: Altered expression of hippocampal $Kv_{1.1}$ after experimental SE may contribute to epileptogenesis and the appearance of spontaneous seizures.

Loss of axonal $Kv_{1.1}$ may be due to a decrease in subunit trafficking, or reduced stability of the synaptic complex due to down-regulation of LGI1.

Therapeutic strategies aiming to increase expression or prevent down-regulation of $Kv_{1.1}$ may prove useful in treating temporal lobe epilepsy.

p125
EFFECTS OF VAGUS NERVE STIMULATION ON KINDLING EPILEPTOGENESIS AND BLOOD–BRAIN BARRIER INTEGRITY IN RATS WITH CORTICAL DYSPLASIA

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Purpose: Cortical dysplasia (CD) is one of the important causes of intractable epilepsy. Among all epilepsy patients the outcome of surgical

and medical treatment is worst in patients with CD. Vagus nerve stimulation (VNS) is an efficacious broad-spectrum add-on treatment for patients with medically or surgically refractory epilepsy. In this study, we investigated the effects of VNS on epileptogenesis and integrity of BBB in kindled rats with CD.

Method: Sprague Dawley rats were used and divided into three groups, VNS (-), VNS 0.5 and 1 mA. A VNS electrode was implanted around the left vagus nerve and stimulation was performed through the cuff electrode for 48 h (pulse duration: 0.5 ms, output current: 0.5 or 1 mA, at 30 Hz frequency). EEG electrodes were implanted bilaterally into the hippocampus of animals and EEG recordings were obtained. BBB permeability was evaluated by determining the extravasation of horseradish peroxidase (HRP) tracer.

Results: The delivery of VNS at 0.5 and 1 mA decreased the severity and intensity of seizures induced by pentylenetetrazole (PTZ) in kindled rats with CD and these findings were also confirmed by EEG tracing. VNS delivery at 0.5 and 1 mA attenuated the increased BBB permeability to HRP during PTZ induced seizures in kindled animals with CD.

Conclusion: The present results suggest that VNS exerts protective effects on BBB integrity and provides seizure control in the treatment of epilepsy associated with CD.

p126
THE ROLE OF ET_B RECEPTORS IN DEVELOPMENT OF ET-1 INDUCED SEIZURES IN IMMATURE RATS

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Purpose: In our previous studies we have shown that intrahippocampal injection of endothelin-1 (ET-1, a nonselective agonist of ET receprors) in doses 10–40 pmol induces acute seizures and hippocampal lesion in immature rats (Tsenov et al., Epilepsia 48 (Suppl.5):7–13, 2007). Mechanism of seizure initiation in this model is unknown and therefore we have studied the role of ET_B receptors in development of ET-1 induced seizures in immature rats.

Methods: Male Wistar 12-day-old rats (P12) were implanted with left and rigth hippocampal electrodes and left dorsal hippocampal cannula. Animals were then video/EEG-monitored for 2.5 h and monitoring was repeated 22 h later. After 30 min of monitoring ET-1 or selective ET_B receptor agonist [$Ala^{1,3,11,15}$]-Endothelin 1 (Ala-ET-1) in a dose of 10 pmol (in total volume 0.5 μl) were injected into the hippocampus. Parameters of electrographic seizures (number of seizures and their duration) as well as pattern of their behavioral correlates were evaluated.

Results: Seizures were observed in both groups; however incidence of seizures longer than 5 s was higher in ET-1 rats (ET-1 87.5%, Ala-ET-1 50%). Animals with Ala-ET-1 exhibited lower number of seizures especially during first part of monitoring and total seizure duration in these animals was shorter. Differences in behavioral correlates were not found.

Conclusions: Potential of Ala-ET-1 to induce seizures when applied intrahippocampaly indicates an important role of the ET_B receptors in the initiation of seizures in the ET-1 model.

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p127
EXPRESSION OF THE CALCIUM-SENSING RECEPTOR AND THE METABOTROPIC GLUTAMATE RECEPTOR 1 IN HIPPOCAMPUS OF PATIENTS WITH TEMPORAL LOBE EPILEPSY

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Purpose: The excessive release of glutamate, with a consequent increase in intracellular calcium influx, is one of the primary events in seizure-induced cell death in the hippocampus. This loss of neurons and synaptic reorganization in the hippocampal sclerosis (HS) cause altered expression of neurotransmitter receptors such as metabotropic glutamate receptor 1 (mGluR1). However, there are controversies about the mGluR1 expression in mesial temporal lobe epilepsy (MTLE). In animal models of epilepsy and in human patients it has been shown to either increase or decrease on the mGluR1 mRNA and protein expressions. The most accepted hypothesis is that the mGluR1 decreases in the hippocampus of patients with MTLE due to the selective hippocampal and cortical degeneration of neurons containing mGluR1. The calcium-sensing receptor (CASR), whose role in brain is not well defined, dawns as a relevant target in the MTLE study not only because of the importance of the calcium in cerebral events but also because of its structural similarity to the mGluR1.

Method: We used immunohistochemistry to analyze the protein expression of the mGluR1 and the CASR in eight patients and two post mortem control subjects. To confirm the protein expression results, we measured by RT-qPCR the mRNA expression using the same targets and two endogenous controls: β-actin (ACTB) and glyceraldehyde-3-phosphate dehydrogenase (GAPDH).

Results: When we compared the hippocampi from patients with the control ones, there was not just a significant reduction on the neuronal number, but also a significant reduction on positively stained neurons for both proteins in the patients. Moreover, the RT-qPCR results for the patients indicated a significant hypoexpression of the targets compared with ACTB and GAPDH.

Conclusion: Our results suggest that both mGluR1 and CASR are downregulated in MLTE patients. This particular modulation of the CASR expression in MTLE patients supports a relation between epilepsy and CASR. Nevertheless, the specific role of the CASR on changes in permeability to neuronal calcium in patients with epilepsy remains poorly elucidated.

Poster session: Basic sciences II
Monday, 29 August 2011

p128
IN VIVO IMAGING OF GLIA ACTIVATION IN ADULT RATS AS A BIOMARKER OF EPILEPTOGENESIS USING QUANTITATIVE MAGNETIC RESONANCE SPECTROSCOPY (MRS)

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Purpose: Long-term activation of glia occurs in brain during epileptogenesis which develops after various CNS injuries. Since glia contributes to the production of proinflammatory molecules that play a key role in the onset and recurrence of seizures, we hypothesized that the extent and/or the duration of glia activation in crucial brain areas may be a predicitive marker of epilepsy development. We set up a MRS study to determine if glia activation can be imaged and quantified in vivo during epileptogenesis, since this technique detects changes in myo-inositol (m-Ins) and lactate (*Lac*) levels reflecting astrocytes and microglia/macrophages activation, respectively.

Method: Status epilepticus (SE) was induced by pilocarpine in adult male rats. ^{1}H-MRS measurements were performed in the hippocampus

every 24 h for 7 day post-SE and in chronic epileptic rats, using a 7 Tesla Bruker Biospec. Spectra were processed and analyzed using jMrui and TARQUIN freeware softwares. MRS results were validated in separate groups of rats by immunohistochemistry using astrocytes and microglia markers.

Results: The quantitative analysis of MRS spectra showed a progressive increase in *m-Ins* levels from 24 h to 7 day post-SE vs control spectra: plateau levels were reached 7 day post-SE and were maintained in epileptic rats. *Lac* peak reached its maximum increase 48 h post-SE, progressively declining thereafter. These changes were confirmed by immunohistochemisty.

Conclusion: MRS is a valuable in vivo technique for quantification of glia activation during epileptogenesis. Studies are in progress to determine if MRS measurements predict the development of epilepsy in rats.

p129
ROLE OF MITOCHONDRIAL FUNCTION IN SEIZURE-INDUCED NEURONAL CELL DEATH

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Purpose: (1) To determine the sequence of events leading to cell death during prolonged seizure activity. (2) To test whether mitochondrial substrate supplementation can prevent neuronal death.

Method: We applied fluorescence imaging techniques to the low magnesium seizure model in rat glio-neuronal cocultures from neocortex to monitor calcium signals, mitochondrial membrane potential ($\Delta\psi$m) and ATP consumption.

Results: With low magnesium, we observed synchronized calcium signals in neurons that induced sustained depolarizations of $\Delta\psi$m ($p < 0.001$). $\Delta\psi$m depolarization was cyclosporine A (CsA) sensitive, suggesting mitochondrial permeability transition pore opening. ATP levels, measured as a change in $[Mg\ (2+)]_{(c)}$, decreased significantly during prolonged seizures and correlated with the oscillatory calcium signal frequency ($r = 0.513$; $p < 0.01$), indicating activity-dependent ATP consumption. Blocking mitochondrial complex I with rotenone (1 μM), complex V with oligomycin (0.2 μg/ml) or uncoupling mitochondrial oxidative phosphorylation under low magnesium conditions with FCCP (0.5 μM), accelerated activity-dependent ATP consumption leading to rapid cell collapse. FCCP induced acceleration was delayed by blocking mitochondrial depolarization with CsA ($p < 0.001$). Neuronal death was increased after 2 and 24 h of low magnesium, compared to control treatment ($p < 0.001$) and was reduced significantly by supplementing mitochondrial complex-1-substrate pyruvate.

Conclusion: (1) Calcium dynamics, mitochondrial membrane potential depolarization, ATP decreases and neuronal death are interrelated and occur sequentially. (2) Therapies that rescue mitochondrial function can prevent seizure-induced cell death and may thus prevent the neurological sequelae of prolonged seizures.

p130
LACK OF ASTROCYTE POTASSIUM CHANNEL KIR4.1 IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY

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Purpose: All neuronal activity is accompanied by elevation of extracellular potassium. High extracellular [K+] causes neuronal depolarization and propensity to epileptic seizures. The glial inwardly rectifying potassium channel Kir4.1 is responsible for clearance of K+ from the extracellular space and thus prevents hyperexcitability. Malfunctioning or lacking Kir4.1 is assumed to be associated with epilepsy.

Method: To investigate the distribution of Kir4.1 in the epileptic/non-epileptic human brain, immunohistochemistry was used in hippocampus specimens from patients with refractory mesial temporal lobe epilepsy with hippocampal sclerosis (referred as MTLE, n = 8) and compared with TLE without hippocampal sclerosis (referred as non-MTLE, n = 8) and neurologically normal autopsy subjects (n = 5). Immunohistochemistry was also conducted in molecules presumed to be involved in astrocyte membrane anchoring of Kir4.1 as dystrophin, alpha-1-syntrophin, and beta dystroglycan, in the same patient/autopsy material.

Results: Kir4.1 immunoreactivity was observed around blood vessels and in astrocyte processes and cell bodies throughout the entire hippocampus formation. Kir4.1 blood vessel immunoreactivity was consistent with the anatomical distribution of the hippocampal vasculature, while Kir4.1 astrocyte immunoreactivity predominantly was observed in the hilus and molecular layer of the dentate and in stratum lacunosum-moleculare and stratum oriens of the hippocampus. There was no difference in Kir4.1 immunoreactivity between specimens classified as non-MTLE and those derived from autopsy. Dystrophin and alpha-1-syntrophin immunohistochemistry showed results comparable to those for Kir4.1 staining, with lack of vessel and astrocyte staining in the sclerotic areas of the MTLE hippocampi. In contrast beta dystroglycan staining did not show any differences between MTLE and non-MTLE or autopsy, or any interregional differences in MTLE hippocampi.

Conclusion: Our findings underline the theory that loss of Kir4.1 contributes to epileptogenesis in MTLE. We hypothesize that deficient Kir4.1 in MTLE may be a consequence of disrupted membrane integrity due to altered anchoring via dystrophin associated glycoprotein complex.

p131
INCREASED EXPRESSION OF TUMOR NECROSIS FACTOR-ALPHA IN THE RAT HIPPOCAMPUS AFTER ACUTE HOMOCYSTEINE ADMINISTRATION

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Purpose: To evaluate the effect of acute homocysteine administration on inflammatory cytokine TNF-α expression and neuronal apoptosis in the rat hippocampus, and to investigate the effects of vitamin C treatment on homocysteine-induced inflammation and neuronal death.

Method: Three-week-old Sprague-Dawley male rats were used. Rats in the control group had saline solution injected into their abdominal cavities for 1 week; rats in the second group had one injection of homocysteine (11 mmol/kg) into their abdominal cavity after administration of saline solution for a week. Rats in the third group were injected once with homocysteine after administration of vitamin C (100 mg/kg) for a week. The hippocampus was stained with an anti-TNF-α antibody and apoptosis was evaluated using the TUNEL staining method.

Results: The homocysteine-injected rats had strong expression of TNF-α in every region of the hippocampus. The expression of TNF-α in the CA1 region of the hippocampus was reduced significantly by administration of vitamin C. Acute homocysteine administration did not cause apoptosis in the hippocampus.

Conclusion: The contribution of elevated homocysteine levels to inflammatory reactions may be mediated by the proinflammatory

cytokine TNF-α, and vitamin C has some protective effect on the inflammatory reaction in the CA1 region of the hippocampus.

p132
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. Twelve hours–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. 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.

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

p133
INHIBITORY EFFECTS OF MINOZAC ON PROINFLAMMATORY CYTOKINES AND CHEMOKINES IMPROVE HIPPOCAMPAL NEURONAL INJURY AND EPILEPTIC BEHAVIOR IN PILOCARPINE INDUCED MICE MODEL

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Purpose: An intriguing suggestion has been put forward that seizures may be facilitated and triggered by inflammatory signaling in the brain, and that proinflammatory cytokines as well as chemokines may play a critical role in epileptogenesis. Minozac, a small molecule can attenuate the enhanced cytokines responses, decrease the susceptibility of seizure in a neonatal rat model of kainic acid (KA)-induced epilepsy. Here, we investigated the effects of minozac on cytokines and chemokine responses, seizure behavior and hippocampal neuronal injury in a typical epileptic mice model for temporal lobe epilepsy (TLE).

Method: Pilocarpine-induced seizure in mice was used as a TLE model. Minozac (5 mg/kg) was intraperitoneally (i.p.) injected to mice 30 min before administration of pilocarpine (300 mg/kg, i.p.). Latency proir to the first episode of limbic seizures and status epilepticus (SE), the mean seizure severity scores and mortality were quantatively analyzed. The levels of proinflammatory cytokines (IL-1β, TNFα), chemokine (CCL2) and neuronal injury in the hippocampus of epileptic mice were measured 12 h after administration of pilocarpine.

Results: Administration of minozac attenuated the enhanced cytokine (IL-1β, TNFα) and chemokine (CCL2) responses in the hippocampus of epileptic mice. Treatment of minozac significantly reduced hippocampal neuronal injury, delayed the onset of the first episode of limbic seizures and the occurrence of SE, alleviated the severity of seizures, but did not reduce the mortality of epileptic mice induced by pilocarpine.

Conclusion: The present study suggests that minozac can modulate seizure generation and propagation, reduce hippocampal neuronal injury, probably due to attenuation of acute increase in proinflammatory cytokines and chemokine responses in the hippocampus of epileptic mice induced by pilocarpine.

p134
MICROGLIA IN EPILEPSY ARE ACTIVATED IN A REGION SPECIFIC MANNER: A MORPHOLOGIC ANALYSIS IN THE EPILEPTIC RAT HIPPOCAMPUS

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Purpose: Microglia cells are resident macrophages in the central nervous system. In addition to serving brain's innate immunity, microglia activation coincides with neuronal excitatory activity and has been recognized as one or the early changes during epileptogenesis. Despite the fact that the definition of microglia activation relies mostly on morphological observations, the correlation between morphology and function is still blurry, partially due to insufficient morphometric quantification. This study presents a precise morphologic description of microglia cells in the chronic state of the pilocarpine model of temporal lobe epilepsy in Wistar rats.

Method: Microglia cell-reconstructions were compared for somatic and process-tree properties. The soma size and shape index (size to area ratio) were used for the description of somata. The quantification of length and complexity of microglia branches was based on Sholl analysis.

Results: The shape index of somata in the epileptic rat hippocampus was less variable in comparison to controls, which indicated a somatic shape preference upon activation. The somatic size of microglia cells in epileptic rats was increased exclusively in the CA1 region. Considering the changes in microglia cell processes, reduction of process ramification occurred in a domain-confined manner between 20 and 30 μm from the centre of the soma. No changes were found below and beyond this radial distance.

Conclusion: Microglia activation in epilepsy is subregion-specific and implies changes in somatic shape, size and ramification pattern of their process trees. A correlation between microglia activation morphology and degree of neuronal dysfunction is suggested.

p135
INTRINSIC BRAIN INFLAMMATION AND ENHANCED SEIZURE SUSCEPTIBILITY IN A TRANSGENIC MOUSE MODEL OF INHERITED CREUTZFELDT–JAKOB DISEASE

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Purpose: Transmissible spongiform encephalopathies (TSEs) are neurodegenerative disorders caused by a misfolded form of the cellular prion protein (PrP^C). Creutzfeldt-Jakob disease (CJD) is the most common human TSE, characterized by PrP deposition, gliosis, cell loss and by global cortical dementia, myoclonus and an increased incidence of epilepsy. Tg (CJD) mice express the mouse homolog of the D178N/V129 PrP^C mutation and are associated with a familial form of CJD. We examined whether *presymptomatic* Tg (CJD) and mice *lacking* PrP^C (PrPKO) show proinflammatory changes in the brain, and we tested their seizure susceptibility as compared to mice expressing the Wild Type form of PrP^C (WT).

Method: IL-1beta and microglia activation were investigated in the hippocampus by immunohistochemistry at presymptomatic stages in 60, 120, 240 days old WT, Tg (CJD) and in 60 day-old PrPKO mice. Seizures were induced in mice by intrahippocampal injection of kainic acid (KA) and were quantified by EEG analysis.

Results: Immunohistochemical analysis of presymptomatic Tg (CJD) mice show hippocampal activation of microglia and increased expression of IL-1beta. EEG analysis of 60 and 240 days old Tg (CJD) mice after intrahippocampal KA injection showed a two-fold increase in number and duration of EEG seizures vs PrPKO and WT mice. Seizures were not different between PrPKO and WT mice.

Conclusion: The intrinsic forebrain activation of proinflammatory processes possibly due to deposition of misfolded protein may alter neuronal excitability and decrease seizure threshold in presymptomatic Tg (CJD) mice, highlighting a mechanism whereby seizures can occur in CJD patients.

p136
INCREASE OF ALBUMIN IN THE RAT HIPPOCAMPUS ENHANCES INTERICTAL SPIKING BUT NOT ICTAL EVENTS DURING ACUTE SEIZURES

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Purpose: Blood–brain barrier (BBB) breakdown occurs during seizures, and artificial BBB opening increases seizure frequency in epileptic rats. Prominent BBB breakdown occurs 24 h after status epilepticus (SE) and lasts for ~2 h after spontaneous seizures. Brain albumin extravasation may contribute to neuronal hyperxcitability by altering K^+ and glutamate buffering capacity of astrocytes.

To provide direct experimental evidence for a role of extravasated serum albumin in seizures: (1) we quantified the amount of serum albumin in the brain parenchyma and CSF during seizures; (2) we reproduced this brain concentration by intraventricular albumin injection in naïve rats, then we tested their seizure susceptibility.

Method: Albumin concentration was measured in the adult rat hippocampus 24 h after SE by Western blot, its brain distribution was studied by immunohistochemistry. Seizures were induced in rats by intrahippocampal injection of a low dose of kainate and quantified by EEG analysis.

Results: The concentration of albumin into the hippocampus 24 h post-SE was 0.8 ± 0.2 μM (n = 7). Intraventricular administration of albumin (500 mg/4 ml) in naive rats accumulates predominantly in the hippocampus resulting in a local concentration of 1.1 ± 0.5 μM (n = 4) after 2 h. When kainate was intrahippocampally applied to albumin-injected rats the onset, number and duration of seizures was not modified but the number of interictal spikes/3 h recording was significantly increased by two-fold on average ($p < 0.05$).

Conclusion: Short-term hippocampal exposure to albumin levels similar to those reached after prominent BBB breakdown did not modify ictal activity while increasing interictal spiking. Long-term tissue exposure to albumin may be required to affect ictal events.

p137
ANALYSIS OF HIPPOCAMPAL CELL PROLIFERATION AND NEURONAL PROGENITOR CELLS IN A MODEL OF VIRUS ENCEPHALITIS ASSOCIATED EPILEPSY

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Purpose: Alterations in hippocampal neurogenesis have been suggested as a factor contributing to epileptogenesis, disease progression, and comorbidities. Here, we analyzed respective cellular alterations in naturally occurring canine distemper virus encephalitis, which serves as an excellent animal model for symptomatic epilepsies associated with virus infection.

Method: We compared postmortem tissue from 76 nonlaboratory dogs of different ages (1 month–18 years) with epilepsy of nonviral etiology, with CDV infection with and without seizures, and dogs without central nervous system diseases using immunhistochemistry methods.

Results: The majority of animals with epilepsy of nonviral etiology and with infection exhibited neuronal progenitor numbers below the age average in controls. Virus infection with and without seizures significantly decreased the mean number of neuronal progenitor cells by 43% and 76% respectively compared to age-matched controls. Ki-67 labeling demonstrated that hippocampal cell proliferation was neither affected by virus infection nor by nonviral epilepsy. A high interindividual variance in the number of lectin-reactive microglial cells was evident in dogs with CDV infection.

Conclusion: In conclusion, virus encephalitis with and without seizures can exert detrimental effects on hippocampal neurogenesis with a significant reduction in neuronal progenitor cells. In animals with CDV-associated seizures an increased variance in the number of proliferating cells and progenitor cells indicated that the impact of seizure activity might vary depending on disease parameters such as seizure density.

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Poster session: Basic sciences III
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p138
ABNORMAL MATURATION OF NONDYSMORPHIC NEURONS IN FOCAL CORTICAL DYSPLASIA: IMMUNOHISTOCHEMICAL CONSIDERATIONS

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Purpose: Dysmorphic neurons and balloon cells in focal cortical dysplasia (FCD) reportedly show immaturity and abnormal differentiation with neuronal and glial components. Although nondysmorphic neurons in FCD are major constituent elements, their biological characteristics have never been identified. The aim of this study was to investigate maturation of nondysmorphic neurons with the focus on neuronal developmental lineage.

Method: Eighteen FCD surgical specimens and controls were examined immunohistochemically using the antibodies for nestin, mammalian achaete-scute complex homolog 1 (Mash1), prospero-related homeobox 1 (Prox1), neuron-specific beta-III tubulin (Tuj1) and microtubule-

associated protein 2 (MAP2) of neuronal lineage, glutamic acid decarboxylase (GAD), calretinin (CR) and calbindin (CB) of interneuron markers, and glial fibrillary-acidic protein (GFAP) of glial cell marker. Additionally, we performed fluorescent-double staining with these markers, and semiquantitative analysis.

Results: Nondysmorphic neurons in FCD had both mature and immature components, without interneuron components. Nondysmorphic neurons in FCD showed abnormal maturation with the combined expression of MAP2 and Mash1/Prox1. Prox1-containing cell distribution in the deep layer was different from that of Mash1-containing cells in the superficial area. The MAP2-containing cell concentration decreased in the order of type I-A, I-B, II-A and II-B, but the Tuj1-containing cell concentration increased.

Conclusion: These findings may reflect differences in neuronal function and expression timing in developmental stages. From the standpoint of molecular expression, abnormal maturation of nondysmorphic neurons may initiate synaptic dysfunction, resulting in intractable seizures of FCD.

p139
NEW MODEL OF REFRACTORY CONVULSIVE STATUS EPILEPTICUS INDUCED WITH ORPHENADRINE IN RATS

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Purpose: The current study was aimed to evaluate a new model of secondarily generalized status epilepticus (SE) induced with orphenadrine (ORPH) in rats, together with a screen of different new-generation antiepileptic drugs (AEDs) on their potency to suppress it.

Method: ORPH was administered in doses of 50–80 mg/kg, i.p in male Wistar rats (n = 8–20 animals/group). The latency to first seizure, the number of seizure episodes and the duration of overt SE as well as the incidence of deaths was scored with simultaneous EEG recordings. Subsequently, the effects of new-generation and selected experimental AEDs on ORPH-evoked (80 mg/kg) seizure incidence were studied.

Results: ORPH dose-dependently induced seizures in increasing number of animals, reaching 100% at a dose of 80 mg/kg, associated with low mortality and no drug-related neurotoxicity as described recently (Rejdak et al., Brain Res Bull, 2011). Among conventional AEDs: valproate ($p < 0.001$), diazepam ($p < 0.01$), and phenobarbital ($p < 0.001$) dose-dependently suppressed seizure activity. Carbamazepine, ethosuximide, felbamate, levetiracetam, topiramate, lamotrigine and progabide did not affect the seizure incidence. Among the experimental drugs, only dizocilpine dose-dependently affected the occurrence of the SE ($p < 0.001$) while scopolamine and mecamylamine were not effective.

Conclusion: All above unique characteristics make the new model, a useful, easy to perform experimental tool to study the pathophysiology of refractory SE as well as the effects of new AEDs.

p140
FEBRILE SEIZURE AS A LONG-TERM PRECONDITIONING CONTEXT WHICH MAY REGULATE EPILEPTOGENESIS IN DOUBLECORTIN KO MICE

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Purpose: According to the ''dual pathology''concept, a relationship between cortical dysplasia and the occurrence of febrile seizures has been suggested to promote the development of mesial temporal lobe epilepsy. We addressed this hypothesis by examining the consequences of Hyperthermic Seizures (HS) applied at P10 on the focal epilepsy developed by doublecortin knock-out mice (Dcx KO).

Method: C57Bl6 DcxKO and wild type littermates (WT) were exposed at P10 to either 40°C (HS) or 20°C (control) temperatures for 30 min. At 2 months, mice were implanted with bipolar hippocampal electrodes and recorded for up to 20 h over 2 months. Hippocampal upregulation of neuropeptide Y (NPY) was monitored between groups.

Results: In WT/controls, no seizures were recorded (n = 7) whereas one hippocampal seizure with cortical spread was observed in the WT/HS group (n = 8). In the DcxKO/control group, 60% of the mice (n = 5) developed seizures with a total of 15 seizures (11 tonic–clonic). In the DcxKO/HS group (n = 8) only 25% of the animals exhibited seizures, with a total of two seizures. No ectopic expression of NPY was observed in WT mice, contrary to all DcxKO mice with seizures, with or without HS.

Conclusion: The rare occurrence of spontaneous seizures observed in adult WT/HS mice is in agreement with previous reports in rats. The lower rate of seizures observed here in DcxKO/HS mice, as compared to DcxKO/controls, suggests that HS could represent a long term preconditioning effect protecting against epileptogenesis.

p141
INHIBITORY EFFECTS OF FOCAL BRAIN COOLING FOR MOTOR CORTICAL SEIZURES IN CATS AND NONHUMAN PRIMATES

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Purpose: Focal brain cooling is expected to be tested in clinical trials of status epilepticus patients. To provide evidence of the safety and effectiveness of such therapeutic intervention, we investigated the placement of a cooling device over the motor cortex of animals, and investigated whether focal brain cooling can prevent and/or terminate focal neocortical seizures without any significant impact on behavior.

Method: Two cats (n = 2) and a macaque monkey (n = 1) were chronically implanted with an epidural focal brain cooling device over the somatosensory and motor cortex, with adjacent EEG electrodes, a CBF probe, and a microinjection tube. Via the tube, Penicillin G (PG) was delivered for induction of local seizures (1000 and 1500 I.U., respectively). Recordings were performed in both awake and anesthetized conditions. In addition, the ability of the monkey to extract small pieces of food from narrow wells of a Klüver board was analyzed. All of the experiments were performed according to the Guidelines for Animal Experimentation of the Yamaguchi University School of Medicine.

Results: The cats and monkey exhibited spontaneous seizures with repetitive epileptiform discharges after the administration of PG, and these were observed to decrease after 15°C cooling. It was also found that

the CBF decreased temperature-dependently. Hand grasping movements by the monkey were appropriately performed in an attempt to grasp morsels of food.

Conclusion: The results suggest that epidural focal brain cooling represents a safe and effective potential treatment modality for status epilepticus.

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p142
ASSESSMENT OF THE ROLE OF POLYUNSATURATED FATTY ACIDS IN THE UNDERLYING MECHANISMS OF THE KETOGENIC DIET

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Purpose: The ketogenic diet (KD) is a high-fat and low-carbohydrate diet used as a treatment of intractable epilepsy. We study if polyunstaturated fatty acids may support the efficacy of the KD.

Method: We used three groups: a control group, a ketogenic diet group (KD) and a ketogenic diet group with mainly saturated fatty acids (KD-Sat group). We assess the anticonvulsant effect using intraveinous pentylentetrazol (PTZ) thresholds and we also assess the ketone bodies pathways.

Results: As previously observed, there is an increased PTZ thresholds (th.) in the KD group (48.2 ± 2.6 mg/kg myoclonic th.; 52.7 ± 2.3 mg/kg seizure th.) compared to the control group (38.3 ± 2.7 mg/kg myoclonic th.; 43 ± 2.7 g/kg seizure th. $p < 0.05$). We did not observe any difference between the KD group compared to the KD-Sat group (48.8 ± 1.4 mg/kg myoclonic th.; 52.6 ± 1.7 mg/kg seizure th.). The levels of β-OH butyrate and acetoacetate were increased in both KD and KD-Sat groups compared to the control group. We did not find any linear correlation between the ketone bodies' level and the PTZ threshold. The fatty acid serum profiles among the groups reflected the level of the intakes. Using quantitative RT-PCR in the brain and in the liver, we did not find any upregulation of PPARα and PPARγ genes.

Conclusion: Our data suggest that PUFA are not an essential component supporting the anticonvulsant efficacy of the KD. We are currently investigating the ketone bodies and the fatty acids pathways. The quantity of fat rather than the quality of fatty acids may be involved in the anticonvulsant properties of KD.

p143
A KINDLING MODEL OF TEMPORAL LOBE EPILEPSY IN RHESUS MACAQUE INDUCED BY *CORIARIA* LACTONE

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Purpose: To observe the behavior and electroencephalogram of rhesus macaque model of kindling temporal lobe epilepsy induced by Coriaria Lactone (CL) and evaluate the effect of classical antiepileptic drug carbamazepine (CBZ) and valproate (VPA).

Method: Six rhesus macaques were divided into two groups: four in test group and two in control group. Test group received CL injection at subthreshold dosages 0.4 ml/kg at the interval of 72 h repetitively, and the control group received normal saline (NS) injection. The maximal human adult dosage of CBZ and VPA were administered as monotherapy to test groups of kindled rhesus for 1 month respectively. Then the behavioral changes of monkeys, including seizure latency, manifestation, severity, duration were observed and the electroencephalogram (EEG) of monkeys were recorded.

Results: Three monkeys in test group were kindled and the clinical manifestation is from complex partial seizures or general tonic–clonic seizure following complex partial seizures. The manifestation including motionless, chawing, clonus of one limb and suddenly occurred general tonic-clonic seizure. Electrocorticogram (ECoG) including hippocampal (EHG) monitoring revealed the temporal lobe origins of epileptiform potentials, which were consistent with the behavioral changes observed. The antiepileptic drug CBZ and VPA lacked a satisfactory seizure control result. Seizure was not observed in control group.

Conclusion: The study provided an ideal TLE (temporal lobe epilepsy) kindling model in rhesus induced by CL. This model resembles partial seizures evolving into secondary generalization, as observed in human temporal lobe epilepsy and is refractory to classical antiepileptic drug CBZ and VPA. This method is easy to operate, without direct hurt to brain. This model might be used in further investigations of the mechanisms involved in drug resistance in TEL and for developing new antiepileptic drugs.

p144
MYO-INOSITOL AND KAINIC ACID INDUCED CELL LOSS IN RAT HIPPOCAMPUS

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Purpose: Epilepsy treatment has significant limitations; therefore the development of new antiepileptic medications is still urgent problem.

According previous data, Myo-inositol (MI), important osmolyte and precursor for inositol lipid synthesis, prevents some biochemical and behavioral alterations provoked by epileptic activity. In the present study we elucidate if MI would prevent the hippocampal cell death provoked by kainic acid (KA); in rats treated with KA or MI+KA we studied: (1) spatial distribution of cell loss in different areas of hippocampus, (2) ultrastructure of CA1. Age-matched control rats received comparable volume of 0, 9% normal saline.

Method: Ninety-day-old male Wistar rats were treated intraperitoneally with KA (10 mg/kg); for subsequent study the animals that developed seizures of grade 5/6 (Racine) during 60 min were used. Other rats were treated, first, with MI (20 mg/kg, i.p.) and after 30 min – with KA. Cell loss was investigated on Thionin-stained sections prepared from animals 2, 14 and 30 day after treatments; statistical analysis was performed using two-way ANOVA. For electron microscopic analysis brains were analyzed 14 day after treatments.

Results: After KA injection the most prominent cell loss (>70%) was observed at 14 and 30 day after KA treatment in pyramidal cell layer of CA1, lesser in oriental and radial layers of CA3. After MI pretreatment the cells were preserved in all three layers of CA1 and CA3 but mostly in pyramidal cell layer of CA 1 – the most damaged after KA treatment. Electron-microscopic investigation confirms protective effect of MI: after KA treatment the significant alterations in some neurons and presynaptic terminals were observed, after MI + KA alterations were predominantly superficial and rare.

Conclusion: Our results indicate that pretreatment with MI attenuate not only biochemical and behavioral changes provoked by KA, but also hippocampal cell loss – the most overt form of seizure-induced bran injury.

p145
HIPPOCAMPAL NEUROGENESIS INCREASES AFTER SEIZURES IN MICE TREATED WITH BETA-HYDROXYBUTYRATE

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Purpose: We recently reported that ketogenic diet (KD) enhanced hippocampal dentate granule cell neurogenesis after seizures in mice. KD

remains a therapy in search of explanation although it is an established treatment for patients with intractable seizures. It was originally devised to mimic the biochemical changes seen upon fasting, specifically the formation of ketone bodies: β-hydroxybutyrate (BHB), acetoactate, and acetone. Recent data suggest that the anticonvulsant efficacy of KD may be due in part to direct actions of ketone bodies. This study was designed to investigate effects of BHB on neurogenesis after pilocarpine-induced seizures in mice.

Method: Mice were divided into two groups. Experimental mice (n = 5) were injected intraperitoneally with BHB (20 mmol/kg), while control mice (n = 6) with normal saline. Fifteen minutes later, seizures were induced by pilocarpine (300 mg/kg. i.p.) in both groups. Then, bromodeoxyuridine (BrdU, 50 mg/kg) was subsequently administered once a day for six consecutive days, starting at 24 h after pilocarpine injection. Thereafter, BrdU-positive cells in the hippocampus were counted.

Results: Blood BHB levels in the experimental group were significantly higher than in the control group. In BHB-treated mice, BrdU-positive cells of the hippocampal dentate granule cell layer increased significantly compared to control mice (377.57 ± 150.40 vs. 230.55 ± 59.50, $p < 0.001$).

Conclusion: In this study, we found a significantly increased proliferation rate of neuronal progenitor cells after seizures in BHB-treated mice. These results suggest that BHB may enhance hippocampal dentate granule cell neurogenesis after seizures.

p146
BEHAVIORAL, EEG AND NEUROPATHOLOGICAL FEATURES OF AN EPILEPSY FOCAL MODEL INDUCED BY CONTINUOUS LOW INTENSITY ELECTRICAL PERFORANT PATH STIMULATION IN WISTAR RATS

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Purpose: Temporal lobe epilepsy (TLE) is characterized by complex partial seizures with a focus in the temporal lobe, associated with hippocampal sclerosis (HS). Most available animal models of TLE are developed after the induction of a generalized status epilepticus episode, which induces widespread neuron loss and spontaneous recurrent seizures (SRS) with multifocal onsets. In this study, we describe electrographic, behavioral and neuropathological features of an epilepsy model induced by perforant path (PP) continuous electrical stimulation.

Method: Freely moving awake male Wistar rats received 20 Hz 10 s trains PP stimulation, during 8 h. The animal response was analyzed according to the parameters: presence of afterdischarges (ADs) and behavioral changes during stimulation, presence of SRS over 2 months, cell density in hippocampal subfields in NeuN immunohistochemistry-stained sections, EEG oscillatory patterns and ADs profile, frequency and duration.

Results: PP stimulation elicited intermittent ADs, associated with behavioral changes and absence of generalized seizures. Animals presented electroencephalographic, behavioral and histological features typical of TLE, as evidenced by: (1) occurrence of ADs associated with behavioral changes, (2) increased slow oscillation (3) preictal eletrographic signatures (fast ripples, periodic epileptiform discharges, rhythmic sharp waves, rhythmic activities spike-and-wave and polyspikes discharges), (4) neuronal loss predominantly in hippocampal CA1 and hilus. Nearly 50% of animals presented SRS within 2 months after stimulation.

Conclusion: The proposed stimulation induces electrographic changes that are highly associated to focal epilepsy and a pattern of cell loss closely resembling HS. The present model may contribute to the understanding of the pathophysiology of TLE and to further preclinical pharmacological studies.

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SCREENING OF KEY PROTEINS INVOLVED IN REFRACTORY EPILEPSY USING THE KINDLING TEMPORAL LOBE EPILEPSY MODEL OF RHESUS INDUCED BY CORIARIA LACTONE

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Purpose: To confirm a new primate animal model of pharmacoresistant temporal lobe epilepsy (TLE) and to explore the mechanisms that might be involved in refractory epilepsy.

Method: Behavioral observation and EEG were performed during establishment of the kindling model of the epilepsy in rhesus. The ultrastructure was examined with electron microscopy. Several drug resistant related proteins were detected by immunohistochemistry. By using iTRAQ method, hippocampus tissues of rhesus were labeled and followed by peptides by LC/MS/MS.

Results: For the first time, the kindling model of temporal lobe epilepsy in rhesus was established by repeated intramuscular injection of Coriaria Lactone (CL). The model showed repeatable behavioral manifestations, and EEG, which are very similar to the TLE in human patient. Mitochondrial ultrastructural damage in neuron and astrocyte, varying from swelling to disruption of membrane integrity, was observed in the hippocampus including CA1 or CA3 subfield in the rhesus model. Both MRP-1 and GST-Pi increased significantly in brain tissue of the epilepsy model, comparing with normal control. A total of 755 proteins were identified in the hippocampus of rhesus, with 47 differentially expressed proteins.

Conclusion: (1) The rhesus kindling model induced by CL has great potential in the pathogenesis study of pharmacoresistant epilepsy.

(2) With state-of-the-art proteomics, our experiments have identified many more novel proteins that have not yet been associated with but probably involved in pathogenesis of pharmacoresistant epilepsy. If validated, these proteins may reveal new mechanisms for pathogenesis of epilepsy or provide new therapeutic targets for therapy of epilepsy.

p148
EFFECT OF SEIZURES DURING BRAIN DEVELOPMENT ON PREPULSE INHIBITION OF THE ACOUSTIC STARTLE REFLEX IN A RAT MODEL OF SCHIZOPHRENIA

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Purpose: Perinatal events may be related to the development of schizophrenia. Individuals with epilepsy are at increased risk of having psychotic symptoms that resemble those of schizophrenia. We investigated the effects of epileptic seizures during a postnatal vulnerable period of brain development, on Prepulse inhibition (PPI) and locomotor activity in rodents tested on postpuberal phase.

Methods: Male Wistar rats were randomly divided into three groups: control (CTRL, n = 8), maternal separation (MS, n = 8) and pilocarpine (PILO, n = 6). For induction of status epilepticus, the animals were isolated from their dams and received intraperitoneal injections of pilocarpine hydrochloride 2% (380 mg/kg, Pilo, Merck) in postnatal days (PD) 7, 8 and 9 and were observed for 5 h. CTRL group received saline solution 0.9%. MS group was left undisturbed with their dam in the experimental room for the same period of time. This group was used to assess

the effects associated with maternal separation. After puberty (56 days), each animal was tested for PPI and locomotor activity (open field).

Results: The two-way ANOVA revealed statically significant [$F_{2,65} = 6.42$, $p < 0.003$] differences among groups. No difference was found between the prepulse intensities [$F_{2,65} = 0.06$, $p = 0.93$] and there was no correlation between treatment and prepulse intensity [$F_{4,65} = 0.41$, $p = 0.79$]. Rats of the PILO group showed impaired PPI (Post hoc Tukey test, $p = 0.003$). There was no difference in the mean amplitude of startle reflex among groups [$F_{2,21} = 0.76$, $p = 0.47$]. Rats of the PILO group showed a significant decrease in the number of crossings in the open field test [$F_{2,21} = 4.01$; $p = 0.03$].

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LOCAL APPLICATION OF VALPROATE ENHANCES SURVIVAL IN THE NOVEL TETANUS TOXIN/COBALT CHLORIDE RAT MODEL OF NEOCORTICAL EPILEPSY

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Purpose: In focal neocortical epilepsies not satisfactorily responsive to systemic antiepileptic drug therapy, local application of antiepileptic agents directly onto the individually identified epileptic focus may enhance treatment efficacy and tolerability. We aimed to investigate the effects of focally applied valproate (VPA) in a newly developed rat model of neocortical epilepsy induced by tetanus toxin (TeT) and cobalt chloride ($CoCl_2$).

Method: VPA (n = 5) or sodium chloride (NaCl) (n = 5) polycaprolactone (PCL) implants constructed by 3D-bioplotting were applied on the right rat motor cortex pretreated with triple injection of 75 ng TeT and 15 mg $CoCl_2$. Intermittent longitudinal video-EEG monitoring was performed with intra- and extrafocal intracortical depth electrodes to assess interictal and ictal epileptic activity and seizure semiology.

Results: All rats randomized to the NaCl PCL group died within 1 week after surgery. In contrast, the rats treated with local VPA PCL survived significantly longer ($p < 0.01$). Witnessed deaths occurred in the context of seizures. At least 75% of the TeT/$CoCl_2$ model rats surviving the first postoperative day developed neocortical epilepsy with recurrent spontaneous clonic, tonic or secondary generalized tonic–clonic seizures. Statistical comparison of the two treatment groups with respect to frequency of interictal epileptic activity and seizures failed, as only few rats treated with NaCl PCL could be studied by long-term video-EEG.

Conclusion: The novel TeT/$CoCl_2$ model of neocortical epilepsy appears to be a valid tool for the investigation of local epilepsy therapy strategies. In this vehicle-controlled pilot study, local application of VPA significantly enhanced survival in rats, most probably by focal suppression of epileptic activity or by counteracting epileptogenesis.

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EFFECT OF 7-NITROINDAZOLE A NEURONAL NITRIC OXIDE SYNTHASE INHIBITOR ON CORTICAL EPILEPTIC SEIZURES IN RATS

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Purpose: An inhibitor of neuronal nitric oxide synthase (nNOS) 7-nitroindazole (7-NI) was found to have an anticonvulsive effect on low-Mg seizures in vitro when applied in combination with potent NO scavenger cPTIO. Our aim was to elucidate an effect of nNOS inhibition on cortical myoclonic seizures in freely moving adult rats.

Method: Adult albino rats (250–350 g) were anesthetized with isoflurane and 2 stimulation electrodes were implanted over right sensorimotor cortex. Recording epidural silver EEG electrodes were implanted over contralateral and ipsilateral cortices. After 1 week recovery biphasic constant current suprathreshold stimulus (2–5 mA, 8 Hz, 15 s) was applied to induce cortical myoclonic seizures. The duration and total number of spike and wave afterdischarges (AD) were assessed offline from EEG recordings (Pentusa, TDT, USA). Ten minutes after initial AD stimulation 7-nitroindazole (25 mg/kg in DMSO) or DMSO was injected intraperitoneally. Thirty and 180 min after the application the stimulation of AD was repeated to assess effect of nNOS inhibition on cortical myoclonic seizures.

Results: The 7-NI significantly increased both duration (30 min to 190% and 180 min to 220% of initial values) and number (30 min to 160% and 180 min to 215% of initial values) of ADs in both time intervals when compared to DMSO or Saline group.

Conclusion: The present findings suggest that inhibition of nNOS in vivo has in contrast to in vitro conditions a proconvulsive effect. The project was supported by grant from Czech Science Foundation no.P303/010/0999.

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EFFECT OF TEMPOL ON BRAIN SUPEROXIDE ANION PRODUCTION AND NEURONAL INJURY ASSOCIATED WITH SEIZURES IN IMMATURE RATS

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Purpose: To examine generation of superoxide anion in brain of immature rats during seizures and to evaluate potential protective effect of SOD mimetic Tempol.

Method: Seizures (having a character of status epilepticus [SE]) were induced by bilateral icv infusion of either DL-homocysteic acid (DL-HCA, 600 nmol/side) or 4-aminopyridine (4-AP, 100 nmol/side) in 12-day-old male Wistar rats with implanted cannulae. Control animals received the corresponding volumes of vehicle. Dihydroethidium (Het) method was employed for detection of superoxide production in brain in situ. Het was given i.p. immediately before infusion of convulsant substances (final concentration 10 mg/kg). After 60 min lasting seizures, the determination of the oxidized products of Het (reflecting superoxide production) was assessed microscopically by fluorescence (>600 nm). Tempol was given i.p. in two doses (150 mg/kg each), 10 min before and 15 min after the infusion of convulsant drugs, respectively. Neuronal injury was evaluated using Nissl and Fluoro-Jade B staining.

Results: The fluorescent signal of the oxidized product of Het was significantly increased ($p < 0.05$) in all the studied regions (CA1, CA3 and DG of hippocampus, cerebral cortex and thalamus), in both models of seizures studied. The treatment with Tempol prevented increased superoxide formation and partially attenuated neuronal injury associated with SE.

Conclusion: The present findings suggest that substances with antioxidant properties combined with conventional therapies might provide a beneficial effect in treatment of epilepsy.

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THE EFFECTS OF ANDROSTERONE ON CALBINDIN-D_{28K} EXPRESSION BY INTERNEURONS IN THE HIPPOCAMPI OF A PILOCARPINE-INDUCED SEIZURE MODEL

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Purpose: Systemic administration of pilocarpine results in status epilepticus (SE) and death of pyramidal cells in the CA1 and CA3 fields of the hippocampus. This is due to excessive elevation of intracellular Ca^{2+} levels caused by the overactivation of glutamate receptors. Therefore, regulation of intracellular Ca^{2+} levels is an important factor in ensuring neuronal survival after SE. We examined whether androsterone affects expression of calbindin (CB) in order to understand the relationship between the neuroprotective effects of androsterone in pilocarpine-induced SE.

Method: ICR mice were induced into SE by injection of pilocarpine. Two hours after SE, the mice were treated with androsterone 200 mg/kg i.p. group. We compared the experimental group with a control group that received only a saline injection. Two days after, immunohistochemistric staining for CB was performed on a hippocampus slices from mice in the two group. We also used cresyl violet staining to compare changes in the hippocampal structures.

Results: Androsterone increased expression of CB in the interneurons of the hippocampus when the test subjects were compared with the control SEl mice. Also, 2 days after pilocarpine administration, numerous CB-expressing astrocytes were found in the androsterone-injected mice, but not in the control mice.

Conclusion: These results suggest that the neuroprotective effect of androsterone on pilocarpine-induced SE may be mediated via an increase in expression of CB.

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STATUS-LIKE ACTIVITY INDUCED BY SOME DRUGS IN ANIMALS WITH GENETICAL ABSENCE EPILEPSY

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Purpose: Absence epilepsy status can arise under inappropriate antiepileptic drugs, antidepressants, hormones and toxic compounds [Panayitopolos, 1999]. In a genetic animal model of absence epilepsy (WAG/Rij rats) status-like state was also observed under various drugs [van Luijtelaar, Coenen, 1999; Depaolis, van Luijtelaar, 2004, van Rijn et al. 2010]. The task of this work was the analysis of the time-frequency structure of spike-wave discharges (SWDs) in absence statuse.

Method: We used WAG/Rij rats with chronic electrodes implanted in cortex and thalamus. Modified wavelet transform was used for the analysis. Rats were injected with haloperidol, vigabatrine, imipramine, fluoxidine, clonidine, CB1 receptor agonist WIN55, 212-2.

Results: Under all these drugs an absence status-like state was observed and characterized by extraordinary long SWDs. Time-frequency dynamics of these discharges was developed in two ways: 1) discharges were initiated with the short burst of 10–12 Hz in somato-sensory cortex followed by the activity about 6–7 Hz during the whole discharge, this pattern was observed under vigabatrine; 2) discharges were consisted of numerous repeated fragments 4–5 s length beginning with 10–12 Hz and then decreasing up to 6–7 Hz. This pattern was observed under haloperidol, fluoxidine, WIN55, 212-2.

Conclusion: The time-frequency analysis of SWDs structure in cortex and thalamus showed that long epileptic activity during absence status can be supported by stable rhythmic activity of the thalamic pacemaker or by multiply triggering of short SWDs from the cortex.

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DEVELOPMENT AND CHARACTERIZATION OF NEW PRODRUGS OF BUMETANIDE IN COMBINATION WITH THE MONOOXYGENASE INHIBITOR PIPERONYL BUTOXIDE FOR ANTIEPILEPTOGENESIS

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Purpose: Downregulation of the K^+-Cl^- cotransporter KCC2 and upregulation of the Na^+-K^+-$2Cl^-$ cotransporter NKCC1 after proepileptogenic brain insults lead to increased intracellular Cl^-, causing a shift from inhibitory to excitatory GABA actions that may contribute to a critical development of neuronal hyperexcitability and, thus, epileptogenesis. Therefore cation-chloride cotransporters provide a potential target for antiepileptogenic treatment. Bumetanide, a selective NKCC1-inhibitor, might counteract NKCC1-up-regulation, but effective brain levels are difficult to achieve and maintain due to a short half-life in rodents and ineffective blood brain barrier passage.

Method: We tried (1) masking of the carboxylic group of bumetanide (esters, alcohol, and amide as potential prodrugs), (2) inhibition of bumetanide degradation (pretreatment with the monooxygenase inhibitor piperonyl butoxide), and (3) modification of solvents (e.g., complex compounds).

For all strategies female Sprague–Dawley rats and NMRI mice were treated intravenously with bumetanide (prodrugs). Plasma and brain concentrations were measured by HPLC.

Results: Low drug concentrations at different time points after injection of the potential prodrugs of bumetanide in plasma and brain tissue pointed to a rapid metabolism of the *N*-butyl sidechain by monooxygenases in rodents. Pretreatment with piperonyl butoxide resulted in a marked enhancement of the half-life, diuretic action, and brain penetration of bumetanide.

Conclusion: A combination of our strategies, i.e., pretreatment with piperonyl butoxide before injection of potential prodrugs of bumetanide in an adequate solvent, should achieve and maintain effective bumetanide brain levels. We currently test whether such treatment exerts antiepileptogenic effects in mouse and rat models of epileptogenesis.

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EFFECTS OF RO-25-6981, A SELECTIVE ANTAGONIST OF NMDA RECEPTORS CONTAINING NR2B SUBUNIT ON CORTICAL PHENOMENA IN DEVELOPING RATS

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Purpose: NMDA receptors (NMDARs) containing NR2B subunit prevail at early postnatal brain development. Therefore we compared effects of a selective antagonist of NMDARs containing NR2B subunit Ro-25-6981 on cortical evoked potentials with older data about 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 low-frequency stimulations. Ro-25-6981 was injected 10 min after first ADs in a dose of 1 or 3 mg/kg. Changes in total duration of ADs were evaluated. The effects of the same doses of Ro-25-6981 were studied in a model of physiological phenomena—cortical interhemispheric responses elicited by single and paired pulses. Amplitude of the first components

was used to construct input-output curves for single responses and excitability cycles for paired-pulse responses.

Results: Single and paired pulse evoked potentials as well as duration of ADs were influenced by 1 mg/kg dose of Ro-25-6981 in 12-day-old animals. Dose of 3 mg/kg resulted in a tendency to shorten subsequent ADs and slightly decreased cortical excitability. Possible rebound effect was observed as a prolongation of the 5th ADs in comparison to 1st one. There was no significant effect of Ro-25-6981 in 18- and 25-day-old rats.

Conclusion: Ro-25-6981 suppresses both physiological and pathological cortical phenomena only in the youngest, 12-day-old group but not in 18-, 25-days-old rat pups.

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ELECTROENCEPHALOGRAPHIC AND BEHAVIORAL EFFECTS OF INTRACEREBROVENTRICULAR INJECTION OF GRAYANOTOXIN IN ADULT WISTAR RATS

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Purpose: Grayanotoxin (GTX) is found in honey obtained from nectar and pollen of rhododendron and rhododendron-like plants which are members of Ericaceae family. Excessive amount of mad honey containing GTX cause dizziness, fatigue, excessive perspiration, hypersalivation, vomitting, paresthesia, seizures and convulsions. Our aim was to investigate the changes in EEG activities and accompanying motor movements when mad honey extract containing GTX is applied intracerebroventricularly (icv) to adult Wistar rats.

Method: Adult male Wistar rats were implanted with icv cannula and bilateral cortical recording electrodes. After recording of baseline EEG (PowerLab 8S) flower honey extract was applied icv. EEG and behaviors were monitored for 3 h (9:30–12:30 a.m.). After a 2-day wash out period the extract corresponding to 5 mg mad honey was injected icv. EEG and behavioral changes based on the Racine's seizure scale were evaluated (Ethics approval; 9.12.2010–90.2010 March).

Results: The administration of flower honey extract did not cause any change in EEG or behavior. After the injection of mad honey extract, latency to the first generalized spikes in EEG was 5.3 ± 0.9 min and reached a maximum at 30 ± 10 min. In the 3-h-EEG recording mean seizure activity was 1470.4 ± 709.9 s. Latency to the first behavioral changes was 10.7 ± 4.5 min after the injection. Changes in behavioral activity reached maximum of stage 3 in the 30–60 min and disappeared 2 h after the injection.

Conclusion: Icv administration of mad honey extract containing GTX causes the generalized cortical seizures characterized by spike discharges in EEG and accompanying behavioral changes in adult Wistar rats.

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SESAMOL 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 sesamol, 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 sesamol was administered for seven successive days at doses of 2, 4 and 8 mg/kg/day i.p. Rats were administered KA (10 mg/kg i.p.) and behavioral changes, incidence and latency of convulsions was observed for 4 h. 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 sesamol against neuronal damage induced by kainic acid. In addition, histopathological and ultrastructural studies were performed to validate the effect of sesamol on hippocampus.

Results: Pretreatment with sesamol (4 and 8 mg/kg, i.p.) significantly increased the latency of seizures as compared to the vehicle-treated KA group. Sesamol (4 and 8 mg/kg, i.p.) significantly prevented the increase in MDA levels and ameliorated the decrease in glutathione. There was also increase in expression of HSP-72 in the KA group; sesamol dose-dependently attenuated the expression of HSP-72. In addition, sesamol protected against neuronal damage and apoptosis in the hippocampus after KA administration, as analyzed by using immunohistochemistry and TUNEL assay. Ultrastructural study revealed swollen or shrunken degenerating neurons in the CA1, CA3 subfields and hilus of the DG and hypertrophied astrocytes showing accumulation of intermediate filament bundles in the cytoplasm were observed after administration of KA. Sesamol (4 and 8 mg/kg, i.p.) protects against ultrastructural changes induced by kainic acid. Furthermore, sesamol-induced neuroprotection was accompanied by marked improvements in memory impairment, as determined by passive avoidance tests.

Conclusion: The results of the present study suggest that sesamol holds potential for the treatment of pathologies associated with KA-induced brain damage. These neuroprotective effects are due to its antioxidant and antiapoptotic properties.

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THE EFFECT OF INTRACEREBROVENTRICULAR NIMODIPINE INJECTIONS ON KINDLING-INDUCED LOCOMOTOR ACTIVITY CHANGES IN WISTAR RATS

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Purpose: It is known that following different types of seizures, including those seen in temporal lobe epilepsy, postictal behavioral changes occur. Amygdaloid kindling is a validated animal model of temporal lobe epilepsy. The aim of this study was to evaluate postictal behavioral changes by locomotor activity measuring, and the effect of intracerebroventricular (ICV) nimodipine, a Ca^{2+} channel blocker, on this processes.

Method: Experiements were carried out with male and female wistar rats, aged 4–6 months. All experimental procedures were approved by the local ethical committee (20 2008 March). A bipolar electrode stereotactically implanted in the right basolateral amygdala and a guide cannula implanted in to the lateral ventricle of each rat, according to the coordinates taken from the rat brain atlas (Paxinos, Watson 2007). All rats were tested for baseline locomotor activity before the stimulations began. Rats were electrically stimulated until they had three successive grade five seizures. EEG activity were recorded during electrical stimulations. Following the third grade five seizure, nimodipine (150 μg/2 μl; dissolved in dimethylsulfoxide) or vehicle were given to the lateral ventricle through the implanted guide cannulas.Twenty minutes after ICV nimodipine

injection, rats were stimulated for the last time and then tested for locomotor activity.

Results: In the kindled rats, locomotor activity measurements showed a decrease in the activity following the stimulation induced seizures whereas this decrease was not statistically significant. ICV nimodipine administration before the electrical stimulus caused a significant decrease in the locomotor activity. A decrease in the after discharge duration, but not in seizure grade, has also been observed during the stimulus induced seizures.

Conclusion: The effect of ICV nimodipin on the kindling induced locomotor activity changes may suggest that nimodipine might influece the postictal behavioral changes in epilepsy patients.

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EFFECTS OF TOPIRAMATE ON THE APOPTOSIS OF HIPPOCAMPUS OF ELECTRICAL KINDLED RATS AND EPILEPSY

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Purpose: To observe the effect of topiramate (TPM) on the apoptosis in the basolateral amygdala electrical (BLA) kindled epilepsy rats' hippocampus; to explore the possible mechanism of topiramate's antiepileptic effect.

Method: Bipolar electrodes were implanted in BLA of rats, through which the rats received chronic electrical stimuli for kindling. Their seizure processes were observed, and electroencephalogram (EEG) recording were performed during and after kindling. Hippocampus apoptosis was detected by TdT-mediated dUTP-biotin nick end labeling (TUNEL). TPM treatment group, control group, sham group were arranged for comparison.

Results: Mean stimuli needed for fully kindled was 13.50 ± 3.99. The mean afterdischarge duration (ADD) recorded was (78205.67 ± 32567.93) ms. The seizure duration was (52.83 ± 23.02) ms; while in the TPM treatment group, the ADD was (23880.83 ± 20184.50) ms, the seizure duration was (13.67 ± 11.34) ms, and all the difference were significant compared to the kindled group ($p < 0.05$). The mean seizure class the kindled rats displayed after topiramate treatment was reduced from 5 to 3 ($p < 0.05$). Significant increase of apoptosis was observed in hippocampus of kindled rats ($p < 0.05$). These kindling-mediated increases of apoptosis were prevented by topiramate treatment ($p < 0.05$).

Conclusion: In seizures induced by electrical kindling, apoptosis possibly participate in the process of kindling. TPM might alleviate epilepsy state through inhibiting the apoptosis of epileptic hippocampus.

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EFFECTS OF INFANTILE ACUTE REPEATED HYPERGLYCEMIA ON NEURONAL DENSITY OF HIPPOCAMPUS AND SEVERITY OF PENTYLENETETRAZOL INDUCED EPILEPTIFORM CONVULSIONS IN WISTAR RATS

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Purpose: Hyperglycemia and metabolic disturbances may induce morphological and behavioral changes in some neuronal structures such as hippocampus. The aim of our study was to investigate the effects of infantile repeated acute hyperglycemia on neuronal density of hippocampal CA3 region in newborn Wistar male and female rats and its effect on pentylenetetrazol induced generalized seizures in adult rats.

Method: Ten-day-old male and female Wistar rats were randomly divided into four groups (n = 20 for each): female and male hyperglycemia and control. Hyperglycemia was induced by intraperitoneal injections of 2 g/kg dextrose solution, two times/day for 14 days. Control animals received saline solution. Blood glucose regularly was measured. After that, the brains of rats (n = 10 for each group) were removed for histological (stereological) analysis. Other animals were kept until 2.5 month old. Then, seizure was induced in all groups by an intraperitoneal pentylenetetrazol injection (45 mg/kg) and latency periods of epileptiform convulsions were recorded. All experiments were approved by Local FUM Committee for Animal Ethics.

Results: Showed that the difference of hippocampal CA3 neuronal density and susceptibility to pentylenetetrazol induced convulsions in hyperglycemic and control groups were significant, but these differences between male and female rats were not significant.

Conclusion: The present study determined that acute repeated increments in daily blood sugar levels in infantile period of rats may induce damage of neuronal structures of the central nervous system especially in hippocampus and such morphologic disturbances may elevate the susceptibility to pentylenetetrazol induced epileptiform convulsions.

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DISRUPTION OF LONG-TERM MEMORY BY HIGH MOBILITY GROUP BOX 1 PROTEIN: A POSSIBLE MECHANISM UNDERLYING MEMORY IMPAIRMENTS ASSOCIATED WITH TEMPORAL LOBE EPILEPSY

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Purpose: High mobility group box 1 (HMGB1)–mediated brain inflammation plays critical role in precipitating seizures in models of temporal lobe epilepsy (TLE; Maroso et al., Nat Med; 2010; 16: 413). We examined whether HMGB1-activated pathways via Receptor for Advanced Glycation End Products (RAGE) and toll-like receptor 4 (TLR4) may elicit memory deficits, as the latter represent frequent comorbidity of TLE.

Method: Nonspatial long-term memory was examined using novel object recognition test (NORT) in wild type, TLR4 knockout, and RAGE knockout adult male mice. Recombinant HMGB1 was injected into the lateral brain ventricle (i.c.v.; 10 μg) at relevant time points in order to examine its effects on memory encoding, consolidation and retrieval. A selective TLR4 antagonist, *Rhodobacter sphaeroides* lipopolysaccharide (LPS-Rs; 20 μg, i.c.v.) was injected 5 min prior to HMGB1.

Results: Neither TLR4 knockout, nor RAGE knockout mice exhibited memory deficits in NORT. HMGB1 disrupted memory encoding equally in wild type, TLR4 knockout and RAGE knockout animals, but did not affect memory consolidation and retrieval. Pharmacological blockade of TLR4 in RAGE knockout mice by means of LPS-RS abolished the detrimental effect of HMGB1 on memory encoding.

Conclusion: Along with its established involvement in ictogenesis (primarily through TLR4, Maroso et al., 2010), HMGB1 signaling may be involved in epilepsy- associated memory deficits by cooperative stimulation of TLR4 and RAGE. Furthermore, considering the role of

RAGE in pathophysiology of Alzheimer disease (AD), the established effects of HMGB1 may also contribute to the high incidence of comorbidity between AD and epilepsy.

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EXPERIMENTAL STUDY ON THE EFFECTS OF EPO, C-EPO ON THE PROTEIN EXPRESSION OF JAK2/STAT5 AND PI3K/AKT IN HIPPOCAMPUS OF EPILEPSY RATS INDUCED BY KAINIC ACID

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Background: Carbamylated EPO (C-EPO) is a derivative of erythropoietin (EPO), it can protect brain from injury as EPO except for stimulating erythropoiesis. The aim of this study is to observe the effects of EPO, C-EPO on the expression of Jak2/STAT5 and PI3K/akt in hippocampus of epilepsy rats and explore the neuroprotection mechanism of both.

Methods: One hundred twenty male rats were divided into four groups: A control group; B epilepsy group; C EPO group; D C-EPO Group. Epilepsy models were made by injecting kainic acid into amygdala under stereotaxic instrument. Rats were decapted at 0, 2, 6, 12, 24 h after epilepsy; The expressions of Jak2/STAT5 and PI3K/akt in the rat hippocampus were tested by the methods of Western blot, and the grey values were calculated.

Results: The protein expression of Jak2/STAT5 after kindling increased from 2 to 24 h in B, C group, Jak2/STAT5 expression in C group are much higher than that in B group at 24 h. There are no difference of Jak2/STAT5 expression between B and C group. The protein expression of PI3K/akt increased from 2 to 24 h after kindling, which increased significantly in D group, compared with other groups.

Conclusion: EPO increase the protein expression of Jak2/STAT5, C-EPO have no effect on the pathway of Jak2/STAT5; C-EPO increase the protein expression of PI3K/akt, EPO have no effect on the pathway of PI3K/akt.

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EXPERIMENTAL STUDY ON THE NEUROPROTECTION ROLE OF EPO, C-EPO ON HIPPOCAMPUS INJURY OF EPILEPSY RATS INDUCED BY KAINIC ACID

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Purpose: Carbamylated EPO (C-EPO) is a derivative of erythropoietin (EPO), it can protect brain from injury as EPO except for stimulating erythropoiesis. The aim of this study is to observe the neuroprotection role of EPO/C-EPO on hippocampus injury of epilepsy rats induced by kainic acid.

Method: One hundred twenty male rats were divided into four groups: the control group; epilepsy group; EPO group; C-EPO Group. Epilepsy models were made by injecting kainic acid into amygdale under stereotactic instrument. Rats were evaluated by the neurological function score and decapted at 24 h after epilepsy. The quantity of apotosis in different group were caculated by Tunnel staining.

Results: The neurological function score were 1.3 ± 0.5; 2.3 ± 0.9; 1.7 ± 0.7; 1.5 ± 0.6, respectively; The quantity of apotosis in different group were 38.4 ± 9.5; 59.03 ± 11.5; 43.5 ± 8.2, respectively. The number of apotosis cells were decreased in EPO, C-EPO groups, compared with epilepsy group ($p < 0.05$).

Conclusion: EPO, C-EPO reduced the neurological function score, reduced the number of apotosis cells and protect the hippocampus from Injury.

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IMPACT OF THE CNTF-DERIVED PEPTIDE MIMETIC CINTROFIN ON A RAT POST–STATUS EPILEPTICUS MODEL

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Purpose: Peptide mimetics selectively include beneficial and exclude undesirable effects of their parent molecules and offer interesting opportunities to develop putative therapeutic or prophylactic strategies. Here, we evaluated the impact of the ciliary neurotrophic factor-derived peptide cintrofin on a rat post–status epilepticus model.

Methods: In female Sprague Dawley rats a status epilepticus (SE) was induced by stimulation of the basolateral amygdala. The impact of cintrofin (10 mg/kg twice daily over five consecutive days) on development of spontaneous seizures was investigated. Furthermore, the development of SE-associated alterations in behavior and cognition was analyzed.

Results: Treatment with cintrofin did not affect frequency and duration of spontaneous seizures. As a consequence of SE mean velocity and distance moved in the open field were significantly increased. Cintrofin did not attenuate these behavioral alterations. On the other hand, the time spent in the periphery of open-arms in the elevated plus maze was significantly increased in cintrofin-treated SE animals. Moreover, SE resulted in a disruption of learning and memory in the Morris water maze, whereas cintrofin significantly attenuated these deficits. In addition, possible effects of cintrofin on cellular processes, such as neurodegeneration, -regeneration, and neurogenesis after SE are currently analyzed.

Conclusions: The results indicate that cintrofin seems to prevent the long-term consequences of a SE regarding learning and memory. Therefore, treatment with CNTF-derived peptide mimetics, such as Cintrofin offers promising opportunities for the development of putative disease-modifying strategies in epilepsies.

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THE ERYTHROPOIETIN-DERIVED PEPTIDE MIMETIC PHBSP AFFECTS CELLULAR AND COGNITIVE ALTERATIONS IN A RAT POST–STATUS EPILEPTICUS MODEL

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Purpose: Erythropoietin (EPO) has been suggested as a promising therapeutic and prophylactic for epilepsies. However, its application is limited by side effects. Therefore, it is of interest to evaluate whether the nonerythropoietic EPO-derived peptide pHBSP can affect epileptogenesis and associated alterations.

Methods: In Sprague-Dawley rats a status epilepticus (SE) was induced and rats were treated with either pHBSP, EPO or scrambled peptide. Behavior of animals was evaluated in different paradigms. The effects on hippocampal neurogenesis and neurodegeneration were investigated

based on immunohistochemistry as well as thionin staining. Data were compared with those of control animals without SE.

Results: Both, pHBSP and EPO further enhanced SE-associated increase in hippocampal cell proliferation. Thereby, pHBSP seemed to promote neuronal differentiation and survival resulting in a significant increase in neurogenesis. Neither pHBSP nor EPO affected the number of animals exhibiting spontaneous recurrent seizures as well as seizure frequency in the chronic phase. However, EPO significantly lowered the mean duration of spontaneous seizure activity. Anxiety-associated behavior was reduced by SE in different paradigms. In the elevated plus maze EPO further enhanced this SE-induced behavioral alteration. In the Morris water maze, pHBSP attenuated cognitive deficits in epileptic animals.

Conclusion: In conclusion, pHBSP can modulate the cellular and cognitive long-term consequences of a status epilepticus. Based on these data, further studies in chronic epilepsy models are necessary to evaluate the potential of pHBSP especially focusing on its disease-modifying effects.

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p166
THE EFFECT OF RESPONSIVE HIGH FREQUENCY STIMULATION OF THE SUBICULUM IN THE INTRA-HIPPOCAMPAL KAINIC ACID SEIZURE MODEL IN RATS

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Purpose: The subiculum is one of the major output structures in the hippocampus and might be involved in the generation and propagation of limbic seizures. In this study, the effects of responsive high frequency stimulation (HFS) of the subiculum were investigated in an acute kainic acid (KA) induced seizure model in rats.

Method: Wistar rats (n = 15) were implanted with an electrode-cannula complex in the CA3 area of the hippocampus, a bipolar stimulation electrode in the subiculum and a tripolar electrode in the contralateral motor-cortex. Two weeks later rats were injected with KA (0.05 μg/0.1 μl) intermittently for 3 days with an interval of 48 h. HFS (125 Hz, 100 μs) was delivered at a predetermined intensity (100–500 μA) in the subiculum stimulation group (n = 7) when seizures were visually detected, while no stimulation was delivered in the control group (n = 8).

Results: All rats reached Stage V (Racine's scale) at Day 1 and various severities of seizures were obtained (Stage I–V). The stimulation group had less focal number ($t_{13} = 2.84$, $p < 0.05$) and longer interseizure intervals of focal seizures ($t_{13} = 2.38$, $p < 0.05$) at Day 1. Significant day effects were found for the latency ($F_{2,26} = 6.94$, $p < 0.01$), number of focal seizures ($F_{2,26} = 11.50$, $p < 0.01$), duration of focal ($F_{2,26} = 5.65$, $p < 0.01$) and generalized seizures ($F_{2,26} = 19.41$, $p < 0.01$).

Conclusion: Responsive HFS of the subiculum has antiepileptic effects on focal seizures at Day 1. The decrease in seizure sensitivity over days might point toward an endogenous anticonvulsant mechanism.

p167
FAST FOURIER TRANSFORMATION ANALYSIS ON THE AFTERDISCHARGE INDUCED BY ACUTE KINDLING OF THE RABBIT HIPPOCAMPUS

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Purpose: Kindling is a widely used animal model of intractable temporal lobe epilepsy. We have performed fast Fourier transformation (FFT) analysis on the afterdischarge (AD) induced by chronic hippocampal kindling of the rabbit and revealed that enhancement of the higher frequency band (HFB: 12–30 Hz) component is associated with kindled stage. In the present study, we examined FFT analysis on ADs induced by acute kindling of the rabbit hippocampus to reveal the underlying mechanism of kindling-induced epileptogenesis with using agonists as well as antagonists of hippocampal neurotransmitters.

Methods: We performed all experiments under appropriate conditions in accordance with the Declaration of Helsinki and the Guide for Animal Experimentation at Soka University. Seven adult rabbits were used. Under deeply anesthesia, we delivered acutely stimulations (1 ms, biphasic 50 Hz, 1 s train) with suprathreshold intensity for AD at 20-min intervals to the right hippocampus. FFT analysis on each AD was performed with sampling frequency of 1 kHz by Power Lab (Chart, ADInstrument).

Results: The power spectral density ratios of the lower frequency band (LFB: 0–9 Hz), the middle frequency band (MFB: 9–12 Hz) and HFB components against total PSD were calculated. The ratios of LFB/MFB/HFB were 71.1 ± 14.6 (mean ± SD), 8.2 ± 4.6, and 17.3 ± 8.9% at the initial stage, while they changed to 37.1 ± 24.4 ($p < 0.05$), 7.7 ± 3.3, and 54.2 ± 23.2% ($p < 0.05$) at the final stage, respectively.

Conclusions: An enhancement of HFB component also occurred in the acute kindling. Effects of agonists or antagonists of hippocampal neurotransmitters on HFB enhancement will be discussed.

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THE EFFECTS OF THE KETAMINE AND DANTROLENE ON THE SPATIAL LEARNING IN RATS EXPOSED TO REPEATED ELECTROCONVULSIVE SEIZURES AS A MODEL OF EPILEPSY

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Purpose: To investigate the effects of ketamine and dantrolene on the spatial learning of rats exposed to repeated electroconvulsive seizures (ECS) as a model of epilepsy.

Method: Thirty-two rats (male, 2 month-old, Wistar albino) were assigned to four groups. (1) Sham; (2) ECS: Rats received ECS (150 V for 2 s/day) via ear electrodes with 24 h interval for five consecutive days, then the 6th ECS was applied 2 h after the last ECS. The same ECS protocol was applied to the three and four groups which received dantrolene (5 mg/kg i.p.) or ketamine (40 mg/kg s.c.) administered 1 h before each ECS, respectively. Following 1 month of recovery, the cognitive status of the animals was evaluated via Morris water maze test for five consecutive days by calculating mean escape latency time (MELT). The same experimental protocol was repeated 14 days afterward to evaluate the retention of the memory.

Results: No significant difference was found in MELT values between the four groups for each day. MELT values for retention for each group were not different from those of the values obtained on the fifth day. Intragroup comparison of the percent change in MELT values for 5 days in each group was also assessed. In group 1, day 2, 4 and 5 values were significantly lower from day 1. In group 2, day 5 value was lower from day 1. In group 3, significant difference in MELT values was found between all days indicating a regular decrease. In group 4, only day 4 was different from the days 1 and 2. Although there was no significant effect of ECS and chemicals, it seems that the animals in four groups learned the task at different rates. ECS and ECS + ketamine treated rats showed impairment in learning rates. ECS + dantrolene treated rats exhibited a consistency and improvement in learning rate.

Conclusion: The treatment strategies targeting the cognitive impairment in epilepsy may contribute to minimize the complications of the disease.

p169
THE ENDURING EFFECTS OF EARLY-LIFE STRESS ON LIMBIC EPILEPTOGENESIS ARE MEDIATED BY HPA AXIS HYPERREACTIVITY

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Purpose: Enduring effects of early-life stress on the brain may contribute to the development of limbic epilepsy later in life. This process is possibly mediated by hyperreactivity of the hypothalamic-pituitary-adrenal (HPA) axis with increased corticosterone release. Using the maternal separation (MS) model of early-life stress in rats, this study assessed whether inhibiting the synthesis of corticosterone could ameliorate the adverse effects of MS stress on kindling epileptogenesis.

Method: From postnatal days 2–14, female Wistar rats were exposed to maternal separation stress for 3 h/day (MS) or early-handled for 15 min/day (EH). At 8 w, rats were assessed for seizure threshold via a bipolar electrode implanted in the left amygdala, and subsequently subjected to the electrical amygdala kindling model of limbic epileptogenesis. Throughout the kindling period, rats were administered with either metyrapone (corticosterone synthesis inhibitor: 50 mg/kg, s.c) or vehicle 60 min prior to each stimulation.

Results: Vehicle-treated MS rats displayed reduced seizure threshold ($p = 0.03$), and longer seizure duration ($p = 0.02$) compared to EH rats. Metyrapone treatment in MS rats significantly increased seizure threshold ($p = 0.0001$) and reduced seizure duration during kindling ($p = 0.018$) to levels of EH rats. In MS rats only, metyrapone treatment delayed the progression of kindling, with rats requiring more stimulations to reach the fully-kindled state ($p = 0.03$).

Conclusion: Inhibition of corticosterone synthesis with metyrapone alleviated the enduring effects of MS stress on seizure threshold, seizure duration and kindling, suggesting that HPA hyperreactivity with increased corticosterone release is critical to the effect of MS stress in increasing vulnerability to limbic epileptogenesis.

p170
CORRELATION OF HYPOXIA-INDUCIBLE FACTOR-1A EXPRESSION WITH P-GLYCOPROTEIN IN THE MECHANISM OF PHARMACORESISTANCE IN REFRACTORY EPILEPSY RAT MODEL INDUCED BY CORIARIA LACTONE

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Purpose: Overexpression of multidrug efflux transporters, e.g., P-glycoprotein (Pgp) may elucidate refractory epilepsy. The hypoxia-inducible factor-1a (HIF-1a) could accumulate in brain tissue following epileptic seizure. In order to test the hypothesis that expression of Pgp is up regulated by HIF-1a in refractory epilepsy, which has been observed in cancer pharmacoresistance research, we explored the correlation of HIF-1a expression with Pgp in refractory epilepsy rat model.

Method: We established refractory epilepsy model in Sprague-Dawley rats by intramuscular injection of subthreshold dosages of Coriaria Lactone (CL), while control group by Normal Saline. The CL injection which was extracted from a herb mainly contains tutin and coriamyrtin has been proved to induce pharmacoresistant epilepsy in Sprague-Dawley rats in our previous studies. HIF-1a and Pgp expression in brain tissue were detected by immunohistochemistry (IHC), Real-time PCR and Western-blot analysis.

Results: IHC indicated that HIF-1a was expressed by microvessel endothelial cells, astrocytes and neurons in line with Pgp in model group. Furthermore, compared with control group, the mRNA and protein levels of HIF-1a increased significantly ($p < 0.05$) in hippocampus and temporal lobe. An accordant result was obtained in the expression of Pgp.

Conclusion: Our study demonstrates that HIF-1a expression increased in accordance with Pgp on spatial distribution in refractory epilepsy rat model induced by CL. The finding indicates that there may be a similar underlying mechanism in multidrug resistance of epilepsy as cancer pharmacoresistance. Further study focusing on siRNA-HIF-1a to distinguish the role of HIF-1a in refractory epilepsy is needed.

p171
TEMPORAL LOBE EPILEPSY: NEW BIOMARKERS IDENTIFIED BY PROTEOMIC ANALYSIS OF HIPPOCAMPI

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Purpose: Temporal lobe epilepsy (TLE) is among the most frequent types of drug-resistant epilepsy. Hippocampal sclerosis is commonly accepted as a hallmark of TLE. Many efforts have been made in order to enhance the understanding of the etiology of TLE and to find new targets for treatment or prevention of epilepsy. In order to get insight into the protein expression profile we used proteomic approach to analyze hippocampal specimens from patients.

Method: For two-dimensional electrophoresis, epileptic hippocampi ($N = 6$) and normal hippocampi from autopsy ($N = 6$) were homogenized in a lysis buffer and applied to isoelectrofocusing separation. Protein spots were analyzed by PDQuest (7.3.1) software, and by MALDI-TOF, MS and MS/MS analysis.

Results: Fourteen proteins were diferentially expressed in the epileptic hippocampi compared to control. Among the 40 proteins, 10 proteins were significantly altered in TLE. In the seven overlapping protein, six were up-regulated (HSP-70, dihydropyrimidinase-related protein 2, transmembrane channel-like 3, anexin, mielin 1-isoform and albumin 1-isoform), and one protein was down-regulated (isoform 3 of spectrin alpha chain). Three proteins were expressed only in TLE, such as heat shock cognate 71, V-type proton ATPase catalytic subunit A and glutathione S-transferase. At date, antibodies have been used to validate proteomic data by Western blotting and imunohistochemistry.

Conclusion: This study suggests that mitochondrial disfunction, as well as signaling pathways in T-cells proliferation could be involved in the pathological mechanisms underlying TLE. These data offer new insight into the complex pathways involved with epileptogenesis.

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p172
BISPHOSPHONATES FOR ALLEVIATION OF PHENYTOIN-INDUCED BONE DISEASE IN MICE

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Purpose: Chronic administration of phenytoin (PHT) has been associated with bone metabolism. Bisphosphonates [alendronate (ALD), ibandronate (IBD) and risedronate (RSD)] being potential candidates to prevent PHT-induced bone disorders, the present study evaluated their effect on the PHT-induced changes in biochemical markers of bone

turnover and on the antiepileptic efficacy of PHT. An attempt was also made to unravel the PHT's and bisphosphonates's effect on hcy.

Methods: Male mice received PHT (35 mg/kg, p.o.) for 90 days to induce bone loss. ALD, RSD and IBD were administered orally at doses 0.65, 0.33, 0.17 mg/kg respectively, for prevention and 1.3, 0.65, 0.33 mg/kg respectively, for treatment of PHT-induced bone loss. The bone loss was confirmed by bone mineral density (BMD) analysis and bone turnover markers. Serum levels of hcy and FA were estimated alongwith hydrogen peroxide levels and total antioxidant capacity.

Results: The induction of bone loss by PHT was marked by lowered BMD and altered bone turnovers. ALD and RSD administration to PHT treated groups significantly reverted the bony adverse effects. No such effects were observed with IBD. In the bisphosphonates treated groups, hcy levels were statistically at par with the control group. PHT at 35 mg/kg, p.o. could compromise bone mass and thus, could be a model of bone demineralization in mice. The ALD, IBD and RSD have no pharmacodynamic interaction when administered along with PHT at the experimental level.

Conclusion: The usage of bisphosphonates in the management of PHT-induced bone disease could be worthwhile if clinically approved.

p173
CELL RECOGNITION MOLECULES MAY TRIGGER THE EPILEPTOGENESIS DURING DEVELOPMENT IN THE HIPPOCAMPUS OF EPILEPTIC MUTANT EL MICE

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Purpose: The cell recognition molecules together with neurotrophin receptors play crucial roles for the development and the function of the brain. Among them, neural cell adhesion molecule (NCAM) has been shown to regulate an inwardly rectifying K^+ channel. Since inhibition of K^+ channel enhances neuronal activities, cell recognition molecules may be involved in the pathophysiology of epilepsy. In the present study, we investigated changes of NCAM, extracellular matrix glycoprotein tenascin-R (TN-R), cadherins and reeling during development of epileptic mutant EL mice.

Method: EL mice and their control animal, DDY mice were used. EL mice show secondary generalized seizures, which initiate primarily at the parietal cortex and generalize through the hippocampus. In the interictal period during development, changes of NCAM, polysialylated NCAM (PSA-NAM), cadherin, TN-R and reelin were investigated by Western blotting in the hippocampus as the seizure generalization site.

Results: In EL mice, levels of the PAS-NCAM, cadherin, tenascin-R and reelin significantly increased during early developmental stages (3–7 weeks) and then, decreased at 10 weeks and remain very low thereafter. The sharp withdrawal was observed before experiencing frequent seizures. In contrast, the expression of NCAM expressions showed no remarkable changes.

Conclusion: In the brain of EL mice, PAS-NCAM, cadherin, tenascin-R and reelin are upregulated before experiencing repetitive seizures, which may trigger the ictogenesis and epileptogenesis through the contribution to abnormal plastic phenomena. NCAM may compensate the hyperexcitability during development.

p174
INFLUENCE OF CAFFEINE ON THE PROTECTIVE ACTIVITY OF NEWER ANTIEPILEPTIC DRUGS IN THE 6 HZ PSYCHOMOTOR SEIZURE MODEL

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Purpose: Caffeine is most commonly ingested stimulant. Experimental studies have demonstrated that caffeine, in relatively low doses, diminished the protective effects of classical antiepileptic drugs (AEDs) against electrocoshock-, pentylenetetrazol-induced and amygdala-kindled seizures. It is thus of interest to find out whether acute or chronic caffeine can affect the anticonvulsant activity of selected newer (AEDs): oxcarbazepine (OXC), levetiracetam (LEV) lamotrigine (LTG) and tiagabine (TGB) in the 6 Hz psychomotor seizure model in mice.

Method: Tetracaine hydrochloride (0.5%) was applied to the cornea of male Swiss mice before corneal stimulation (0.2 ms duration pulses at 6 Hz for 3 s) delivered by constant-current device (ECT Unit 57800; Ugo Basile). AEDs and acute or chronic (twice daily for 14 days) caffeine were administered intraperitoneally. The anticonvulsant activity of the AEDs was determined by their respective ED50 values (in mg/kg). The neurotoxic effects of AEDs alone or combined with caffeine were evaluated in the chimney test (motor coordination) and grip-strength test (muscular strength).

Results: Caffeine administered acutely or chronically at doses of 23.1 and 46.2 mg/kg reduced the protective potency of LEV. The anticonvulsant activity of OXC was also decreased by chronic caffeine. Neither acute nor chronic caffeine affected the protective action of LTG and TGB. Caffeine (acute or chronic) had no effect on OXC, LTG, TGB and LEV associated neurotoxic effects.

Conclusion: Only the anticonvulsant activity of some newer AEDs was reduced by caffeine. Nevertheless, the intake of caffeine by epileptic patients should be discouraged.

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EFFECTS OF SUBCONVULSIVE PENTYLENETETRAZOLE INFUSION ON EPILEPTOGENESIS IN A STATUS EPILEPTICUS MODEL IN SPRAGUE–DAWLEY RATS

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Purpose: Temporal lobe epilepsy (TLE) belongs to the most prevalent forms of epilepsy. A variety of brain insults, including status epilepticus (SE), have the potential to induce TLE in a process, which is termed epileptogenesis. During epileptogenesis the brain undergoes alterations, which increases its excitability and eventually lead to the occurrence of spontaneous recurrent seizures (SRS). One hypothesis links this hyperexcitability with enhanced GABAergic inhibition after the insult, which increases network synchronization and results in synchronized firing of glutamatergic neurons after collapse of GABAergic inhibition. In this context the $GABA_A$-receptor antagonist pentylenetetrazole (PTZ) could be a useful pharmacological tool to prevent epileptogenesis.

Method: We used female Sprague-Dawley rats. SE was induced by intrahippocampal microinjection of kainic acid. Either 16 h or 7 days following onset of SE, a subconvulsive dose of PTZ (10 μg/ml plasma) was administered as intravenous infusion (60 μg/kg/min) for 48 h in two separate groups of rats. Controls received a saline infusion instead of PTZ. The occurrence of SRS was evaluated 8 weeks after treatment by EEG- and video monitoring.

Results: The subconvulsive target PTZ plasma concentration of 10 μg/ml, which was based on preliminary dose-finding and pharmacokinetic experiments in rats, was reached in all rats. However, treatment with PTZ following SE did not alter the occurrence of SRS in comparison to controls.

Conclusion: Treatment with a subconvulsive dose of PTZ over 2 days had no effect on the development of SRS in the kainate model of TLE. One explanation can be that we used the wrong time window after SE-induction for PTZ-infusion. It is also possible that the processes we want to influence with our treatment occur in restricted brain areas and thus a systemic treatment with PTZ is ineffective.

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LONG TIME EFFECT OF CHRONIC GAMMA-BUTYROLACTONE ADMINISTRATION IN WISTAR RATS

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Purpose: Absence epilepsy is an idiopathic, noncolvulsive form of epilepsy characterized by 3–4 Hz spike-wave discharges (SWDs) in elektroencephalography (EEG). Each SWD is accompanied by behavioral immotility and interrupted consciousness. The aim of this study was to determine EEG and behavioral changes with systemic administration of GBL in Wistar rats which is a model of the chemical absence seizures.

Method: Adult male Wistar rats (n = 12) were implanted with bilateral cortical recording electrodes under stereotaxic surgery. After recovery period for 1 week, rats were given 100 mg/kg GBL i.p. twice daily over the course of 30 injections. In order to monitor spontenous SWDs, EEGs were recorded for 90 min on subsequent Monday mornings after the injection free weekends. Results are expressed as mean ± SEM. Statistical analysis of the data was done by applying the analysis of one way variance (ANOVA).

Results: After the last injection of the week on Friday, SWDs were monitored for 90 min in basal EEG recording on subsquent Monday morning. Over the course of 3 weeks, cumulative durations of spontenous SWDs were increased. The cumulative duration of spontaneous SWD were 2.8 ± 1.6 after the first weekend, and 7.2 ± 3.6 after the third weekend. There was a significant increase in the cumulative duration of spontenous SWDs monitored after the third weekend.

Conclusion: In this study, there was a time-dependent increase in the duration of spontenous SWDs due to repeated injections of GBL.

p177
INVESTIGATION OF CALCIUM CHANNEL SUBUNITS EXPRESSION IN GENETIC ABSENCE EPILEPSY RATS FROM STRASBOURG

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Purpose: Genetic absence epilepsy rats from Strasbourg (GAERS) is one of the well validated genetic models of typical absence epilepsy. Voltage-activated calcium channels are thought to play a key role in the generation of spike and waves discharges characteristic of absence epilepsy and regulating neuronal excitability. Voltage activated calcium channels are composed of a_1, a_2, β and γ subunits. There are three members of a_1 subunit (a_1G, a_1H, a_1I) and their important role in the absence epilepsy has been shown in several studies.

Method: To analyze the protein levels of calcium channel subunits we performed Western blot using polyclonal antibodies specific for the a_1G and a_1I calcium channel subunits. The cortex and hippocampus were dissected from brains of GAERS (n = 4) and nonepileptic control Wistar rats (n = 4). The experimental protocol was approved by the Marmara University Ethics Committee for animal experimentation (22 2008 March).

Results: We found increased calcium channnel a_1G subunit protein levels in the cortex and hippocampus from GAERS compared with control Wistar rats. The other calcium channel subunit a_1I protein levels were also increased in the cortex and hipocampus from GAERS.

Conclusion: These results have shown that enhanced expression of T-type calcium channel subunits may contributes to epileptic phenotype in this strain. Further experiments will be performed to investigate the implication of other calcium channel subunits.

p178
"HERCULES": MEDICAL GENETICS AND BIOMEDICAL INFORMATICS INFRASTRUCTURE IN SUPPORT OF EARLY DIAGNOSIS, MONITORING AND TREATMENT OF CHILDREN WITH NEUROLOGICAL DISORDERS IN GREECE

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Purpose: Epilepsy is one of the most common chronic neurological disorders. Particularly, the estimated number of children and adolescents in Europe with active epilepsy is 0.9 million. Approximately 1% of children are affected and a significant proportion up to 30% of them does not respond to the treatment with occasionally catastrophic results. In this work, the Hercules project is demonstrated, which aims to the development of an integrated health care scheme specified for childhood neurological disorders.

Method: The main idea is to provide cohesive integration of medical, behavioral and genetic information. Current systems have been analyzed in order to build innovative tools and networks for providing state-of-the-art quality of care, through better disease classification, knowledge discovery and decision support systems.

Results: The overall architecture of the Hercules project includes: (1) the development of a biobank, (2) the development of an electronic health record, (3) the creation of a Web-collaborative environment and (4) the acquisition of a video-electroencephalogram monitoring system.

Conclusion: The objective of this paper is twofold: to present the general scope of the Hercules project and to provide all the issues related with the technological requirements, architectural design and functional specifications that render Hercules electronic health record innovative.

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RELATIONSHIP OF THE MOLECULAR GEOMETRY AND QUANTUM-CHEMICAL CHARACTERISTICS SOME AMINOACIDS WITH THEIR INHIBITOR POSSIBILITY IN CNS. SHILAU G.N. REPUBLICAN SCIENTIFIC PRACTICAL CENTRE OF PSYCHICAL HEALTH, MINSK, BELARUS

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Purpose: Of this investigation has been turned out searching natural endogen agonists GABA-benzodiazepine's receptors and synthesis new such kind Act on the basis their similarity.

Method: In our observe we studied: (1) Molecular geometry and quantum chemistry of the barbiturates and benzodiazepines pharmacophores, α-amino-vinegar (glycine), β-amino-propionic (β-alanine), γ-amino-buthiric (GABA and its three main conformers – linear, cyclic, scoop), δ-amino-valerian asides in the approximation of molecular mechanics with the use of the MM2 force field (2) Influence introventrical injection of aforementioned amino-asides on the cerebral neurophisiological activity in white rats (taking of EEG) (3) Anticonvulsant activity new class

compounds, containing glycine's pharmacophores using picrotoxin, pentylenetetrazol and maximal electroseizure models.

Results: (1) Molecular geometry all investigated amino-asides by its molecular geometry in largest remind cyclic and scoop GABA-conformer. (2) Introducing in same dosage as GABA as all aforementioned amino-asides produces inhibition of the brain cortex bioelectrical activity, depending from their similarity with cyclic or scoop GABA-conformer (3) It was confirmed good anticonvulsant activity new class compounds, containing glycine's pharmacophore.

Conclusion: (1) Apparently, pharmacophore of GABA-cyclic conformer appropriate to the pharmacophore of the natural endogen agonists GABA-a-benzodiazepines receptor (2) All investigated amino-asides, in different degree, possess inhibitor activity in CNS. (3) Development of new antiseizure drugs with glycine pharmacophore in their structure could be perspective direction of antiepileptic neuropharmacology.

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EFFECTS OF ELECTRICAL STIMULATION OF THE THALAMIC MEDIODORSAL NUCLEUS ON SPIKE AND WAVE DISCHARGES IN WAG/RIJ RATS

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Purpose: Pharmacological inhibition of mediodorsal (MD) nucleus suppresses of SWDs and this effect appears specific to the MD. The aim of this study was to investigate effect of bilateral electrostimulation of MD nucleus on pattern of SWDs in WAG/Rij rats.

Method: Two groups (n = 6 each) were included: low (10 Hz) and high frequency (130 Hz) DBS. All animals were equipped under general anesthesia (chloralhydrate 400 mg/kg i.p.) with two recording monopolar cortical stainless-steel electrodes placed bilaterally over the frontal cortex and bilateral bipolar stimulation electrodes aimed at the MD nucleus. The rats were stimulated for 1 h, the current intensity was 30 % of the threshold amplitude (0.1–0.3 mA, mean 0.2 mA). The duration and number of SWDs were calculated.

Results: A statistically significant ($p < 0.05$) decrease in the number and duration of SWDs was found after after 10-Hz stimulation, a significant increase of the number and duration of SWDs after 130 Hz stimulation.

Conclusion: Although low frequency stimulation is generally proepileptic, here inhibitory effects were found, probably through an arousing effect. Interestingly, high frequency stimulation showed proepileptic effects. This is in contrast to most of the DBS literature on convulsive seizures. The results also demontrate a modulatory role of the MD nucleus on absence seizures.

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SPONTANEOUS SPIKE-WAVE DISCHARGES IN SPATIALLY EXTENDED MODELS OF EPILEPTIC DYNAMICS

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Purpose: We challenge the concept that the transition from background activity to epileptic seizure activity, particularly in the neocortex, necessarily requires some changes in system parameters to occur.

Method: We study spatially extended models of macroscopic spike-wave-discharges in mathematical neural mass and neural field models. We use analytical techniques and numerical simulations to characterize the parameter space and the typical solutions of these models.

Results: Analytical results on low-dimensional versions of the models indicate robust spike-wave discharges (SWD) for a large number of parameter combinations. These are therefore considered robust representations of epileptic EEG waveforms. In spatially extended versions of the models, there are regions of intermittent bursting. Under these conditions sequences of SWD spontaneously occur amidst background dynamics, even in the absence of noise in the model. Intermittency, while considered rare in low-dimensional dynamical systems, is a generic solution in spatially extended models, particularly, when spatial heterogeneities are considered. In addition, the model demonstrates that the transition from a desynchronized background to a highly synchronized SWD can be entirely due to self-organization of the cortical field. The results are compared to studies of SWD in genetic models of absence seizure in rats as well as in children with typical absence seizures.

Conclusion: Mathematical Modelling of Epileptic Dynamics offers new theoretical concepts to discuss the sudden onset and offset of epileptic discharges in the human brain. We argue that models which neglect spatial features of cortical networks cannot fully account for specific features of generalized SWD like spatial heterogeneity, fragmentation and spontaneous termination. The modelling studies also predict the existence of microdomains with abnormal activity in an apparently normal background dynamics which can be tested experimentally in animal models. Detailed in silico studies of such models allow the design of external stimuli (realizable e.g. with direct electrical stimulation of the cortex) to either induce or terminate spike-wave activity.

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THE EFFECT OF INTRACEREBROVENTRICULAR U-92032 INJECTIONS ON GENETIC ABSENCE EPILEPSY RATS FROM STRASBOURG

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Purpose: Absence epilepsy is characterized by generalized nonconvulsive seizures with loss of consciousness and spike-and-wave discharges (SWDs) in the EEG. Low-threshold Ca^{2+} currents have been suggested to underlie the firing of thalamocortical neurons during SWDs in absence epilepsy. Genetic absence epilepsy rats from Strasbourg (GAERS) is a well defined animal model of absence epilepsy sharing pharmacologic and many clinical characteristics of absence epilepsy in humans. The aim of this study was to investigate the antiabsence effect of intracerebroventricular (ICV) U-92032, a novel T-type Ca^{2+} channel blocker, and the possible mechanisms of its action.

Method: Experiments were carried out with male GAERS animals, aged 5–12 months. All the experimental procedures were approved by the local ethical committee. U-92032 (50, 100 and 250 nM; dissolved in dimethylsulfoxide and diluted with saline) was given to the lateral ventricle through the implanted guide cannulas. Electrical activity of cortex was recorded 1 h before and 6 h after each injection. The total duration of SWDs, the number and the mean durations of SWD complexes, were analyzed over 20-min periods.

Results: A significant dose dependent decrease in cumulative duration, number and mean durations of SWD complexes were observed after ICV administration of 50, 100 and 250 nM U-92032.

Conclusion: The suppression of SWDs in GAERS by ICV injection of U-92032 shows that U-92032 is of value as an antiabsence agent.

Acknowledgement: U-92032 was provided by Pfizer Inc.

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IN VIVO STUDY OF THE IMPACT OF AMYGDALA KINDLING ON THE FIRING PATTERN OF SINGLE NEURONS IN A GENETIC ABSENCE EPILEPSY RAT MODEL

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Purpose: Genetic absence epilepsy rats from Strasbourg (GAERS), a well validated model of idiopathic generalized epilepsy, are resistant to the progression of kindling. Rhythmic reciprocal oscillatory firing between the cortex and the thalamus plays a critical role in absence seizures. We hypothesized that, the progression to the convulsive stages of amygdala kindling involves acquired alterations to firing properties in the thalamus that predisposes to rhythmic synchronized epileptiform firing in GAERS.

Method: GAERS and nonepileptic control (NEC) rats were implanted with a stimulating electrode in amygdala and stimulated at afterdischarge threshold twice daily to a maximum of 30 stimulations. Thereafter extracellular single neuron recordings were performed in vivo under neurolept anesthesia from the thalamic reticular nucleus (TRN), ventrobasal thalamus (VB), hippocampus and the cortex.

Results: The interictal firing patterns recorded in the cortex, hippocampus and TRN were similar between control-NEC and control-GAERS groups. However the thalamocortical cells in VB thalamus in control-NECs interictally had a lower firing frequency compared to control-GAERS. Following kindling the TRN firing had evolved a bursting (epileptiform) low frequency pattern interictally in kindling-NEC but this was not seen in kindling-GAERS subjected the same number of stimulations as NEC. In the VB and hippocampus, neurons in kindling-NEC, developed more bursting than kindling-GAERS group but the cortical neurons did not show this alteration.

Conclusion: Amygdala kindling induces the thalamus (TRN and VB) and to a lesser extend the hippocampus to fire in bursting pattern, which provide the new insight of involvement of the thalamus and hippocampus during secondary generalization of limbic seizures.

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THE EFFECT OF IL-1B AND SPECIFIC ICE/CASPASE-1 BLOKER ON SPIKE-AND-WAVE DISCHARGES

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Purpose: Interleukin (IL)-1β plays a crucial role in the mechanisms of limbic seizures induced in rodent models of temporal lobe epilepsy. We addressed whether activation of the IL-1β signaling occurs in rats with genetic absence epilepsy (GAERS) during the development of spike-and-wave discharges (SWDs). Moreover, we studied whether inhibition of IL-1β biosynthesis could affect SWD activity.

Method: IL-1β expression and glia activation were studied by immunocytochemistry in the forebrain of nonepileptic control Wistar rats and in GAERS postnatal days (PN) 90.

Results: In Wistar rats no detectable IL-1β immunoreactivity was observed in any of the areas studied, and glial cells showed a resting morphology. In adult PN90 GAERS, when mature SWDs are established, IL-1β immunostaining was observed in numerous reactive astrocytes in the somatosensory cortex.

Inhibition of IL-1 β biosynthesis using a specific ICE/Caspase-1 blocker, significantly reduced both SWDs number and duration in PN90 GAERS over 4 days of systemic administration.

Conclusion: These results show that IL-1β is induced in reactive astrocytes of the somatosensory cortex of GAERS. IL-1β induction has pro-ictogenic properties in this model, thus it may play a role in the mechanisms underlying the occurrence of absence seizures.

Poster session: Pediatric epileptology I
Monday, 29 August 2011

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PERINATAL STROKE AND THE RISK OF DEVELOPING EPILEPSY

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Purpose: Perinatal arterial ischemic stroke (PAS) is an acute cerebrovascular event occurring in 1/2300 to 5000 births. Little data are available on the risk and timing of developing epilepsy later in life.

Method: We retrospectively reviewed data of children with acute and delayed diagnosis of PAS in a tertiary care children's hospital, from January 2004 to December 2010. Only patients with MRI-documented stroke were included.

Results: We identified 132 patients. Eight were lost to follow-up. Middle cerebral artery was involved in 121/124, 97.5%, left side more than the right (58% vs 42%). 24/124 (19.3%) patients were diagnosed at birth, and 100 (80.6%) had a delayed presentation at a mean age of 8 months. Twenty out of 24 babies (83.3%) diagnosed at birth presented with neonatal seizures. Children with delayed diagnosis presented with hemiparesis (86%), with epilepsy (7%), or had an MRI for unexplained psychomotor delay (7%). Fifty-six children out of 124 (45%) developed epilepsy (mean age: 30 months). Forty-four children out of 56 (78.5%) presented with focal seizures, 3/56 (5.3%) with generalized seizures, and 15 (26.7%) developed West syndrome. Six of them had infantile spasms and focal seizures. Incidence of epilepsy was higher after neonatal onset (14/20, 70% vs 40/100, 40%). While in 32/56 (57%), seizures were controlled with AEDs, 24/56 (42.8%) had AEDs resistant epilepsy. Two children were successfully treated with surgery.

Conclusion: Childhood epilepsy is a frequent resulting morbidity of PAS, mainly focal epilepsy and epileptic encephalopathy. Neonatal seizures are an important risk factor. Drug-resistance is not uncommon and epilepsy surgery should be considered.

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INVOLVEMENT OF CHROMOSOMAL ABERRATIONS IN PATIENTS WITH EARLY EPILEPTIC ENCEPHALOPATHY

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Purpose: West syndrome and Ohtahara syndrome are associated with many underlying conditions. We aimed to evaluate the contribution of chromosomal aberrations as the cause of these two disorders.

Method: We investigated the etiologies of these disorders examined in Epilepsy Center, Nishi-Niigata Chuo National Hospital between 2000 and 2010. In most patients without specific causes for epileptic encephalopathies, chromosome G-banding was examined. In addition, we carried out copy number analysis using genomic microarrays in 16 patients.

Results: There were 158 patients in this study. The causative etiologies are migration or brain anomalies in 25 (15.8%), tuberous sclerosis in 16 (10.1%), chromosomal abnormalities in 11 (7.0%), mutations of affecting genes in six (3.8%), other congenital factors in eight (5.1%), perinatal incidents in 15 (9.5%), postnatal incidents in 12 (7.6%), and unknown etiology in 65 (41.1%). Details of chromosome anomalies are as follows: trisomy 21 in four, 4p- in one, chromosomal translocations in two, premature chromatid separation syndrome in one, carrying supernumerary marker chromosome in one, and microdeletion in two patients. Two patients showed microdeletion in 9q33.3-q34.11 and 14q13.1-q13.3, respectively. One patient with marker chromosome showed an increased dosage of 14q11.2-q12.

Conclusion: The ratio of involvement of chromosomal abnormalities is almost equal to that of tuberous sclerosis or postnatal incidents. Contribution of chromosomal abnormality to these two disorders is important enough to be noticed. Detection of submicroscopic chromosomal aberrations could elucidate the causes in etiologically unexplained patients, and may lead to the identification of candidate genes for early epileptic encephalopathies.

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SPECTRUM OF IDIOPATHIC FOCAL EPILEPSIES

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Purpose: Investigation of the spectrum of idiopathic focal epilepsies (IFEs) in our Institute.

Method: The study enrolled 1118 patients with established diagnosis of epilepsy, with age of seizure onset from the first day of life to 18 years.

Results: Out of 1118 patients, in 189 cases the IFEs have been diagnosed, which comprised 16.9% from the total group. In 8.8% of patients the diagnosis of idiopathic focal epilepsy with centrotemporal spikes was established. The idiopathic occipital epilepsy (IOE) was found in 4.2% of cases. The idiopathic focal epilepsy with pseudogeneralized seizures (IFE-PGS) was found in 2.8% of cases. The idiopathic focal epilepsy of infancy (IFEI) was observed in 0.5% of the total group of patients. The idiopathic focal epilepsy with affective symptoms (IFEAS) was found in 0.6%. Rolandic epilepsy was most often seen in the IFEs group (52.4% of cases). The IOE was found in 24.9% of cases. The IFE-PGS was seen in 16.4% of patients, IFEAS – 3.7%, IFEI – in 2.6%. Valproates is the drug of choice in the treatment of IFEs.

Conclusion: The IFE is not a homogeneous disease. Each form of disease has its specific electroclinical picture, age of onset and prevalence rate. It is not always fulfill the criterion of ''benign epilepsies.''

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A CASE OF CONTINUOUS SPIKES AND WAVES DURING SLOW SLEEP SYNDROME IN A KOREAN CHILD

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Continuous spikes and waves during slow sleep (CSWS) syndrome is not a common epileptic syndrome in children. It is diagnosed by a special type of electroencephalogram (EEG) pattern called status epilepticus during sleep, which is characterized by near-continuous spike-wave discharges at a frequency of 1.5–3.5 Hz on the EEG in slow sleep. The first seizure generally occurs between ages 1 and 10 years, with a peak at 4–5 years. In nearly one-third experience delays, predominantly in language.

I represent a case of a 10-year-old girl who showed continuous spikes and waves during slow sleep on her EEG. The patient was normal at birth. Her EEG recording taken at the age of 3 months was normal. She had mental retardation and developmental delay but did not show any seizure activities until age 10. She had her first seizure during sleep in April of 2008. Her EEG showed brief bursts of diffuse spike-wave activities and frequent multifocal spikes and waves. Her brain MRI was normal. She was started on lamotrigine and had no seizures until December of 2008. In January of 2009, she had a clinical seizure with CSWS at a frequency of 2–2.5 Hz on her EEG. Treatment with lamotrigine was discontinued and valproic acid and clonazepam was started. She has been seizure-free for 2 years and her last follow-up EEG was normal. Her cognitive function and language skill showed gradual improvement. Here, a case of CSWS syndrome in a Korean child is reported.

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BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES (BCECTS): EARLY RESPONSE TO TREATMENT WITH REGARD TO AGE AT SEIZURE ONSET AND LONG-TERM OUTCOME

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Purpose: To follow the clinical course of children with BCECTS treated with antiepileptic drugs (AEDs), estimate the percentage of early response to treatment and correlate findings with age at seizure onset and long-term outcome.

Method: The study population consisted of 102 children with BCECTS (66 boys & 36 girls; age range 2–14 years, mean 7.4) treated with AEDs for a minimum of 2 years. Based on response to treatment during the first year (early response) and long-term outcome the patients were divided into the following groups: (1) without early response to treatment, (2) with relapse, (3) with remission, (4) drug-resistant. The documented results were correlated with age at seizure onset and individual elements from the history of the patients.

Results: Patients included in the study were followed for 2–8 years. In 22.5% of children with BCECTS (N = 23/102) seizures were recorded during the first year of therapy. At the time of data collection, 21/23 were in remission, 1/23 in relapse and 1/23 was drug-resistant. Among the remaining 77.5% of children (N = 79/102) who exhibited early response to treatment, all had achieved remission at the time of data collection, while in 9/79 relapse has been reported during the clinical course of the syndrome followed by remission. Children with seizure onset at age 4 years or younger had a greater tendency to exhibit no initial response to treatment ($p = 0.0006$) and relapse ($p = 0.0031$) of seizures, although favorable long-term outcome was not altered.

Conclusion: (1) The outcome of BCECTS is excellent, with over 97% of children achieving complete remission, regardless initial nonresponse to treatment or further relapse, (2) A statistically significant tendency for initial nonresponse to treatment or later relapse is evident in children with seizure onset before the age of 4 years.

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CLINICAL ANALYSIS OF CHILDREN WITH CATASTROPHIC EPILEPSY REGISTERED IN THE FAR-EAST ASIA CATASTROPHIC EPILEPSY (FACE) STUDY GROUP

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Purpose: We studied on children aged younger than 5 years who manifested catastrophic epilepsy and were registered in the FACE study group to clarify their clinical characteristics. Subjects: Subjects were 261 children with epilepsy who satisfied the following criteria and underwent intensive study during the registration period (2009–2011): an age younger than 5 years, and more than 10 seizures/month refractory to more than two antiepileptic drugs and/or ACTH or ketogenic diet therapy. The data were provided by 14 collaborative Japanese, Korean, and Taiwanese hospitals.

Method: We analyzed the age at onset of epilepsy, predominant seizure type, etiology, EEG findings, neurological and neuropsychological findings at the onset, and syndromic classification.

Results: Among the 261 patients, the most frequent type of epileptic syndrome was West syndrome (WS) accounting for 34.5%, followed by unclassified epilepsy at 22.6%, neocortical epilepsy at 18.8%, Lennox-Gastaut syndrome at 9.6%, Dravet syndrome at 4.2%, Rasmussen syndrome at 2.3%, and other miscellaneous syndromes at the remaining 8.0%. Epilepsy developed at an age under 12 months in 75% of all patients. The most frequent and disabling seizure type was epileptic spasms (ES), comprising 90 cases (34.5%), followed by generalized tonic seizures in 52 cases (20%), and partial complex motor seizures in 40 cases (15.3%). The etiology in 41% of all patients remained unknown.

Conclusion: The highest proportion of catastrophic epilepsy patients aged <5 years had WS and related syndromes featuring ES, followed by neocortical epilepsy, whose etiology largely remained undetermined despite cortical dysplasia being the most prevalent.

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A POPULATION-BASED STUDY OF EPILEPSY IN CHILDREN FROM THE SOUTHERN PART OF SWITZERLAND

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Introduction: Epidemiological studies of childhood epilepsy are of importance in order to compare incidence and prevalence rates, age distribution, inheritance, seizure types, epilepsy syndromes and treatment strategies.

Aim: To analyze epilepsy characteristics, outcome and antiepileptic drug (AED) use in a children's neurological department located in the southern part of Switzerland.

Method: All the children referred to and analyzed by our department were aged from birth to 16 years with the epilepsy diagnosis recognized between January 2002 and December 2009.

Results: One hundred eighty-three children (99 male/84 female) were included in the study. Mean age at first attack (range) was 5.2 (0–16) years. A majority of the patients, 58%, had focal or focal plus secondarily generalized seizures. Epilepsy was classified in 45% of patients. The most common syndrome of childhood absence epilepsy occurred in 20%, and rolandic epilepsy in 14%. Thirty-four percent showed different disorders associated with epilepsy: The most common associated disorders are cortical malformation (8%) and chromosomal abnormality (7%). Seventy-two percent were seizure-free at the last follow-up visit after at least 6 months. Antiepileptic drug (AED) treatment was used in 89% of patients (most common: valproate 38%, carbamazepine 11%, topiramate 10 %, sultiam 8%). Eighty-eight percent were on monotherapy, 9% on two drugs and 3% on three or more.

Conclusion: This study provided valuable information on epilepsy characteristics, outcome and AEDs in a child population in the southern part of Switzerland. Epilepsy was classified in 45% of the patients, more than two-thirds were seizure-free and the majority were on monotherapy.

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THE PREVALENCE OF ATYPICAL PRESENTATIONS OF BENIGN CHILDHOOD EPILEPSY WITH CENTRO-TEMPORAL SPIKES

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Purpose: Benign childhood epilepsy with centrotemporal spikes (BCECTS) is the most common epileptic syndrome in childhood. The outcome is usually excellent, but there are some atypical forms of BCECTS with less favorable outcome. The aim of this study was to delineate the frequency of these atypical features among BCECTS patients.

Methods: We conducted a retrospective chart study by retrieving the medical records of all consecutive patients with BCECTS who were evaluated in four pediatric neurology outpatient clinics in Israel between the years 1991–2008.

Results: A total of 196 BCECTS patients were identified (78 females and 118 males, mean age at time of diagnosis 7.64 years, range 1.5–14). The mean duration of follow-up was 4.43 years (range 2–11). Nine patients (4.6%) developed electrical status epilepticus in sleep (ESES) during follow-up, four (2%) had Landau-Kleffner syndrome, three (1.5%) had BCECTS with frequent refractory seizures, two (1%) had BCECTS with falls at presentation, one (0.5%) had a ''classic'' atypical variant, and one (0.5%) had oromotor dysfunction. None had rolandic status epilepticus. Sixty-one (31%) patients had attention deficit hyperactivity disorder (ADHD), 43 (21.9%) had specific cognitive deficits, and 23 (11.7%) had behavioral abnormalities, including aggressiveness, anxiety disorders, depression and pervasive developmental disorder.

Conclusions: The prevalence of most atypical forms of BCECTS other than ESES is low. There is, however, a high prevalence of ADHD and specific cognitive deficits among BCECTS patients.

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CLINICAL FEATURES, DIAGNOSTIC PITFALLS AND PROGNOSIS IN JUVENILE MYOCLONIC EPILEPSY: A SERIES OF 83 PATIENTS

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Purpose: Juvenile myoclonic epilepsy (JME) is common genetic electroclinical syndrome of adolescents and adults. Despite of typical clinical and EEG features it is often under- and misdiagnosed.

Method: We retrospectively analyzed clinical and diagnostic data and prognosis of 83 JME patients (36 male, 47 female) aged from 16 to 41.5 years (mean 25.7), with mean seizure onset of 14.3 years (range 8.5–20.5).

Results: Myoclonic jerks were associated to generalized tonic–clonic seizures (GTCS) in 79.5% and to typical absences in 22.9% cases. Only 43.4% patients were correctly diagnosed at entry visit. In 21.7% the misdiagnosis of focal epilepsy was related to failure in eliciting a history of myoclonic jerks and their misinterpretation as focal motor seizures (11) or absences as complex partial seizures (7). Initial EEG asymmetry/focal abnormalities were misleading in 27.7%. A mean diagnostic delay of 2.14 years was found. Complete seizure control was achieved in 63 (75.9%) patients mainly with valproate (54 patients). Pseudo-resistant seizures occurred in 8 9.6%, while JME was refractory in14.5% patients. Therapy was discontinued in 35 (42.1%) patients (in16 by own initiative). In 21/35 subjects seizures relapsed after mean 1.1 year (range 7 days to 4 years) and AED was restarted. In 4/35 the AED was reintroduced because of EEG aggravation. Seizure and drug freedom of mean 5.1 years (range 3.5–12 years) was noted in12% patients.

Conclusion: Failure in eliciting a history of myoclonic jerks and misinterpretation of seizures and EEG abnormalities as focal epilepsy are the main diagnostic pitfalls. Seizure and drug freedom was noted in 12% patients.

Poster session: Pediatric epileptology II
Monday, 29 August 2011

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MENTAL DEVELOPMENT OF INFANTS AT CORRECTED AGE OF 24 MONTHS AT HIGH RISK OF IMPAIRED DEVELOPMENT AND EPILEPSY ATTRIBUTED TO PERINATAL INSULTS DISCHARGED FROM NEONATAL INTENSIVE CARE UNIT

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Purpose: To determine the mental development (MD) of infants at corrected age of 24 months at high risk of impaired development and epilepsy attributed to perinatal insults (EAPI) discharged from neonatal intensive care unit (NICU).

Method: Newborns at risk for neurodevelopmental abnormalities were included. Follow-up visits were performed after they were discharged from NICU. Because of multiple perinatal insults, all of them were considered at increased risk for long-term neurodevelopmental deficits. MD Index (MDI) of infants was evaluated through the Bayley Scales of Infant Development (BSID-II) when they were at corrected age of 24 months. One-sample Kolmogorov-Smirnov test was performed to analyze the normal distribution of the sample. ANOVA and Tukey HSD post hoc test were used for statistical analysis. To determine the association or independence between neonatal seizures (NS) and EAPI, a χ^2 test was performed. MDIs from 15 healthy infants were used as control data (HIgroup).

Results: Thirty-eight infants discharged from the Hospital de Especialidades del Niño y la Mujer were followed-up. All of them had neurohabilitation therapy. NS were documented in 13 (34%) of the patients (NSgroup); 12 (32%) developed EAPI (Egroup), and 13 (34%) had increased risk for long-term neurodevelopmental deficits but no NS background or epilepsy was documented in any of them (RFgroup). The Kolmogorov-Smirnoff test showed normal distribution in the sample ($Z = 1.162$, $p = 0.134$); homogeneity of variance showed no differences between the groups ($p = 0.459$). Since χ^2 value was 6.2 ($p < 0.02$) it was accepted that epilepsy attributed to perinatal insults was independent of NS. MDI showed differences between the groups ($p = 0.004$) and epileptic infants had the worst MDI; when Egroup and NSgroup were compared with HIgroup, statistical differences were seen ($p = 0.008$ and $p = 0.014$, respectively). However, there were no differences between RFgroup and HIgroup and between Egroup and NSgroup.

Conclusion: Infants at risk of impaired development and NS background or EAPI may have poor prognosis in MD; EAPI is independent of NS. Both of them have a negative effect on MD despite infants received neurohabilitation.

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NEONATAL SEIZURES WITH DIFFUSION RESTRICTION LESIONS ON BRAIN DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING: ARE THESE FIFTH DAY FITS?

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Purpose: We have experienced the neonates with seizures who showed diffusion restriction lesions in the cerebral white matter on brain diffusion-weighted magnetic resonance imaging (DWI). We aim to describe the clinical characteristics and DWI findings of these neonates.

Methods: A total of 30 term neonates who presented with seizures were admitted at Ulsan University Hospital between January 2008 and October 2010. Of these neonates, 13 (group A) had the following characteristics in brain DWI: (1) diffuse lesions in the bilateral cerebral white matter, including the corpus callosum; and (2) no cerebral cortical lesions. The remaining 17 patients (group B) did not have the aforementioned characteristics in brain DWI. We compared clinical characteristics between the two groups.

Results: The 5-min Apgar score was more than 9 in all group A patients, while it was diverse in group B patients. Patient age at seizure onset was 4.62 ± 0.65 days (range, 4–6 days) in group A, and 8.29 ± 7.37 days (range, 1–27 days) in group B. Twelve (92.3%) of 13 patients in group A and 2 (16.7%) of 12 in group B were positive for stool rotavirus antigen tests ($p < 0.001$). Six of 10 patients in group A showed normal development, but four had a neurodevelopmental delay between 6 and 30 months of age.

Conclusion: The clinical characteristics of neonates with seizures who had the aforementioned characteristic DWI findings seem to be similar to those of fifth day fits. Rotavirus infections might be one of their main causes.

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CHARACTERISTICS OF BENIGN CONVULSION WITH ROTAVIRUS GASTROENTERITIS

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Purpose: To identify the characteristics of benign convulsion with rotavirus gastroenteritis by comparing cases with and without fever among children with seizures accompanying rotavirus gastroenteritis.

Method: The medical records of patients aging from 5 to 59 months old with positive stool rotavirus antigen tests, who were admitted to our hospital, between January 1999 and June 2010 were retrospectively reviewed on the aspects of epidemiologic characteristics, clinical symptoms, treatment, etc. Subjects were divided into three groups: control (rotavirus gastroenteritis without seizure), febrile (rotavirus gastroenteritis with seizure and fever), nonfebrile (rotavirus gastroenteritis with seizure and without fever).

Results: Among the 690 subjects, the number of patients for each group was 652 (94.50%) for the control group, 19 (2.75%) for the febrile group and 19 (2.75%) for the nonfebrile group. The mean age was 19.56 ± 9.57 months (control), 20.37 ± 7.26 months (febrile), 20.84 ± 7.41 months (nonfebrile), respectively. All three groups showed high annual incidence between December and May. There was no significant difference in the aspects of gastroenteritis symptoms such as vomiting, diarrhea, decreased activity, poor oral intake. However there was a statically significant difference between the febrile group and the nonfebrile group on aspects of the duration of diarrhea before the 1st episode of seizure and after the 1st episode of seizure. The onset of the 1st episode of seizure in patients of the nonfebrile group appeared to occur later than patients of the febrile group after diarrhea first began ($n = 2.95$ days, $n = 1.16$ days, $p = 0.0002$). Moreover, diarrhea appeared to cease earlier after the 1st episode of seizure in patients of the nonfebrile group than patients of the febrile group ($n = 1.84$ days, $n = 3.42$ days, $p = 0.0337$). However, there was no statistical difference in the total duration of diarrhea in both groups ($n = 4.79$ days, $n = 4.58$ days, $p = 0.7686$).

Conclusion: The differences in the duration of diarrhea before and after the onset of the 1st episode of seizure in the febrile group and the nonfebrile group might occur due to the differences in the pathophysiology of both diseases.

p197
CHARACTERISTICS OF THE PEDIATRIC PATIENTS WITH POSTSTROKE EPILEPSY

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Purpose: Ischemic stroke in children is a rare disorder occurring in about three cases per 100,000 children per year. A history of acute brain ischemia is burdened with consequences such as motor impairment (hemiparesis observed most commonly), speech impairment and intellectual regression. Particularly, noteworthy is the problem of epilepsy after an ischemic stroke in children. The aim of the study was to characterize a group of children with epilepsy that occurs as a consequence of stroke and assessment of serum lipids and fibrinogen in these patients.

Method: We examined 12 stroke patients with epilepsy (mean age: 5.33 ± 4.38) and 15 healthy children (mean age: 11.60 ± 3.20). Levels of total serum cholesterol (TC), HDL-cholesterol and triacylglycerols (TG) were measured using enzymatic methods. Fibrinogen concentrations were measured using coagulometer method and commercial kit. Data were analyzed with the STATISTICA 7.1 software.

Results: The most common stroke subtype was TACI, present in seven patients (58%). The PACI stroke was present in 17%, LACI – in 17% and POCI – in 8%. Epileptic seizures in all of the patients were focal in nature, some children had seizures with secondary generalization. Most of the patients received treatment with carbamazepine and seizure control in monotherapy has been satisfactory. One patient was even able to discontinue anticonvulsant therapy. Forty-two percent of the patients were treated with two or three antiepileptic drugs. Ninety-two pecent of the patients had focal cerebral arteriopathy (FCA). We observed that levels of total cholesterol, LDL-cholesterol, triacylglycerols and fibrinogen were higher, although not significantly, in children with epilepsy after stroke than in controls ($p = 0.567$, $p = 0.249$, $p = 0.138$ and $p = 0.280$ respectively).

Conclusion: Epilepsy after stroke seems to be related to FCA. Tendency to higher level of triacylglycerols in epilepsy patients compared to healthy children was also observed.

p198
EPILEPTIC AND NONEPILEPTIC SEIZURES ASSOCIATED WITH INFLUENZA A/B AND PARAINFLUENZA III IN CHILDREN DURING THE 2008–20011 INFLUENZA SEASON AT NEUROPEDIATRIC UNIT OF UH SESTRE MILOSRDNICE IN ZAGREB, CROATIA

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Purpose: The aim of this study was to describe the clinical characteristics and viruses isolated from patients who presented with seizures associated with influenza A/B and Parainfluenza III infection and were hospitalized from January 2008 to March 2011.

Method: We reviewed the medical and laboratory records of all children who were hospitalized at Neuropediatric Unit with seizures and had no clinical evidence of influenza virus infection, but infection was proven by rapid antigen testing.

Results: Twenty one children aged 1–16 years with seizures associated with influenza A (13), B (3), A + Parainfluenza III (1) and Parainfluenza III (4) were identified. None of the children had received the influenza vaccine. Nine presented with febrile seizures, two with first afebrile seizures, five with afebrile fits having previously diagnosed and well

controlled epilepsy, four had syncopal attacks and one had acute somnambulism. All had influenza A/B or Parainfluenza III viral antigen detected in nasal wash samples. None of the patients had serum metabolic abnormalities or bacterial superinfection. All patients were treated with symptomatic therapy and had complete recovery.

Conclusion: Febrile seizures and epileptic or nonepileptic convulsions were associated with influenza A/B or Parainfluenza III virus infection in children during the 2008–20011 influenza season (November to February) at the Neuropedatric Unit of UK Sestre milosrdnice in Zagreb. Influenza should be considered in the differential diagnosis in patients with febrile and afebrile seizures, exacerbation of epileptic fits and in nonepileptic seizures, even if they present without respiratory symptoms during an influenza period.

p199
SYNDROMIC CLASSIFICATION OF EPILEPSY IN PATIENTS WITH EYELID MYOCLONIA

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Purpose: One of the difficulties in the delineation of Jeavons syndrome (JS) is the impossibility to determine the age of seizure onset since many patients are unaware of eyelid myoclonia (EM), which is misinterpreted as tic or mannerism and the brief absence seizures are frequently overlooked. Although considered as an idiopathic syndrome, intellectual impairment has been described. Our aim was to classify epileptic syndromes in a series of patients with EM.

Method: Patients with EM were submitted to video-EEG and had clinical features evaluated.

Results: EM was recorded in 17 patients. Twelve met criteria for JME diagnosis (Commission, 1989) presenting limb myoclonia beginning between 7 and 26 years old. Among these, only three could inform EM onset between 14 and 18, the others being unaware of them. One female patient had features of JS with EM onset at four. Another female had generalized spike-wave complexes 3/s described in JS but presented learning disability. Two female patients had EM and the features described by Capovilla et al. (Epilepsia 2009;50:1536–41) as impaired intellectual function and ictal generalized polyspikes with intermixed slow waves. The last patient, a male, had convulsions at two, limb myoclonia at seven and EM at 18. We considered him as a possible JME patient with an extreme age of onset. Taken altogether, familiar history for epilepsy was present in nine and consanguinity in three. All patients, except three older than 30 in the JME group, had eye-closure and photo sensitivity with generalized discharges.

Conclusion: A syndromic diagnosis is generally possible for patients with EM.

p200
VISUAL INDUCED SEIZURES IN REFLEX EPILEPSIES AND EPILEPSIES WITH REFLEX SEIZURES

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Purpose: To determine any differences or similarities between children with reflex seizures alone (Reflex Epilepsies = RE) and those with both spontaneous and reflex seizures (Epilepsies with Reflex seizures = E + RS).

Method: We studied 209 patients (103 males and 106 females; mean age13.14 ± 7.02 years; mean follow up 6.57 years) with RE (49) or E + RS (160). RS were identified on the basis of medical history, semi-structured interviews with patients and parents, and questionnaires on environmental risk factors for visual stimuli. Visual sensitivity was confirmed by video-EEG recording with standardized procedures of visual stimulation (IPS, Pattern-Stimulation, and 30 min of TV watching). Statistical analysis was performed by chi squared and ANOVA test.

Results: RS were more frequently focal in RE (63% vs 51%) and predominantly generalized in E + RS (38% vs 18%) (p 0.03079). Differences were found in the distribution of paroxysmal EEG abnormalities at rest: occipital foci were more common in RE than in E + RS (71% vs 52.5%), whereas generalized abnormalities (10%) and not occipital foci with secondary generalization (5.5%) were observed only in E + RS (p 0.04879). Moreover, significant differences were found for CT/MR brain imaging, with prevalence of normal findings in RE (81% vs 51%) and focal not occipital lesions in E + RS (38% vs 18%) (p 0.03079). Self-induced seizures were more common in RE than in E + RS (51% vs 31%; p 0.0146).

Conclusion: RE differ from E + RS for the prevalence of focal seizures with occipital EEG abnormalities, normal brain imaging, and higher recurrence of self-induction.

p201
VISUAL EVOKED POTENTIALS AND NEUROLOGIC OUTCOME IN CHILDREN WITH SYMPTOMATIC EPILEPSY

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Purpose: In infants with symptomatic seizures it is very difficult to predict accurately neurologic outcome and evaluate the visual functions.

Visual evoked potential (VEP) is a reproducible measure of cortical function and can predict the neuro developmental outcome. We performed VEPs on 56 patients from 2 months to 3 years to investigate the relationship between VEPs and neuro developmental outcome.

Method: The 1st group consisted of 30 infants with focal symptomatic epilepsy, the 2nd – 16 infants with generalized symptomatic seizures, the 3rd – healthy infants.

Results: The maximum delay of latency (37, 4 ± 30 mc) of component P100 of the VEPs and more expressed disturbances of carrying out of impulses on visual ways were found in 1st group. In patients from second group the latency delay and decrease of amplitude have been less expressed in comparison to patients with focal epilepsy. At 32% of patients from the first group the cortical visual impairment with disturbance of visual reactions and optic nerve hypoplasia have been determined. Severe motor and psychological disorders at 36 % of children from the 1st and 26% in 2nd group were observed. In 3rd group all had normal VEPs and neurodevelopment during the first 6 months of life.

Conclusion: Delay of latency and decrease of amplitude of the main VEPs component are very specific findings in children with symptomatic epilepsy.

VEPs demonstrate quite good correlation with neuro developmental outcome in infants with symptomatic epilepsy and very useful in the clinical management of these infants.

Poster session: Pediatric epileptology III
Monday, 29 August 2011

p202
JEAVONS SYNDROME; OCCIPITAL CORTEX INITIATING GENERALIZED EPILEPSY

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Purpose: Jeavons syndrome (JS) is one of the underreported epileptic syndromes characterized by eyelid myoclonia (EM), eye closure-induced seizures/EEG paroxysms, and photosensitivity. JS has been proposed as idiopathic generalized epilepsy (IGE) because of normal posterior dominant background activity and paroxysmal generalized ictal epileptiform discharges (EDs). However, we noticed subtle occipital EDs preceding EM and interictal posterior EDs using digital video EEG. We studied clinical and EEG findings in JS to determine the specific occipital lobe relation to this ''eye closure induced''reflex IGE.

Methods: We identified 12 children who met the diagnostic criteria of JS from January 2004 to April 2009 at the Hospital for Sick Children, Toronto, Canada. All patients had EM captured by video-EEG. We reviewed and described ictal EEG patterns, interictal abnormalities, demographics, clinical and neuroimaging findings.

Results: All patients but one were female (92%). Age at seizure onset ranged from 1.5 to 9 years, with a mean age of 4.9 years. Six patients (50%) were previously diagnosed as having absence epilepsy and 10 patients were on antiepileptic medications. All of them had normal posterior dominant alpha rhythm, reactive to eye opening and closure. Spiky posterior alpha activity was noted with sustained eye closure in six patients (50%). Interictally, there were generalized EDs found in 10 patients (83%); four of them also had focal interictal EDs over the posterior head region. Eleven patients (92%) had evidence of focal posterior ictal EDs. EM and/or paroxysmal EDs were induced by photic stimulation in 9 (75%) and hyperventilation in 7 (58%).

Conclusion: We observed two neurophysiological findings in JS; 1, focal interictal EDs from posterior head region; 2, predominant focal posterior ictal EDs preceding generalized EDs. Further clinical observations of seizures induced by eye closure, photic stimulation and hyperventilation along with EEG paroxysms would raise the possibility of the occipital cortex initiating generalized epilepsy network involving the brainstem, thalamocortical and transcortical pathways in JS.

p203
EXERCISE THERAPY IN CHILDREN WITH BENIGN ROLANDIC EPILEPSY

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Purpose: To evaluate the benefits and safety of exercise in children with epilepsy focused on benign rolandic epilepsy (BRE).

Method: Ten school age children with BRE (boys = 4, girls = 6, aged 8–12 years (M = 9.7, SD = 1.42) were participated in therapeutic exercise program, consisting of 10 times supervised exercise and 6 weeks home-based exercise. EEG, seizure frequency, neuropsychological and psychological battery (evaluation on attention, executive function, depression, anxiety, sociobehavioral problem, quality of life) were assessed before and after exercise program.

Results: (1) Seizure frequency was not changed. (2) Computerized EEG analysis showed significant decrease in sharp wave amplitude after exercise program. (3) Significant improvement was seen in neurocognitive domains such as visual and auditory simple attention, sustained attention, divided attention, psychomotor speed, and inhibition-disinhibition ability and despite not up to significant level, working memory had also a tendency of improvement. (4) In Child Behavior Checklist (CBCL) and depression/anxiety scale, internalizing and externalizing behavioral problems were reduced. Internalizing problems were up to significant level of reduction, among them, somatic and social problems were declined by significant level. (5) In quality of life assessment, physical, mood, cognition, and social function were improved.

Conclusion: Adequate, well-designed exercise program showed significant benefits mostly in neurocognitive and psychobehavioral function without seizure worsening in children with epilepsy.

p204
VITAMIN B12 DEFICIENCY: AN IMPORTANT CAUSE OF INFANTILE SEIZURES

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Purpose: Deficiency of B_{12} due to low amounts of intake alone, is quite rare, and generally limited to vegan children, who are at risk due to higher needs of the vitamin, no intake of animal products that contain it, and low body stores. In our country the incidence of nutritional B12 deficiency is increasing in all age groups. Hematologic, dermatologic, gastrointestinal and neurologic findings are main features. Neurologic findings can occur in the absence of anemia or macrocytosis. In the case of breast-fed infants of vitamin B12-deficient mothers, symptoms and signs usually consisted of movement disorder, developmental delay and seizures.

Method: Seven cases (five female, two male) with B12 vitamin deficiency are presented. Metabolic tests including urine organic acids, amino acid chromotography, homocystein, biotinidase, lactic and pyruvic acid, EEG and cranial magnetic resonance imaging were done.

Results: All of the cases were only breast-fed. Three of the cases hospitalized with afebrile seizures, otherwise the reminder admitted with developmental delay. Hypotonia, failure to thrive, feeding difficulties were the most significant clinical symptoms. EEG displayed epileptic discharges in three cases. Cranial magnetic resonance imaging demonstrated cortical atrophy in five of the cases.

Conclusion: Although symptomatic cobalamin deficiency is rare in childhood, it can occur as a consequence of inadequate dietary intake especially in children who are only breast-fed. It must be keep in mind in infants with developmental delay and seizures.

p205
CLINICAL PRESENTATIONS AND SEIZURE RECURRENCE IN THAI CHILDREN WITH FIRST UNPROVOKED SEIZURE

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Purpose: To determine chance of seizure recurrence and its risk factors in children with first unprovoked seizure in Thai children for further application in the country.

Method: From January 1st 2004 to March 31st 2010, children aged from 1 month to 15 years presenting with first unprovoked seizure at a university hospital located in Bangkok, Thailand, were included into this cohort study. Demographic data, initial investigations and duration to seizure recurrence were collected for descriptive analysis. Predictions of seizure recurrence were determined by Kaplan–Meier and Cox regression analysis.

Abstracts

Results: There were 57 children (28 boys and 29 girls) aged 8 ± 3.7 years (ranged 1–15) included to a cohort study. They were followed from 12 to 79 months (mean 39.4 ± 19.4 months). Thirty children had focal with secondarily generalized seizures. All had standard EEG recording which revealed epileptiform discharges in 68.4%. Benign epileptic syndromes were diagnosed in 23 children. Among 28 children who had brain imaging, 10 had nonspecific abnormality. Twenty-six children received continuous antiepileptic drug due to parental request. Thirty children (52.6%) experienced subsequent seizures. The cumulative risk of seizures recurrence was 47%, 49%, 51% and, 59% at 1, 2, 3 and 4 years, respectively. Multivariate analysis identified developmental delay as the only risk factor for seizure recurrence.

Conclusion: Recurrent seizure after first unprovoked seizure in Thai children is similar to previous studies. Delay in developmental milestones is the predictor of recurrent seizure. Long-term prophylactic treatment with antiepileptic drug did not change risk of recurrence.

p206
STATUS EPILEPTICUS IN CHILDHOOD ENCEPHALITIS: A 13 YEAR RETROSPECTIVE SINGLE CENTER STUDY

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Purpose: Encephalitis (brain inflammation) is a potentially devastating illness in childhood with significant morbidity and mortality. Seizures are common in encephalitis however there is limited literature on status epilepticus in childhood encephalitis.

Method: A clinical retrospective chart review of all immunocompetent children between ages of 1 month to 17 years presenting with acute encephalitis from 1998 to 2010 at the Children's Hospital at Westmead was approved by the hospital ethics committee. Patients with acute disseminating encephalomyelitis were not included in this cohort. One hundred and twenty-four patients were identified.

Results: Status epilepticus was present in 25 of 124 patients at some stage during the illness (20%), and 14 patients presented with status epilepticus on admission (11%). The median age was 4.8 years (range: 0.7–15.1 year) and the male to female ratio was 1.3:1. CSF pleocytosis was present in 13 of 25 patients (52%) and the brain MRI (n = 24) was abnormal in 17 patients (71%). The EEG was abnormal in 23 of 24 patients (96%). Admission to the intensive care unit was required for 20 of 25 patients (80%) with a median length of stay of 7.5 days (range 1–280 days). An infectious etiology was identified in 10 patients (40%); confirmed (n = 3, enterovirus), probable (n = 2, Mycoplasma pneumonia) and possible (n = 5). The only noninfectious etiology identified was voltage gated potassium channel antibodies in three female patients (12%). The outcome data (n = 20) was unfavorable in 15 patients and included death (n = 1) and ongoing epilepsy (n = 12) at median follow up of 22 months (range 1–86 months).

Conclusion: Status epilepticus in children with encephalitis highlights an at risk population who require aggressive symptomatic seizure control, supportive management and a detailed investigation of potential infective and noninfective etiologies.

p207
SCN1A-RELATED SPECTRUM OF FOCAL EPILEPSY WITH FEBRILE SEIZURES PLUS IN POLISH FAMILY

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Introduction: Mutations in the gene *SCN1A,* coding for the α1 subunit of the sodium channel NaV1.1, have been associated with various types of epilepsy. Clinical spectrum of *SCN1A* mutations ranges from febrile seizures (FS) and quite benign generalized epilepsy with FS plus (GEFS+) to severe epilepsy syndromes such as Dravet syndrome. *SCN1A* mutations have been also found in patients with other epilepsy syndromes, e.g., focal epilepsies and in rare cases of familial hemiplegic migraine and familial autism as well.

Purpose: To presend the family with *SCN1A*-related spectrum of focal epilepsy with febrile seizures plus.

Method: Clinical, EEG and genetic data of proband and other family members were analyzed.

Results: The proband is 4-year-old girl with normal cognitive development. Onset of focal seizures always involving left side of the body, with sometimes secondarily generalization was in 8 months of life. Only minorities of her seizures were induced by hyperthermia. EEG samples were normal or showed single sharp waves/sharp and slow waves in both centro-parietal regions, predominantly on right side. Family history revealed FS and FS plus in five members out of 3-generation family. Molecular analysis showed the single nucleotide change in the exon 25 – genotype [c.4787G>A] + [=]; missense mutation p.Arg1596His, of paternal inheritance. The mutation was also found in proband's affected sister and the other family members, who showed epileptic phenotype.

Conclusion: The phenotype of proband epilepsy (focal, and not side-alternated seizures, and in majority of fits not being induced by hypertermia) indicated rather cryptogenic than genetic etiology. The suggestion of channalopathy as the possible etiology of epilepsy was provided by family history showing the autosomal dominant pattern of disease inheritance.

Identification of the molecular defect allowed us to avoid further unnecessary investigations and to choose appropriate management.

p208
EPILEPTIC ENCEPHALOPATHY WITH EPILEPTIC ATONIA OF THE MUSCULUS MENTALIS DURING SLEEP

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Purpose: Epileptic atonia of musuclus mentalis (EAMM) which is associated with diffuse spike-waves during non–rapid eye movement (REM) sleep can only be detected by performing PSG together with EMG of the musclus mentalis. The outcome in those patients with EAMM remains unclear.

Method: The study included eight patients who had daily seizures with multiple types, and were diagnosed with intractable epileptic encephalopathy (e.g. Lennox-Gastaut syndrome, Doose syndrome, West syndrome). These patients were admitted to Tokyo Medical University Hospital for treatment and examination between 1990 and 1994, and were prospectively followed-up for the average of 16 years.

Results: EAMM developed from the average age of 4 years (range 6 month–7 year 3 month). During EAMM episodes, the sleep EEG showed abundant diffuse spike-waves with focal abnormalities. These EEG abnormalities became localized after EAMM disappeared. In overnight PSG, EAMM episodes were observed 130–317 in 1 night with reduction of %REM sleep. Patients who had EAMM for more than 2 years (range 2 year 9 month–4 year 2 month) had uncontrolled seizures and severe mental deficits (IQ/DQ range 20–34), and those who had EAMM for <1 year (range 1–2 month) were seizure-free and had mild mental retardation (IQ/DQ range 48–92). In most cases where EAMM disappeared, the patients had been prescribed valproate and benzodiazepines.

Conclusion: Patients with EAMM have mental retardation together with epilepsy that has poor prognosis. Although the sample size of our study is

small, our results suggest that frequent EAMM episodes, i.e., more than 100 episodes in 1 night, can aggravate epilepsy.

p209
SHORT-TERM PROGNOSIS OF MYOCLONIC ASTATIC EPILEPSY (MAE)

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Purpose: Retrospective study was conducted at the Iashvili Children's Central Hospital to evaluate influence of EEG patterns and clinical signs of MAE on seizure control and mental development.

Method: Twelve patients with MAE were evaluated and monitored at least 1 year. Patients evolved to MAE from West syndrome were excluded. All patients underwent regular EEG monitoring and developmental assessment. Mental development was assessed by Kaufman Assessment Battery for Children before treatment and once per year regularly.

Results: A total of 12 children were enrolled; mean age of 5 years, 8 (66%) were male; mean age at MAE onset was 32 months. All children had a normal development by the time of MAE diagnosis. Two children had a positive family history of seizures; 8 (66.7%) had a stormy onset of MAE. Two of them had second stormy episode. Among children with stormy onset three had epileptic encephalopathy (EE) Seizure freedom was achieved in 8 (66.67%) children. Duration of remission varied from 2 to 5 years, mean 30 months. Development remain normal in 5 (41.67%). Half of the children experienced more than three seizure types. Having of more than three seizure types was associated with unfavorable outcome with OR 2.1 CI (0.091, 48.871). Supposedly because of the very small sample size statistical significance was not detected. Four patients continued to have seizures, three of them frequent seizures. Existance of second stormy phase and EE was associated with poor seizure outcome and mental retardation. Mental retardation was mild in all cases. Nocturnal tonic seizures, age at onset of MAE, duration of active epilepsy did not influance outcome.

Conclusion: Children experiencing more than three types of seizures might have an increased risk of poor outcome in terms of development and seizure control. Nocturnal tonic seizures, age at onset of MAE, duration of active epilepsy are not predictors of prognosis. Further research on larger sample size is necessary.

Poster session: Pediatric epileptology IV
Monday, 29 August 2011

p210
NEUROPSYCHOLOGICAL FINDINGS AND PSYCHIATRIC COMORBIDITIES IN CHILDHOOD IDIOPATHIC GENERALIZED EPILEPSIES

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Purpose: Idiopathic generalized epilepsies (IGE) represent the 31% of pediatric epilepsy syndromes; seizures are easily controlled by AEDs, therefore they have always been considered among epilepsies with a benign course and still little data exist about social and academic long-term outcome.

Method: We describe the neuropsychological and psychopathological profile and the assessment of reading, writing and calculation skills in 14 patients. All the patients had absence seizures, four of them had experienced also tonic–clonic seizures. Epilepsy was easily controlled by medication, EEG was normal in all of them. Attention, short-term verbal and spatial memory and reading abilities were compared with a control group. Correlations with disease-related factors have been searched.

Results: A diagnosis of learning disorder (LD) was present in 9 out of 14 patients: three patients had only reading impairment, two had an impairment of calculation ability, in three patients both disorders were present and in one patient a writing disorder was associated with calculation difficulties. Attention or memory deficit could not explain the disorders and significant difference was found only in reading abilities between the two groups. Children affected by IGE showed also a higher score on internalizing problems on CBCL (particularly somatic complaints) than healthy controls.

Conclusions: In our study diagnosis of IGE was a risk factor for LD. We confirm the need of neuropsychological and psychopathological evaluation to avoid overlooking of problems that can lead to a poor social and academic achievement described in these children.

p211
SOCIAL STATUS OF PATIENTS WITH EPILEPSY ACCORDING TO THE EPILEPSY REGISTER IN SELECTED REGIONS OF KAZAKHSTAN (EREKA)

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Purpose: To determine the forms of employment of epileptics.

Method: A national, multicenter, uninterventional studies (EREKA).

Project Supervisor: Sanofi Aventis.

Inclusion criteria: Patients with any type of epilepsy, including newly diagnosed, without reference to the tactics used in treatment.

Results: During the period of 2008–2009 there had been identified and comprehensively studied 1897 patients with epilepsy aged from 0 to 63 years. Status of patients with epilepsy based on 18 standardized groups featured on the form and type of seizure, duration of disease, treatment. Evaluation of the social status of patients according to EREKA proved to be disappointing. Only 43.8% are studying, do physical or mental job. Patients at the age of 7–18 years, enrolled in secondary school - 247 (50.7%), children in special schools 6.37%, 8.62% studying at home. At the age of 19–25 the ratio of employed at mental and physical labor 151:40 (3.8:1), and over 25 years–181:140 (1.3:1).

Registered in social security authorities 24.6%. 31.6% of people suffering from epilepsy are not studying, not working, do not receive state subsidies.

Conclusion: Epilepsy is essentially maladjusted patients: 24.6% of patients are disabled, 31.6% were not registered yet, but do not work. Patients with epilepsy have lower level of education, social activity. Treatment of patients with similar social problems is complicated by low komplaentiency of these patients. There should be additional efforts in order to obtain and adequately analyze the burden of epilepsy in the structure of disability of the Republic of Kazakhstan.

p212
DEVELOPMENTAL ABNORMALITIES IN CHILDHOOD EPILEPSY

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Abstracts

Purpose: Developmental abnormalities of CNS, which occur as a result of errors in the process of normal morphogenesis and lead to malformation syndromes, are commonly related with appearance of childhood epilepsy. The aim of this work is to present different kind of developmental abnormalities in our group of children with epilepsy.

Methods: The files of eighty-four children are evaluated by taking in consideration their sex, age and diagnosis; pediatric and neurological examination; CTM, MRI of the brain and EEG results; presence of mental retardation and the applied therapy.

Results: From a total of eighty-four children (thirty-five girls and forty-nine boys, born between 1999 and 2009, with epilepsy), morphological abnormalities are verified in twenty-nine children with neuroimaging methods. Most common developmental abnormalities are: agenesis of the corps callosum in two children; hypoplasia of corpus callosum in one child; lissencephaly in one child; schizencephaly in one child, polymicrogyria in one child; dysplasia in four children; porencephalic cysts (single and double) in four children; colpocephaly in two children; hydrocephalus in five children, empty sella in two children; mega cisterna magna in five children; congenital demyelinization in one child. It was not uncommon to find combinations of above-mentioned abnormalities and additional changes like gliosis, global cerebral atrophy, widened subarachnoid spaces, asymmetry in volume and dimension of the hemisphere. In ten children, there were neurological disorders; mild mental retardation in sixteen children; moderate mental retardation in three children and two children with severe mental retardation; sy Aicardi in one child; sy West in four children; absence epilepsy in one child. EEGs in all children are with epileptiform changes. Monotherapy was applied in eight children, polytherapy in the rest (most used being the classic antiepileptic drugs, equally the new generation like levetiracetam, topiramate, lamotrigine and stiripentol in diverse combinations).

Conclusion: Epilepsy in developmental disorders of CNS is generally pharmacoresistant, associated with intellectual deprivation. Ante natal prevention, regular examination (echo, biochemistry, etc.) during pregnancy and genetic counseling are indispensable.

p213
EXTENSIONAL CHANGES IN CURRENT-SOURCE DENSITY IN BENIGN ROLANDIC EPILEPSY PATIENTS

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Purpose: Interictal spikes are diagnostic markers of benign rolandic epilepsy (BRE). Their frequency, location, and persistence do not appear to indicate the clinical manifestations, severity, or frequency of seizures or the prognosis of BRE. However, it has been suggested that seizure control is associated with changes or suppression of interictal changes although the underlying neurophysiological mechanisms have not been clarified. In this study, we evaluated whether seizure control or clinical manifestations were associated with changes in the epileptogenic neuronal area.

Method: In this pilot study, we assessed five children (aged 7–11 years) with BRE using low-resolution brain electromagnetic tomography (LORETA) for comparing interictal spikes with the maximum negativity between EEG recordings obtained just before treatment and after 6–12 months of antiepileptic drug medication. Patients who remained seizure-free for a minimum of 6 months with no breakthrough seizures were defined as patients with effective seizure control or good clinical course.

Results: Of our five patients, three had effective seizure control; these three showed a decrease in the extension of current-source density. In contrast, the two patients who suffered multiple breakthrough seizures were noted to have increased extensions of current-source density.

Conclusion: Our results suggested that seizure control patterns or the clinical course of BRE may be associated with extensional changes in the current-source density, and therefore, with changes in the epileptogenic neuronal areas.

p214
ADOLESCENTS' KNOWLEDGE AND ATTITUDES TOWARD EPILEPSY COMPARED WITH ASTHMA IN PORTUGAL

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Epilepsy is one of the most common chronic diseases among children and teenagers and is associated with an important social stigma. Asthma is the most prevalent chronic disease in this age group.

Purpose: To evaluate knowledge and attitudes towards epilepsy compared with asthma, among Portuguese teenagers.

Method: Two questionnaires on knowledge and social impact of epilepsy and asthma, respectively, were applied to teenagers attending three schools from three different places in Portugal. Each student answered both questionnaires individually.

Results: A total of 110 students aged between 13 and 16 participated in this study. Most teenagers have heard about epilepsy (96.4%) and asthma (97.2%). There were significant differences ($p < 0.05$) between the students' knowledge on both diseases: there were less correct answers regarding the definition of epilepsy, its treatment and prevalence, and more correct answers about the clinical course of the disease, when compared to asthma. The majority of students disclosed they would be more low-profile in revealing their own epilepsy diagnosis. Whereas most teenagers stated they would date or marry someone with asthma, in what concerns epilepsy there is a 10% reduction in positive answers. Only 6.3% of the surveyed students would act properly while assisting someone with a seizure.

Conclusion: According to the results, among teenagers there is still a lack of knowledge, incorrect attitudes and some degree of social stigma in what concerns to epilepsy, when compared to asthma. This pilot study highlights the need to improve teenagers' knowledge and attitudes regarding epilepsy.

p215
ADAPTATION AND VALIDATION OF LIVERPOOL ADVERSE EVENTS PROFILE (LAEP) IN PEDIATRICS PATIENTS WITH EPILEPSY AND ITS CORRELATION WITH THE LEVEL OF QUALITY LIFE OF CHILDREN WITH EPILEPSY (CAVE)

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Purpose: Adverse effects of antiepileptic drugs (AEDs) are common in pediatric patients suffering from epilepsy. In adults there are standardized and validated questionnaires on patients with epilepsy, such as LAEP, but not the pediatric population.

Objective: Adapt and validate the scale LAEP on pediatric population as a means of detecting the adverse effects of AEDs. Analyze the correlation between the modified LAEP and the quality of life scale CAVE.

Method: An observational, cross-sectional multicenter study during a period of 12 months. We adapted LAEP scale to pediatrics patients with 21 item questionnaire. Each item is assessed on a 4-point Likert scale, and a global summary score ranging from 21 to 84. Sociodemographic and clinical (epilepsy etiology, seizure type, and antiepileptic drug treatment) data were collected at the moment of inclusion. The scale was applied in each patient less frequently than every 3 months.

Results: Modified LAEP and CAVE was applied to 411 children under 18 years with epilepsy. We find correlation between the LAEP scale and the CAVE (r Pearson -0.4037). Time for the test was < 5 min in 99% and the difficulty level was low in 88% of cases. The effects most frequently found in children under 3 years were agitation, weight loss, drowsiness, and over 3 years, behavior problems and difficulty in concentrating.

There was statistical significance between the frequency and intensity of seizures, polytherapy and the high score in LAEP. Improved scores on the LAEP to withdraw the medication and the maintenance dose at the time.

Conclusion: • Modified LAEP is the first scale to detect adverse effects of the AEDs applied in children.

• The systematic use of scales to predict the adverse effects of AEDs and the proper selection of AEDs can improve the quality of life.

p216
SCHOOL-AGED CHILDREN WITH PARTIAL EPILEPSIES AND MIGRAINE

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Epilepsy and migraine are two entities with various similar features, and differential diagnosis in some cases can be very hard, due to some overlapping features. Possible relationship is not completely understood; common underlying mechanisms are presumed, genetic and environmental factors probably play role.

Purpose: Aim of the study was assessing similarities and dissimilarities that should be worth of further investigation for better understanding of possible mutual mechanisms.

Method: Patients from two separate hospital-based studies, one on partial epilepsies in school aged children and other on migraine headaches in same population, were cross compared. We looked for similarities and dissimilarities in clinical presentation and results of diagnostic procedures.

Results: There were 62 school-aged children in migraine study group, 81 in partial epilepsies group, aged 6–18 years. No statistically significant sex differences were found in both groups. In migraine study group 1 patient had epilepsy (1.6%), but 4 had specific changes on EEG (6.4%). In partial epilepsy group 13.6% of patients had migraine headaches unrelated to seizures. Five children (6.2%) in partial epilepsy group did not have impaired consciousness ictaly, while 7 (11.29%) had impaired consciousness in migraine group. Seizure related headaches were not uncommon in partial epilepsy group, 6 (7.4%) had preictal or prodromal headaches, unilateral or bilateral, 3 (3.7%) had ictal headaches, interestingly all of them with intellectual disabilities. Postictal headaches resembling migraine were most common, 28 (34.6%) reported them. Only one patient was observed as migralepsy. Aura was more common in migraine group (21% versus 14.8%). Types of aura were different, as well as their duration. Ictal and postictal aphasia, dysphasia, paresthesias, hemiparesis and other features also showed some similarities and dissimilarities.

Conclusion: We conclude that epilepsy and migraine remain two substantially different conditions, showing interesting similarities and differences, that deserve further investigation.

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NEUROCOGNITIVE DEVELOPMENT IN PRE-SCHOOL-AGED PATIENTS WITH MYOCLONIC-ASTATIC EPILEPSY (MAE, DOOSE SYNDROME)

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Purpose: We assessed neurocognitive and sensomotor development as well as neuronal capacity for auditory language-related processing in five male patients born 2004–2006 and fulfilling the diagnostic criteria of MAE (normal development prior to the onset of seizures, seizure onset between ages 2–4 years, generalized 2–3Hz spike/polyspike wave in EEG, normal brain MRI, and myoclonic-astatic seizures + other types of seizures) to uncover developmental trails in MAE.

Method: The patients underwent extensive neuropsychological assessment and detailed evaluation by speech and occupational therapists. As an electrophysiological estimation of neuronal capacity for auditory language-related processing, electric multifeature mismatch negativity (MMN) was recorded with a 32-channel EEG.

Results: Epilepsy has remained active in the youngest boy; he was on lamotrigine, valproate, and clobazam combination therapy. The others were seizure-free and on monotherapy (topiramate in 1, ethosuximide in 1, valproate in 1 and levetiracetam in 1). All patients showed developmental difficulties. These appeared most evident in language domain (verbal IQ, receptive and/or expressive language skills) and executive functions (e.g., attention, inhibition), while performance IQ and visual perception were within normal range. The electrophysiological analysis is still ongoing.

Conclusion: In our patients, specific neurocognitive difficulties were detected shortly after the MAE diagnosis. In addition to drug treatment, large-scale developmental monitoring and detailed rehabilitation program are necessary to remedy the neurocognitive obstacles and to accomplish optimal outcome within the individual neuronal constraints.

p218
CLINICAL EVALUATION OF NEUROPSYCHOLOGICAL FUNCTION IN CHILDREN WITH BENIGN ROLANDIC EPILEPSY

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Purpose: Benign rolandic epilepsy (BRE) is a benign condition, but may display different degrees of neuropsychological deficits such as cognitive, ADHD, and other behavioral deficits. The aim of this study was to assess the neuropsychological function in children with BRE at the time of first visit.

Method: A total of 33 children with BRE (19 males/14 females, 8.2 ± 2.4 years) were involved in the study from 2008 to 2010. All children underwent a sleep EEG and a comprehensive neuropsychological battery including Korean versions of Wechsler Intelligence Scale for Children III (K-WISC-III), Frontal Executive Neuropsychological Test (K-FENT), Rey Complex Figure Test (RCFT), Wisconsin Card Sorting Test (WCST), Attention Deficit Scale (K-ADS), Child Behavior Checklist (K-CBCL).

Results: The average monthly seizure frequency of the subjects was 0.8 ± 0.8. Spike index was 14.1 ± 18.4/min (Rt) and 18.8 ± 22.1/min (Lt). On the whole, the subjects exhibited normal cognitive function (FIQ 102 ± 15, VIQ 105 ± 15, PIQ 99 ± 15), frontal executive function (EIQ 105 ± 14), memory (MQ 104 ± 16) and other neuropsychological subdomain scores. The group with higher spike index on the left hemisphere scored lower on AVLT ($p < 0.05$) and the group with higher spike index scored lower on Wiscosin card sorting test ($p < 0.05$). In addition, a few

of them showed attentional difficulties, social, behavioral and emotional difficulties, though statistically not significant.

Conclusion: The data partly has limited predictive value, but shows the evidence that contrary to the presumed benign nature of BRE, the condition may cause cognitive, attentional, behavioral and emotional impairment. Despite the fact, further studies are needed to elucidate the core nature of BRE.

p219
A COMMUNITY-BASED STUDY OF DEVELOPMENTAL OUTCOMES OF CHILDHOOD-ONSET TEMPORAL LOBE EPILEPSY

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Purpose: Chronic illness and cognitive disturbance in childhood are known risk factors for poor developmental outcomes, yet the effect of habitual seizures in this context remains poorly understood.

Method: As part of a community-based longitudinal study commencing in 1992–1993, we prospectively examined the achievement of developmental tasks in a cohort of 55 individuals with childhood-onset temporal lobe epilepsy (TLE) at review in 2004–2006. Developmental tasks are age-specific psychosocial achievements tied to particular phases of the lifespan against which we can assess individual outcomes.

Results: Individuals clustered into three groups representing distinct developmental trajectories: (1) a Typical group (51%) who achieved most of their developmental tasks, (2) an Altered group (38%) who achieved some, and (3) a Delayed group (11%) who achieved few. There were significant differences in cognitive functioning between the three groups on a range of measures, with the Typical group outperforming the Altered and Delayed groups on all tasks ($p < 0.05$). Multiple discriminant function analysis indicated that membership of the groups was independently predicted by the chronicity of seizures, cognitive functioning, having surgically remedial epilepsy, and gender ($p < 0.001$). The first two variables discriminated between all three developmental trajectories, while the latter two variables primarily discriminated between the Altered and Delayed trajectories.

Conclusion: We found that childhood-onset TLE disrupts mastery of normative developmental tasks that is independently predicted by the chronicity of seizures and cognitive factors. Assessment of developmental tasks across the lifespan provides a practical framework for guiding prognostic counseling of patients and families.

p220
MATHEMATICAL PERFORMANCE IN CHILDREN AND ADOLESCENTS WITH EPILEPSY: PRELIMINARY RESULTS

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Purpose: To evaluate the mathematical performance in epileptic children and adolescents with normal intelligence and correlate it with clinical and neuropsychological issues.

Methods: A transversal, descriptive and analytical study. Twenty-one patients with epilepsy and an IQ > 80 were evaluated by the Academic Performance Test (items reading, writing and arithmetic), Arithmetic Test (Capovilla) and Mathematics Test (Boller and Faglione). The results were compared with clinical and neuropsychological data. The neuropsychological measures used were: total IQ (WISC-III), Sustained Attention Test and WCST (Wisconsin Card Sorting Test). We used the following nonparametric statistical tests (small sample without normal distribution): Mann–Whitney and Kruskal–Wallis (comparison of means), Spearman (linear correlation of quantitative data). The proposed level of significance was 0.05.

Results: Twelve patients (57.1%) were male. The average age and education level were respectively 11.2 years (SD 2.7) and 6.4 years (SD 2.9). The mean time of epilepsy was 60 months (SD 38). The mathematical performance was below than expected for schooling in 12 (57.1%) patients. The syntax and lexical math skills were impaired in 8 (38.1%) patients. The calculation abilities were below the average level of results in (N -%): sum (5–23.8%), subtraction (12–57.1), multiplication (7–33.3), division (8–38, 1) and problems (8–38.1). There were no significant differences between the mathematical performance and types of epileptic seizures, or significant correlation with disease duration and frequency of seizures. There was a correlation between math performance and reading ability, IQ, level of attention and executive functions.

Conclusion: Epileptic children with normal intelligence have mathematical performance below than expected for their schooling in a higher frequency than expected. Factors such as IQ, executive functions, attention and reading difficulties are involved in these results.

Poster session: Pediatric epileptology V
Monday, 29 August 2011

p221
LACOSAMIDE: OUR CLINICAL EXPERIENCE IN TREATMENT OF PARTIAL DRUG-RESISTANT EPILEPSIES IN CHILDREN

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Purpose: Lacosamide (LCM) is one of the latest antiepileptic drugs (AEDs) commercialized, that using the slow inactivation of voltage-gated sodium channels. LCM is approved for been prescribe in politherapy for the treatment of partial drug-resistant epilepsies in children older than 16 years old (yo).

This is a prospective observational open label assay about our experience in the use of LCM as an adjunctive therapy in focal and multifocal partial epilepsies, in a 3rd level children hospital.

Method: Prospective observational, open-label clinical assay from October 2009 in 115 children, showing dates from the 82 followed at least for 12 weeks. Efficacy (EF) and adverse outcomes (AO) are recorded at least at 6th and 12th week of treatment. Dose was 5 mg/kg/day (maximum 10 mg/kg/day), divided into two to three doses, and achieved in 6–8 weeks.

Results: Forty-seven boys and 35 girls; medium age 10 year 7 months (R 23 month–18 year); range of associated AEDs 1–3 (more frequent: carbamazepine, sodium valproate and levetirazetam). Epileptic etiology: cryptogenic (35), cortical dysplasia (15), tumoral (6), others (Dravet, Aicardi S., Tuberous sclerosis, 26). Suppressed in 19/82 (10 no efficacy and 9 AO). EF (58/82) (seizure reduction in >75%: 22; neurocognitive: 34). EA (39/82) (dizziness, visual disorders).

We have the follow-up of 28 patients for more than 1 year. In 16 (57%) the good response continued and in 12 (43%) we suppressed the LCM because it was no efficacy (six patients) or for AO (four patients).

Conclusion: LCM is an effective drug for the treatment of partial drug-resistant seizures in children. Adverse outcomes are frequent but mild. There is a high prevalence in positive neurocognitive effects. Dosage at 5 mg/kg/day seems adequate but higher ones do not show more adverse outcomes. Adjust doses and intervals when using LCM and carbamazepine together.

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LONG-TERM OUTCOME OF VAGUS NERVE STIMULATION THERAPY IN YOUNG CHILDREN WITH INTRACTABLE EPILEPSY

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Purpose: Vagus nerve stimulation (VNS) has been approved by FDA for treatment of intractable epilepsy in children over 12 years of age. However, it is often used in younger children with intractable seizures. There is little data on the efficacy of VNS therapy in the preadolescent patient cohort.

Our goal was to assess the long-term efficacy of VNS therapy in young children. We hypothesized that their seizure reduction with VNS therapy would be at least as good as that reported for patients over 12 years of age.

Method: We retrospectively reviewed medical records of intractable epilepsy patients who were under 12 years of age at the time of VNS implantation. We included all such patients who underwent VNS implantation surgery at the University of Chicago from 1/1/2002 to 5/19/2009 and who had a minimum of 6 months of follow-up after VNS implantation. Outcome was quantified as percent seizure decrease from baseline. Statistical analysis of the data was done to determine if any of the parameters significantly influenced the outcome.

Results: Out of 42 patients studied, 28 (67%) had at least 50% decrease in seizures frequency, one-half had 75% decrease in seizures, and three became seizure-free. Most of seizure reduction was achieved within the first 6 months of VNS therapy. There was a trend for further seizure reduction over 5 years of follow-up. In addition, 69% of patients reported improvements in mood and alertness. Age at VNS implantation, duration of epilepsy prior to VNS implantation, and EEG focality did not significantly influence the outcome. Complication rate was 7% and included cough, gag, hypopnea, dystonia, and a a delayed surgical site infection.

Conclusion: Our cohort demonstrated a lasting benefit of VNS therapy over 5 years, including seizure reduction and improved mood and alertness. VNS therapy in preadolescent children with intractable epilepsy is effective and safe. Larger scale studies are needed to evaluate predictors of greatest VNS response in this vulnerable group of children.

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FIRST REPORT OF TAIWAN CHILD NEUROLOGY SOCIETY PROJECT ON VAGUS NERVE STIMULATION RESULTS FOR INTRACTABLE EPILEPTIC CHILDREN

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Purpose: Vagus nerve stimulation (VNS) is approved by FDA in 1997 for adjunctive therapy for intractable epilepsy. In Taiwan, the first Model102 VNS was implanted since August, 2007 under informed consent and IRB certification. To investigate indication of implantation and VNS effect for pediatric patients, we collected questionnaire for VNS insertion by cohort study about refractory epileptic children.

Method: Fifty-three refractory epileptic patients aging from 1~37 Y/O were enrolled into this study for completion of questionnaire, and 26 children among them had received VNS implantation after questionnaire (averaged 11.2Y/O). The data of 3 months before VNS implantation, including epilepsy classification, seizure dairy and quality of life variables were collected, and the patients were followed for more than half year. Patient's classification of epilepsy included post-West syndrome, Lennox-Gastaut syndrome, autism with localized epilepsy, mesial temporal epilepsy, epilepsy related to encephalitis, severe myoclonic epilepsy in infancy, cryptogenic localized epilepsy, symptomatic occipital lobe epilepsy, tuberous sclerosis & CSWS. The seizure reduction rate, EEG, brain MRI and intelligence test were done before or after performance of VNS for 1/2–1 year.

Results: The seizure reduction rates were more than 50% in most patients, and life quality quotient test and Depression quotient test were both improved, but IQ test improved little without significant change. The prolonged seizure (status) & frequent seizure with poor life quality are the most important indication for VNS implantation among our cases.

Conclusion: (1) Seizure reduction rates were more than 50% after implantation for half year; (2) Quality of life, such as: alertness, mood and language function improved prominently; (3) Poor life quality with prolonged seizure and frequent seizure are the important fators for VNS replacement.

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NEUROLOGICAL AND RADIOLOGICAL CHANGES IN PATIENTS WITH SCHIZENCEPHALY

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Purpose: To make the analysis of neurological and radiological presentations in seven patients with schizencephaly.

Method: We have included seven children aged from 2 to 13 years into research using special formalized medical history that had been developed at pediatric department of Russian Medical Academy of Post-graduate Education. EEG, brain CT and/or MR investigations were carried out for all patients.

Results: Cerebral palsy forms among patients: 71.5%, hemiparetic form; 28.6%, double hemiplegia. Cognitive deficit: 57.2%, moderate degree; 42.9%, heavy degree. Symptomatic focal epilepsy was diagnosed in 100% of cases: 42.9%, complex focal seizures; 28.6%, simple focal seizures; 57.2%, complex focal seizures with secondary generalization; 14.3%, generalized (tonic) seizures. Combination of different types was available. All schizencephaly cases were confirmed with radiological methods. Schizencephaly forms: 42.9% of cases, close-lip form; 28.6%, open-lip form in combination with inner hydrocephaly; 14.3%, bilateral close-lip form to the right and open-lip form to the left in combination with inner hydrocephaly. Additional verifications:100 % of cases, heterotopy of gray matter; 71.5%, corpus callosum agenesis; 14.3%, septum pellucidum agenesis; 57.2%, optic nerves hypoplasia.

Conclusion: Clinical dominance of hemiparetic form of cerebral palsy in 71.5%; 57.2%, complex focal seizures dominance. Close-lip schizencephaly in 42.9% of cases. Gray matter heterotopy was combined with schizencephaly in all patients, confirming epileptic seizures presence.

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HIPPOCAMPAL SCLEROSIS IN A CASE OF FRAGILE X SYNDROME

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Background: Hippocampal sclerosis is a relatively frequent cause of epilepsy in children. Fragile X syndrome is the most common inherited form of mental retardation, caused by a mutation in the FMR1 gene. The

association of hippocampal sclerosis and fragile X syndrome rarely is cited in the literature, despite of numerous animal models that had been developed to investigate the substrate of epileptogenesis in this syndrome.

Case report: A 12-year-old boy with Fragile X syndrome (full mutation of the FMR-1 gene) started to experience epilepsy at the age of 4 years. This child presented with the classical clinical and EEG picture of mesial temporal lobe epilepsy. The MRI study revealed the presence of right hippocampal sclerosis already at the age of 4 years. Because the epilepsy became resistant to standard treatment, he was referred for epilepsy surgery. Neuropsychological assessment revealed a nonverbal working memory deficit and a specific impairment on learning and delayed recall of complex verbal material, which is less consistently found in fragile X syndrome, but is common in temporal lobe epilepsy. An en bloc right anterior temporal lobectomy was performed, after which the patient remained seizure-free. The histopathological examination confirmed an extensive right hippocampal sclerosis.

Conclusions: This case underline the importance of the hippocampus in the pathogenesis of epilepsy associated with fragile X syndrome.

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TIMELY TREATMENT AS A PREDICTOR OF SHORTER DURATION OF CONVULSIVE SE

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Purpose: Convulsive status epilepticus (SE) is a life-threatening emergency that requires urgent treatment. A cross-sectional study was conducted between September 2009 and December 2010 to assess association between lead time for convulsive SE treatment and the seizure duration.

Method: Patients were evaluated by Standardized Admission Proforma, approved and used in two previous studies: North London convulsive Status Epilepticus in Childhood Surveillance Study and Incidence and Outcome of Convulsive Status Epilepticus study conducted in UK and Kenya, 2002–2006, respectively. The patients receive treatment according to NICE guideline (Protocol of treating status epielpticus in adults and children).

Results: A total of 29 children were evaluated; mean age was 5 years, 13 (45%) were female. Five (17%) were diagnosed with a CNS infection, 9 (36%) had some type of epilepsy, 11 (38%) had a febrile convulsive SE, 4 (14%) had the first episode of convulsive SE. Ten (35%) patients presented with generalized seizures. Only 12 (41%) received treatment timely, within 15 min of seizure initiation. Mean lead time for the treatment was 19 min. Median convulsive SE duration was 40 min. There was a significant negative correlation between lead time to SE treatment and SE duration when assessed using Spearman's correlation coefficient ($\rho = -0.16$, $p < 0.05$).

Conclusion: Urgent treatment of convulsive SE is necessary to avoid serious complications associated with long duration convulsive SE. In our study shorter lead time for treatment was significant predictor of shorter duration of convulsive SE, thus to favorable outcome.

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A POPULATION-BASED STUDY OF LONG-TERM OUTCOME OF EPILEPSY IN CHILDREN WITH POTENTIALLY RESECTABLE LESION ON NEUROIMAGING

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Purpose: To evaluate long-term seizure outcome in children with epilepsy and a potentially resectable lesional etiology.

Methods: All children (<18 years in Olmsted County, Minnesota), with new onset epilepsy between 1980 and 2004 and a single focal lesion on neuroimaging were identified by review of the Rochester Epidemiologic Project database. Outcomes were divided into three categories: (i) seizure freedom for 1 or more years at last follow up, (ii) ongoing seizures but not medically intractable and (iii) medically intractable epilepsy or undergoing epilepsy surgery.

Results: Of the 359 children with newly diagnosed epilepsy, 37 (10%) had a focal or hemispheric lesion on neuroimaging. Median age of follow up was 145 months. Eighty-six percent of children with MCD, 67% with MTS, 33% with encephalomalacia, and 40% with vascular malformations had intractable epilepsy or underwent surgery for medically intractable epilepsy. Among the different etiologies, presence of encephalomalacia predicted least likelihood of being intractable or undergoing surgery ($p = 0.012$). At final follow-up, 23 (62%) of our entire cohort were seizure-free. Following surgery, seizure freedom was achieved in 80% with MTS, 67% with encephalomalacia, 50% with vascular malformation, and 40% with MCD. There was no statistically significant difference between the different etiologies and seizure freedom after surgery. Twelve children (32%) achieved seizure freedom with medical management alone.

Conclusion: Focal lesions on neuroimaging confer a higher risk of medical intractability amongst children with new onset epilepsy. However, 32% of this cohort achieved seizure remission with medical management alone, including 58% with encephalomalacia and 33% with MTS.

p228
CHILDREN WHO HAVE EXPERIENCED >5 AEDS ARE MORE LIKELY TO RESPOND TO VAGAL NERVE STIMULATION (VNS) THAN TRIALS OF FURTHER AEDS

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Purpose: To compare the effect of VNS with further AEDs in children with difficult to treat epilepsy with respect to seizure frequency, severity and quality of life (QOL).

Method: A prospective, controlled trial with randomization to VNS or further AEDs for 1 year. Further stratification into those who had had 3–5 AEDs previously (''Early'') and those who had had >5 AEDs (''Non Early''). Primary outcome measure was the numbers with a > 50% reduction in seizure frequency (''responders'').

Results: One hundred forty-one children were randomized. One hundred five completed the study (49 VNS 56 AEDs). Forty-eight percent in the Non Early VNS group were responders vs 23% in the Non Early AED group ($p = 0.045$). QOL improved in the ''Early''VNS group by comparison with deterioration in the ''Early'' AED group ($p = 0.03$).

Conclusion: Children who have experienced >5 AEDs are more likely to respond to VNS than further trials of AEDs. VNS improves QOL independent of its effect on seizure frequency

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EFFICIENCY AND SAFETY OF USING NEW ANTIEPILEPTIC DRUGS IN TREATMENT OF FOCAL FORMS OF EPILEPSY IN CHILDREN

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Purpose: Comparison of the efficiency and the safety of using antiepileptic drugs topiramate and lamotrigine in treatment of symptomatic focal forms of epilepsy in children.

Method: We observed patients aged from 1 month to 17 years old with focal forms of epilepsy and divided them into two groups according to using antiepileptic drugs: 1 group (31 patients) were treated by topiramate in doses 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 (31 patients) received therapy by lamotrigine in doses from 25 up to 250 mg/day, from 0.5 up to 6 mg/kg/day (on the average 3.6 mg/kg/day). All drugs were used in monotherapy or in combine therapy with other antiepileptic medication.

Results: Seizures freedom was achieved in 8/31 patients (26 %), used topiramate, and in 8/31 patients (26%), treated by lamotrigine. Reduction in seizure frequency more than 50% were observed in 19/31 (61%) cases in topiramate group and in 14/31 (45%) cases in lamotrigine group. In 3 patients were detected seizure aggravation (in 3% cases, used topiramate and in 6% cases, used lamotrigine). Side effects registrated in 23% patients in topiramate group and in 32% patients in lamotrigine group.

Conclusion: This study has shown topiramate and lamotrigine is high effective and safe new antiepileptic drugs for treatment focal forms of epilepsy in children.

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EFFICACY AND TOLERABILITY OF ORAL LACOSAMIDE (LCM) AS ADJUNCTIVE THERAPY IN 130 PEDIATRIC PATIENTS WITH PHARMACORESISTANT FOCAL EPILEPSY

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Introduction: LCM is a third generation antiepileptic drug (AED) that operates through the slow inactivation of sodium channels without affecting fast inactivation. There are few studies in the literature about efficacy and tolerability of LCM in children.

Purpose: We report our experience with LCM as adjunctive therapy in patients under 16 years of age with pharmacoresistant focal epilepsy.

Method: Observational, prospective and multicenter study in which 18 Spanish Neuropediatrics Units have been involved. We established a follow-up of ≥6 months. Treatment efficacy was assessed at the end of follow-up considering reduction in seizure frequency compared to 3 months prior to begin LCM. We accepted that there was response when this reduction was >50%.

Results: Total: 130 patients (24.6% simple partial seizures, 71.5% complex partial seizures, 64.6% secondarily generalized seizures and 55.3% combination). Etiology: 63% symptomatic, 27.6% presumably symptomatic and 9.2% idiopathic. Sex: 60% male. Mean age: 8.01 years (±4.25). AED associated: 45.3% VPA, 39.2% LEV, 17.6% ZNS, 13.8% OXC, 13.8% CLB and 13% TPM. Initial dose: 89.2%: 1–2 mg/kg/day. Mean period to reach the final dose: 2.66 weeks ± 4.98. Mean final dose: 6.80 mg/kg/day ± 2.39. Follow-up: 66% of patients were followed for ≥6 months. 62.3% had reduction seizure frequency ≥50% (16.15% full control seizures). There was no response in 30% and 3.8% of patients increased seizure frequency. The associated AEDs in groups with better response were VPA and LEV and in groups with worse response were what operate on sodium channel. Tolerability: side effects ocurred in 30% (39/130) and in 10% (13/39) LCM had to be retired. The most common side effects were: Nausea, vomiting, unsteadiness, dizziness, nystagmus, weakness, and adynamia.

Conclusion: LCM is effective in children with pharmacoresistant focal epilepsy. Our data suggest that LCM in pediatric patients is safe at doses of 6–9 mg/kg/day, twice daily. Its introduction should be slow and progressive in 4–6 weeks. It is advisable to associate it with VPA or LEV and inadvisable with AEDs that operate on sodium channel.

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MESIAL TEMPORAL LOBE EPILEPSY IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Children with acute lymphoblastic leukemia (ALL) rarely develop mesial temporal sclerosis (MTS), and the clinical course in such cases remains unclear.

Method: We have reported the clinical courses of two patients who developed epilepsy with MTS after chemotherapy for ALL. They were longitudinally followed-up by EEG and MRI.

Results: The first patient was a girl who was diagnosed with ALL at 6 years old. She gained complete remission after undergoing chemotherapy that included 11 times of intrathecal methotrexate (IT-MTX). During the MTX therapy, she experienced two partial seizures, subsequently carbamazepine was initiated. The follow-up EEG and MRI yielded normal results until she was 9 years old, at that point, irregular spike-waves were observed for the left hemisphere. At 11 years old, she started experiencing refractory complex partial seizures (CPSs), and MRI showed left MTS for the first time. After 1 year, she underwent multiple subpial transection, thereby achieving freedom from seizures. The second patient was a boy who was diagnosed with ALL at 5 years old. His treatment regimen was the same as that used for the first patient. He experienced no seizure during chemotherapy. At 11 years old, he started experiencing CPSs. EEG showed diffuse irregular spike-waves with focalization, whereas MRI showed no abnormality. He was observed without anticonvulsant therapy. At 13 years old, the frequency of seizures increased, EEG showed diffuse irregular spike-waves predominantly in the left posterior head region and MRI revealed left MTS.

Conclusion: In the case of our patients, the detection of MTS by MRI was preceded by that of epileptic discharges on the EEG. Chemotherapy that includes IT-MTX may be a major cause of MTS in ALL patients.

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FRONTAL LOBE AUTOMATISMS IN CHILDREN WITH SURGICALLY VERIFIED EPILEPTOGENIC ZONE

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Purpose: To analyze semiology of seizures with automatisms originating from frontal lobe in children who became seizure-free after surgery.

Methods: We analyzed 17 videotaped seizures from six patients with FLE aged 5.5–13.8 years (mean 7.3 years). In an average follow-up was 28 months (range 3–31 months). Fourteen symptoms and signs were looked for in every seizure. Each seizure was divided in three equal parts. The time of symptoms onset was determined in relation to each part of seizure. Analysis was performed both for patients and seizures.

Results: Patients had high seizure frequency from 3 to 30 attacks/day (mean 9), with cluster tendency in 33%, mean duration of seizures was 25 s (range 5–142 s). Secondary generalized seizures were not recorded. Proximal automatisms were seen in 12 (71%) seizures in 4 (67%) patients and were registered in first (3 seizures) and middle (nine seizure) third of the ictal event and were ipsilateral (six seizures) or bimanual (two seizures). Distal automatisms were registered in 8 (47%) seizure in 4 (67%) patients, were seen in the middle (three seizures) and last third (five seizures) and were more frequently bimanual (six seizures). Oral

automatisms (seven seizures 41% in three patients 50%) occurred only in last third of seizure.

Conclusion: Automatisms in frontal lobe seizures have specific order of appearance: proximal are prevalent early within the seizure while distal and oral ones appear later.

Poster session: Clinical neurophysiology I
Monday, 29 August 2011

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THE SLEEP-DEPRIVED BRAIN IN NORMALS AND PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY: A PERTURBATIONAL APPROACH TO MEASURING CORTICAL REACTIVITY

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Purpose: Simultaneous electroencephalography-transcranial magnetic stimulation (EEG-TMS) investigates cortical reactivity to external perturbations. TMS evoked potentials (TEPs) are a series of positive and negative EEG deflections elicited by magnetic stimulation. They have been described in normals during sleep and wake but not after sleep deprivation or in pathologically enhanced excitability, i.e., epilepsy. The aim of our study was to identify TEPs and their modifications via EEG-TMS coregistration in healthy controls and patients with juvenile myoclonic epilepsy (JME) during wake, sleep deprivation and sleep

Method: To study vigilance-related modifications of cortical reactivity by measuring variability in TEP, we performed EEG-TMS coregistration with a compatible equipment (Brain-Vision Recording System, 32 electrodes) in twelve healthy subjects and ten JME patients, stimulating the dominant motor area in a standard wake condition, after partial sleep deprivation, and during sleep. At least 150 TMS were delivered randomly every 8–15 s during wake, sleep deprivation and sleep conditions. Sleep scoring and peaks analysis was performed ofline.

Results: We identified positive peaks approximately after 15, 45 and 100 ms after the TMS artifact, and negative peaks after 30, 60 and 190 ms. We observed overall higher amplitudes in the EEG recorded from epileptic patients compared to controls. In both groups sleep deprivation had a marked augmentation effect on peaks' amplitude compared to wake and sleep, more evident over the late deflections. Finally, a different topographical distribution of sleep-deprivation induced amplitude increase distinguished the two groups, with a major enhancement over the anterior areas for the JME patients, and over the posterior cortex for controls

Conclusion: Cortical reactivity to the external perturbation of TMS is modulated – i.e. augmented – by sleep deprivation. A globally enhanced cortical response to TMS is recognized in JME patients, particularly after sleep deprivation and over the anterior cortical areas. This phenomenon could be related to the cortico-thalamic circuit dysfunctions believed to cause myoclonic epilepsy and a higher susceptibility of the frontal and prefrontal areas to the effects of sleep deprivation

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A COMPARATIVE STUDY OF HEART RATE VARIABILITY IN HOT WATER EPILEPSY

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Purpose: Alteration in thermoregulatory centre i.e., hypothalamus might be implicated in hot water epilepsy (HWE), a type of reflex epilepsy. Involvement of autonomic nervous system has not been evaluated in HWE. In this study, heart rate variability (HRV) was performed to characterize the autonomic function in patients with HWE.

Method: Twenty patients with HWE (Age: 27.1 ± 7.6 years; M: F = 16:4) and 20 age and gender matched healthy controls were recruited. Five minutes resting Lead II ECG was obtained (AD instruments) under standard conditions and analyzed for time and frequency domain HRV parameters using Chart software.

Results: Independent-samples *t*-test result showed mean heart rate was higher in patients with HWE compared to controls (74 ± 3/min vs. 69 ± 2/min; $p < 0.05$). The time domain parameters of HRV were significantly reduced in HWE patients compared to controls [SD of RR intervals (SDNN): 46.41 ± 3.6 ms vs. 55.21 ± 2.5 ms, $p < 0.05$; square root of mean of sum of squares of successive differences of RR intervals (RMSSD) 37.9 ± 3.3 ms vs. 51.2 ± 4.1 ms; $p < 0.05$; number of successive NN intervals >50 ms (NN50) 56.3 ± 8.2 vs. 95.8 ± 11.4, $p < 0.05$]. The frequency domain parameters were also reduced in HWE patients [Total power (TP) 2201.1 ± 309.8 ms^2 vs 3103.5 ± 299.4 ms^2; $p < 0.05$ high frequency power (HF) 556.6 ± 141.1 ms^2 vs 951.7 ± 165 ms^2 $p < 0.05$]. Significant changes were noted in the parameters denoting parasympathetic dysfunction (RMSSD, NN50 and HF).

Conclusion: Our study demonstrates distinct parasympathetic dysfunction in HWE patients and supports the hypothesis of a common origin for HWE and autonomic dysfunction. Understanding of autonomic dysfunction in HWE may help to diagnose and treat disease.

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P300 IN PATIENTS WITH EPILEPSY—THE DIFFERENCE BETWEEN THE TARGET AND NONTARGET ANSWERS: PILOT STUDY

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Introduction: The P300 is the method of choice for evaluation of cognitive processing. Determined by the latency and amplitude of evoked responses N1, N2 and P3. Epilepsy and antiepileptic drug use reduces cognitive function. Therefore, the object of our interest is the impact of disease and drugs on P300, latency and amplitude of evoked responses.

Patients and Methods: The study includes 20 subjects of both sexes, who are being treated for epilepsy, grand mal type. Everyone we have done recording auditory cognitive evoked potential, audio-P300. The measurement was done on the machine Medelec Synergy – Oxford Instruments apparatus. All subjects were determined target and not target-evoked response. All subjects were recorded auditory cognitive evoked potentials, with clear auditory stimuli regular and irregular click stimuli to which they should pay attention.

Results: The study includes 20 patients, six women and 14 men. The mean age of examinees was 56 ± 3.4 years. Median duration of disease was 14 ± 3.6 years. Latency of nontarget evoked response was 323.6 ± 3.1 ms, a target response 295.35 ± 2.7 ms.

Discussion: The research revealed that the latency of nontarget auditory stimuli of cognitive, audio-P300, is longer than the target audio-P300 evoked responses in patients with epilepsy. From these results we conclude that patients with epilepsy direct their attention have appropriate cognitive response. However, if they do not direct attention their cognitive response was significantly worse than expected.

Conclusion: Epilepsy and long-term use of antiepileptic drugs affect the characteristics of audio-P300 nontarget responses, and significantly prolonged latency of cognitive evoked response.

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MISMATCH NEGATIVITY FOR PHONETIC SOUNDS IN TEMPORAL LOBE EPILEPSY

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Purpose: Mismatch negativity (MMN/P) is known as an objective index of temporal lobe function. We utilized a phonetic MMN paradigm and analyzed MMN at midlines and MMP at mastoids separately to examining the change in temporal lobe epilepsy (TLE).

Method: Twenty-six patients with TLE (10 females; mean age 32.7) and age- and sex-matched 26 healthy right-handed controls were recruited. Stimuli were vowel-speech (`a` and `o`). Electrodes at Fz, Cz, and bilateral mastoids were used for analysis. Average waveforms were obtained separately for deviant and standard stimuli, with a minimum of 95 deviant trials for each participant. After all, 19 TLE patients (seven females; mean age 33.6 years ± 10.1) and 22 controls (eight females; mean age 33.6 ± 9.3 years) were analyzed. We analyzed the mean MMN amplitude between 150 and 180 ms, and peak latency between 70 and 200 ms. We used three-way repeated ANOVA for statistical analysis.

Results: The ANOVA examining amplitudes at Fz and Cz revealed a significant main effect of STIMULUS, such that deviant amplitudes were greater than standard amplitudes, however there was no significant interaction between GROUP and STIMULUS. ANOVA examining amplitude at mastoids showed a significant interaction between STIMULUS and GROUP, indicating that the difference between deviant and standard amplitudes in TLE was smaller than in controls. The latency between TLE and controls did not show differences.

Conclusion: The differences between standard and deviant responses at mastoids were smaller in TLE compared to controls at mastoids, while it was not significant at midline electrodes.

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ELECTRICAL PROBING OF THE BRAIN FOR THE MEASUREMENT OF CORTICAL EXCITABILITY

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Purpose: This presentation introduces a new method for measuring cortical excitability using an electrical probing stimulus via intracranial electroencephalography (iEEG). The aim is to measure cortical excitability for the purpose of epileptic seizure anticipation.

Method: Stimuli consisted of 100 single biphasic electrical pulses, delivered 3 s apart, every 10 min. Stimuli were targeted to the suspected epileptic focus. Neural excitability was estimated by extracting iEEG phase clustering features from the cortical responses to the stimuli.

Results: We will present results showing how the neural responses vary with interictal discharges, sleep-wakes cycles, and in the preseizure period. Importantly, the phase clustering measure increases up to 3 h before seizures.

Conclusion: Our results show that the probing method has a potential to solve the important problem of epileptic seizure anticipation.

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WHICH PHYSICAL ENTITIES OF ENVIRONMENTAL VISUAL STIMULI CAUSE EEG DISCHARGES IN PHOTOSENSITIVE EPILEPSY PATIENTS? A PILOT STUDY WITH AMBULATORY EEG AND ARTIFICIAL EYE

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Purpose: Photosensitive patients report seizures when exposed to flickering lights, TV, computers and video games. From laboratory studies we know that intensity, frequency and contrast of the visual stimulus are important parameter for provocation of photoparoxysmal epileptiform discharges (PPRs). We do however not know how often discharges are provoked in daily life and which of the above parameters or combination of parameter is most important.

Method: An "artificial eye," a small optical sensor with electronic storing system, has been developed by Broadcast Project Research. This device can be attached on a cap such that it absorbs and measures changes in luminance, frequency and contrast of the visual stimuli seen. After validation, patients with a PPR were, after informed consent, registered with a 24 h ambulatory EEG system. They kept a diary and exposed themselves as much as possible to a variety of stimuli and situations.

Analysis of the EEG and the variables from the artificial eye, were done independently and blinded. Epileptiform discharges (ED) were time-marked in epochs of 5 s before onset. Artificial eye data were imported in Matlab, combined with the selected epochs and analyzed.

Results: Four patients (2 F; 12–40 years) were investigated; three had a history of visually induced seizures, the drug naive patient a positive family history. Neither during the photic stimulation procedure, nor in the 24 h registration period, symptoms or signs were reported during ED. Data analyses revealed that frequency and contrast changes in real-life situations were found to be related, and the combination was found to be especially provocative, while light intensity changes seem to be less provocative and not related to other parameters

Conclusion: The photosensitive patients all showed ED evoked by a combination of physical properties of visual stimuli in their daily life. Data were concordant with the findings in the EEG laboratory. In daily life situations the epileptogenic visual stimuli showed a great variety. These results encourage us to enlarge our sample.

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COMPLEX EMOTIONAL VOCALIZATIONS TRIGGERED BY ELECTRICAL STIMULATION OF THE CEREBRAL CORTEX

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Purpose: The electrical stimulation of the cerebral cortex has greatly contributed to the knowledge of brain functioning.

Method: We describe the results of cortical stimulation of the frontobasal area in a patient undergoing epilepsy surgery in our epilepsy unit.

Results: Fifty-five year old man with a history of symptomatic epilepsy with onset at 24 years old secondary to low grade glioma submitted to surgery for the first time in May 2002. In spite of polytherapy, he had frequent complex partial seizures (vocalization, coprolalia and hypermotor activity). The surface EEG recordings did not allow a precise localization of ictal onset. Reassessment imaging revealed the presence of residual tumor in the posterior-basal boundary of the earlier removal. The patient

underwent a new presurgical evaluation with invasive study to allow the registration of electroclinical seizures, electrical stimulation and cortical mapping of the brain. During frontobasal stimulation a complex emotional vocalization of an unpleasent emotion without a true emotional state was obtained in a consistent way.

Conclusion: We intend to present a case of a patient whose electrical stimulation of the frontobasal region produced a complex emotional vocalization without a true emotional state, leaving us the question about the role that this area can play in the modulation of the emotional-prosodic-melodic components of the speech commonly associated with an emotional state.

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MOBILE PHONE EMISSIONS MODULATE BRAIN EXCITABILITY IN FOCAL EPILEPSY PATIENTS

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Purpose: It has been shown in healthy subjects that electromagnetic fields (EMF) emitted by mobile phones increase cortical excitability. The aim of our study is to assess via transcranial magnetic stimulation (TMS) the effects of the acute exposition to EMF of a mobile phone operating in the Global System for Mobile Communication (GSM-EMFs) on the cortical excitability in patients affected by focal epilepsy.

Methods: Ten patients affected by cryptogenic focal epilepsy originating outside the primary motor area (M1) were studied using a double-blind, cross-over, counter-balanced design. Single and paired-pulse TMS were applied to the M1 of the hemisphere ipsilateral (IPSIH) to the epileptic focus and the contralateral one (CONTRAH) before and immediately after real/sham exposure to the GSM-EMFs (45 min).

Results: The real exposure over the CONTRAH side induced an increase of brain excitability in the same exposed hemisphere paired with an excitability decrease in the other one (IPSIH). Focusing on the EMF effect across interstimulus intervals, we observed in the same condition a clear increase of intracortical facilitation (ICF) in the CONTRAH (exposed), and concurrently an increase of short intracortical inhibition (SICI) in the IPSIH. These results could be due to interhemispheric inhibition mechanisms. There were no significant changes of the brain excitability in the sham and the real IPSIH exposure conditions. No significant changes of rest motor threshold were found in all conditions.

Conclusion: Our findings suggest that in patients with focal epilepsy GSM-EMFs acute exposure of the CONTRAH but not the IPSIH significantly modulates cortical excitability, subtending an IPSIH refractoriness to ipsilateral stimulations but a possible inhibition through CONTRAH stimulation.

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EYE CLOSURE AND PHOTOSENSITIVITY IN PATIENT WITH JUVENILE MYOCLONIC EPILEPSY—OUR EXPERIENCE IN 104 CASES

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Purpose: To evaluate eye closure and photosensitivity (PS) frequency in patients with juvenile myoclonic epilepsy (JME).

Method: In retrospective study we analyzed 104 patients with JME diagnosed and treated in period of 2002–2009 in Clinic of Neurology and Psychiatry for Children and Youth. Eye closure sensitivity (ECS) is epileptiform discharges after eye closing lasting 1–4 s. An inclusion criterion was appearing ECS phenomena at least two times during standard EEG on four montages. PS was defined by Waltz criteria during standard intermittent photic stimulation (IPS).

Results: We analyzed 104 patients with JME aged 12–39 years, mean old 21.8 years (SD-5.3 years), 61 (58.7%) females and 43 (41.3%) males. PS was detected in 49 (31 females) patients. Forty patients (81. 6%) were photosensitive at flash frequencies between 10 and 30. Photoparoxysmal responses (PPRs) tip IV was detected in 38 (22 females), and tip III in 11 (6 females) patients. ECS was detected in only 9 (8.7%) patients (7 females). Focal EEG discharges was found in 20 (20.2%) patients, two females with ECS.

Conclusion: It is difficult to evaluate the true prevalence of photo and eye closure sensitivity in JME because of the different definitions of PS and the different protocols used for IPS in various neurophysiology departments. PS and ECS are frequent in JME females. PPRs type IV is most frequent in both genders.

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VESTIBULAR-EVOKED MYOGENIC POTENTIALS AND THE POSTURAL REFLEXES AFFECTED BY ANTIEPILEPTIC DRUGS IN OLDER PEOPLE

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Purpose: Dizziness and unsteadiness are common adverse effects in epilepsy patients taking antiepileptic medications. The purpose of this study was to quantitatively evaluate balance impairment in epilepsy patients of aged-people and to determine whether saccular function is affected by antiepileptic drugs.

Method: Eighty-two patients who were at least 50 years old, without complaint of dizziness or imbalance, and on a stable dose of carbamazepine or levetiracetam were enrolled. All the subjects underwent balance measurements that included an activities-specific balance confidence scale, quantitative caloric and rotational chair testing and vestibular-evoked myogenic potentials (VEMP). The amplitude and latency of VEMP were measured from the sternocleidomastoid muscles of the subjects. Their scores on the measures of balance were compared with newly diagnosed untreated age and sex matched epilepsy patients (N = 30).

Results: The EMG-corrected VEMP amplitudes significantly reduced in the patients treated with carbamazepine. CDP showed no significant differences on SOT results among the groups, but on motor control test, there were significant increase of latencies and slowed adaptations in the carbamazepine group.

Conclusion: These findings suggest that newer drugs such as lamotrigine or levetiracetam may induce less disequilibrium than does carbamazepine in older people on monotherapy for epilepsy. The disturbance is likely related to slowed central postural reflexes.

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SoC INTEGRATING OF NEURAL SIGNAL ACQUISITION UNIT, BIO-SIGNAL PROCESSOR, RADIO-FREQUENCY TRANSCEIVER, AND WIRELESS POWER TRANSMISSION CIRCUITRIES FOR EPILEPSY TREATMENT

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Purpose: In this project, common circuitry building block of neural prothesis are integrated into an SoC (system-on-a-chip) to minimize implanted device. Treatment for epilepsy is chosen as the first test-bed of proposed design, which can also be applied to other neural disease.

Method: There are four blocks in proposed SoC, neural-signal acquisition unit, bio-signal processor, radio-frequency transceiver, and wireless power transmission circuitries. The acquisition unit first acquires and digitizes the patient's ECoG signals. The unit contains multichannel low-noise amplifiers, filters, and analog-to-digital converters. The bio-signal processor receives the acquired ECoG signals and detects seizures by our real-time algorithm. It controls the firing of the off-chip stimulator for seizure inhibition. The third block, RF transceiver, sends out the acquired neural signals for monitoring and receives the command from the external remote controller for parameter setting. Wireless power transmission circuitries, inclusive of rectifier and regulator, are included in the SoC to prolong the battery life. The embedded rectifier converts the received AC power to a DC one which is further regulated by the regulator to stabilize supply voltage for the rest circuits in the chip.

Results: Currently, the circuitry IP design of the building blocks are fabricated and verified. In vivo experiment on animal models using a prototype system built with discrete components reveal the seizure detection and suppress rate of at least 92%. The prototype system using designed SoC components are designed and fabricated and the animal tests using such device will be conducted in 2nd quarter of 2011.

Conclusion: The successful of proposed system-on-chip design yield a miniaturized, low-power and longer battery life neural signal detection and stimulation system. Comparing to previous discrete component design, a thirty-time power reduction is expected. Using such devices can extend the life of implanted devices into tens of years, which will be a very promising solution for alternative treatment for epilepsy seizures.

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CHARACTERISTICS, CLINICAL AND ECONOMIC OUTCOMES IN MEDICAID PATIENTS 17 YEARS AND YOUNGER RECEIVING VAGUS NERVE STIMULATION (VNS) THERAPY FOR THE TREATMENT OF REFRACTORY EPILEPSY

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Purpose: The purpose of this study is to evaluate the clinical and economic benefits associated with VNS Therapy in patients aged 17 years and younger with refractory epilepsy in a real-world setting.

Method: A retrospective cohort study design was applied using data from 5 US Medicaid state claims databases. Patients had ≥1 neurologist visit with an epilepsy diagnosis (ICD-9 345.xx, 780.3, or 780.39), ≥1 procedure claim for VNS implantation, ≥1 AED, ≥6 months of pre- and post-VNS continuous enrollment are included. Health resource utilization (HRU) was measured by frequency of hospitalizations, hospital length of stay, emergency room (ER) visits, outpatient visits, neurologist visits, fractures, head injuries, and status epilepticus events.

Results: Of the 445 patients meeting the inclusion criteria, 238 were between 1 and 11 years old and 207 were between to 12–17 years old. For patients 1–11 years old, hospitalizations and ER visits were reduced during post-VNS versus pre-VNS period (adjusted IRR = 0.73 [CI: 0.61–0.88] and 0.74 [CI: 0.65–0.83], respectively). Average total health care costs were numerically lower during post-VNS versus pre-VNS period ($17,831 vs. $18,220 quarterly [p = 0.052]). For patients 12–17 years old, hospitalizations and ER visits were reduced during post-VNS versus pre-VNS period (adjusted IRR = 0.43 [CI: 0.34–0.54] and 0.44 [CI: 0.39–0.51], respectively). Average total health care costs were lower during post-VNS versus pre-VNS period ($14,068 vs. $19,047 quarterly [p = 0.002]).

Conclusion: VNS Therapy in patients 17 years and younger is associated with decreased HRU and epilepsy-related events such as hospitalizations and ER visits, resulting in net cost savings for public payers.

Poster session: Clinical neurophysiology II
Monday, 29 August 2011

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STANDARDIZED COMPUTER-BASED ORGANIZED REPORTING OF EEG (SCORE)

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Background: The EEG signal has a high complexity, and the process of extracting clinically relevant features is achieved by visual analysis of the recording. The interobserver agreement in EEG interpretation is only moderate. This is partly due to the method of reporting the findings in free-text format.

Purpose: To create a computer-based system for EEG interpretation and reporting, where the physicians would construct the reports by choosing from predefined elements for each relevant EEG feature, as well as the clinical phenomena (for video-EEG).

Method: A working group of EEG experts took part in a consensus workshop in Dianalund, Denmark, in January 2010. The faculty was approved by the Commission on European Affairs of the ILAE. The working group produced a consensus proposal, which has been submitted to a pan-European review, organized by the European Chapter of the IFCN.

Results: The main elements of SCORE are: personal data of the patient, referral data, recording conditions, background activity, sleep, nonictal findings, ictal findings, normal variants and patterns, artefacts, polygraphic channels, interpretation and diagnostic significance. Specific aspects of the neonatal EEGs are scored: alertness, temporal organization and spatial organization.

Conclusion: SCORE will provide quality control for the EEG assessment and reporting, it will help incorporating the results of computer-assisted analysis into the report, it will make possible the build-up of a multinational database, and it will help in training young neurophysiologists.

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IMBALANCE OF MESIAL SYNCHRONIZATION IN TEMPORAL LOBE EPILEPSY

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Purpose: Temporal lobe epilepsy is commonly associated with synchronous, hypersynchronous and desynchronous activity. The aim of the present work is to explore synchronization activity in both mesial areas in temporal lobe epileptic patients during the interictal state

Method: Using a cluster technique, we analyzed 17 temporal lobe epilepsy patients' records of foramen ovale electrodes activity during the interictal state.

Results: There exists a clear tendency in the mesial area of the epileptic side to be organized as isolated clusters of electrical activity as compared with the contralateral side, which is organized in the form of large clusters of synchronous activity. The number of desynchronized areas is

larger in the epileptic side than in the contralateral side in 16 out of 17 temporal lobe epileptic patients.

Conclusion: The mesial area responsible for the seizures is less synchronous than the contralateral; the different kind of synchronous organization accounts for a lower synchronization activity at the epileptic side, suggesting that this lack of synchronous cluster organization would favor the appearance of seizures. Our results shed new light regarding synchronization issues in temporal lobe epilepsy and also it would help in reducing drastically the lateralization time.

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SYNTHETIC APERTURE MAGNETOMETRY-KURTOSIS (SAM(G2)) FOR PRESURGICAL EVALUATION FOR SINGLE/MULTIPLE EPILEPTIC FOCI IN CHILDREN WITH NEOCORTICAL EPILEPSY

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Purpose: Synthetic aperture magnetometry-kurtosis (SAM(g2)) is an adaptive spatial filtering algorithm for magnetoencephalography (MEG). To evaluate SAM(g2), we applied SAM(g2) in children with intractable neocortical epilepsy.

Method: Forty-four children (mean 9.9 years) were analyzed. We selected epileptic voxels of SAM(g2) (evSAM(g2)) with local peak kurtosis higher than half of maximum value. We defined a case as ''concordant'' when ≥50 % of grouped evSAM(g2) overlapping with ECD clusters; ''partially concordant'' when <50 %; ''discordant'' when there was no overlap.

Results: The rate of evSAM(g2) overlapping with ECD clusters ranged from 0 to 100 % (mean 73.1%). Thirty-four patients (77.3%) showed ''concordant'' with 20 single clusters (11 lesions; 9 nonlesion) and 14 multiple clusters (12 lesions, 2 nonlesion). Seven patients (15.9%) showed ''partially concordant'' with two single clusters, (two nonlesions) and five multiple clusters (three lesions, two nonlesions). Three patients (6.8%) showed ''discordant.'' Eleven patients with single cluster with lesion showed higherst concordant rate (mean 88%) than that of 12 patients with a comparing with single cluster without lesion (12 patients, mean 67.4%). Sixteen patients with multiple clusters with lesion also reached higher concordant rate (16 patients, mean 74.6%) than that of five patients and without lesion (five patients, mean 49.4%).

Conclusion: SAM(g2) showed highest concordant evSAM(g2) with the single clustered ECDs secondary to lesion. In multiple clustered ECDs, lesional epilepsy presented highly concordant evSAM(g2) comparing with those without lesion. SAM(g2) can assist ECD especially for the cases with multiple foci to determine epileptogenic hemisphere and surgical candidates.

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MULTISCALE ANALYSIS OF EEG SIGNAL OF JUVENILE MYOCLONIC EPILEPSY: DOES THE LOW FREQUENCY ACTIVITIES CONTROL THE DISCHARGES?

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Purpose: To study the multiscale characteristics of the EEG signal in juvenile myoclonic epilepsy (JME) by wavelet transform.

Method: Perform the multiscale analysis of the EEG signals for 12 patients of JME by continuous wavelet transform (CWT) with the time scale ranging from 0.00075 to 1.5 s, observe the time-frequency dynamics of JME discharges, analysis their multiscale power spectrum, and compar them with the 12 normal controls

Results: The primary visual EEG signals of discharges in all 12 JME patients showed rapid, generalized, spike-waves or polyspike-waves. Frequency information of the discharges from 0.1 to 100 Hz was presented at 30 scales by CWT, and enhanced rhythmic activities at 4.5 Hz enveloped in the 0.6 Hz packet were observed in discharges of JME, and they were closely correlated with each other. The low frequency activities at 0.6 Hz started with a positive-phase, followed by a negative-phase and ended with a positive-phase in all discharges. Each low-frequency envelope of 0.6 Hz contained several rhythmic activities at 4.5 Hz. The enhanced rhythmic activities at 4.8 1.7 Hz could be observed in all these 0.6 Hz low-frequency discharge packets, and both rhythmic activities of frequency at 4.8 1.7 Hz and 0.5 0.2 Hz are significant in contrast to normal controls. We also analyzed the subscale power percentage of the total power across all the analyzed scales. There existed two narrower and more significant power peaks at frequency of 0.6 Hz and 4.5 Hz in discharge of JME by wavelet power spectrum, in contrast with the normal case showed wider frequency band with three lower power peaks at 0.05 Hz, 1.35 Hz and 10 Hz respectively.

Conclusion: Enhanced rhythmic activities at 4.5 Hz enveloped in the 0.6 Hz packet were the key characteristics of EEG signals in JME discharges. The low frequency packet at the frequency peak of 0.6 Hz had not been found previously. It may give important insight on understanding the dynamics of discharge in JME. Does the low frequency packet at 0.6 Hz control the discharge mechanism?

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BEYOND SPIKES AND SEIZURES: DETECTION OF INTERICTAL EEG ASYMMETRIES IN FOCAL EPILEPSY

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Aim: To investigate whether people who suffer from refractory focal epilepsy, but do not show any spikes or seizures in the EEGs, demonstrate significant asymmetries in their background EEG signals. Patients without clear focal onsets are less likely to be considered for epilepsy surgery. Therefore, finding a surrogate measure for detection of a focal onset would be valuable.

Method: Algorithms were developed (Matlab2009b) for detecting EEG asymmetries from interictal background EEG recordings. Using the standard 10–20 system, the first 18 channels are analyzed and homologous channels are chosen for comparison between hemispheres. For each homologous region, the signal is split into epochs, filtered by a Hanning window, Fourier transformed and band-pass filtered. Two asymmetry detection methods have been developed: one based on the statistical *t*-test and one based on the Brain Symmetry Index (BSI). A measure is calculated for quantification of the asymmetries that are found. To make the distinction between asymmetries that are possibly epileptic versus non-epileptic, five threshold values are used. There is a minimum and a maximum value for the asymmetry measure, skewness and kurtosis are taken into account and the asymmetry is required to meet a minimum duration condition. Default values for the thresholds were chosen in consultation with a physician experienced with EEG data.

Results: Datasets from patients with different pathologies are checked with the program. For patients who suffered from hippocampal sclerosis, the most significant region of asymmetry was found in the parietal lobe (P7-P8). Patients with temporal lobe lesions showed asymmetries in the

parietal lobe (P3-P4). For the ones that suffered from subpial layer gliosis, asymmetric regions were detected at the center of the head (C3-C4).

Conclusion: This study demonstrated that asymmetric regions in epilepsy patients can be determined. While insufficient datasets were analyzed to validate the program and link the asymmetric regions to the focal onset, additional assessment of a larger number of patients may provide a potentially useful clinical tool.

p250
ELECTROENCEPHALOGRAPHY AND DIFFUSION-WEIGHTED IMAGE FINDINGS IN TGA PATIENTS

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Purpose: The etiology of transient global amnesia (TGA) is uncertain. Recently some reports showed that diffusion MRI could detect high signal intensity in TGA patients. In this study, we reviewed electroencephalography (EEG) and diffusion-weighted image (DWI) and compared with each other to know the sensitivity and reveal the clue of etiology.

Method: Nineteen patients were included (M:F = 7:13, 58 ± 12.1) All of them were diagnosed as TGA at Dongguk university international hospital during 2 years (2007 and 2008). All patients underwent EEG and DWI.

Results: Thirteen out of 20 patients (65.0%) showed abnormalities in EEG. All of them showed slowing in left side (n = 3) or bilaterally (n = 10). Spikes or sharp waves were detected in three patients. Diffusion-weighted MRI revealed unilateral hippocampal high signal intensities in eight patients. Five patients had left hippocampal lesions, and the other three patients had right hippocampal lesions. Comparing the results between two modalities, four patients showed ipsilateral (left) abnormalities, one patient showed contralateral abnormality (EEG: Left, DWI: Rt). One patient showed bilateral EEG abnormality with right DWI MRI lesion. Six patients showed only EEG abnormality without DWI abnormality. One patient had high signal intensity lesion on DWI without EEG abnormality. Six patients were normal in both EEG and DWI. Interestingly, there is no case with only right temporal EEG abnormality.

Conclusion: These findings suggest that left temporal dysfunction is important for developing TGA. EEG and DWI are complementary to each other mutually and EEG might illustrate the memory dysfunction better.

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CAN SPIKE VOLTAGE TOPOGRAPHY PREDICT THE ICTAL PATTERNS IN TEMPORAL LOBE EPILEPSY?

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Purpose: To study whether voltage topographic analysis of interictal epileptiform discharges (IEDs) in temporal lobe epilepsy (TLE) help to predict the type of scalp ictal onset pattern.

Methods: IEDs from 74 patients with drug resistant TLE and strictly unilateral mesial temporal sclerosis (MTS) who underwent presurgical evaluation were categorized according to dipolar fields into Types A and B temporal IEDs. Type A IEDs were defined as those with dipolar fields (tangential/vertical) with sharply defined negativity over the infero-lateral temporal scalp, and positivity over contralateral centro-parietal scalp. Type B IEDs included all other IEDs other than Type A. Scalp ictal electrographic patterns were classified into rhythms confined to temporal lobe ipsilateral to MTS *(''focal'')*, lateralized to the hemisphere *(''regional'')*, and diffuse, nonlateralized and nonlocalized rhythms *(''diffuse'')*.

Results: A total of 5476 IEDs and 377 seizures were analyzed. They were divided into *four categories* based on the side of MTS: (1) Type A IEDs ipsilateral to MTS (44 patients); (2) bilateral Type A IEDs (16 patients); (3) Type B IEDs ipsilateral and Type A IEDs contralaterally (seven patients) (4) Bilateral type B IEDs (seven patients). In 51 of 60 (85%) patients with only Type A IEDs (either ipsilateral and/or bilateral to MTS), the ictal pattern was either focal or regional and only in nine patients (15%) it was ''diffuse.'' Twelve of 14 (86%) patients with either ipsilateral or bilateral Type B IEDs showed a diffuse ictal onset, whereas 2 (14%) showed a contralateral ictal onset.

Conclusion: In patients with unilateral MTS, Type A IEDs are associated with clearly localized and lateralized ictal onset, whereas Type B IEDs are associated with diffuse ictal onset. Interictal spike topography can thus help to predict ictal patterns in TLE in majority of patients.

p252
SPATIOTEMPORAL ANALYSIS OF THE LEADING FREQUENCIES AND THEIR ENERGY IN EEG SIGNALS WITH EPILEPTIC DISCHARGES

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Purpose: This report concentrates on the problem of illustrating evolution of the cerebral functional states during epileptic activity reflected in the pattern of background EEG activity. This practical problem of documenting changes of the functional brain states associated with ictal or interictal epileptic activity results from complexity of EEG patterns not necessarily presenting clear sharp waves, spikes or typical discharges of sharp and slow waves. The optimal analytical method for solving this problem appears to be evaluation of the leading frequencies and their energy based on wavelet transform or fast Fourier transform of EEG records.

Method: The study was performed on selected EEG records in a group of five patients in conditions of nonconvulsive status epilepticus. The EEG was analyzed in conventional 10–20 system of electrode localization and in different montages with different localizations of reference electrodes. The EEG was recorded with sampling frequency 250 Hz using ELMIKO recording system. Frequency analysis included wavelet analysis of the leading frequencies and the analysis of frequency spectrum of EEG records using fast Fourier transform (FFT). The results of analysis of selected multichannel EEG samples were transformed into color maps illustrating spatiotemporal evolution of the brain states in terms of changes of leading frequencies of background EEG activity in different cerebral regions.

Results: These techniques provided information concerning contribution of different cortical regions in formation of epileptic discharges and evolution of the functional brain states in terms of frequency changes within wide spectrum of delta, theta, alpha and beta waves. Especially, it concerns such phenomena as existence of localized epileptic discharges or interhemispheric asymmetries during and after seizures.

Conclusion: The results of this investigation illustrate potential utility of the spatiotemporal mapping of the frequencies of background activity during evaluation of EEG records.

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CONCORDANCE OF SOURCE LOCALIZATION MODELS APPLIED ON SCALP AND SUBDURAL RECORDINGS AND VALIDATION AGAINST OUTCOMES OF EPILEPSY SURGERY

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Abstracts

Purpose: Source localization methods applied in scalp and recently also in subdural EEG recordings may provide useful information complementary to conventional visual evaluation in presurgical workup validated against postoperative outcomes in epilepsy surgery. The appreciation of correlations between scalp EEG and its subdural (ECoG) substrates constitutes a fundamental issue in electrophysiology, which has obvious implications in the identification and meticulous delineation of the epileptogenic zone. Furthermore, despite the progress in source modeling approaches, data regarding their reciprocal validation in a clinical setting remains scarce.

Method: We analyzed the long-term scalp- and subdural-EEG recordings of 14 patients suffering from refractory frontal lobe epilepsy due to focal cortical dysplasia. Scalp EEG was mounted according to an extended 10–20 system and subdural coverage included lateral coverage in all patients, as well as frontobasal, frontopolar and interhemispheric grid and strip electrodes in 4, two and nine patients respectively. Interictal scalp EEG and ECoG spikes visually identified and annotated in sleep segments were consequently averaged and served as a template for source analysis using the MUSIC and sLORETA algorithms.

Results: Eleven patients presented with at least one scalp EEG spike population with 12 patients showing multiple spike populations in ECoG. The MUSIC and sLORETA source reconstruction derived from scalp and subdural recording data was congruent between different recording scales and correlated with the findings of conventional electroclinical analysis as well as with seizure freedom following resective surgery. sLORETA tended to provide solutions that appeared blurred for sources far from subdural contacts. In nine cases source analysis facilitated the study of spike spread within the frontal lobe.

Conclusion: The correlations of source reconstruction models derived from EEG signals on variable levels and their matching with clinical outcomes in individual cases could serve to clarify the significance of these methods but most importantly promote our understanding of cortical generators of epileptic phenomena regarding their localization and delineation and thus contribute to the improvement of outcomes in epilepsy surgery.

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INDICATORS OF FAVORABLE OUTCOME WITH VAGUS NERVE STIMULATION (VNS) IN 50 PATIENTS WITH DIFFERENT KINDS OF EPILEPSY

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Purpose: Most VNS efficacy studies have been carried out in patients with focal epilepsy, or Lennox-Gastaut syndrome (LGS). It is nevertheless important to compare different types of epilepsy, to better understand which candidates may be most suitable for VNS. The aim of this study was to analyze the whole population of generalized and focal drug-resistant epileptic patients, who were implanted with a VNS device in Marseille, and to evaluate VNS antiepileptic effect but also the improvement of the global condition of the patient, and to delineate clinical indicators of good VNS response.

Methods: In this retrospective study, we included the 50 patients suffering from drug-resistant epilepsy (either focal or generalized), for whom VNS was implanted in Marseille. We analyzed different clinical variables, including epilepsy characteristics, and VNS response (with particular attention to VNS parameters, tolerance, but also mood evolution if available).

Results: Our study included 29 men and 21 women, mostly adults (mean age: 30.6 years ± 14.8). Eighteen patients suffered from generalized epilepsy and among them, 10 had LGS; other epilepsy syndromes were myoclono-astatic epilepsy, GEFS+, drug-resistant absence epilepsy or IGE, and Lafora disease. The 32 other patients had unilateral focal epilepsy (16 patients), bilateral focal epilepsy (13 cases), or multifocal epilepsy (three cases). After VNS, the best outcome was obtained in LGS patients. However, patients with focal epilepsy had also a good response to VNS, with ~55% of them displaying a major or a mild improvement; in this latter group, one patient experienced a transient worsening in seizure frequency, that relapsed after VNS discontinuation, and three patients became seizure-free.

Conclusion: In this study, VNS therapy was effective in both generalized and focal epilepsy. These results show that VNS could be an interesting option when the epilepsy is drug-resistant and when surgery is not indicated (or contraindicated). Besides, even if a dramatic seizure improvement is not always achieved, VNS could be effective in improving the global condition of the patient.

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CLOSE-LOOP EPILEPSY PROSTHESIS DEVICES WITH SPATIAL-TEMPORAL SEIZURE DETECTION AND RESPONSIVELY THERAPEUTIC STIMULATION

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Purpose: In recent years, alternative treatments and devices are proposed to investigate and treat epilepsy in addition to pharmacological and surgical treatments. Several prosthesis devices with deep brain stimulation (DBS) or vagus nerve stimulation are becoming popular treatment for epilepsy clients. These devices use the open-loop continuous neural stimulations to control medical refractory epilepsies complementarily with the limited effective rate around 45%. Besides, by using continuous stimulations and an implantable battery, lifetime of such a device is often limited and periodically operations for clients are required to replace the battery/devices. To overcome above limitations, this research proposed close-loop epilepsy prosthesis devices with temporospatial seizure detection and responsively therapeutic stimulation.

Method: The proposed prostheses devices contain: (1) three-dimensional micromachining electrodes and highly compact flexible planner electrods with localize cortical stimulation drivers; (2) a system-in-a-chip (SIP) with ECoG recoder, bio-signal processing unit, and current stimulator. The low-power ECoG recorder and bio-signal processing circuitries are used to detect the seizure's signal before it propagates to the whole cortex and activating localized cortical stimulation on the electrodes. The prototype SIP system and ECoG flexible electrodes will be developed and verified in this project.

Results: A portable seizure controller assembled by commercial discrete devices with our real-time seizure detection algorithms has been developed for two epileptic animal models for evaluation of the algorithm. Preliminarily experimental result on Long-Evans rats reveals at least 92% of seizure detection rate and stopping of seizure activity by responsively stimulation. Animal tests with integrated prototype using our designed chips and electrodes is carring on in this project. And the prototype will also be used in epileptic animal models for further studies in their ictogenesis.

Conclusion: The successful of this research yields the first close-loop temporal seizure detection and spatial cortex stimulation prosthesis devices with more than 92% detection and suppression rate, which is a promising treatment for absence epilepsy.

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RANDOMIZED CONTROLLED TRIAL SHOWS QUALITY-OF-LIFE BENEFITS WITH VNS ADDED-ON TO BEST MEDICAL THERAPY VERSUS BEST MEDICAL THERAPY ALONE IN ADULTS WITH DRUG-RESISTANT EPILEPSY

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Purpose: To assess the impact of vagal nerve stimulation (VNS) on quality of life in patients with drug resistant epilepsy.

Method: Patients 16 years and older with refractory epilepsy were enrolled in an open-label prospective randomized long-term trial comparing the impact of VNS added on to best medical therapy versus best medical therapy alone on quality-of-life (QOLIE-89 score, primary outcome) and seizure frequency. The study was prematurely terminated due to slow recruitment.

Results: One hundred twenty-one patients were enrolled at 28 European and Canadian sites. Twelve-month follow-up data are available for 55 patients (28 VNS/27 controls). Median age at enrollment was 35 years in the VNS group, and 40 years in controls. The median VNS output current was 1.8 mA (0.75–2.75). A new antiepileptic drug (AED) was introduced during the study in 81.5% of controls, and in 46.4% of VNS patients. Despite a much lower sample size than initially planned, a significant difference in QOLIE-89 score was observed at 12 months between the two groups, with greater improvement in the VNS group (mean ± SD: 6.0 ± 6.9) than in controls (1.4 ± 7.2) (p = 0.016). Seizure reduction (expressed as 50% responder rate) did not differ significantly between the VNS group (36.5%) and controls (22.2%).

Conclusion: VNS therapy used adjunctively to best medical management in patients with refractory epilepsy was associated with a significant improvement in quality of life compared with best medical management without VNS.

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Poster session: Clinical neurophysiology III
Monday, 29 August 2011

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NEUROPHYSIOLOGICAL FINDINGS IN A CLINICAL CASE OF KABUKI SYNDROME

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Purpose: To show the neurophysiological findings in a case of Kabuki syndrome. Description/Method. Kabuki syndrome is an uncommon syndrome which was first defined in 1981. It is caused by a frameshift mutation and it associates facial features, neurological problems (the majority have localization-related epilepsy), joint laxity, hearing loss, dermatologic abnormalities, intelectual dissability, esqueletic, cardiac, genitalurinary disorders and immunity disorders with susceptibility to have infections.

Temporooccipital spikes have been documented in sleep electroencephalogram in these patients.

Clinical case: A 3-year-old patient with facial features of Kabuki syndrome with dismorphic ears, high arched palates and paralysis of the uvula, hand with thin distal phalanges, genu valgus and flat feet. The patient has a dysarthric language but there is no intelectual disability.

The patient is sent to our department to evaluate the myoclonic seizures during sleep that he is suffering from and to study the possibility of an epileptic origin.

Results: A deprivation polisomnography is performed, which shows left and right temporooccipital spikes and polyspikes in phase I, II and III of sleep. The iniciation of treatment with levetiracetam shows a clinical improvement with a clinical control of night seizures.

Conclusion: The findings in the polisomnography which was performed showed the epileptic origin of the myoclonic movements and helped to control the night seizures.

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CLINICAL PROFILE AND OUTCOME OF CONSECUTIVE 179 PATIENTS SEEN IN THE ACTIVATION CLINIC FOR PSYCHOGENIC NONEPILEPTIC SEIZURES (PNES)

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Purpose: To evaluate the clinical profile of patients with suspected PNES seen in the activation clinic (AC) and to classify the PNES based on the AC results. Also to compare the success rate of AC in the diagnosis of PNES with that of standard inpatient diagnostic video-telemetry (VT).

Methods: Consecutive 179 patients seen in our AC over the last 5 years (2006–2010) formed the study cohort. The PNES were classified based on the classification proposed by Seneviratne et al, Epilepsia 2010.

Results: The mean age of patients was 34.3 years (range: 16–87 years). Male to female ratio was 1:3. Mean duration of seizures was 10.3 years. Ninety-three patients were on AEDs. At least 14 had associated epileptic seizures. Photic stimulation (PS) alone was used as an induction procedure in 72 (40.7%), and combined PS and hyperventilation were used in another 31 cases. Habitual PNES could be induced in 105 (60%), six were confirmed to have organic conditions (3.4%) and no events were recorded in 52 (29.3%). The most common recorded PNES was dialeptic PNES (36/105, 34%), followed by complex motor PNES (33/105, 31%) and rhythmic motor PNES (12/105, 11%). AC diagnosed the habitual paroxysmal spells in 13 out of 24 patients (52%) who had negative VT earlier. Subsequent VT diagnosed the habitual spells in only 3 out of 11 patients (27%) who had negative AC earlier.

Conclusions: Activation clinic confirmed the diagnosis in about 2/3rd of referred patients with suspected PNES. AC appeared to be more successful than standard inpatient VT in the diagnosis of PNES.

Abstracts

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CASE REPORT OF ABNORMAL EEG BASIC RHYTHM AND ITS DYNAMIC STATE CAUSED BY AFTEREFFECT OF SERIOUS HEAD INJURY WITH COMPLETE APHASIA AND RIGHT HEMIPLEGIA

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Purpose: Inspecting this case, we prove the usefulness of our original computer programs which analyze digital EEG data.

Method: The case is middle-aged male who was involved in a traffic accident. During the acute phase of cerebral contusion (L > R), the hematoma was removed, then cranioplasty was performed. He was left with complete aphasia and right hemiplegia. We rehabilitated him and examined his EEG.

Results: Ten hertz waves which correspond to alpha rhythms and beta-1 rhythms whose center is 18 Hz waves were observed at relatively healthy right hemisphere. Half width of 10 Hz spectre peak is relatively small at occipital, and relatively large at frontal. Corresponding components are small at relatively diseased left side, and laterality of alpha component is extremely large (central 134% – occipital 54%.) 6.25 Hz activities were found at frontal and central, and 8.59 Hz activities were also found at relatively diseased left occipital and temporal region. The amplitude (fo = 10.16 Hz) while rest and awake is dominant at right temporal, central, and occipital region. Phase shift is the same as normal, but the amount is one half or one-third compared to normal. Without comprehensive observation of dynamic states, other theta-2 ~ alpha-s components are difficult to distinguish with dominant alpha component. To verify some kind of evoked potentials, we examined the case's averaged evoked potential of electronic flash stimulus (3, 6, 10 Hz), and measured their amplitude of response, phase mapping, and laterality comparing with EEG diagnosis while resting.

Conclusion: Our computer programs seem to have shown proper conclusion.

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ICTAL HEADEACHE IN NONPHOTOSENSITIVE PATIENTS

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Purpose: Several studies support the hypothesis of a clinical relationship between some types of migraine and some types of epilepsy, sometimes with evidence of complete overlap.

Recent reports of cephalalgia as ictal symptom in photosensitive patients have been described (Piccioli et al, 2009, Parisi et al, 2008).

Method: We selected four patients (three females and one male, average 17 years ± 9.9) in which EEG was performed in our laboratory because of cephalalgia of short duration or long lasting migraine with visual discomfort (amaurosis, diplopia). EEG at rest, 3 min of hyperventilation (HV) and intermittent photic stimulation (IPS) (eyes closure) was recorded. Micromed rectangular lamp flash 10 S was used with frequencies from 5 to 30 Hz in all patients extended to 60 Hz in two. In one case IPS was repeated using Grass Lamp PS 33 Plus, according to the UE protocol (Kasteleijn et al, 1999).

Results: EEG showed epileptiform discharges in all patients: generalized sharp and spike-waves during HV in two of them; occipital sharp and spike-waves with generalization, increased by HV in one of them; generalized spike-waves increased by HV in the last one. We ask this patient to count every breath during HV; she stopped during discharges.

None of the patients presented photo paroxystic response.

Conclusion: Our study confirms the hypothesis of a clinical relationship between some types of migraine and some types of epilepsy, also in nonphotosensitive patients.

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USE OF EEG IN PATIENTS WITH AUTOIMMUNE ENCEPHALOPATHY

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Purpose: Autoimmune encephalitis (AE) is associated with antibodies against neuronal and thyroidal antigens. EEG has been shown to be more sensitive compared to MRI and CSF antibody titers in AE. Little is known about serial EEG findings in this setting. Here we describe EEG findings in correlation to the clinical course and in response to immunotherapy in patients with AE.

Method: We retrospectively reviewed the EEGs of 14 among 16 patients who had AE associated with neuronal or thyroidal antibodies.

Results: Median age was 54 (range 15–88) years, ten were women. Clinical manifestations included memory impairment in 11, seizures in 9, confusion in 9, sleep disturbance in 8, psychosis in 7, autonomic involvement in 3, and abnormal movements in three patients. Antibodies were found against the NMDA-receptor in 3, VGKC in 2, GABA-b-receptor in 1, unclassified neuronal antigens in 4, and TPO-antibodies in four patients. Multihour and follow-up EEGs were done in five out of 14 patients with median monitoring duration of 12 (range 4–24) hours, median number of EEGs 3 (range 3–7) per patient, and median time between EEGs 1 (range 0–14) day. The remaining nine patients had single 30 min EEGs. The first EEG showed generalized continuous slow in 8, and slow posterior background, generalized intermittent slow, regional intermittent slow, regional EEG seizures, periodic pattern and normal findings in one patient each. Improvement of EEG findings after immunotherapy heralded clinical improvement in four out of five patients.

Conclusion: EEG improvement may indicate clinical response to immunotherapy in patients with AE.

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A EUROPEAN DATABASE ON EEG AND CLINICAL INFORMATION IN EPILEPSY PATIENTS

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Purpose: So far, resources for researchers to develop methods of EEG analysis are limited. We here describe a European database developed in the EU-sponsored project EPILEPSIAE (EU-Grant 211713) containing continuous long-term recordings from more than 200 epilepsy patients.

Method and Results: Based on data from three European Epilepsy Centers (Freiburg, Paris and Coimbra), data from patients with focal epilepsy, long-term recordings of a minimum duration of 96 h and a minimum of

five recorded clinically manifest seizures were included in this database. Fifty patients with intracranial EEG recordings (depth and/or subdural), and more than 150 patients with surface EEG recordings have so far been introduced. Data underwent standard annotations including information on ictal onset, spread and interictal potentials. In addition, metadata on seizure semiology and clinical history as well as 3D imaging data from all patients are included in the database. Overall, the database contains more than 25.000 h of long-term recordings and more than 2000 seizures.

Conclusion: The EU database of the project EPILEPSIAE is by more than one order of magnitude larger than any other presently available resource of clinical information in epilepsy patients. It will be possible to use the database for external research groups from 2012 on for research related to EEG analysis and seizure detection/prediction. Interested researchers can contact the Freiburg epilepsy center for access.

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ZONISAMIDE AS ADD-ON TREATMENT DOES NOT AFFECT NOCTURNAL SLEEP AND VIGILANCE IN PATIENTS AFFECTED BY FOCAL EPILEPSY: A POLYSOMNOGRAPHIC STUDY

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Purpose: Epilepsy are particularly sensitive to the sleep disruption induced by antiepileptic drugs (AEDs). AEDs have the potential to either improve or worsen sleep and sleep disorders in epileptic patients (Placidi et al., 2000). Zonisamide (ZNS) is a new AED approved in USA and Europe as adjunctive therapy for focal epilepsy. To date the effects of ZNS on sleep and vigilance in focal epilepsy are not yet studied. The purpose of our study is to evaluate the effects of ZNS adjunctive therapy on nocturnal sleep by means of ambulatory polysomnography (A-PSG) and Pittsburgh Sleep Quality Index (PSQI) and on daytime somnolence by means of multiple sleep latency test (MSLT) and Epworth Sleepiness Scale (ESS) in focal epilepsy with a standard methodology (Romigi et al., 2011).

Method: Twelve patients affected by focal epilepsy underwent A-PSG, MSLT, and a subjective evaluation of nocturnal sleep by means of PSQI and daytime somnolence by means of the Epworth Sleepiness Scale (ESS), before and after 3-month treatment with ZNS. Recordings were evaluated according to standard criteria. The study was single-blind. PSG data, MSLT, PSQI and ESS scores were calculated before and after ZNS treatment. Statistical analysis was performed by means of the nonparametric Wilcoxon test. Bonferroni correction was applied when required.

Results: ZNS induced a decrease of seizures >50% in 9 out of 12 patients (75%). ZNS did not induce any significant differences of nocturnal PSG parameters (A-PSG) and mean sleep latency as measured by means of MSLT. No significant changes were detected in both PSQI e ESS scores after ZNS addition.

Conclusion: To our knowledge this is first study focusing on the effects of ZNS on nocturnal sleep and diurnal sleepiness. Firstly ZNS adjuntive treatment seems to be effective in focal epilepsy in our narrow sample as reported in clinical trials (Zaccara et al., 2009). In addition ZNS does not induce negative effects on sleep and vigilance in focal epilepsy.

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ELECTROENCEPHALOGRAPHIC FINDINGS IN 200 EPILEPTIC SEIZURE PATIENTS IN LAGOS NIGERIA

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Purpose: Epilepsy is one of the most common neurologic problems worldwide, which affects more than 50 million people (the vast majority of them being in the developing countries). This study show the continuous investigative value of electroencephalography (EEG) in the management of epilepsy in Nigeria.

Method: A total of 200 epileptic patients who fulfilled the criteria for selection were recruited into the study. Demographic and other clinical data were obtained from the patients using the modified version of the questionnaire for investigation of epilepsies in the tropics. All the patients had an electroencephalogram that was analyzed for epileptiform discharges, nonspecific EEG abnormalities or an entirely normal record.

Results: Sixty-one percent of the 200 patients with definite epilepsy were classified as partial seizure, 37.5% had generalized epileptic seizure and only 1.5% was unclassified. The male to female ratio was 2.3:1; and 61.5% of the 200 patients were in the first and second decades of life. Eighty-one patient (40.5%) had epileptiform EEG abnormalities, while 16 patients had nonspecific EEG changes (8%) and 103 (51.5%) had normal EEG records.84 % of the epileptiform EEG abnormalities were focal while the generalized spike and wave discharges were present in 16%. Out of 97 patients that were assessed as having generalized seizures clinically, 21 (21.7%) turned out to have focal discharges following an EEG and so were reclassified as partial epileptic seizure.

Conclusion: The study has demonstrated the continuous value of EEG in the management of epilepsy, and focal epileptiform EEG activities were the most frequent findings.

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QUALITY MANAGEMENT IN EPILEPTOLOGY: CAN IT REALLY IMPROVE CARE FOR PATIENTS?

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Quality monitoring is taking centre stage as proofs of results from the health care services provided begin to be demanded. Thousands of organizations have obtained quality certifications worldwide and numbers are increasing spectacularly. On the other hand, health care professionals require a generally accepted and implemented means for incorporating and organizing an ever-growing scientific knowledge into their work, in a systematic way that optimizes patient management. Epileptology cannot be left behind.

Purpose: Our study is a pioneering attempt to scrutinize quality management within the epileptology domain. We suggest novel quality measures specific to the video-EEG/epilepsy monitoring unit and offer a practical view by focusing on determining whether or not a quality management system (QMS) can truly improve care for epilepsy patients through its impact on such quality measures.

Method: A total of 98 patients, undergoing video-EEG/epilepsy monitoring studies at a quality certified service, were selected from three different periods (P1-P2, before; P3, after; implementation of the QMS). Quality indicators were developed and compared between periods, while confounding factors were systematically monitored.

Results: After implementing a QMS and certifying our service under the International Organization for Standardization (ISO) rules, clear improvements are observed with regard to cost-effectiveness and efficiency. Stagnation and decline in the quality of services have been overcome, the number of studies has increased and recording times have been reduced, while statistically significant improvements have been evidenced in terms of ''quality of the EEG study and report'' (P3vsP2: $p = 0.000$), ''quality in the evaluation of ictal/periictal semiology'' ($p = 0.039$), ''study-derived improved diagnosis'' measures ($p = 0.000$) and ''quality of report storage/retrieval'' ($p = 0.028$). Furthermore, an analysis of the demand has harvested a growing number of satisfied petitioners.

Conclusion: ISO certification is an excellent tool incorporating and driving quality improvement in a way that enhances other actions in the

epileptology domain, improving care for patients. Our results should encourage the journey of undertaking standardized processes that will benefit and correct an efficient use of resources following an efficacious quality strategy.

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SEIZURE AWARENESS IN FOCAL EPILEPSY PATIENTS: DATA FROM AMBULATORY-EEG MONITORING

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Purpose: The management of epilepsy patients relies on self-reported seizure frequency, which might be unreliable. A few studies assessing seizure recognition by patients undergoing EEG monitoring suggested that more than 30% of patients are not aware of having seizures. Twenty-four-hour ambulatory EEG recordings (AEEGs) provide a real-life setting to analyze seizure reporting.

Method: To evaluate the frequency of unreported focal seizures during AEEGs, we reviewed 951 AEEGs performed with various diagnostic purposes in 835 outpatients with epilepsy or suspected seizures (455 males; mean age 41.4 ± 18.9 years, range 8–89 years) consecutively referred between January 2004 and December 2010. The overall occurrence of focal ictal EEG discharges (IDs) was assessed. Individual IDs were categorized as either lateralized left, lateralized right or nonlateralized, and as occurring during wake or sleep. The ID occurrence was analyzed in relation to the presence of coincident event-marker activation and seizure description on the patient's diary, to verify the possible lack of seizure recognition.

Results: IDs were detected in 51 out of 951 AEEGs (5.4%) performed in 45 patients. We identified a total of 90 IDs (1 ID in 29 AEEGs; 2–7 IDs in 22 AEEGs). Of the 90 IDs, 43 were right-sided and 42 left-sided, while 5 IDs did not show a reliable lateralization.

Twenty-eight out of 90 IDs (31.1%) occurred during sleep (19 during NREM, 3 during REM and 6 during drowsiness periods). Event marker activation or diary entry were correlated with IDs in 39/90 IDs (43.4%): 38.6% with right lateralization, 53.8% with left lateralization and 7.6% without lateralization. Fifty-one of 90 IDs (56.6%) were unrecognized by the patient, 54.9% of them with right lateralization, 41.1 % with left lateralization and 4% nonlateralized. Nineteen of unrecognized IDs (37.2%), versus 9 of those recognized (23.0%), occurred during sleep.

Conclusion: These data suggest that unrecognized focal seizures in the outpatient setting might be a frequent eventuality, which should be considered in patient management. Right-sided IDs resulted to be more frequently unrecognized.

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REFRACTORY EPILEPSY WITH NORMAL MRI: CORRELATION BETWEEN THE SEMIOLOGY, EEG (LECTROENCEPHALOGRAM) AND ICTAL SPECT (SINGLE PHOTON EMISSION TOMOGRAPHY)

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Purpose: Our study tests the ability of the surface EEG and ictal SPECT in identifying the ictal onset zone in patients with refractory epilepsy and normal MRI.

Method: Retrospective study of 4 years which includes patients with refractory epilepsy and normal MRI that had been investigated with surface EEG and ictal SPECT. We proceeded to compare seizure semiology, paroxysmal activity in EEG and its pattern of perfusion in ictal SPECT.

Results: Of a total of 41 patients, 8 met inclusion criteria with a mean age of 23 years. Interictal epileptiform activity was obtained in 75% of patients (n = 6) that was predominantly lateralized in 100%. The ictal EEG showed clear paroxysmal activity in 88% of cases (n = 7) that was lateralized in 63% of them (n = 5). The interictal epileptiform activity had a positive correlation with ictal EEG in 50% of cases. Ictal SPECT had a pattern of focal perfusion in all patients with absolute positive correlation with lateralized EEG. Seizure phenomenology had a positive correlation with perfusion patterns in 75% of cases (n = 6). The ictal SPECT localized seizure onset zones on frontal lobe in 63% (n = 5) with the remaining localized to the temporal lobe. The semiology mismatch was 20% (n = 1) on frontal lobe perfusion patterns.

Conclusion: Despite the small sample, the analysis allowed to establish a positive correlation between the variables. Our study showed that like in temporal epilepsy, the SPECT also seems to have importance in the study of extratemporal seizures.

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QUANTITATIVE ELECTRIC TOMOGRAPHY (QEEGT) APPLICATION IN A CASE OF EPILEPTIC STATUS NO CONVULSIVE

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DIGITAL EEG CRITERIA IN DIAGNOSTIC REMISSION IN EPILEPSY

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Poster session: Genetics I
Monday, 29 August 2011

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NIPA2 GENE LOCATED AT 15Q11.2 IS MUTATED IN PATIENTS WITH CHILDHOOD ABSENCE EPILEPSY

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Purpose: Childhood absence epilepsy (CAE) is one type of idiopathic generalized epilepsy (IGE) with complex genetic basis. Copy number variations (CNVs) at 15q11.2 were recently reported in Caucasian patients with IGEs, but epilepsy-associated genes in North China are still unknown. Our study investigates whether CNVs at 15q11.2 are associated with CAE in Chinese patients and whether the selective magnesium transporter NIPA2 gene, which is affected by 15q11.2 microdeletions, is the susceptibility gene for CAE.

Method: We assessed IGE-related CNVs by Affymetrix SNP 5.0 microarrays in 198 patients with CAE and 198 controls from North China. Direct sequencing of the coding region and exon-intron boundaries of *NIPA2* was conducted in all 367 patients with CAE and 700 controls.

Results: We found 15q11.2 microdeletions in 3 of 198 (1.5%) CAE patients, but none were detected in 198 controls. Furthermore, we identified point mutation or indel in a heterozygous state of the *NIPA2* gene in 3 of the 367 patients, whereas they were absent in the 700 controls

(p = 0.040). These mutations included two novel missense mutations (c.532A>T, p.I178F; c.731A>G, p.N244S) and one small novel insertion (c.1002_1003insGAT, p.N334_335EinsD).

Conclusion: Our findings suggest that 15q11.2 microdeletions are important pathogenic CNVs for CAE and have a higher frequency in the Chinese population than that previously reported in Caucasians. Our study is the first to identify *NIPA2* as a susceptibility gene for CAE and also suggests that haploinsufficiency of selective magnesium transporter *NIPA2* may be a mechanism underlying the neurologic phenotypes of 15q11.2 microdeletions.

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LINEAR SCLERODERMA OR PARRY–ROMBERG SYNDROME: A RARE CAUSE OF EPILEPSY WITH STILL UNKOWN ETHIOLOGY

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Purpose: We present four patients with linear scleroderma or Parry-Romberg syndrome. These rare syndromes share clinical features and the craniofacial forms can be associated with epilepsy, migraine and unilateral white matter lesions. Their etiology is still not clear. In this study we tested the hypothesis that the localized, strictly unilateral structural abnormalities may be caused by a somatic mutation resulting in somatic mozaicism.

Method: Clinical and radiological characteristics of the four patients are presented. In one patient we performed array comparative genome hybridization (aCGH) on DNA extracted from lymphocytes and cultured fibroblasts obtained by skin biopsy of affected skin. Copy number variants (CNVs) were compared between the two tissues in order to search for a CNV present in fibroblasts and absent in the blood.

Results: Two patients had linear scleroderma. The first patient had imaging consistent with a right-sided cerebral vasculitis. The other patient had the diagnosis of Rasmussen encephalitis. Two patients had Parry-Romberg syndrome. One patient had aspecific gliosis of the right frontal brain. The last patient had Rasmussen encephalitis, with intractable epilepsia partialis continua.

Results of the CNV analysis in the first patient will be presented.

Conclusion: Linear scleroderma and Parry-Romberg can be associated with epilepsy, migraine and unilateral white matter lesions. There can be overlap with Rasmussen encephalitis. The etiology and best treatment of these disorders is not clear. There are speculations about viral, autoimmune or vascular origin but genetic somatic mozaicism is also an interesting hypothesis needed to be explored further.

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GENETIC ANALYSIS OF *SLC2A1* GENE CODING GLUCOSE TRANSPORTER GLUT1 IN TURKISH IDIOPATHIC GENERALIZED EPILEPSY PATIENTS

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Purpose: Epilepsy is one of the most common neurological disorders with prevalence of 1% and approximately 30% of all epilepsy cases are classified as idiopathic generalized epilepsy (IGE). Twin studies demonstrate that genetic factors have significant impact on the etiology of IGEs. In uncommon cases with Mendelian inheritance and sporadic cases of IGE, it has recently been connected with glucose transporter type 1 (GLUT1) deficiency. Generalized epileptiform activity can be seen in the cases with GLUT1 deficiency syndrome is due to heterozygous mutations in *SLC2A1* gene. In this study, we aim to screen *SLC2A1* gene in seventeen patients with absence seizures.

Methods: Seventeen patients from Turkey who all had absence seizures and generalized spike-wave (>2.5 Hz) records on electroencephalogram were included. All exons and exon-intron boundaries of *SLC2A1* gene were PCR amplified in ten fragments from genomic DNA extracted from whole blood of these patients. Subsequently, mutation analysis was carried out on all fragments were subjected to DNA sequence analysis via denaturating high performance liquid chromatography (DHPLC) and/or direct DNA sequencing techniques. DNA sequencing results were aligned to reference sequence NM_006516.

Results: DHPLC is a mutation prescreening technique that can distinguish even one single variation in the amplified sequence. In our research, DHPLC results were confirmed with direct DNA sequencing technique in the rate of 95%. We found six different common polymorphisms, three of them in exons, two of them in introns and one of them in 3' UTR region. Also a novel variant in intron 4 was encountered in one patient.

Conclusion: According to our results of the mutation screening of *SLC2A1* gene, we have not detected any novel or reported mutations in our patient cohort with absence seizures. All polymorphisms in exons are synonymous variations. For further research, the novel variant in intron 4 can be evaluated if it results with any splice site aberrations. Also, the novel variant can be screened in healthy individuals to test if it is a new common polymorphism.

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GAIN-OF-FUNCTION OF THE INWARDLY RECTIFYING K^+ CHANNEL KIR4.1 CONTRIBUTES TO AUTISM WITH SEIZURES AND INTELLECTUAL DISABILITY

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Purpose: The inwardly rectifying potassium channel Kir4.1 is a major player in the astrocyte-mediated regulation of $[K^+]_o$ in the brain, which is essential for normal neuronal activity, excitability, and synaptic functions. *KCNJ10*, encoding Kir4.1, has been recently linked to seizure susceptibility in humans and mice, and is a possible candidate gene for autism spectrum disorders (ASD). We have investigated the frequency of *KCNJ10* variants in patients with cryptogenic epilepsy, fourteen of whom had a concurrent diagnosis of ASD.

Method: Mutation analysis of *KCNJ10* was performed in 52 patients with cryptogenic epilepsy associated with impairment of either cognitive

or communicative abilities, or both. The effects of mutations on channel activity were functionally assayed using a heterologous expression system.

Results: We detected two heterozygous *KCNJ10* mutations (p.R18Q and p.V84M) in three children (two unrelated families) with seizures, ASD, and intellectual disability. These mutations changed highly conserved residues and were undetected in about 500 healthy chromosomes. Our functional studies indicated that the molecular mechanism contributing to autism/epilepsy with intellectual disability tentatively relates to an increase in either surface-expression or conductance of Kir4.1 channels, or both.

Conclusion: Gain-of-function defects of Kir4.1 are associated with ASD, seizures, and intellectual disability. Unlike previous syndromic associations of genetic variants in *KCNJ10*, the pure neuropsychiatric phenotype in our patients suggests that the new mutations affect K^+ homeostasis mainly in the brain. Dysfunction in astrocytic-dependent K^+ buffering may contribute to autism/epilepsy phenotype, by altering neuronal excitability and synaptic function, and may represent a new target for novel therapeutic approaches.

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PHENOTYPIC STUDY OF A FAMILY WITH EPILEPSY AND EPISODIC ATAXIA TYPE 2

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Purpose: Epilepsy has been reported in some patients and families with episodic ataxia (EA) type 2 related to *CACNA1A* mutation. Mutated mice in P/Q-type Ca^{2+} channel alpha (1) 2.1 subunits gene exhibit also absence-like seizures in association with EA. Here we describe a new family with genetically proved EA type 2 associated with different idiopathic generalized epilepsy (IGE) phenotypes.

Method: The proband, a 36-year-old male, harbours a *CACNA1A* gene point mutation in exon 33 (c.5088_5091del). Six other members of his family are clinically affected, on three generations. All were evaluated with awake EEG and intermittent light stimulation. Cerebral MRI was performed in five members, sleep EEG in four.

Results: The proband (II-2) suffers from progressive ataxia and history compatible with juvenile myoclonic epilepsy (JME). First clinical manifestations were tonic–clonic generalized seizures and myoclonia at 14 years of age, with 3 Hz spike-waves (sw) on the EEG. Clinical examination showed nystagmus. Phenytoin was administrated during 11 years. Seizures persisted and progressive ataxia appeared. He is currently seizure-free under valproate but ataxia persists. MRI shows severe cerebellar atrophy. His father (I-2) has late onset EA. His older brother (II-1) presents mild EA, discrete cerebellar atrophy and history of febrile seizures during early childhood. His younger brother (II-3) suffers from severe EA, his EEG showing rare 3 Hz sw. Among his four children, the first three are affected, all with some degree of mental retardation. The elder (III-2) has 3 Hz sw and photosensitivity on the EEG, without clinical seizure. The second (III-3) presents EA only. The third (III-4) is followed for EA and childhood absence epilepsy (CAE) with photosensitivity. She had one febrile seizure during infancy.

Conclusion: This report confirms the link between IGE and *CACNA1A* mutation. Clinical expression is variable: febrile seizures, subclinical EEG abnormalities, JME or CAE. Photosensitivity, demonstrated in two patients, was not yet reported with *CACNA1A* mutation. The more severe cerebellar atrophy, found in the proband, could have been worsened by chronic phenytoïn use.

p275
THE ROLE OF *SCL2A1* IN EARLY ONSET AND CHILDHOOD ABSENCE EPILEPSIES

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Purpose: Early onset absence epilepsy (EOAE) constitutes an idiopathic generalized epilepsy syndrome with typical absences starting before the age of 4 years. Mutations in *SLC2A1*, encoding the glucose transporter of the blood–brain barrier (GLUT-1), account for approximately 10% of EOAE cases. The role of *SLC2A1* mutations in absence epilepsies with a later onset has not been assessed so far. Therefore, we aimed to compare the role of *SLC2A1* mutations in EOAE and Childhood and Juvenile Absence Epilepsy (CAE, JAE).

Method: Twenty-six cases with EOAE and 40 probands with CAE or JAE were screened for *SCL2A1* mutations by sequence analysis. Extensive phenotyping was performed in patients and family members.

Results: Mutations in *SLC2A1* were detected in 2/26 EOAE patients and 0/40 patients with familial absence epilepsy. One EOAE patient with a mild phenotype had a variant in exon 8 (c.1008G>C) leading to an amino acid exchange (336Leu>Val), the family history was unremarkable. The other EOAE patient with a very early onset of a severe epilepsy phenotype and movement disorder had a base exchange at position c.1189C>T causing a stop codon (p.Q397X) in exon 9. Familial GTCS were reported in his brother and the paternal grandmother.

Conclusion: Our study confirmed the role of *SLC2A1* mutation carriers in EOAE and demonstrated that *SLC2A1* do not seem to play a major role in CAE and JAE. Since ketogenic diet is a well known treatment option in GLUT-1-deficiency, pediatricians as well as neurologists may revisit the age of onset in patients diagnosed with absence epilepsies.

p276
FAMILIAL CLUSTERING SUGGESTS GENETIC CONTRIBUTION TO COMMON EPILEPSY-RELATED EEG PATTERNS

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Purpose: Many common epilepsy syndromes present with distinct age-related EEG patterns. While the heritable component to many common epilepsy syndromes is clearly established through twin and family studies, the genetic contribution to the related EEG phenotypes is less clear. We aimed to assess the genetic contribution to five common EEG phenotypes through family segregation analysis.

Method: In order to examine familial aggregation of EEG patterns, 251 families (cohort 1) were phenotyped for theta waves, generalized spike

wave (GSW), photoparoxysmal response (PPR), focal spike-wave (FSW) and alpha EEG. Results were followed up in an independent cohort of 134 families phenotyped for the five EEG patterns including additional information about age at the time of the EEG (cohort 2). In cohort 1, permutation analysis with 10,000 permutations was used to test the hypothesis that the number of families concordant for presence or absence of a given EEG abnormality was greater than expected by chance. In cohort 2, logistic regression analysis was performed.

Results: In cohort 1, concordance for theta, GSW, FSW and PPR in families was greater than expected by chance ($p < 0.0075$). Logistic regression analysis in cohort 2 confirmed familial aggregation for GSW, FSW and PPR ($p < 0.002$), but not for theta. Alpha rhythms did not aggregate in families in either cohort.

Conclusion: Using two complementary statistical approaches in two independent cohorts, we demonstrate significant familial clustering of common epilepsy-related EEG patterns (theta, GSW, FSW, PPR) in families. This clustering is likely to reflect a strong genetic contribution to these EEG patterns.

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EXON-DISRUPTING DELETIONS OF *NRXN1* PREDISPOSE TO IDIOPATHIC GENERALIZED EPILEPSY

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Purpose: Neurexins are neuronal adhesion molecules located in the presynaptic terminal where they interact with postsynaptic neuroligins to form a transsynaptic complex which is required for formation of synaptic contacts and efficient neurotransmission in the brain. Recently, partial deletions and point mutations of the neurexin 1 (*NRXN1*) gene have been associated with a broad spectrum of neuropsychiatric disorders. This study aimed to investigate if exon-disrupting deletions of *NRXN1* also increase risk for idiopathic generalized epilepsies (IGE), representing the most common group of genetically determined epilepsies.

Method: We screened 1569 IGE patients of North-Western ancestry and 2788 German controls for exon-disrupting deletions involving the *NRXN1* gene using microarray data. Validation of *NRXN1* deletions was performed by qPCR or array CGH.

Results: We identified exon-disrupting deletions of *NRXN1* in 5 of 1569 individuals with IGE, whereas none was observed in 2788 controls ($p = 0.006$, Fisher's exact test). The identified deletions were verified by either array CGH or qPCR. The inheritance of these deletions was tracked in four families. Two were de novo, one was inherited from a parent affected by IGE, and one was transmitted from an unaffected parent. The deletion cosegregated with IGE in 1/3 multiplex families whereas 2/3 pedigrees included other family members with IGE who lacked the deletion. Nonpenetrance of the deletion was identified in one deletion carrier in 1/4 pedigrees.

Conclusion: Our results provide evidence that exon-disrupting deletions of *NRXN1* are a risk factor for common IGE syndromes.

p278
MOLECULAR INVESTIGATION OF DRAVET AND DOOSE SYNDROMES: ADVANCING THE KNOWLEDGE OF CLINICAL USE OF GENETIC TESTING FOR MONOGENIC EPILEPSIES

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Purpose: Dravet (DRS) and Doose (DOS) syndromes are severe forms of epilepsy included in the clinical spectrum of generalized epilepsy with febrile seizures plus. Mutations in *SCN1A* have been identified in patients within this spectrum. The purpose of this study was to test patients with DRS and DOS for mutations in *SCN1A* in order to further advance the knowledge of its role in clinical epileptology.

Method: Mutation screening in *SCN1A* was performed in 15 patients with DRS and 13 with DOS. Four different prediction algorithms were used to analyze the impact of the mutations in putative protein function. Furthermore, we genotyped 100 control chromosomes. In addition, MLPA technique was used to detect copy number variations within *SCN1A*.

Results: Patients with DOS showed no mutations, whereas twelve mutations were identified in patients with DRS: six missense mutations (50%) which were predicted to affect protein function, three frameshift mutations and three splice-site mutations. The mutations are mostly located in the pore region and the C-terminal of the protein. No copy number variants were identified.

Conclusion: Patients with DRS showed a high frequency of *SCN1A* mutations (80%), confirming that molecular testing is useful to identify these patients. In addition, our strategy for predicting deleterious effect of mutations was able to provide valuable information helping clinicians with decision making. Moreover, DOS does not seem to share the same genetic basis as DRS. Furthermore, our results confirm that missense mutations can cause severe phenotypes depending on its location and the type of amino-acid substitution.

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MUTATIONAL ANALYSIS OF *SCN1A* IN KOREAN DRAVET SYNDROME PATIENTS

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Purpose: The aim of this study was to characterize the *SCN1A* mutation spectrum and genotype-phenotype correlation of Korean Dravet syndrome patients

Method: Twenty-three patients diagnosed as Dravet syndrome in Seoul National University Children's Hospital were included. Direct sequencing and multiplex ligation-dependent probe amplification (MLPA) were used for screening of *SCN1A* mutations. Mutation type was classified as truncation (nonsense, frame-shift) or missense. The mutation spectrum was analyzed according to the clinical phenotype (classic VS. borderline).

Results: Seventeen pathogenic mutations (17/23, 74%) and three unclassified variants were identified. No large deletion/duplication mutation which could be detected by MLPA was found. Thirteen

mutations out of these 17 *SCN1A* mutations were found to be novel. The type of *SCN1A* mutations were nine truncation (five frame-shift, four nonsense), seven missense, and one splice site (in-frame deletion) mutations. While truncating mutations span throughout the whole SCN1A location, all missense mutations were localized to either the voltage sensor (S4) or ion pore region (S5-S6). As for genotype- phenotype correlation, *SCN1A* mutations were more frequently found in classic group (87% vs. 50%). Most of the truncating mutations (eight of nine) were found in classic group.

Conclusion: The genotype-phenotype correlation of Korean Dravet syndrome patients is consistent with the current understandings. Furthermore, this study could expand the spectrum of *SCN1A* mutations associated with Dravet syndrome.

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GENOTYPE-PHENOTYPE CORRELATION IN PATIENTS WITH COMORBID EPILEPSY AND INTELLECTUAL DISABILITY

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Purpose: Intellectual disability (ID) affects 1–3% of the western population. The prevalence of epilepsy in this group is approximately 26 %. Causes and clinical course of comorbid ID and epilepsy are often unknown. Copy number variations (CNVs) have been described as the underlying etiology of both epilepsy and ID. However, little data exist on the phenotype-genotype relationship among persons with comorbid epilepsy and ID. This study aimed to characterize the genotype-phenotype correlation in this particular group of patients.

Method: We examined 76 persons with unexplained epilepsy and ID. Detailed phenotyping was performed and genotype was determined by array-CGH, sequencing and karyotyping.

Results: Median age of epilepsy debut was 18 months (1 day–18 years). At time of examination, >60% had intractable epilepsy. The most frequent seizure types were GTCS and complex focal seizures. Thirty-one percent had cognitive decline after seizure onset. Genetic analysis revealed CNVs in 9/76 (11.8%) all detected in patients with generalized epilepsy. Among others, an intragenic deletion of *NRXN1*, unmasking a recessive mutation, was detected in a patient with severe ID, West syndrome and GTCS; and a de novo partial deletion of *SETDB1* and *LASS2* was detected in a patient with mild ID and progressive myoclonic epilepsy (PME).

Conclusion: CNVs were detected in 11.8% of patients and our data show that CNVs play an important role in the etiology of comorbid ID and generalized epilepsy. This study provides new candidate genes and chromosomal loci for different epilepsy disorders, including early onset epileptic encephalopathies and PME.

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MOLECULAR AND FUNCTIONAL STUDY OF 9 FAMILIES WITH BENIGN FAMILIAL NEONATAL SEIZURES (BFNC)

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Benign familial neonatal seizures (BFNS) are one of the three autosomal dominant epileptic syndromes occurring in the first year of life with generally favorable outcome. They are characterized by nonfebrile seizures starting within the first days of life and that usually stop spontaneously or under treatment after a few weeks or days, although 10–15% of patients develop febrile seizures or epilepsy later in life and some have cognitive delay. Mutations in two genes can cause BFNS, *KCNQ2* and *KCNQ3*, which encode for Kv7.2 and Kv7.3 neuronal voltage-gated potassium channel subunits, respectively.

We report nine families with at least two first degree related individuals who experienced seizures with onset between day 2 and 2.5 months and that stopped spontaneously or under treatment The clinical presentation and family history were consistent with the diagnosis of BFNS. Five patients had psychomotor retardation or learning difficulties. We resequenced the exons and intronic boundaries of *KCNQ2* and *KCNQ3* genes and search for large deletions/duplication using Multiplex Ligation-dependent Probe Amplification. We identified a mutation of *KCNQ2* in each family. Among these mutations, there are seven missense involving highly conserved amino acids, a deletion of two base pairs leading to frameshift and one deletion of exons 16 and 17. Six mutations have not been reported so far. All mutations are inherited and are not found in 100 control individuals. Functional studies are under way to assess the molecular pathophysiology of the disease in each BFNS family.

Poster session: Genetics II
Monday, 29 August 2011

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A PILOT STUDY OF COPY NUMBER VARIATION IN ROLANDIC EPILEPSY

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Purpose: Rolandic Epilepsy (RE) is a common childhood epilepsy of complex genetic inheritance, with comorbid speech, reading and attentional impairments. Recent reports suggest an association between copy number variation (CNV), neurodevelopmental disorders and epilepsy.

This study gives a pilot evaluation of the potential role of CNVs in RE and the types of CNV that may be encountered.

Method: We analyzed thirteen RE cases, comorbid with speech and/or reading impairment, were analyzed for copy number variation using the Affymetrix Human SNP 6.0 Array. We carried out CNV detection was carried out using the PennCNV-Affy protocol.

Results: 8/13 cases had deletions or duplications at the proximal end of the 15q11.2 hotspot for intellectual disability, language delay, schizophrenia and epilepsy. Two deletions and one duplication were also found within breakpoint4 and one deletion within breakpoint5 of the 15q13.2 hotspot. Three novel CNVs encompassing several genes were discovered on 19p12, 11q22.3 and 14q11.1, with potential causality. One case had a large (1.6 Mb) deletion on 16p11.2 which matches the deletion highly enriched in families with benign infantile convulsions with paroxysmal dyskinesia. One case also had a 600 Kb deletion at terminal 1p36, although smaller than those most commonly seen in 1p36 deletion syndrome.

Conclusion: This pilot study gives evidence for extension into a larger cohort, as it appears that copy number variation might play an important role in the etiology of RE. These results also consolidate findings of genetic overlaps in developmental neurological disorders. Further inheritance and validation assays will now be carried out.

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WHOLE EXOME SEQUENCING IN STATUS EPILEPTICUS

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Purpose: Studies in animals and humans suggest that genetic factors may contribute to status epilepticus (SE). However, no genes involved in human SE have been identified so far. Recent advances in genetics suggest that rare genetic variants with large effect size play a major role in the susceptibility to common diseases. Sequencing of individuals with extreme phenotypes has been proposed as a way to uncover these rare variants. In this study we consider SE as a biologically extreme phenotype of seizures. The purpose of the study is to identify rare genetic variants that play a role in human SE through whole exome sequencing (WES) in selected cases of SE.

Method: WES was conducted in two groups of patients with SE: (1) cryptogenic (i.e. absence of acute precipitating factors or history of prior neurologic insult), de novo (i.e., no history of epilepsy) SE (N = 7), and (2) recurrent SE without obvious cause (N = 7). One patient was represented in both groups. Therefore, 13 samples underwent WES. Raw sequence image data were processed and compared to WES data of 335 control samples. Identified single nucleotide variants (SNVs) and small insertions/deletions were annotated, interpreted and prioritized. We looked for enrichment of (putatively) functional variants in cases compared to controls considering both recessive (including compound heterozygotes) and dominant disease models. The nature and distribution of genetic variants in SE was explored.

Results: A large number of genetic variants were significantly overrepresented in SE versus controls. The most significant result was obtained for variants in the gene COX*10*, encoding cytochrome C oxidase assembly protein. Genotyping of the 29 most promising variants in further cases of SE, as well as in patients with epilepsy and controls is currently ongoing.

Conclusion: We successfully completed WES in 13 cases of SE. Identification of genetic variants involved in SE will improve our understanding of the pathophysiology of SE and may lead to the development of novel treatments for SE and epilepsy.

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ASSOCIATION OF POLYMORPHISM OF THE SODIUM CHANNELS GENE *SCN1A* WITH THE EFFECTIVENESS OF PHENITOINE TREATMENT IN PATIENTS WITH EPILEPSY

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Purpose: Establish the association between the type of polymorphism of (Na) channels B3 receptor and phenitoine effectiveness in patients with epilepsy

Method: We examined 201 patients with a diagnosis of epilepsy. To establish the (Na) channels B3 receptors polymorphism used biological material (whole blood) from patients with epilepsy. Investigated patients were divided into two groups: first group included 135 patients with effective drug treatment and the second group – 69 pharmacoresistent patients that was 66.2% and 33.8% respectively. Pharmacoresistence of the patients was evaluated on the basis of adequate long-term medication, using international criteria developed by Brodie and others. [3].

Results: Using PCR reaction was established three polymorphisms of the *SCN1A* – TT, CT, and CC combination of alleles of this gene. Distribution in the study group was: 76 patients had a CT polymorphism (37.4%), 65 patients – TT polymorphism (31.8%), and in 63 patients was set CC polymorphism of *SCN1A* (30.8%). The distribution analysis of polymorphism of *SCN1A* receptor in groups according to the efficiency of phenitoine was performed.

Conclusion: Based on the above is possible to assume a clear association between the effectiveness of phenitoine as AED and CC polymorphism of *SCN1A*. There is also a clear association between resistance to the phenitoine and TT polymorphism *SCN1A*. We understand the need for further research in this area, but we consider it appropriate to investigate of *SCN1A* receptor polymorphism before prescribing phenitoine. This would avoid the long-term drug titration in the presence of ineffective cases with TT polymorphism.

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INFLUENCE OF A FUNCTIONAL *SCN1A* POLYMORPHISM ON MAXIMUM AND MAINTENANCE DOSES OF ANTIEPILEPTIC DRUGS IN NEWLY DIAGNOSED EPILEPSY

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Purpose: An intronic polymorphism (rs3812718) found in the *SCN1A* gene affects the 5' splice donor site of exon 5 of the alpha-1 subunit of the neuronal voltage-gated sodium channel and has previously been shown to influence maximum prescribed doses of phenytoin and carbamazepine. We assessed whether this SNP shows a similar association with the maximum and maintenance doses of several antiepileptic drugs (AEDs) when used as monotherapy in individuals with newly diagnosed epilepsy.

Method: A total of 586 patients originally enrolled in the SANAD trial were genotyped for the rs3812718 polymorphism. Maximum and maintenance AED doses were identified from trial notes and standardized according to the World Health Organization daily defined dose. Four sodium channel blocking AEDs (carbamazepine, phenytoin, oxcarbazepine, lamotrigine) and four non–sodium channel blocking AEDs (sodium valproate, gabapentin, topiramate, levetiracetam) were included in the

analysis. Associations were investigated using linear regression adjusted for clinical variables, age, sex and epilepsy type.

Results: There was no association between rs3812718 genotype and maintenance dose of all AEDs or sodium channel blocking AEDs. However, there was an association between maximum dose and genotype when all AEDs were analyzed (n = 586, p = 0.030 uncorrected) and when only the sodium channel blocking AEDs were analyzed (n = 389; p = 0.002 uncorrected). Though only the rs3812718 genotype association with sodium channel blocking AEDs survived correction for multiple testing (p = 0.024, r^2 = 2.8%).

Conclusion: These results support the hypothesis that rs3812718 influences maximum dose of AEDs in general, and of sodium channel blocking AEDs in particular, and may be a susceptibility marker for the limit of AED tolerability. However, the modest effect size would question its clinical utility in this regard.

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VALIDATION OF THE AUSTRALIAN FIVE-SNP GENETIC CLASSIFIER OF EARLY TREATMENT OUTCOMES IN NEWLY DIAGNOSED EPILEPSY

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Purpose: This study investigated whether the recently reported Australian five-SNP k nearest neighbour (kNN) classifier for predicting early seizure control in newly diagnosed epilepsy could also predict treatment outcome in a UK epilepsy cohort.

Method: A total of 491 newly treated epilepsy patients from the SANAD trial were genotyped for each of the five SNPs reported to predict outcome in the Australian classifier. Patients were considered responders if they remained seizure-free in the first 12 months of follow-up. Nonresponders were those who continued to experience seizures over the same period despite adequate drug exposure. The performance of the five SNPs was assessed in 70% of the UK cohort (training group), employing a cross-validation approach, and used to predict outcome in the remaining 30% (test group). Machine learning parameters were consistent with the original study.

Results: The original five SNPs in a kNN model significantly predicted treatment outcome for the UK training group (p = 0.0003, n = 343). However, this training group did not, in turn, successfully predict treatment outcome for the UK test group (p > 0.05, n = 148).

Conclusion: The Australian kNN classifier did not provide robust prediction of treatment outcome in a UK epilepsy cohort. This failure may be due to genomic and/or phenotypic differences between the respective clinical populations or may reflect relatively limited patient numbers. The predictive performance of the classifier in the UK training group is, however, encouraging and may be indicative of an underlying influence of these five genomic regions on treatment response. This merits further detailed examination.

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HUMAN GENETIC POLYMORPHISMS AND THE RISK OF MALARIA-ASSOCIATED SEIZURES IN AFRICAN POPULATIONS

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Purpose: To determine the genetic risk of acute symptomatic seizures in malaria by comparing the distributions of genetic polymorphisms among children admitted with malaria-associated seizures (MAS) to those among children admitted with *Plasmodium falciparum* malaria without seizures.

Method: We used logistic regression to investigate genetic associations with MAS, particularly complex phenotypes (focal, recurrent or prolonged), in four sites across Africa: Blantyre, Malawi; Kilifi, Kenya; Kumasi, Ghana and Muheza, Tanzania. The analysis was repeated for four inheritance models (dominant, heterozygous, recessive and additive) adjusting for ethnicity, age, hyperparasitemia and temperature. Pooled estimates were determined by analyzing the summed raw data or by combining individual site estimates using the fixed or random effect models (where heterogeneity was evident). P-values of ≤0.05 and ≤0.009 were considered significant for clinical features and genotypic tests, respectively.

Results: Complex MAS constituted 71% of the 2095 admissions with MAS in all sites. The polymorphisms associated with the risk of MAS or complex MAS were interleukin (IL)10-rs1800890 (odds ratio [OR] = 0.6 [95% confidence interval (CI), 0.5–0.9, p = 0.005]) in Kilifi, IL10-rs1800896 (OR = 0.7 [CI, 0.6–0.9, p = 0.004] and OR = 0.5 [CI, 0.3–1.0, p = 0.009] in Blantyre and Kumasi, respectively), IL4-rs2243250 (OR = 0.5 [CI, 0.3–0.8, p = 0.005]) in Blantyre, complement receptor-1-rs17047660 (OR = 4.6 [CI, 1.8–11.8, p = 0.001]) in Kilifi, epidermal growth factor module-containing mucin-like hormone receptor (EMR)1-rs373533 (OR = 5.2 (CI, 1.8–14.5, p = 0.001)) and OR = 0.5 (CI, 0.4–0.7, p = 0.0004) in Blantyre and Kumasi, respectively), EMR1-rs461645 (OR = 0.2 (CI, 0.1–0.7, p = 0.004) and OR = 0.4 (CI, 0.3–0.7, p = 0.0006) in Blantyre and Kumasi, respectively), Glucose-6-phosphate dehydrogenase (G6PD)-rs1050828 (OR = 0.3 [CI, 0.1–0.6, p = 0.001]) in females in Kumasi, G6PD-rs1050829 (OR = 0.3 [0.1–0.6, p = 0.003]) in females in Kumasi and cluster of differentiation-40-rs1126535 (OR = 0.4 (0.2–0.8, p = 0.009)) in females in Blantyre. No polymorphism was significant in Muheza or in the pooled analysis for the same inheritance models.

Conclusion: The risk of MAS is associated with a number of different polymorphisms. The lack of significant polymorphisms in the pooled analysis for the same inheritance models suggests that the genetic risk of MAS could be site/population specific.

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DEVELOPMENT AND VALIDATION OF CLINICAL ASSESSMENT TOOLS FOR POPULATION GENETIC STUDIES OF EPILEPSY IN RURAL CHINA: A GREAT STUDY

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Purpose: GREAT (Genetic Repository for the study of Epilepsy And related Therapy) is being established as a nationwide genetic repository in China with the goal of identifying genetic markers for the development of epilepsy and treatment response in Chinese. Research and application

of findings in epilepsy genetics in rural areas are hampered by lack of validated clinical assessment tools for phenotyping at the primary care level, agreed investigation protocols, established logistics and network, and trained personnel. This study aims to overcome these barriers with emphasis on building research infrastructure and capacity.

Method: A total of 2000 people with epilepsy will be recruited from rural areas of four provinces. In stage 1, rural primary care doctors will perform phenotyping using clinical assessment tools (questionnaires) in 600 people. Patients will attend the provincial hospitals for independent phenotyping by the ''gold standard,'' consisting of neurologist assessment, EEG and brain MRI. In stage 2, 1400 patients will be phenotyped by rural doctors only. Blood/mouthwash samples will be collected from patients in both stages for DNA extraction and subsequent genotyping. To develop locally valid clincial assessment tools, reference was made to screening questionnaires previously employed for seizure classification and provincial neurologists were consulted. Their feasibility was pilot tested in 80 patients in the rural areas. Common EEG and brain MRI protocols were checked for compatibility with local equipment and practice.

Results: After piloting testing and revision, clinical assessment tools covering epilepsy history and seizure semiology were developed. Common EEG and brain MRI protocols were employed in the provincial hospitals. Provincial neurologists and rural doctors were trained in clinical and research skills and ethics. By February 2011, 297 patients have completed stage 1. Preliminary findings will be presented.

Conclusion: Results will help overcome barriers in epilepsy genetics research and application in rural China. The model developed may be adopted in other low- and middle-income countries where 80% of the world's people with epilepsy live.

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THE DEVELOPMENT OF THE DNA CHIP WHICH AIMED AT THE CLINICAL APPLICATION IN EPILEPSY

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Purpose: Despite the continuous development and release of new AEDs, about 30 % patients are resistant to AED therapy. Furthermore, current therapy for epilepsy requires trial and error method to determine the most effective AED. The development of individualized medicine based on genetic information for epilepsy is critical for improving AED treatment. The aim of this study, therefore, was to develop DNA chip for genetic diagnosis of epilepsy to assist individualized medicine. Furthermore, we searched for new gene mutations related to epilepsy with this DNA chip.

Method: We designed a custom resequencing array (Affymetrix based), in which 26 epilepsy genes and nine genes for AED-induced severe adverse reaction were tiled. We examined performance of this chip using 60 SMEI patient's samples.

Results: Average call rate was 91%, and overall accuracy was 99%. The present data indicate that the DNA chip can determine gene mutations with comparatively high performance. Furthermore, we found novel missense mutations not only *SCN1A* but other gene mutations in about 10% of SMEI patients.

Conclusion: It is possible that coexistence of several gene mutations are implicated in the pathogenesis of SMEI. Because of small number of control samples, significance of newly identified mutations in the pathogenesis of epilepsy is yet to be clarified. This DNA chip can be applied in clinical settings for the individual medicine in the near future. The development of individualized medicine based on genetic information is expected to improve epilepsy treatment immeasurably.

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FINDING MUTATIONS FOR GENERALIZED EPILEPSY WITH PHOTOPAROXYSMAL RESPONSE BY A COMBINATION OF LINKAGE AND WHOLE-EXOME SEQUENCING IN MULTIPLE FAMILIES

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Purpose: Photoparoxysmal response (PPR) is an EEG trait associated with idiopathic generalized epilepsy (IGE), and may be considered an endophenotype within IGE-families. We aimed at finding the mutations responsible for PPR within IGE-families with a predominantly myoclonic IGE phenotype.

Method: We collected ten moderately large families presenting with IGE and PPR, and we performed linkage analysis. The results showed two peaks, one at 16p13, and one at 7q32, which have been published before. To identify the mutations responsible for the linkage results, we have used next-generation sequencing under the linkage peaks in two affected individuals per family. Probes were designed for all exons of coding genes as well as for microRNA genes, and printed on an enrichment chip. After a number of filtering steps, we searched for genes that had cosegregating mutations in multiple families. Special care was necessary not to miss mutations that had low coverage in some samples. For this we used in-house scripts.

Results: An overview of the mutations found, and their relevance, will be given.

Conclusion: Exome sequencing is a valuable tool for finding genes in Mendelian diseases.

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ANALYSIS OF *MDR1* AND *MRP2* POLYMORPHISMS IN DRUG-RESISTANT EPILEPSY (2ND REPORT)

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Purpose: Epilepsy is a most common neurological disorder. About 20–30% of epilepsy do not respond to antiepileptic drugs. We investigated the frequency of *MDR1/MRP2* polymorphism in Japanese patients with epilepsy (drug-resistant/drug-responsive). We defined that drug-responsive patient was that ''patient with complete seizure freedom for ≥1 year'' and drug-resistant patient was that ''patient with any seizure for ≥1 year.''

Method: *MDR1* and *MRP2* polymorphisms were genotyped in 121 drug-resistant epilepsy patients, 184 drug-responsive patients. Highly

specific real-time PCR was applied to detect the variants by using TaqMan allelic discrimination method and direct sequencing method. Differences in genotype and allele frequencies between the three groups were compared using chi-square test (significance was accepted at $p < 0.05$). The haplotype associations were estimated using haplo.stat. These statistical analyses were carried out using the language and environment for statistical computing, R version 2.11.

Results: We obtained genotypic data on all 12 SNPs (*MDR1*: T-129C, A61G, C501T, C1236T, G2677T/A, C3435T; *MRP2*: C-24T, A1019G, G1249A, A1549G, C3972T, G4544A) in 305 patients. No significant differences were observed in the frequencies of genotypes, alleles, haplotypes of the *MDR1/MRP2* polymorphisms between drug-responsive and drug-resistant.

Conclusion: Association between drug-resistance and *MDR1* SNPs is incongruous with this results and previous studies. The precise definition of drug-resistance may very according to epileptic syndromes, substrate AEDs and other important factors.

Poster session: Genetics III
Monday, 29 August 2011

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MOLECULAR GENETIC STUDIES OF PATIENTS WITH FAMILIAL GENERALIZED EPILEPSY WITH FEBRILE SEIZURES PLUS IN CHINESE HAN POPULATIONS FROM SICHUAN PROVINCE

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Purpose: This study is to analyze clinical and genetic features of familial patients with generalized epilepsy with febrile seizures plus (GEFS+) in Chinese Han populations from Sichuan province.

Method: Eight families with GEFS+ from Chinese Han population in Sichuan province were studied. Clinical data were collected in a retrospective survey. Genomic DNA was extracted from peripheral blood lymphocytes of probands in five families using standard phenol-chloroform procedures. Polymerase chain reaction was used to amplify the entire coding region and the exon/intron boundaries of *SCN1A*, *SCN1B* and *GABRG2* genes. The sequences of three genes were analyzed by direct sequencing. The association between gene variants and the clinical features of GEFS+ were analyzed.

Results: Forty patients from eight families with GEFS+ were included in this study. In one patient from family E, a base substitution c.636C>T in exon 5 of *SCN1A* gene was detected; and this was not observed in other patients of this family or healthy control individuals. The c.636C>T transversion didn't result in the substitution of Valine. A new synonymous mutation (V212V) was verified. The entire coding regions of *SCN1B* and GABRG2 were also sequenced and no mutation was observed.

Conclusion: *SCN1A*, *SCN1B* and *GABRG2* mutations may be not the main reasons contributing to familial GEFS+ of Han ethnicity in Sichuan province. The c.636C>T substitution may create a new exonic splicing enhancer consensus sequence; so V212V may be a functional mutation in the *SCN1A* gene.

p293
NOVEL *SCN2A* GENE MUTATION IN A FAMILY WITH BENIGN NEONATAL INFANTILE SEIZURES FROM MALAGASY

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Mutations in *SCN2A*, encoding the brain sodium channel Na (V)1.2, have been described in different types of epilepsies. The most common phenotype caused by *SCN2A* mutations is benign neonatal-infantile seizures (BFNIS), a self-limiting disorder with good outcome, while several de novo mutations have been found in patients with sporadic intractable childhood epilepsy. We report on a French family from Malagasy, including nine individuals over three generations, with phenotypes consistent with BFNIS. Seizure onset extended from 3 to 5 months of age. Seizure frequency during the initial phase was variable from one patient to another. They were not triggered by fever. They often occurred in clusters and one patient had a status epilepticus episode. Interictal EEGs were normal. In two patients, ictal EEG recording showed partial discharges with or without secondary generalization. Seizure offset occurred from 5 to 18 months in all patients, with or without antiepileptic therapy. Psychomotor and intellectual development was normal in all patients. One obligate carrier did not experience seizures. We performed direct sequencing of all exons and intronic boundaries of *KCNQ2*, *KCNQ3* and *SCN2A* genes. We identified a heterozygous missense mutation, c.4766A>G, in exon 26 of *SCN2A*, expected to affect a tyrosine residue (p.Tyr1589Cys), which is highly conserved through evolution, in D4/S6. This mutation has not been reported so far. It was not found in 100 control subjects. It segregates with the phenotype in the family. Functional studies using a heterologous expression system and whole cell patch clamping are currently performed to prove an expected change-of-function of the mutation predicting a neuronal hyperexcitability.

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A NEW FORM OF PROGRESSIVE MYOCLONUS EPILEPSY WITH EARLY ATAXIA AND SCOLIOSIS DUE TO MUTATION IN THE GOLGI PROTEIN GOSR2

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Purpose: The progressive myoclonus epilepsies (PMEs) are a group of predominantly recessive disorders, which present with action myoclonus, tonic–clonic seizures and progressive neurological decline. Many PMEs have similar clinical presentations yet are genetically heterogeneous making accurate diagnosis difficult. We studied an Australian case from a consanguineous union where known causes of PME had been excluded.

Method: Linkage mapping using SNPs was performed on the proband, her healthy sibling and parents. The mapped locus was captured and analyzed by massive parallel sequencing. The identified variant was validated in other cases and its function explored in vitro.

Results: A novel locus for PME to chromosome was identified in 17q21. We identified an identical by descent, homozygous mutation in *GOSR2* (c.430G>T, p.G144W), that codes for a Golgi vesicle transport protein. Following screening of a 73 cases with unsolved PME we identified the same variant in five other cases from four unrelated sibships. All six subjects had difficulty walking in early childhood followed by the onset of action myoclonus around the age of 6 years. Tonic–clonic seizures were infrequent. By mid teenage subjects were usually wheelchair dependent due to sudden epileptic falls. Cognition was preserved. All six cases had scoliosis. EEGs showed active generalized epileptiform activity with prominent photosensitivity. All cases had borderline or mildly elevated serum creatine kinase levels. MRI brain scans were normal with the exception of mild cerebellar atrophy in one. We show that this mutation is equivalent to a loss of function and results in GOSR2 protein mislocalization.

Conclusion: This PME syndrome with early onset ataxia and subsequent scoliosis and raised creatine kinase is a distinct new disorder, due to mutation in a Golgi transport protein GOSR2. Like many other causes of PME, GOSR2 is involved in the posttranslational processing of proteins suggesting a convergence of mechanisms causing this devastating form of epilepsy.

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PREDICTION METHOD FOR *SCN1A*-RELATED EPILEPSY PHENOTYPES BASED ON AMINO ACID SUBSTITUTION

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Purpose: More than 650 mutations in the voltage-gated sodium channel α1 subunit gene *SCN1A* have been identified in epileptic patients with benign and severe phenotype. However, the reason why similar missense mutations in *SCN1A* result in different phenotypes has not been fully clarified yet. We analyzed genotype-phenotype correlation based on the effects of physicochemical property changes by amino acid substitution and estimated the accuracy of *SCN1A*-related epilepsy phenotypes prediction using the bioinformatic approach.

Method: First, we obtained a total of 249 *SCN1A* missense mutations from the *SCN1A* Variant Database. We describe a computational model for phenotype prediction of *SCN1A*-related epilepsies involving the Support Vector Machines (SVMs) or Random Forest algorithms that were trained the significant value difference of physicochemical properties for *SCN1A* missense mutations.

Results: The accuracy of prediction model for SVMs that were trained "isoelectric point" + "polarity" + "polar requirement" is very high (accuracy = 99%, sensitivity = 100%, specificity = 99.23%).

Conclusion: In the future, this model can help predict the *SCN1A*-related epilepsy phenotype of de novo missense mutation in *SCN1A*, and will provide new insights into *SCN1A* gene functions and a new strategy for genetic diagnosis, genetic counseling, and epilepsy treatment.

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PREDICTING *SCN1A*-RELATED EPILEPSY PHENOTYPES BASED ON THE PREDICTED DELETERIOUS EFFECT IN SCN1A FUNCTION WITH THE AMINO ACID SUBSTITUTION

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Purpose: More than 650 mutations in the voltage-gated sodium channel subunit (*SCN1A*) gene have been identified in epileptic patients with various phenotypes. However, the genotype-phenotype correlation in *SCN1A*-related epilepsy has not been fully understood yet. We tried, in this study, an *SCN1A*-related epilepsy phenotype prediction based on the amino acid substitution in possible epileptic SCN1A sequences, by using a bioinformatics approach.

Method: First, we extracted 249 *SCN1A* missense mutations in total (SRIEE group, 215; GEFS+ group, 31) from the *SCN1A* Variant Database. We applied PolyPhen (a program for predicting deleterious effects on protein function based on the amino acid substitution) to these mutated *SCN1A* sequences to examine whether their functional damages are predicted correctly or not. The missence mutations predicted in this step to have a deleterious effect were treated as epileptic ones.

Results: Setting the parameter value in PolyPhen appropriately, we attained the prediction accuracy of 0.80 (sensitivity, 0.87; specificity, 0.32) as the best one, and the second best 0.70 (sensitivity, 0.74; specificity, 0.42).

Conclusion: In near future, this prediction model would make a great contribution to the *SCN1A*-related epilepsy phenotype prediction for future missense mutations in *SCN1A* and also provides a new strategy for genetic diagnosis, genetic counselling, and epilepsy treatment.

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SODIUM CHANNEL *SCN3A* MUTATIONS IN PATIENTS WITH EPILEPSY AND MENTAL RETARDATION

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Abstracts

Purpose: *SCN3A* is one of the four voltage-gated sodium channel genes that are widely expressed in the CNS and plays an important role in controlling the excitability of neurons. Contrast to other sodium channel genes, *SCN3A* has been less investigated as a candidate gene for epilepsy. This study screened *SCN3A* gene for mutations in patients with epilepsy and mental retardation.

Method: A total of 82 patients were recruited. Their clinical information and blood samples were collected. DNA was extracted and screened for *SCN3A* mutation in all 26 coding exons by using PCR and direct sequencing.

Results: Five missense mutations, including c.602C>T (A201V), c.1388C>T (A463V), c.1559G>C (R520T), c.1589A>G (D530G), and c.3282C>A (D998E) were identified, each in one patient. c.602C>T (A201V) was a homozygous mutation, while the others were heterozygous. Three cosense mutations, c.2118G>A (V706V) from five patients, c.4731C>T (L1577L) and c.5232A>G (P1744P) from one patient each, were also detected. These variants in *SCN3A* were not detected in 100 neurologically normal controls.

Conclusion: *SCN1A* mutations may be associated with epilepsy and mental retardation. Further studies are required to know the impact of the mutations on channel function and their roles in the pathogenesis of epilepsy.

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FAMILIAL MOVEMENT-INDUCED REFLEX EPILEPSY: A NOVEL GENETIC EPILEPSY SYNDROME

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Purpose: To describe clinical features, neurophysiology and molecular genetic data of a family with a previously unreported familial reflex epilepsy.

Method: Observational family study including clinical, neurophysiological and molecular genetic data.

Results: Two siblings presented with a reflex epilepsy syndrome not previously described. Parents were healthy and unrelated. The older, male sibling described lifelong movement-induced attacks. His sister developed identical attacks with onset aged 8 years.

Repetitive voluntary movement of any body part would evoke involuntary clonic movements and dystonic posturing in the repetitively active muscles. Cessation of voluntary movement would usually result in involuntary movements subsiding within 2–5 s, but persistent voluntary activity would lead to focal clonus migrating proximally over 5–10 s then culminating in loss of consciousness and a generalized tonic–clonic seizure (GTCS).

Typical triggers included scanning visual targets, speech, chewing, walking and manual tasks such as doing up or undoing buttons, knots or laces. Sodium valproate reduced attack frequency and severity, though multiple other antiepileptic drugs conferred no benefit.

EEGs were repeatedly normal for both subjects. A GTCS evoked by untying a difficult knot was recorded on video EEG. No scalp electrographic abnormalities were seen accompanying the focal clonic movements during attack evolution and EEG was obscured by muscle artefact at the onset of GTCS, preventing electrographic characterization. Visual and somatosensory evoked potentials were normal in both subjects, as was brain MRI.

The segregation pattern favors recessive inheritance, though dominant inheritance with either germ-line mosaicism or low penetrance also possible. In view of the rarity of the condition, recessive inheritance of two identical ancestral alleles is plausible. Attempts at linkage analysis using Affymetrix SNP 6.0 platform with homozygosity models and CNV analysis are ongoing.

Conclusion: We describe a previously unreported familial movement induced reflex epilepsy. Identification of the causative genetic changes may yield insights which are also relevant to motor reflex epilepsies sometimes seen in refractory symptomatic cases.

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EXPLORING THE CAUSATIVE ROLE OF *PCDH19* (XQ22) IN FEMALE PATIENTS WITH EPILEPSY

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Purpose: Confirmation of *PCDH19* mutations in female patients with Dravet Syndrome (DS) and examining a possible extension of the clinical spectrum.

Method: We performed a mutation analysis of *PCDH19* in a cohort of 25 DS or DS-like patients, eight patients with severe early onset epilepsies and seven patients showing a wide spectrum of milder phenotypes including focal and generalized forms. We also screened an epilepsy family with a female-limited autosomal dominant inheritance pattern but without mental retardation. Sequencing data was generated by Sanger sequencing, while CNVs were determined thought multiplex amplicon quantification (MAQ).

Results: Three point mutation were identified in four patients. Consistent with the literature we identified a recurrent missense mutation (p.N340S) in two sporadic cases of DS and one novel missense mutation (p.D341G) in a sporadic patient with a severe early onset epilepsy with clusterd eizures. On top of this another novel missense (p.Y275S) mutation was found in all nine affected females of the female-limited epilepsy family. MAQ analysis revealed no whole gene or partial deletions. These results show that mutations in *PCDH19* are a relatively frequent cause of epilepsy in females and should be considered even in absence of family history and/or mental retardation.

Conclusion: Our research confirms and strengthening previous results about *PCDH19* as an emerging major gene for early onset sporadic and familial epilepsy in female patients with or without mental retardation. It also demonstrates the need for systematic screening of *PCDH19* in *SCN1A* negative female DS patients and epilepsy families with a female-limited autosomal dominant inheritance pattern.

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"BORDERLINE" GENERALIZED EPILEPSY WITH FEBRILE SEIZURES PLUS (GEFS+)

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Introduction: Generalized (or genetic) epilepsy with febrile seizures plus (GEFS+) is the most studied familial epilepsy syndrome, however the characteristics of UK families have not previously been reported. GEFS+ is caused by private mutations in *SCN1A* and *GABRG2* genes in around 10% of families. Initially the family phenotype was tightly defined, but the borders of both epilepsy within GEFS+ families and the epilepsy caused by *SCN1A* mutations are increasingly blurred.

Methods: Consensus as to whether the families met the original criteria for GEFS+ (Scheffer and Berkovic, 1997) was achieved following debate

within a team consisting of two clinical research fellows, a Professor of molecular genetics, a pediatric neurologist and a genetic counsellor. Analysis of the first eighty families recruited by WERN identified four broad familial endophenotypes: classical GEFS+; borderline GEFS+; unclassified epilepsy; and families with a definite alternative syndromal diagnosis.

Results: Borderline GEFS+ families have many of the characteristics of GEFS+ families—such as prominent atypical febrile seizures and early-onset febrile seizures. However, borderline families have more adults with focal epilepsies (as opposed to idiopathic generalized epilepsies predominating in GEFS+) and double the prevalence of migraine. Atypical febrile seizures are rare events but were specific (97.5%, but not sensitive) for identifying GEFS+ or GEFS+ borderline families, where they accounted for 24 and 19% of febrile seizures respectively.

Discussion: Subcategorizing families with epilepsy is important as it helps target both clinical and research resources. As most families with GEFS+ have no identified causal mutation – the process of endophenotyping (both individuals and families) becomes more important to identify genetic homogeneity.

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UNVERRICHT–LUNDBORG DISEASE: REPORT OF A NEW MUTATION

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Introduction: Unverricht-Lundborg disease is the most frequent cause of progressive myoclonic epilepsy. *CSTB* mutations, with cystatin B loss of function, have been described as the major cause of this disease.

Case Report: We present a 33-year-old man with the first epileptic seizure at age 14. He started seeing bright lights followed by a myoclonic seizure. Afterwards he had similar seizures, some with longer duration and consciousness impairment. Occasionally, while walking/running, he had sudden falls, caused by loss of tone in his legs. By the age of 18, upper limb bilateral, irregular myoclonus appeared, worsened by unexpected sounds or bright light. At the age 20 he developed progressive dysarthria, bilateral dismetria and axial ataxia. Currently, he maintains reflexive and negative myoclonic seizures; he has normal cognitive functions, moderate dysarthria, generalized myoclonus, apendicular and truncal ataxia, and an independent gait. Interictal EEG disclosed bilateral synchronous polyspike-and-wave activity, with photosensitivity.

Genetic testing identified a mutation Q22Q in homozygosity that leads to abnormal splicing and partial inclusion of intronic sequence. Potential interference with a splicing consensus region led to the study of the cDNA and subsequent bioinformatics analysis. The data obtained at the RNA level substantiates the causal nature of the CSTB genetic lesion and corroborates the existing clinical suspicion. Concordant results showed activation of an alternative splice site with partial inclusion of an intronic sequence.

Conclusions: We describe a patient with a classic clinical Unverricht-Lundborg disease secondary to a new splicing mutation in homozygosity of cystatin B gene.

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FIRST REPORT AND DESCRIPTION OF PATIENTS WITH DRAVET SYNDROME AND GENETIC CONFIRMATION OF MUTATION ON NEURONAL VOLTAGE-GATED SODIUM CHANNEL ALPHA SUBUNIT TYPE 1 GENE IN CHILE

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Purpose: Description of phenotypic and genotypic characteristics of patients with genetic confirmation of neuronal voltage-gated sodium channel alpha subunit type 1 (SCN1A) gene mutations and Dravet syndrome (DS) in our country.

Method: Retrospective descriptive analysis of first seizure, clinical evolution, electroencephalographic (EEG), neuroimaging findings and mutation analysis in six patients with DS.

Results: Six unrelated patients had normal psychomotor development prior to seizure onset and moderate to severe development compromise was recorded at last visit. Epilepsy family history was found in 1/6 patients. Subjects first seizure was between 2 and 6 months, 5/6 of them with fever and duration of 15 min or more. All but one had normal neuroimaging. EEG findings were normal in all patients during first year of life. No same mutations were found; two intron mutations and four exon mutations.

Conclusion: First national report of genetic confirmation of SCN1A mutations in six patients with classic DS manifestations. Six different point mutations were found in all unrelated patients.

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SPECTRUM AND FREQUENCY OF *SCN1A* MUTATIONS IN DRAVET SYNDROME PATIENTS: THE FIRST ATTEMPT OF MOLECULAR DIAGNOSTIC IN POLAND

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Purpose: Dravet syndrome (DS) is a severe epilepsy syndrome characterized by prolonged febrile hemiconvulsions starting in the first year of life with myoclonic, absence and complex partial seizures appearing later accompanied with psychomotor delay resulting in mental retardation.

About 80–90% cases of DS are caused by dominant mutations of the *SCN1A* gene coding for the sodium channel α-1 subunit ($Na_v1.1$). Because missing knowledge about the frequency of DS and the molecular background of this disorder in Poland we performed the *SCN1A* gene mutations analysis for the group of patients diagnosed as DS. The result of this research—frequency and the type of identified mutations are shown.

Method: The molecular tests of the *SCN1A* gene were performed for 53 patients from different neurological centres in Poland and included sequence analysis and screening for intragenic deletions. DNA sequencing was performed for all, for patients without point mutations, gene deletion/duplication was analyzed by MLPA. The range of identified deletion in *locus* 2q24.3 was established by array CGH.

Results: The *SCN1A* mutations were confirmed in 20 out of 53 DS patients. Nineteen (95%) had point mutations (11 missense, six nonsense, one splice); in one case the deletion of the all *SCN1A* exons was identified. The deletion spans to 1.5 Mb and covers not only *SCN1A* but also adjacent genes (*GSRNP*, *GALNT3*, *TTC212B*, *SCN9A*, *SCN7A* and *XIRP*). For seven patients we were able to perform analysis of parents DNA and confirmed de novo mutations in all cases (point mutations and gene deletion).

Conclusion: The frequency of the *SCN1A* mutations in the analyzed group of DS patients was estimated as 38%. This data were obtained for

rather small group of DS patients and to make them more conclusive more patients have to be analyzed. To continue *SCN1A* mutation screening we have developed the referral form, as the likelihood of mutation identification depend upon the patients' phenotype characterization, and believe that the mutation detection in DS will be increased.

Poster session: Genetics IV
Monday, 29 August 2011

p304
A GENOMIC DELETION SPANNING PART OF LGI1 ASSOCIATED WITH AUTOSOMAL DOMINANT LATERAL TEMPORAL EPILEPSY

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Purpose: To describe the clinical and genetic findings in a family with autosomal dominant lateral temporal epilepsy (ADLTE), a defined condition characterized by lateral temporal seizures with prominent auditory or aphasic auras. Mutations in the LGI1 gene are found in about 50% of ADLTE families. Over 30 LGI1 mutations have been identified so far, all of which are missense or splice-site point mutations or short indels.

Method: All participants were personally interviewed and underwent neurologic examination. Part of the patients underwent EEG examination and neuroradiological investigation (CT/MRI). Sequencing of LGI1 exons was performed by standard methods. The DNAs of all available family members were genotyped with the HumanOmni1-Quad v1.0 SNP array beadchip and copy number variations (CNVs) were analyzed in each subject.

Results: The family had eight affected members over three generations. All of them showed GTC seizures, with partial onset in five and unknown onset in 3. Four patients had partial seizures with auditory features, while for three patients (two of them deceased) there were no data about the occurrence of auditory symptoms. One patient had partial seizures with déjà vu. Age at onset was 12–14 years in six patients, 34 years in 1, unknown in 1. The EEG examination in three patients showed only minor sharp abnormalities over the temporal or central regions. Neuroradiological investigations in three patients were normal. Sequencing of LGI1 exons in the family proband did not reveal any point mutation. By SNP array genotyping and CNV analysis, we identified a genomic deletion about 80 kb in size encompassing the first two exons of LGI1 in all available affected members and in two nonaffected carriers.

Conclusion: This is the first genomic deletion affecting LGI1 identified in ADLTE. As other LGI1 deletions may occur, ADLTE families in which no point mutations are revealed by direct exon sequencing should be screened for possible genomic deletion mutations by appropriate methods.

p305
NO DIFFERENCE IN CLINICAL FEATURES BETWEEN FAMILIAL AND NONFAMILIAL PARTIAL EPILEPSY

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Purpose: To investigate the influence of genetic factors on the clinical features of nonlesional partial epilepsy through comparing patients with sporadic and familial epilepsy.

Method: Patients were recruited from the outpatient clinics of Ain Shams university hospital with a clinical features of partial epilepsy with exclusion of patients with history or investigations evidence of an underlying lesion. Patients evaluation included detailed clinical and family history, neurological examination, EEG and brain MRI. Familial epilepsy was diagnosed based on epilepsy or febrile convulsions in first, second or third degree relatives. Patients were further classified according to presumed lobe of origin into mesial temporal, lateral temporal, frontal, parietal, occipital and undetermined epilepsy.

Results: The study involved 101 patients, 49 familial and 52 nonfamilial. There was no differences between the two groups regarding age at onset, seizure localization, seizure types or frequency, clinical course and response to AEDs. This was true for all group and for each site of seizure localization

Conclusion: Most familial epilepsy syndromes, such as ADNFLE, ADLTE and ADEVF are defined based on seizure localization in different family members. This study showed that no specific clinical feature can distinguish between familial and sporadic nonlesional partial epilepsy. This may be caused by both groups being influenced by similar genetic factors. Alternatively, other features, such as advanced imaging studies or detailed neuropsychiatric assessment might be more valuable in differentiating the two groups than seizure manifestations.

p306
IS BENIGN FAMILIAL INFANTILE EPILEPSY (BFIE) LINKED TO CHROMOSOME 16P11.2-Q12.1 THE RESULT OF AN UNUSUAL MUTATIONAL MECHANISM?

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Purpose: Many families with benign familial infantile epilepsy (BFIE) have been linked to the pericentromeric region of chromosome 16, between 16p11.2 and 16q12.1. However, no protein coding mutations have been identified in these families despite extensive sequencing of candidate genes. We used novel genomic technologies to search for structural and coding mutations in BFIE families linked to chromosome 16.

Method: Linkage analysis was carried out using microsatellite markers and LINKAGE. Comparative genome hybridization (CGH) data was analyzed using SignalMap. Sequence capture arrays were designed to capture promoters, coding sequences and microRNAs within the linkage interval. Captured DNA was sequenced using the Illumina Genome Analyzer *II*. Sequence data was aligned to the whole genome and known SNPs were filtered using SeattleSeq.

Results: Three families showed significant or nearly significant linkage to the chromosome 16 locus. Another seven families were consistent with linkage to chromosome 16. CGH did not show any unusual copy number changes, either in single families or in common to affected individuals. Sequence data with a median coverage of 48 reads was obtained for coding sequences in the region. No variants likely to cause BFIE were identified.

Conclusion: These results suggest that the BFIE mutation may not be a protein coding mutation. It is not a detectable pathogenic copy number

change. The mutational mechanism might be a regulatory mutation, balanced inversion, repeat variation or a small copy number change below the resolution of the specific CGH array used.

p307
CLINICAL GENETIC STUDIES IN BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES (BECTS)

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Purpose: To study the clinical genetics of benign childhood epilepsy with centrotemporal spikes (BECTS).

Method: Participants with BECTS were recruited from the EEG laboratories of three pediatric centers and by referral. Pedigrees were constructed up to three degrees of relatedness for each proband. Affected individuals underwent phenotyping where available using a validated seizure questionnaire. The proportion of affected relatives according to degree of relatedness was calculated.

Results: Fifty-three BECTS probands had a mean age of seizure onset at 7.8 years (range 2–12 years). 34/53 (64%) patients were male. For 50 participants, pedigrees were available for three degrees of relatedness. 28/53 (52.8%) probands had a positive family history of febrile seizures and/or epilepsy. 57/2085 (2.7%) total relatives had a history of seizures: 21/214 (9.8%) first degree, 15/494 (3%) second degree and 21/1377 (1.5%) third degree relatives. Febrile seizures were the most frequent phenotype, occurring in 25/57 affected relatives. Of 21 affected first degree relatives: 8/21 had febrile seizures, 4/21 BECTS, 2 epilepsy-aphasia syndrome, 1 temporal lobe epilepsy with hippocampal sclerosis, 2 focal epilepsy of unknown cause, 2 genetic generalized epilepsies and 3 miscellaneous.

Conclusion: Clinical studies suggest that BECTS has a genetic component consistent with complex inheritance. Focal epilepsies are the most common epilepsy in the relatives especially BECTS and epilepsy-aphasia syndromes. This supports the concept of a BECTS related spectrum and shared genetic determinants.

This study was approved by the Austin Health Human Research Ethics Committee. The study was funded by NHMRC of Australia.

p308
PHARMACOGENOMIC STUDY OF PHENOBARBITAL AND PHENYTOIN: FROM KINETIC TO DYNAMIC TARGETS

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Purpose: Phenytoin and phenobarbital are widely prescribed antiepileptic drugs with narrow therapeutic index. Dosage optimization is an importance issue to avoid side effects such as ataxia, drowsiness and dizziness. The present study aimed to evaluate the possible genetic effect on phenytoin and phenobarbital both in pharmacokinetic and pharmacodynamic pathway.

Method: There were 289 patients in phenytoin cohort and 74 patients in phenobarbital cohort. Genotype analysis was performed by real time-PCR and PCR-RFLP. The associations between genotypes and dosages or concentrations were analyzed using one way ANOVA with post hoc Bonferroni correction.

Results: In the phenytoin cohort, patients with lower phenytoin dose were more likely to carry the variant allele in *CYP2C9* c.1075A>C ($p = 0.0141$). In addition, patients with higher concentration-to-dose ratios tended to carry more of the variant allele in *CYP2C19* c.636G>A ($p = 0.0165$). On the other hand, the variant allele in *ABCB1* c.2677G>T/A and *GABRA1* IVS11 + 15G>A were demonstrated to be associated with lower phenobarbital doses in the phenobarbital cohort ($p = 0.0451$ and 0.0245, respectively).

Conclusion: Our results indicated that the genetic polymorphisms in *CYP2C9* c.1075A>C and *CYP2C19* c.636G>A were associated with phenytoin doses or concentrations. Although the sample size was limited in the present study, the doses of phenobarbital was demonstrated to be influenced by *ABCB1* c.2677G>T/A and *GABRA1* IVS11 + 15G>A. Our results revealed that several genetic polymorphisms may involve in dosage optimization of phenytoin and phenobarbital and need to be confirmed in a larger population.

p309
INVESTIGATING THE EXPRESSION OF INFLAMMATION RELATED GENES IN TEMPORAL LOBE EPILEPSY PATHOGENESIS

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Purpose: In temporal lobe epilepsy it is thought that various genes and signalling pathways take place due to presence of complex changes in hippocampus during the pathogenesis of disease. The inflammation period in this pathogenesis has been exhibited by the studies of animal models. In this study, we used hippocampus materials which are obtained from post amygdalohippocampectomy period after medical indication of four women and five men patients who are diagnosed with mesial temporal lobe epilepsy and resistant to antiepileptic treatment applied in convenient time and combinations.

Method: RNA samples, isolated from these tissues were used for the synthesis of cDNAs by reverse transcriptase PCR method, in order to quantify the inflammation-related gene expressions by real-time PCR. As control tissue, hippocampus material were taken during autopsy from nine different cadaver of which the reason of death excluding neurological reasons. In the normalization of results, abl and cyclophilin genes were used Relative expression values were calculated with deltaCt method. Results were compared statistically by using Mann–Whitney *U* test.

Results: In the analysis of the expression levels of IL12, IL10, IL6, it has been depicted that these genes do not show any significant differences in the materials of epileptic versus autopsy tissues ($p = 0.73$, $p = 0.59$, $p = 0.24$). On the other hand, it is determined that the expression of IL1-beta, TNF-alfa, IFN-gama and TGF-beta in patients indicate significant increase according to healthy controls ($p = 0.001$, $p = 0.0006$, $p = 0.007$, $p = 0.027$). In addition to these, there was no expression of IL1-alfa, IL2 and IL17 detected neither in patients or in healthy individuals.

Conclusion: Results in this study show that an increased level of inflammation related gene expression participates in the pathogenesis of mesial temporal lobe epilepsy.

Abstracts

p310
AUDIT OF THE USE OF ARRAY CGH IN EPILEPSY PATIENTS SEEN AT A TERTIARY CLINIC

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Microdeletions or duplications, also known as copy number variants (CNVs), identified using array comparative genome hybridization (array CGH) constitute the commonest known genetic cause of the epilepsies. Yet, this technique remains underutilized in most clinical services. We audited the yield of array CGH in a tertiary epilepsy clinic before mid August 2010. Until then, this test was only requested in selected cases with epilepsy of unknown etiology, where there was also a personal or family history of learning difficulty, developmental delay or mental health problems including autism. CGH array was performed in 30 cases in this time period. Three with 15q13.3 microdeletion were related to a previously diagnosed case and are thus excluded from the results. In remaining 27 cases the findings were as follows. In 17 (63%) no abnormality was found. In 3 (11%) an imbalance of uncertain significance was detected and was considered most likely a ''benign variant.'' In 7 (26%) significant changes were found, sometimes more than one variant per individual. These included variants in 1p22.1, 7q35, 15q11.2 (detected in two cases), 15q13.1, 15q13.2 (three cases), 16p12.1, 16q13.11 and 17q12. Our results indicate the usefulness of this test in this setting. Identifying underlying genetic susceptibility has value not only in determining the etiology and aiding clinical management but also in genetic counselling.

p311
ELECTROCLINICAL FINDINGS IN DUPXQ28 SYNDROME

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Purpose: Duplications of Xq28 have been described in males with moderate to severe mental retardation, absent speech, progressive spasticity and/or ataxia, recurrent severe respiratory infections and epilepsy. We describe the electroclinical features of four unrelated males (aged 10–24 years) with epilepsy and severe mental retardation carrying microduplications of Xq28.

Method: Clinical data (age at seizure onset, seizure type and frequency, AEDs used, response to treatment) as well as video-EEG recordings and neuroradiological data were collected. Oligo array-CGH was performed on genomic DNA from probands and their mothers.

Results: All patients were found to be carriers of cryptic interstitial duplications of Xq28 (ranging from 186.1 to 474.6 kb), including MECP2 gene in three cases. Neurological examination showed spasticity and severe mental retardation in all of the patients. Epilepsy onset occurred at a mean age of 12 years; one patient had febrile convulsions. All the patients presented atypical absences, myoclonic and atonic seizures. A combination of valproic acid and lamotrigine controlled seizures in two patients; two of them were drug-resistant. The EEG pattern was characterized by slow background activity, slow spike and waves with anterior predominance. Long bursts of frontal theta rhythmic activity has been recorded in one patient, without any clear clinical modification.

Conclusion: In our patients with Xq28 microduplications the electroclinical feature of epilepsy was characterized by atypical absences, myoclonic and atonic seizures. Distinctive EEG pattern consisted of theta rhythmic activity and slow spike and waves with anterior predominance.

p312
EXPRESSION OF GLUTAMATE TRANSPORTERS IN HUMAN MESIAL TEMPORAL LOBE EPILEPSY WITH HIPOCAMPPAL SCLEROSIS: A PRELIMINARY STUDY

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Purpose: Glutamate is an essential excitatory neurotransmitter involved in brain functions. Glutamate uptake system consists of transporter proteins responsible for the removal of potentially excitotoxic glutamate excess from the extracellular space. Over 90% of glutamate uptake activity is mediated by EAAT2 (excitatory amino acid transporter 2), present in hippocampus and cerebral cortex. Dysfunction of EAAT2 and accumulation of excessive extracellular glutamate has been implicated in the onset and progression of diverse neurological disorders like epilepsy. Controversy exists on whether EAATs expression is altered in patients with mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS). We evaluated the expression levels of EAAT2 in patients with MTLE-HS in the lesion and in the adjoining temporal cortex.

Method: EAAT2 expression levels in the hippocampus (lesional and perilesional cortical area) were quantified by real-time PCR in ten patients with refractory MTLE-HS submitted to surgery and in six autopsy controls without neurological disorder. The procedure was included in a larger project and was approved by ethical committee and legal regulators.

Results: EAAT2 expression levels were similar in the hippocampus and temporal cortex of MTLE-HS patients when compared to similar data from matched healthy controls.

Conclusion: Our results, although preliminary, are in agreement with previous reports, and do not exclude the hypothesis of abnormalities in EAATs at functional level. Further studies are needed to clarify the role of these transporters in the etiology of MTLE-HS. We are currently addressing the hypothesis on whether glutamate transport is compromized.

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THE USE OF STEREOPHOTOGRAMMETRY TO DETECT COPY NUMBER VARIATION IN PEOPLE WITH EPILEPSY

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Purpose: An increasing number of genetic causes of epilepsy are being found, particularly an increased rate of copy number variants (CNVs). It is not currently possible to predict which patients will have a relevant CNV. Identification of a pathogenic CNV has major implications for management. Dysmorphism is also associated with CNVs, and may be used clinically to distinguish people with various CNVs. We used a three-dimensional stereophotogrammetric camera to analyze facial shape variation in genotyped epilepsy patients and in control subjects. We hypothesized that stereophotogrammetry could distinguish patients with and without a putatively pathogenic CNV.

Method: One hundred nineteen patients and 336 control subjects were studied. The presence of a CNV was sought. Dense surface modelling of three-dimensional face images was used to compare patients with or without CNVs. Local ethics committee approval was obtained at all sites.

Results: Thirty-seven of the 119 patients had significant CNVs. Prinicipal component analysis of modes showed that the average deviation from the mean age-matched sex-matched face was significantly greater in patients with CNVs compared to those without CNVs for the whole face (PCA: 8.23 vs. 6.91; $p < 0.001$) and the periorbital region (PCA: 7.52 vs. 6.64; $p < 0.01$).

Conclusion: Stereophotogrammetry can be used to assess dysmorphism and may help predict which patients will have CNVs. It could be a useful clinical tool not only for epilepsy but also for other medical specialties.

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GENE HUNTING FOR EARLY-ONSET EPILEPSIES USING GENOME-WIDE CNV ANALYSIS

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Purpose: Severe early-onset epilepsies (SEOE) comprise the most devastating epileptic phenotypes. Given the severe neurological outcome, SEOE usually present as isolated cases. De novo mutations in genes with diverse functions in the brain are increasingly found in patients without an acquired etiology. Furthermore, rare de novo deletions of the same culprit gene are identified in patients with a similar epileptic phenotype as patient with truncating point mutations. This implies that haploinsufficiency of dosage sensitive gene products is an important pathomechanism in SEOE. We aim to identify novel genes implicated in these devastating epilepsies.

Method: We implement genome-wide CNV analysis as a gene hunting strategy to identify loci encompassing dosage sensitive genes. Following literature mining to identify candidate genes in de novo CNV loci, we perform mutation analysis, including local high resolution CNV analysis, in patients with a similar epileptic phenotype as the CNV patient to find additional de novo aberrations in this gene.

Results: We initiated a pilot CNV analysis on a heterogeneous cohort of 31 patients with SEOE. 248 rare CNVs were identified including two deletions >2 Mb mapping to private loci on chromosome 13q13 and 18q22 in two different patients. Segregation analysis confirmed their de novo character. In each respective locus two candidate genes were identified with a prominent neuronal expression profile and an important known function in brain development. Mutation screening of the four functional candidate genes in an appropriate patient cohort is ongoing.

Conclusion: We identified two large de novo private deletions in two SEOE patients (2/31; 6.5%). This finding is relatively consistent with current frequencies of large de novo deletions identified in syndromal intellectual disability. Based on size and de novo character, both deletions are likely pathogenic. However, identification of additional gene defects (point mutations, genic deletions) in patients presenting with a similar epilepsy phenotype is necessary to conclude the causal link with the epileptic phenotype.

Poster session: Neuropsychology/psychiatry I
Monday, 29 August 2011

p315
DEFICITS IN EMOTION RECOGNITION AND EXECUTIVE FUNCTIONS, AND MILD MNESTIC DEFICITS AFTER LIMBIC ENCEPHALITIS

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Purpose: Limbic encephalitis (LE) can affect the amygdalae, involved in emotion recognition and usually leads to temporal lobe epilepsy, characterized by mnestic deficits. We report a 16-year-old male patient with temporal lobe epilepsy (TLE) after possible LE. MRI demonstrated bilateral abnormities of the amygdalae but hippocampi were normal. Various tests were applied in order to describe the patients' neuropsychological deficits.

Method: R.N. suffered from possible LE at age 15 (not paraneoplastic, no screening for autoantibodies). However, he became a good high-school student. A neuropsychological test battery was applied 12 months after possible LE and included test for intelligence (WISC-4), executive functioning, visuoconstruction, motor skills, expressive and receptive language and memory function (visual and verbal short and long term memory). The Ekman 60 faces test was applied to analyze the patients' ability to treat emotional expression of faces.

Results: Tests revealed normal intelligence and motor skills. Deficits were found regarding executive functions, especially working memory, verbal fluency, mental flexibility and planification, as well as denomination and long-term memory. Facial emotion recognition was markedly impaired for disgust and fear, while other basic emotions were recognized without relevant problems.

Conclusion: Limbic encephalitis may cause relevant executive dysfunctioning in addition to the already well described mnestic deficits. In addition, impairment of facial emotion recognition may follow limbic encephalitis in the case of bilateral involvement of amygdalae.

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EMOTIONAL EXPERIENCE AND EMOTION RECOGNITION IN MESIAL TEMPORAL LOBE EPILEPSY PATIENTS

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Purpose: Defective social abilities have been observed in patients with mesial temporal lobe epilepsy (MTLE), particularly in facial expression recognition of negative emotions. To test the existence of a supramodal system for recognizing signals of fundamental emotions, we evaluated the ability to recognize five emotions in a group of MTLE patients from visual and prosodic cues. In addition, we test whether these abilities are linked to the experience of the same emotions.

Method: A group of 35 patients (22 women; mean age 47 years) were included in the study. Patients performed two different tasks of emotion recognition: recognition of facial expressions and prosody of five basic emotions (happiness, fear, disgust, anger and sadness). The subjective experience of emotions of fear, anger and disgust were investigate by

means of different scales. Correlation between emotion recognition and emotional experiences were calculated with Spearman rho.

Results: Correlations were significant between the facial emotion and emotional prosody recognition tasks; no correlation was found between subjective measures of fear, anger, disgust and the recognition of these emotions in the visual and auditory domain.

Conclusion: The results of the present study showed that in a group of MTLE patients the ability of recognizing emotions from visual and prosodic cues correlates; however, no correlation with the subjective experience of fear, anger and disgust emotions was detected. These preliminary data suggest the existence of a supramodal system for recognizing fundamental emotions and that the neuronal systems involved in the recognition of the visual and prosodic expression of emotion may not be necessary for the subjective experience.

p317
THE ANALYSIS OF INTERACTIONAL FEATURES IN NEUROLOGICAL CONSULTATIONS CONTRIBUTES TO THE DIFFERENTIAL DIAGNOSIS OF EPILEPTIC SEIZURES AND PSYCHOGENIC NONEPILEPTIC SEIZURES (PNES): THIRD PARTY REFERENCES AND SEIZURE WITNESSES

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Purpose: PNES are defined by their resemblance to epileptic seizures and the process of distinguishing between the two can be difficult, with high misdiagnosis rates reported. In addition, there is no evidence that factual items can help to differentiate between epilepsy and PNES. Therefore, history taking remains the key tool in this clinical setting. Previous findings from the multidisciplinary team (including neurologists, linguists and sociologists) demonstrate that close interactional and linguistic examination of ''history taking'' between neurologists and patients can contribute to the differential diagnosis of epilepsy or PNES (Reuber et al. Epilepsy and Behav 2009; 16: 139–44).

Method: The current phase of research involves identification of third party references and seizure witness accounts during neurological consultations with twenty unselected patients experiencing refractory seizure disorders and admitted for video/EEG telemetry because of diagnostic uncertainty to a regional NHS seizure clinic. A researcher blinded to diagnosis developed and applied a coding frame to verbatim transcripts and determined strength of association (OR), statistical significance (Fisher's exact (two-tailed) Test) and affect size (Cohen's d) of diagnostically distinguishing interactional features.

Results: Findings indicate statistical significance across a number of diagnostically discriminating variables including ''prompting third party recall'' (PNES mean 4.69, SD 2.95; epilepsy mean 2, SD 2.65 (per consultation); OR = 2.25 (95% CI 1.22–4.15); p = 0.007; d = 0.96), normalization (PNES mean 0.31, SD 0.63; epilepsy mean 3, SD 2.45 (per consultation); OR 12.81 (95% CI 4.32–37.99); p = 0.027; d = 1.51) and ''catastrophization'' (PNES = mean 3.69, SD 2.78; epilepsy = mean 0.43, SD 0.11 (per consultation); OR 9.10 (95% CI 2.80–29.63); p ≤ 0.001; d = 1.54).

Conclusion: Findings complement psychosocial explanations and diagnostically differential interactional features of PNES and epilepsy in the wider literature. We are not aware of any previous attempts to use the analysis of interactional data for the differential diagnosis of medical conditions.

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p318
INCREASED MESIOTEMPORAL DELTA ACTIVITY CHARACTERIZES VIRTUAL NAVIGATION IN HUMANS

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Purpose: Hippocampal theta or rhythmic slow activity (RSA) occurring during exploratory behaviors and rapid-eye-movement (REM) sleep is a characteristic and well-identifiable oscillatory rhythm in animals. In contrast, much controversy surrounds the existence and electrophysiological correlates of this activity in humans. Some human studies argue that hippocampal theta activity appears in short and phasic bursts. On the contrary, our earlier studies provide evidence that REM-dependent RSA recorded from the mesiotemporal region is continuous like in animals but instead of the theta it falls in the delta frequency range.

Method: We used a virtual navigation task to examine mesiotemporal EEG patterns in 18 epilepsy patients implanted with foramen ovale electrodes. SPD values were compared for each 1 Hz wide frequency bin up to 10 Hz between resting, acquisition, recall and a nonlearning route-following condition.

Results: SPD progressively increased across resting, nonlearning, recall and acquisition. SPD values did not differ according to pathologic variables. The affected frequency bins were below the traditional theta band and were similar with those affected by REM sleep in our previous studies.

Conclusion: These data provide further evidence that it is delta rather than theta that should be regarded as a human analogue of the animal hippocampal theta.

p319
THALAMIC T-TYPE CA^{2+} CHANNELS MEDIATE FRONTAL LOBE DYSFUNCTIONS CAUSED BY A HYPOXIA-LIKE DAMAGE IN THE PREFRONTAL CORTEX

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Hypoxic damage to the prefrontal cortex (PFC) has been implicated in the frontal lobe dysfunction found in various neuropsychiatric disorders. The underlying subcortical mechanisms, however, have not been well explored. In this study, we induced a PFC-specific hypoxia-like damage by cobalt-wire implantation to demonstrate that the role of the mediodorsal thalamus (MD) is critical for the development of frontal lobe dysfunction, including frontal-lobe specific seizures and abnormal hyperactivity. Before the onset of these abnormalities, the cross-talk between the MD and PFC nuclei at theta frequencies was enhanced. During the theta frequency interactions, burst spikes, known to depend on T-type Ca^{2+} channels, were increased in MD neurons. In vivo knockout or knock-down of the T-type Ca^{2+} channel gene ($Ca_V3.1$) in the MD substantially reduced the theta frequency MD-PFC cross-talk, frontal-lobe-specific seizures and locomotor hyperactivity in this model. These results suggest a two-step model of prefrontal dysfunction in which the response to a hypoxic lesion in the PFC results in abnormal thalamocortical feedback driven by thalamic T-type Ca^{2+} channels which, in turn, leads to the onset of

neurological and behavioral abnormalities. This study provides valuable insights into preventing the development of neuropsychiatric disorders arising from irreversible PFC damage.

p320
THEORY OF MIND AND EMOTIONAL-BEHAVIOR DISTRESS IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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Purpose: Temporal lobe epilepsy (TLE) may impair the ability to understand others' mental states (theory of mind, ToM) and emotional-behavior well-being. This study explored the relationships between ToM deficits, social relations and emotional-behavior distress.

Method: A hundred and nine patients with TLE and 69 healthy subjects underwent the Faux Pas task (FPT), which evaluates the recognition and comprehension of others' mental states. Thirty-three patients also compiled the Symptom Check List 90 (SCL-90) and the Lubben Social network inventories, which assess the emotional-behavior distress and social relations.

Results: The patients were significantly impaired in ToM and the deficit was associated with age of seizure onset and schooling. Partial correlation analyses (with age of seizure onset and schooling as covariates) showed that the ability to comprehend behavior appropriateness correlated with the number of social relations, while the ability to exclude nonexistent mental states correlated with the SCL-90 Hostility score.

Conclusion: These results suggest that ToM impairment may have relational and emotional-behavioral implications. Future studies are needed to confirm these findings and to clarify their pathophysiological mechanisms.

p321
CORRELATION OF CLINICAL PARAMETERS AND COGNITIVE ASPECTS OF QUALITY OF LIFE IN PATIENTS WITH COMPLEX PARTIAL EPILEPSY

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Purpose: Assessment of cognitive aspect of QOL in patients with epilepsy in routine clinical work, using standardized questionnaire.

Method: Prospective observation study of 18 consecutive patients with complex partial epilepsy. Criteria for including patients in study were: (1) aged ≥18 years; (2) diagnose of complex partial epilepsy set by standard clinical, electrophisiologicaly and neuroradiology protocol; (3) same therapy during last 2 months; (4) ability to give consent and to fill in the questionnaire with minimum help; and (5) absence of chronically disease or use of medicine with potential for cognitive negative side effects. Assessment of cognitive aspect of QOL was done using validated translation of the QOLIE-31 questionnaire. Scores are obtained according to original manual. Descriptive statistic methods, and Spearman's coefficient rho were used for processing of data.

Results: Results show that cognitive aspects of QOL are comparable with referent epilepsy population (T-score). Analyzing the correlation of clinical parameters, it was determinate significantly correlation of age, type of seizure and therapy (efficiency and number of medications) with cognitive aspects of QOL.

Conclusion: The study showed that cognitive aspects of QOL for our patients are similar to referent population. We need further specific studies for all clinical factors in patients with epilepsy, with aim for better profiles and individualized therapy.

Key words: epilepsy, quality of life, cognition.

p322
DIFFERENCES IN QUALITY OF LIFE BETWEEN SUB-GROUPS OF PATIENTS WITH TREATMENT-RESISTANT TEMPORAL LOBE EPILEPSY

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Purpose: To correlate the subscores and overall score of the Quality of Life in Epilepsy Inventory-31 (QOLIE-31) with clinical variables and memory neuropsychological evaluation in patients with treatment-resistant temporal lobe epilepsy (TLE).

Method: Data from sixty consecutive patients with treatment-resistant TLE and complete neuropsychological evaluation including QOLIE-31 were analyzed. Patients were divided according diagnosis in mesial temporal lobe sclerosis (MTLS) and others (non-MTLS), and according the side of ictal onset. Correlation analyses were run to compare clinical data versus the seven subscores (Seizure worry (SW), Overall quality of life (OQ), Emotional well-being (EW), Energy/fatigue (EF), Cognitive functioning (CF), Medication effects (ME), Social functioning (SF)) and the Overall score (OS) of QOLIE-31.

Results: Mean age was 34 (±10), 45% female, with epilepsy onset at 12 (±10) years, monthly seizure frequency 9 (±10), being discognitive seizures (83%) the most common type.

Age at onset showed statistically significant correlations with EW, EF, ME ($p < 0.05$), and SW ($p < 0.01$) scores, all in detriment of an earlier onset; seizure frequency and CF score were inversely proportional ($p < 0.05$); whereas years of evolution showed no correlations.

MTLS patients had lower SW, SF ($p < 0.05$), OQ, EF, CF, and OS ($p < 0.01$) scores than non-MTLS patients. Right and left ictal onset showed significant differences in EW ($p < 0.05$) score.

Regarding neuropsychological memory evaluation, only visual memory reproduction correlated ($p < 0.05$) with CF score.

Conclusion: An earlier age of onset and the diagnosis of MTLS showed to be the most relevant factors associated with a poorer quality of life in TLE patients.

p323
EPILEPSY TYPE AFFECTS HEALTH-RELATED QUALITY OF LIFE IN YOUNG PATIENTS WITH CONTROLLED SEIZURES

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Purpose: A recent controlled study (Eddy et al., Epilepsy and Behavior 2010;19:623–626) showed that epilepsy may exert a negative influence on young patients' health-related quality of life (HR- QOL) even in the context of complete seizure remission. In the present study, we explored

the possible correlations between HR-QOL domains and specific epilepsy types.

Method: We compared HR-QOL ratings in four groups of young patients with controlled epilepsy (n = 13 temporal lobe epilepsy, TLE; n = 10 frontal lobe epilepsy, FLE; n = 7 parietal lobe epilepsy, PLE; n = 10 idiopathic generalized epilepsy, IGE), matched for age and sex. In addition to completing a generic HR-QOL measure (Youth Quality of Life Instrument-Research Version, YQOL-R), all patients underwent standardized psychometric testing for anxiety, depression and behavioral problems.

Results: We found significant differences in the harm avoidance behaviors (a measure of anxiety) and in specific YQOL-R contextual items: patients with PLE exhibited significantly more harm avoidance behaviors than each of the other three groups (FLE: p = 0.016, TLE: p = 0.003, IGE: p = 0.009). In relation to HR-QOL, young patients with PLE reported more communication with adult figures than patients with FLE (p = 0.017), and perceived that their condition caused fewer difficulties for their family than patients with IGE (p = 0.030).

Conclusion: These findings suggest that young patients with PLE are more likely to attempt coping strategies to deal with anxiety than patients with other kinds of controlled epilepsy. This seems to be in accordance with evidence of better communication with or support from adults/caregivers and fewer concerns about a detrimental impact of seizures on family life. These differences between young patients with PLE and other types of epilepsy could reflect poorer coping strategies and family cohesion for patients who are more likely to experience seizure-induced alterations in consciousness (Cavanna and Monaco, Nature Reviews Neurology 2009;5:267–276).

p324
INDUCTION OF PSYCOGENIC NONEPILEPTIC SEIZURES: COMPARISION BETWEEN SIMULTANEOUS HYPERVENTILATION AND PHOTIC STIMULUS VERSUS IV SALINE PLACEBO

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Purpose: To compare safety and effectiveness of two different induction procedures for psychogenic nonepileptic seizures during ambulatory EEG studies; IV saline placebo induction versus simultaneous hyperventilation (HV) with photic stimulation (PS).

Method: We recruited in two different centers 60 patients (30 patients each). Age: 11–63 years old; 48 females and 12 males derived to the laboratory by epileptologists, asking for seizure induction. Center A (Pontificia Universidad Catolica de Chile. PUC) used as routine procedure the placebo technique and Center B (Liga Chilena Contra la Epilepsia) used the procedure of simultaneous HV plus PS, telling the patient that the idea was to register a seizure.

Results: Center A: (22 females and eight males) – 19 patients gave positive for psychogenic nonepileptic seizures with placebo technique (63% effectiveness). None of them registered epileptic seizure or sides effects of the injection. Center B: (26 females and four males) – 24 gave positive for psychogenic nonepileptic seizures using simultaneous HV plus PS (80% effectiveness). No epileptic seizures where induced during the procedure. One patient, who was negative to psychogenic nonepileptic seizure, showed interictal epileptic activity during the activation.

Conclusion: Considering the long time discussion of ethical arguments against placebo induction, the simultaneous use of HV plus PS, seems to be a secure, more effective and even more informative procedure in highly suggestive patients of having psychogenic nonepileptic seizures.

Poster session: Neuropsychology/psychiatry II
Monday, 29 August 2011

p325
CLINICAL CHARACTERISTIC OF ANXIETY IN EPILEPTIC PATIENTS USING STATE-TRAIT ANXIETY INVENTORY

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Purpose: Anxiety is common comorbidity in people with epilepsy. Previous studies have reported the prevalence and factors associated with anxiety. Those studies, however, focused only in existence of anxiety. The current study is designed to analyze anxiety in specific forms, the state and trait.

Method: As cross-sectional study, 95 epilepsy patients were enrolled from January to July 2010. We used State-Trait Anxiety Inventory (STAI) to measure the anxiety. STAI is composed of transitory episodes of anxiety (STAI-S) and stable personality features presenting chronic levels of anxiety (STAI-T). As controls, 113 age-and sex-matched healthy people were included.

Results: The mean score of STAI-S and STAI-T was higher in patient than controls without significance (STAI-S; p = 0.998, STAI-T; p = 0.343). Within patients, patients without occupational engagement had higher STAI-S ($p < 0.001$) and tendency to higher STAI-T (p = 0.052). Patients with depression had higher score in both modalities (STAI-S and STAI-T; $p < 0.001$). Patients with aura showed higher STAI-T (p = 0.031).

Conclusion: STAI-S and STAI-T was not significantly different between patients and controls. Of 3 factors related to anxiety, higher STAI-T in patients with aura is likely to represent misunderstanding internal changes as an aura and worrying about impending seizure. Occupational engagement and depression had relation to both STAI-S and STAI-T and more concern is needed to evaluate the risk of anxiety and manage it appropriately.

p326
A NEW ITALIAN INSTRUMENT FOR THE ASSESSMENT OF IRRITABILITY IN PATIENTS WITH EPILEPSY

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Purpose: The purpose of the present study is to analyze the psychometric properties of a new Italian instrument for the assessment of irritability in adult patients with epilepsy (I-Epi). The I-Epi is an 18-item self-administered questionnaire focusing on four domains: Physical Functioning, Verbal Functioning, Temperament Functioning, and Epilepsy Functioning.

Results: Five hundred four patients from nine secondary and tertiary Italian centers for the care of epilepsy were recruited and interviewed. Each patient was evaluated on a series of demographic and clinical variables recorded before the administration of the I-Epi and of the AQ (Aggression Questionnaire), used for the external validity. The final results supported the reliability and validity of I-Epi as a measure of irritability in the adult epilepsy population. Gender differences were observed in the overall score and in all the subscales (apart from the Physical Functioning), with females having a higher irritability level compared with males; moreover, the irritability score was associated with the number of drugs taken.

Conclusion: The psychometric characteristics of the I-Epi seemed fairly good. We believe that the adoption of this new instrument could be very useful in both clinical and research management of patients with epilepsy.

p327
PREVALENCE OF DEPRESSION IN PATIENTS SUFFERING FROM EPILEPSY IN COMPARISON WITH CHRONIC SOMATIC DISORDERS IN UKRAINE

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Background: Depression is a disorder that very often follows the epilepsy and has influence on patients' quality of life. Depression in patient with epilepsy is very rare assessed in Ukraine and there is no current data about it prevalence in our country.

Purpose: To assess the prevalence of depression in patient with epilepsy and compare it to chronic somatic disorders (type 2 diabetes mellitus).

Method: Three groups of patients were examined: epilepsy group (EG) – 182 patients, age 18–55 (mean = 38.35 ± 10.70); type 2 diabetes mellitus group (DMG) – 135 patients, age 32–61 (mean 50 ± 9.37); rheumatoid artritis group (RAG) – 144 patients, age 34–62 (mean 51 ± 8.55). Beck depression scale was used for assessment of depression.

Results: EG: Depression was found in 91.1 % patients; 34.5 % had mild, 42.6% had moderate, 22.9% had severe depression. Antidepressants were prescribed to 8.5% patients only. DMG: Depression was found in 58.4% patients; 44.3% had mild, 48.2% had moderate, 7.5% had severe depression. Antidepressants were prescribed to 22.5% patients. RAG: Depression was found in 52.3% patients, 73.7% had mild, 26.3% had moderate, no patients had severe depression. Antidepressants were prescribed to 30% patients.

Conclusion: Prevalence of depression in patients with epilepsy in Ukraine is higher than worldwide. Moderate and severe depression in epilepsy group is statistically significant higher (65.5%) compare to chronic somatic disorders groups. Depression is generally underassessed and undertreated in all groups with statistically predominance in EG in Ukraine.

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THE INFLUENCE OF CLINICAL CHARACTERISTICS, INTERICTAL EEG AND NEUROIMAGING FINDINGS TO ASSOCIATED PSYCHIATRIC DISORDERS IN PATIENTS WITH FOCAL EPILEPSIES

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Purpose: To define the influence of some clinical characteristics (the age of onset and duration of the illness), predominant side of interictal EEG and neuroimaging findings to the psychiatric disorders (PD) in two groups of patients: with pharmacoresistant focal epilepsy (PhRE) and controlled focal seizures (CS).

Method: In a group of 60 outpatients, age 18–65 years, both sexes, with diagnosed focal epilepsy, divided in two subgroups of 30 patients with PhRE and CS, we followed the age of onset (up to 20, 21–40, above 40 year), duration of the illness (<15, 16–30, more than 30 year.), EEG with side predominance, neuroimaging findings and presence of PD.

Results: In the PhRE group (nine males, 21 females) average age of onset 26, average duration of the illness 26 year, PD in 18 patients; all with pathological EEG (focal left 22-with PD 13, focal right 8-with PD 5, ratio of side predominance and PD 1.6:1 in both) and 19 with pathological neuroimaging findings (11 with PD). In the CS group (12 males, 18 females) average age of onset 27, average duration of the illness 20 year, PD in seven patients; pathological EEG in 23 (focal left 15-with PD 5, focal right 8-with PD 2, ratio of side predominance and PD 3:1 in left, 4:1 in right) and 15 with pathological neuroimaging findings (four with PD).

Conclusion: The features that could influence the psychiatric disorders in patients with pharmacoresistant focal epilepsy are pathological intericat EEG and neuroimaging findings, and right predominance in interictal EEG-discharge in patients with controlled focal seizures.

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PSYCHIATRIC DISORDERS IN PATIENTS WITH PHARMACORESISTANT AND CONTROLLED FOCAL EPILEPSY

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Purpose: To show the frequency and type of psychiatric disorders (PD) in two group of patients with focal epilepsy: with pharmacoresistant (PhE) and controlled seizures (CS).

Method: A group of 60 outpatients, age 18–65 years, both sexes, with diagnosed focal epilepsy, as well as interictal EEG and neuroimaging findings, divided in two subgroups of 30 patients with PhRE and CS, we diagnosed PD, according to ICD-10 criteria.

Results: In the PhRE group there were nine male and 21 female subjects, average age 53 years; average lasting of the illness 26 years. Interictal EEG findings were pathological in all of them, neuroimaging findings pathological in 19 patients. PD were diagnosed in 18 patients: six with organic mental disorder, five with affective disorder, two with neurotic and somatoform disorders, five with mental subnormality. In the CS group there were 12 male and 18 female subjects, average age 48; average lasting of the illness 20 years. Interictal EEG findings were pathological in 23 and pathological neuroimaging findings in 15 of them. PD were diagnosed in seven patients: four with affective disorders and three with neurotic and somatoform disorders.

Conclusion: Psychiatric disorders are more frequent in patient with pharmacoresistant focal epilepsy than in those with controlled partial seizures, ratio 2.6:1. The most prominent disorders in PhE are organic mental disorder and mental subnormality, and affective disorder in CS group.

p330
EPILEPSY AS A CAUSE OF ANOREXIA—CASE REPORT SPECIAL PSYCHIATRIC HOSPITAL "G. TOPONICA"

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Method: Case report. Anorexia is a reduction in food intake which leads to maintaining minimum body weight, at least 15% under the expected value for a specific age and height. The fear of possible weight gain is always present, and the severity of weight loss is denied. Amenorrhoea always occurs in the last 3 months. Etiological factors are biological, psychological, and sociological factors combined. Serotonin neurotransmitter disorder and genetic predisposition for this disbalance are mentioned as a biological factor. Epileptic etiology of anorexia is not described anywhere.

Our patient is a 15-year-old girl, 163 cm tall. She was eating less and constantly losing weight during 1 year period. When she first saw a doctor she weighed 37 kg, because she lost 8 kg in the previous 6 months. During the same period she demonstrated decline in school grades, as well as absence of menstrual cycle, although her cycle was relatively orderly since she was 13. Personal anamnesis shows that she had absence seizure in her childhood, and she was treated with valproate from the age of 2 until 7. This was a reason for EEG testing. It showed basic activity of average amplitudes with frequencies of 6–7 and rarely 8 Hz. Generalized

spikes of high voltage, polyspikes and polyspike waves appeared during the hyperventilation. Spike-wave complexes of 3–4 Hz frequencies with the duration of 1–4 s were also registered. In the posthyperventilatory period, higher and high voltage beta activity of 15 Hz frequency, which was not blocked by optic perception, was registered in frontotemporal regions bilaterally (more to the left side). No clinical manifestation accompanied described electro cerebral activities.

Conclusion: Subclinical electro cerebral activity could lead to behavioral disorders, even anorexia, which was the case with our patient. Therefore, beside the detailed anamnesis, obligatory EEG would be recommended for every case of anorexia.

p331
CHARACTERISTICS OF EPILEPTIC PSYCHOSIS

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Purpose: Several studies have described risk factors for psychotic episodes in epilepsy. However, their findings are highly controversial. To evaluate the mechanisms of epileptic psychosis, we investigated factors associated with it.

Method: We retrospectively reviewed characteristics of 637 outpatients of Kurume University Hospital in January 2011 known to have had epilepsy. We examined the characteristics of 79 patients who had psychotic episodes (60 patients had interictal psychosis (IIP), 12 patients had postictal psychosis (PIP), and seven patients had both IIP and PIP).

Results: Compared with patients who had no psychotic episodes, those with psychosis had a longer duration of epilepsy, and higher rates of epigastric sensation, complex partial seizure, temporal epileptiform discharge on EEG, extensive abnormality on MRI, and cortical dysplasia (CD). In the subgroup with psychosis, IIP exhibited an earlier onset of epilepsy than PIP or patients without IIP, longer duration of epilepsy than in patients without IIP, and earlier onset of psychosis than PIP. Moreover, IIP featured higher rates of epigastric sensation and left or hemicephalic abnormality on MRI as well as CD. PIP exhibited a higher rate of mesial temporal sclerosis (MTS).

Conclusion: IIP was correlated with earlier onset of epilepsy and psychosis, higher rates of CD and left or extensive focal MRI lesions. In contrast, PIP was associated with a later onset of epilepsy and psychosis and a higher rate of MTS. As reported previously, our findings suggest heterogeneity of features of epileptic psychosis.

p332
EPILEPTIC PSYCHOSIS IN COMPARISON WITH SCHIZOPHRENIA USING PANSS

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Purpose: To investigate psychiatric symptoms in psychosis of epilepsy (POE), and to make comparisons between POE and schizophrenia using the positive and negative syndrome scale (PANSS).

Subjects and Method: Subjects comprised 30 patients with POE (15 men, 15 women; mean age, 40 years) and 62 patients with schizophrenia (41 men, 21 women; mean age, 39 years) who visited Kurume University Hospital and affiliated hospitals in Japan. Evaluation included clinical background and assessment using PANSS.

Results of PANSS: A significant difference was found between POE and schizophrenia with respect to results of the PANSS. Total score, scores associated with negative symptoms (scores of the negative subscale, blunted affect, emotional withdrawal, poor rapport, passive apathetic social withdrawal, difficulty in abstract thinking), conceptual disorganization, motor retardation, uncooperativeness, poor attention, disturbance of volition and preoccupation were higher in schizophrenia than in POE. However, scores for excitement and hostility were higher in POE than in schizophrenia. We also compared interictal psychosis with schizophrenia and postictal psychosis with schizophrenia, yielding similar results.

Discussion: Psychiatric symptoms in both psychoses have been regarded as similar. However, the differences in PANSS between POE and schizophrenia reflect dissimilarities in psychiatric symptoms, particularly in terms of negative symptoms. These results suggest key differences in these psychoses.

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DEPRESSION AND ANXIETY SYMPTOMS IN PATIENTS WITH EPILEPSY

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Purpose: To assess symptoms of depression and anxiety and to define its influence on quality of life (QOL) in patients with epilepsy.

Method: Adult patients (age range 18–65 years) with epilepsy of normal intelligence and without any progressive neurological disease or psychotic disorder were included in the study. They completed Beck's Depression Inventory (BDI), Beck's Anxiety Inventory (BAI), Symptom Check List – 90, QOLIE-31 Inventory (Serbian version). Stepwise multiple regression analysis was performed to assess the predictive effects of some factors on QOLIE-31 Inventory.

Results: 11.8% of patients had clinical diagnosis of depression and were previously treated with antidepressants. According to Beck's depression inventory, symptoms of depression were present in 33% of patients. Multiple regression analysis showed significant correlation between three instruments for depression: BDI, HAMD and SCL-90 depression score and overall score of QOLIE-31. Sixty-four percent of overall score was determined by those scores ($F = 51.88$; $p < 0.001$; $R^2 = 0.63$). Tests of regression coefficients significance showed that only BDI score was significant predictor of QOLIE-31 (beta = −0.55; $t = -5.17$; $p < 0.001$). All subscales of QOLIE-31 were negatively and moderately correlated with instruments of depression ($r = -0.334$ to -0.744). Clinical diagnosis of anxiety disorder was present in 10.3% of patients. Prevalence of anxiety symptoms on BAI was 36%. Multiple regression analysis showed that 49% variance of QOL is determined by BAI and SCL-90 anxiety score ($F = 60.747$; $p < 0.001$; $R^2 = 0.49$). Both instruments are significant predictors of QOLIE-31 score.

Conclusion: Depression and anxiety, frequently coexisting psychiatric conditions in patients with epilepsy, have significant influence on QOL.

p334
EPILEPSY AND MOOD DISORDERS

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Background: Mood disorders are more prevalent among epilepsy patients. The prevalence of these comorbidities is higher in persons with uncontrolled seizures.

Purpose: To find any correlation between epilepsy and mood disorders in an Albanian patients cohort.

Method: We screened the data of 505 patients controlled last year at the outpatient epilepsy clinic, University Service of Neurology, UHC Mother Theresa, Tirana, Albania. The diagnosis of epilepsy is made according the ILAE classification. The Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on

Therapeutic Strategies (2010) is used to identify the resistant cases. The *Diagnostic and Statistical Manual of Mental Disorders* – Fourth Edition, Text Revision – (DSM-IV-TR) (American Psychiatric Association, 2000) is used to diagnose the mood disorders. We looked for the correlation between the form and resistance of epilepsy seizures with mood disorders.

Results: We found 10 patients (1.9%) with mood disorders: one had major depression, six had dysthymia and three had bipolar disorders. There are 86 patients with resistant epilepsy in our cohort (17%). Seven patients with mood disorders belong to this group. The prevalence of mood disorders in the resistant epilepsy cases is 8.1%. There is a correlation between the complex partial seizures and depression too. No significant electroencephalographic changes are observed. Two of patients with mood disorders had cerebral dysplasia.

Conclusion: The mood disorders are more frequent to the resistant epilepsy patients.

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SCREENING SYMPTOMS OF DEPRESSION AND SUICIDAL IDEATION IN PEOPLE WITH EPILEPSY USING THE BECK DEPRESSION INVENTORY

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Purpose: We measured the severity of symptoms of depression and suicidal ideation in people with epilepsy (PWE) before and after epilepsy surgery. We aimed to determine the risk factors (sociodemographic and seizure-related factors) of depression in PWE.

Method: Four hundred sixty-eight adult individuals with a diagnosis of epilepsy for over 2 years and age between 17 and 80 years old were interviewed. The sample (n = 468) was divided into two groups for all the analysis (preoperative (n = 346) and postoperative (n = 122) group). We used the Beck Depression Inventory (BDI). The BDI is widely used as an assessment tool by health care professionals and researchers in a variety of settings and it has a specific suicide item to screen for suicidal ideation. The items constituting the BDI have been separated into two subscales. The first, Affective subscale, evaluate the mental aspect of depression (sadness, pessimism, past failure, loss of pleasure, guilt feelings, punishment feelings, self-dislike, self-criticalness, suicidal ideation, crying, agitation, loss of interest, indecisiveness and worthless). The second, the Somatic subscale, access vegetative and somatic symptoms (loss of energy, sleep problems, irritability, appetite problems, concentration, fatigue and loss of interest in sex).

Results: PWE, regardless of epilepsy type, seizure type, duration or frequency of seizures, and antiepileptic drugs were investigated. Before epilepsy surgery female gender, unemployment and high seizure frequency are associated factors for the occurrence of symptoms of depression. After epilepsy surgery, the only factor associated to high level of depression symptoms was the lack of seizure remission. Suicidal ideation was associated to seizures frequency and control before and after epilepsy surgery.

Conclusion: Our study is the first to discuss depression in epilepsy through the BDI subscales (Affective and Somatic). Our results confirm the prevailing view that symptoms of depression is frequently associated to epilepsy (32% in the preoperatory group and 21% in the postoperatory group). It additionally provides further insight to the association of depression with certain sociodemographic and seizure-related factors before and after epilepsy surgery.

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DISSOCIATIVE EXPERIENCES IN EPILEPSY PATIENTS

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Purpose: Epileptic seizure phenomena sometimes resemble symptoms of dissociative disorders. Although many studies have associated psychogenic pseudoseizures with dissociative experiences, few scrutinized relations between dissociative experiences and epileptic conditions. To clarify relations between dissociation and epilepsy, we evaluated dissociative experiences in epilepsy patients and those of nonclinical individuals.

Method: For the study subjects, 192 epilepsy patients (98 men and 94 women, mean 34.7 years) were recruited multiinstitutionally. For the control subjects, age- and sex-matched 292 nonclinical individuals were recruited from the community. In the epilepsy patients, epilepsy-related factors (e.g. epilepsy type, seizure type and frequencies, and pseudoseizures) were also evaluated. To evaluate dissociative phenomena, the total score and taxon of the Dissociative Experiences Scale (DES) was used.

Results: There was no significant difference in the DES score between the epilepsy group (mean 11.8) and the control group (11.0) (p = 0.432). The epilepsy group showed a slightly higher DES taxon (mean 7.9) than did the control groups (6.1) (p = 0.082). In the epilepsy patients, there was also no difference in DES score between idiopathic generalized epilepsies (mean 12.5, n = 30) and partial epilepsies (11.7, n = 162) (p = 0.753). The patients with pseudoseizures (n = 27) showed a significantly higher DES score (mean 24.1) and taxon (19.7) than those without (DES score 9.8 and taxon 5.8, p = 0.000).

Conclusion: The findings suggested that dissociation experiences in epilepsy patients are almost equivalent with those of the nonclinical individuals. However, as previously reported, patients with pseudoseizures suffer significantly from dissociative experiences.

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ONE-YEAR SEIZURE PROGNOSIS WITH ANTIDEPRESSANT TREATMENT

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Purpose: In patients with epilepsy, treatment with antidepressant drugs (antidepressants) has long been considered to cause aggravation of seizures, as many antidepressants are known to lower seizure thresholds in experimental conditions. However, little is known about whether treatment with antidepressants significantly increases seizure frequency in epilepsy patients properly being treated with antiepileptic drugs (AEDs). To investigate the clinical effects of antidepressants on the seizure frequency of epilepsy patients treated with AEDs, we retrospectively evaluated the 1-year course of seizure frequencies.

Method: One hundred twenty-one epilepsy patients treated with antidepressants (first-generation antidepressants in 63, second-generation antidepressants in 46, and combination in 12) and 300 age-, age at onset of epilepsy-, and epilepsy type-matched epilepsy patients without antidepressant treatment (controls) were the subjects of this study. Seizure frequencies in a 1-year period of the administration of antidepressants were retrospectively evaluated and compared with those of the controls.

Results: In the epilepsy patients with antidepressants, the seizure frequencies at four observation points (1, 3, 6, and 12 months after their administration) were equivalent to those of the same four age-matched periods of the control group. In addition, there was no significant difference in seizure frequencies between first- and second-generation

antidepressants. Other clinical variables (i.e., epilepsy type, number of AEDs taken, psychiatric condition) showed no association with these findings.

Conclusion: Epilepsy patients treated with AEDs can take antidepressants without a significant risk of exacerbation of seizures. Most antidepressants, either first- or second-generation, can be used for psychiatric treatment of epilepsy patients.

Poster session: Drug therapy I
Tuesday, 30 August 2011

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THE METABOLISM AND ELIMINATION PATHWAY THROUGH GLUCURONIDATION OF ESLICARBAZEPINE ACETATE AND ITS METABOLITES

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Purpose: Eslicarbazepine acetate (ESL) is a novel once-daily antiepileptic drug approved in Europe for use in adults as adjunctive therapy for refractory partial-onset seizures with or without secondary generalization. Metabolism of ESL consists primarily of hydrolysis to eslicarbazepine, the major circulating metabolite in humans, which is subject to glucuronidation followed by renal excretion. To date, the glucuronidation of eslicarbazepine has not been evaluated in detail. In the current study, we have identified one eslicarbazepine glucuronide, in human liver microsomes enriched with uridine 5'-diphosphoglucuronic acid.

Method: The kinetics of eslicarbazepine glucuronidation in human liver microsomes (HLMs) was investigated in the presence and in the absence of bovine serum albumin (BSA).

Results: The apparent K_m, determined by fitting to the Michaelis-Menten equation, was 410 and 350 μM in the presence and absence of BSA, respectively. Incubations with recombinant human uridine diphosphate glucuronosyltransferases (UGTs) indicated that UGT1A4, UGT1A9, UGT2B4, UGT2B7 and UGT2B17 appear to be involved in eslicarbazepine conjugation. The UGT with highest affinity for conjugation was UGT2B4 (K_m of 163 and 22 μM in the absence and presence of BSA, respectively). Significant correlation between eslicarbazepine glucuronidation and trifluoperazine glucuronidation, a typical UGT1A4 substrate was obtained, but no correlation was obtained with typical substrates for UGT1A1 and 1A9. Diclofenac inhibited eslicarbazepine glucuronidation in HLMs with an IC_{50} value of 17 μM.

Conclusion: These results suggest that eslicarbazepine glucuronidation results from the contribution of UGT1A4, 1A9, 2B4, 2B7 and 2B17, with UGT2B4 playing a more significant role at the therapeutic plasma concentration of unbound eslicarbazepine.

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INCIDENCE OF ADVERSE EVENTS IN RELATION TO STARTING DOSE AND TITRATION REGIMEN OF ESLICARBAZEPINE ACETATE AS ADD-ON TREATMENT IN PATIENTS WITH PARTIAL-ONSET SEIZURES

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Purpose: The incidence of treatment-emergent adverse events (TEAEs) by starting dose and titration regimen during early weeks of treatment with adjunctive eslicarbazepine acetate (ESL) may define further optimal treatment strategies for patients with refractory partial-onset seizures with or without secondary generalization.

Method: Integrated data from 1049 adult patients enrolled in three phase-III multicentre, randomized, double-blind, placebo-controlled, 12-week studies were reviewed for incidence and time of occurrence of TEAEs by different starting dose and titration regimen.

Results: Approximately 2/3 of TEAEs occurring in >5% of patients (dizziness, somnolence, headache, nausea, diplopia, vomiting, and coordination abnormal) started within initial 21 days of treatment. After 6 weeks of treatment, no relevant difference was found between ESL (18.7%) and placebo (16.6%) in incidence of TEAEs. In 12-week period, overall ratio of patients with TEAEs was not different in 800 and 1200 mg maintenance dose groups. TEAEs were recorded in 40.1% and 54.8% of 400 and 800 mg starting-dose groups, respectively, compared to 33.6% of placebo group whereas neurological TEAEs were found in 19.5% and 26.6% of same starting dose groups, respectively, compared to 14.9% in placebo-group. In groups with slow titration to maintenance-dose, relatively low numbers of patients (39.9% versus 54.8%) treated with ESL were identified with TEAEs.

Conclusion: In this analysis, TEAEs occurred early in the first weeks of treatment with ESL without clinically relevant differences from placebo following 6 weeks of treatment. This supports the possibility that a titration period of 2–3 weeks initiating the treatment on lower ESL starting-doses before achieving maintenance doses may reduce the likelihood of TEAEs.

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STEADY-STATE PHARMACOKINETICS OF ESLICARBAZEPINE ACETATE: INTEGRATED POOL ANALYSES FROM THREE DOUBLE-BLIND PHASE III CLINICAL STUDIES

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Purpose: The antiepileptic activity of eslicarbazepine acetate (ESL), a novel once-daily voltage-gated sodium-channel blocker was demonstrated in three phase-III randomized controlled studies in adult patients with partial-onset seizures unsatisfactorily controlled with 1–3 antiepileptic drugs (AEDs). In these studies, ESL demonstrated a dose-related antiepileptic response. The steady-state pharmacokinetic (PK) profile of ESL's main active metabolite eslicarbazepine and its exposure-response relationship was characterized in patients with partial-onset seizures treated with 1–3 concomitant AEDs.

Method: Plasma concentrations of eslicarbazepine and concomitant AEDs were obtained from 641 patients enrolled on ESL. Data were analyzed using nonlinear mixed-effect modelling (NONMEM) methods. Exposure parameters were calculated from individual parameters estimates derived from the model. A population-PK model of trough eslicarbazepine concentrations at steady-state was fitted.

Results: Eslicarbazepine's apparent clearance (CL/F) was affected by body-weight, height, dose of carbamazepine and coadministration of barbiturates or phenytoin. Concomitant use of lamotrigine, valproate, topiramate, gabapentin, clobazam and levetiracetam showed no effect on the exposure to eslicarbazepine. Interindividual variability of CL/F was 44%. The CL/F of eslicarbazepine was not affected by AST, ALT, ALP, bilirubin, CL_{CR}, age, ethnicity and gender. The probability of being a responder (≥50% reduction in seizure frequency) increased as a function of eslicarbazepine concentrations.

Conclusion: Although the clinical efficacy of adjunctive ESL was shown to be superior to placebo, the addition of ESL to carbamazepine, phenytoin and barbiturates may require monitoring of patients' clinical progress and possible dose adjustment. The concomitant administration of other AEDs did not affect the ESL exposure-response relationship.

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TO WHAT EXTENT CAN ESLICARBAZEPINE ACETATE INFLUENCE THE PLASMA LEVELS OF COMBINED ANTIEPILEPTIC DRUGS? AN EVALUATION BASED ON THREE DOUBLE-BLIND PHASE III CLINICAL STUDIES

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Purpose: Eslicarbazepine acetate (ESL) is a novel once-daily voltage-gated sodium channel blocker approved in Europe for use in adults as adjunctive therapy for refractory partial-onset seizures (POS) with or without secondary generalization. The variability of the population pharmacokinetics (PK) and systemic plasma exposure to concomitant antiepileptic drugs (AEDs) in treating patients with refractory POS were analyzed to determine the potential influence of ESL on the metabolism and PK of concomitant AEDs.

Method: Plasma concentrations of eslicarbazepine (main active metabolite of ESL) and other concomitant AEDs were obtained from 641 patients receiving ESL. Data were analyzed using nonlinear mixed-effect modelling (NONMEM) methods. Plasma exposure PK parameters were calculated from individual parameters estimates derived from the model. A population PK model of trough ($C_{min,ss}$) eslicarbazepine plasma concentrations at steady-state was fitted.

Results: ESL did not affect the clearance of clobazam, gabapentin, phenytoin, phenobarbital, levetiracetam and valproate. ESL slightly increased the oral clearance (CL/F) of carbamazepine, lamotrigine and topiramate up to 14%, 12% and 16%, respectively. Interindividual variability of CL/F for carbamazepine, clobazam, gabapentin, phenytoin, phenobarbital, topiramate and valproic acid was 24%, 77%, 48%, 72%, 42%, 39% and 64%, respectively.

Conclusion: In this integrated data analysis, it appears as though the magnitude of pharmacokinetic effect of ESL on the clearance of concomitant AEDs may not be clinically relevant and therefore may not justify the need for dose adjustment.

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METHODS USED TO EVALUATE COGNITIVE EFFECTS OF ESLICARBAZEPINE ACETATE ADD-ON THERAPY IN EPILEPTIC CHILDREN OF AGE 6–16: THE DESIGN OF A PLACEBO-CONTROLLED CLINICAL TRIAL

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Purpose: Eslicarbazepine acetate (ESL) is a novel once-daily voltage-gated sodium channel blocker approved in Europe for use in adults as adjunctive therapy for refractory partial-onset seizures with or without secondary generalization. Epilepsy is associated with significant cognitive comorbidity, correlated to both the underlying disease and antiepileptic drugs (AEDs). The study aimed to evaluate the effect of ESL as add-on therapy on the cognitive function in children and adolescents with partial-onset seizures, treated with 1–2 AEDs and experiencing ≥2 seizures/4-weeks.

Method: After a 4-week baseline-period, 117 subjects will be randomized in 2:1 ratio to ESL (10–30 mg/kg/day) or placebo once-daily. Potential effects on attention, memory and information processing/psychomotor speed will be assessed by the UBC System, a computerized neurocognitive test battery validated in clinical studies in epileptic children. The primary end point is the change in the composite Power of Attention, over a 12-week double-blind maintenance period. Patients' global cognitive skills, social competence, quality of life, and seizure frequency will also be evaluated. Safety will be assessed by records of adverse events, clinical laboratory tests, physical and neurological examinations and measurement of growth and development. A 1-year open-label will follow the double-blind period.

Results: The study is expected to be completed by the end of 2012 and the results will be available thereafter.

Conclusion: The use of a validated cognitive-battery in a noninferiority study with a placebo control is an appropriate study-design to assess cognitive effects of ESL while accounting for developmental changes and disease progression in children and adolescents.

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THE DESIGN OF A DOUBLE-DUMMY, ACTIVE-CONTROLLED, MULTINATIONAL PHASE-III NONINFERIORITY TRIAL IN 900 PATIENTS WITH PARTIAL-ONSET SEIZURES: ESLICARBAZEPINE ACETATE VERSUS CONTROLLED-RELEASE CARBAMAZEPINE IN MONOTHERAPY

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Purpose: Given the demonstration of efficacy and tolerability of eslicarbazepine acetate (ESL) as adjunctive therapy in partial-onset seizures (POS) in clinical studies, ESL may be an alternative as a first-line agent in monotherapy. This phase-III, randomized, double-blind, active-controlled, noninferiority study aims to demonstrate the efficacy and safety of ESL once-daily as monotherapy treatment for newly diagnosed adults with POS in comparison to controlled-release carbamazepine (CBZ-CR) twice-daily.

Method: Patients (≥18 year) with ≥2 unprovoked seizures in the past year and ≥1 in the last 3-months will be randomized in a 1:1 ratio to receive ESL 800 mg once-daily or CBZ-CR 200 mg twice-daily during a 26-week evaluation-period. In case of seizure occurrence during the evaluation-period, subjects are titrated to dose-levels B (1200 mg once-daily/400 mg twice-daily) and C (1600 mg once-daily/600 mg twice-daily). To assess maintenance of the effect over 1-year, a 26-week maintenance-period will follow. Exit criteria include seizures at dose-level C at evaluation period or at any dose-level in the maintenance-period. The primary end point is seizure freedom in the 26-week evaluation-period at the last received dose level. The sample size was calculated to achieve a ≥ 90% power to establish noninferiority, using a -12% margin. Secondary end points include tolerability, QOLIE-31, sedation and clinical laboratory assessments.

Results: The study is expected to be completed by the end of 2013.

Conclusion: The use of a noninferiority design implies the predefinition of a clinically relevant margin and adequate power to detect

noninferiority versus a gold standard. To our knowledge this is the first pivotal study to fully achieve those requirements.

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THE DESIGN OF A PHASE III CLINICAL STUDY OF ESLICARBAZEPINE ACETATE IN ELDERLY PATIENTS WITH PARTIAL-ONSET SEIZURES IN EPILEPSY

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Purpose: The elderly are the most rapidly growing segment of the population, and incidence of epilepsy is higher in this age group than in any other. Treatment of older patients with antiepileptic drugs (AEDs) is complicated by increased sensitivity to drug effects, altered pharmacokinetics, and an increased risk for drug interactions. However, few elderly patients are normally included in pivotal studies of AEDs, which results in the need for assessment of their safety and efficacy in this particular population. As part of the European postapproval commitment, a study in this population was designed for eslicarbazepine acetate (ESL). In a phase III-b open-label study, the safety and efficacy of ESL as adjunctive treatment for patients ≥65 years-old with partial-onset seizures (POS) using 1–2 AEDs will be evaluated.

Method: Patients with POS experiencing ≥4 seizures in an 8-week baseline period will be enrolled in a 2-week titration-period followed by a 26-week maintenance-period. Patients will receive ESL in doses ranging from 400 to 1200 g once-daily, according to clinical response and adjusted to renal function. Seizures will be recorded in daily diaries. Safety will be assessed by records of adverse events, clinical laboratory tests, electrocardiograms, and a series of visual analogue scales in order to evaluate potential sedative effects.

Results: The study is planned to include approximately 100 subjects and be completed by mid-2012.

Conclusion: The adoption of this design close to everyday treatment conditions is an appropriate approach to increase the knowledge on the effects of ESL in elderly patients.

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THE EFFECT OF ESLICARBAZEPINE ACETATE 800 AND 1200 MG ONCE-DAILY ON THE PHARMACOKINETICS OF A COMBINED ORAL CONTRACEPTIVE IN HEALTHY FEMALE VOLUNTEERS

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Purpose: Eslicarbazepine acetate's (ESL) potential pharmacokinetic (PK) interactions with oral contraceptives (OCs) were investigated.

Method: The effects of ESL 800 and 1200 mg once-daily on the 15-day steady-state pharmacokinetics of both ethinyloestradiol (30 µg) and levonorgestrel (150 µg) and its tolerability were investigated in two identical, single-centre, two-way cross-over, randomized, open-label studies in 40 healthy female volunteers. Bioequivalence with (test) and without (reference) ESL was assumed when the point-estimate (PE) and 90% confidence-interval (CI) for the test/reference ratio of PK-parameters were within 80–125% of the reference-interval.

Results: OCs' C_{max} and t_{max} values were similar both with and without addition of ESL. In ESL 800 mg group, PE (90%CI) for C_{max} and $AUC_{0–24}$ were 0.91 (0.85–0.97) and 0.75 (0.71–0.79) for ethinyloestradiol, and 1.04 (0.95–1.14) and 0.89 (0.82–0.97) for levonorgestrel, respectively. However, PE (90%CI) for $AUC_{0-\infty}$ of ethinyloestradiol and levonorgestrel were 0.69 (0.64–0.75) and 0.83 (0.76–0.91), respectively, outside limits. In 1200 mg group, PE (90%CI) for C_{max} and $AUC_{0–24}$ were 0.80 (0.71–0.92) and 0.68 (0.64–0.71) for ethinyloestradiol, and 0.87 (0.79–0.95) and 0.76 (0.68–0.86) for levonorgestrel, respectively. For the majority of parameters, the 90%CI was not included within the 80–125% reference interval, and therefore bioequivalence was not proven for both OCs concomitantly used with these two dose strengths of ESL. The distribution of adverse events (AEs) was comparable with one serious AE reported in 1200 mg ESL group.

Conclusion: Coadministration of ESL at doses of 800 and 1200 mg was well tolerated; however, it significantly and dose-dependently decreased systemic exposure to ethinyloestradiol and levonorgestrel, which may necessitate additional contraceptive methods.

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IN HEALTHY SUBJECTS, CONCOMITANT USE OF CARBAMAZEPINE WITH ESLICARBAZEPINE ACETATE CAN DECREASE EXPOSURE TO ESLICARBAZEPINE: LACK OF PHARMACOKINETIC EFFECTS OF ESLICARBAZEPINE ACETATE ON CARBAMAZEPINE AND ITS 10,11-EPOXIDE METABOLITE CONFIRMS FINDINGS FROM CLINICAL PHASE III STUDIES

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Purpose: The effectiveness of eslicarbazepine acetate (ESL) as adjunctive therapy in adults with partial-onset seizures was demonstrated in randomized controlled studies. This phase-I study assessed potential pharmacokinetic (PK) interactions between ESL and controlled-release (CR) carbamazepine (CBZ) in two groups of healthy volunteers.

Method: Group A (n = 18) received 35-day (test-day) treatment with ESL 800 mg once-daily, with CBZ-CR (titrated up to 400 mg twice-daily) coadministered from day-7 (reference-day). Group B (n = 20) received 35-day (test-day) treatment with CBZ-CR (titrated to 400 mg twice-daily), with ESL 800 mg once-daily coadministered after day-28 (reference-day). Test/reference ratios and 90% confidence-intervals (90%CI) were calculated for area under the curve (AUC) values over the dosing interval and C_{max} for eslicarbazepine, the main active metabolite of ESL, in group A, and for CBZ and CBZ-10,11-epoxide in group B.

Results: In group A, eslicarbazepine AUC decreased significantly by 31.9% (test/reference ratio: 68.1; 90%CI = 63.3–73.4) following co-administration of CBZ. In group B, decreases in AUC of CBZ and CBZ-10,11-epoxide following coadministration of ESL were within the 80–125% bioequivalence-range (test reference ratios: 90.3; 90%CI = 82.4–99.0 for CBZ and 97.6; 90%CI = 84.9–112.1 for CBZ-10,11-epoxide). There were no statistical differences of C_{max} and t_{max} values for eslicarbazepine, CBZ and CBZ-10,11-epoxide in any group.

Conclusion: In agreement with population PK analysis of phase-III studies, concomitant use of ESL and CBZ results in a significant decrease in exposure to the active metabolite eslicarbazepine, which might require individual adjustment of the ESL dose. There was no influence of ESL on CBZ pharmacokinetics.

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ONE YEAR EXPERIENCE WITH ESLICARBAZEPINE ACETATE ON A COMMUNITY HOSPITAL IN PORTO, PORTUGAL

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Purpose: Eslicarbazepine acetate (ESL) is a new antiepileptic drug available in Portugal since April 1st 2010. Clinical trials have shown good safety and efficacy but little is known about its effectiveness on clinical practice. The aim of our study is to evaluate postcommercialization first year of experience in our tertiary centre.

Method: We included all outpatients who initiated treatment with ESL from April 1st 2010 till March 31st 2011. We retrospectively collected data on demographics, clinical, treatment response, compliance and side effects. Only patients with at least one follow-up (FU) visit were included in the effectiveness and safety analysis.

Results: At baseline (n = 120) mean age was 39.1 yo (range 7–76), 47.5 % were man, mean epilepsy duration was 27.2 years (range 2–50), mean seizure frequency was 28.2/month (range 0–600); 60.0% of the patients were taking ≤2 AEDs and the remaining were taking ≥3 AEDs. At the last FU visit (n = 89), 78.4% of the patients were still on treatment [mean FU 204, 3 days (range 59–350); median ESL dosage 1200 mg (range 400–1600)]. Patients discontinued therapy due to side effects (15.9%) or lack of efficacy (5.7%). Among patients still on therapy (n = 69), 27.5% were responders (≥50% reduction on the seizure frequency); 26.1% were greatly improved or seizure-free (clinician global evaluation [CGE]). The effectiveness was higher in patients treated with ≤2 AEDs vs ≥3 AEDs (Responder rate – 35.1% vs 18.8%, p = 0.13; CGE – 37.8% vs 12.5%, p = 0.017).

Conclusion: Clinically relevant improvements were achieved in a significant proportion of patients, especially in the less refractory ones. The global tolerability was good with few patients discontinuing due to side effects and no new safety issues were observed. These conclusions are limited by the retrospective nature of our data and the short FU time.

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A COMPARISON OF SODIUM LEVELS IN PATIENTS SWITCHED FROM OXCARBAZEPINE TO ESLICARBAZEPINE ACETATE

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Purpose: Eslicarbazepine acetate (ESL) has shown a favorable profile in terms of hyponatremia in regulatory trials performed at dosages up to 1200 mg/day. We here compared sodium levels in patients with focal epilepsy treated at higher dosages of oxcarbazepine (OXC) and switched to similar dosages of ESL.

Methods: Prospective data acquisition in patients with uncontrolled focal epilepsy switched from OXC to ESL, often due to low sodium levels. Switching was performed within 3 days starting at an ESL dose of 0.7× OXC and uptitrated to 1.0× OXC dosage. Sodium levels were obtained prior to switch (T0) and at periods of 1, 6, 12, and 18 months after switching (T1-T4).

Results: From october 2009 until october 2010 19 patients (seven female, mean age 39.6 year (range 25–56 year) with focal epilepsy were switched from OXC to ESL. Mean daily dose of OXC prior to switch at T0 was 1900 mg (range 1050–2850 mg), and of ESL was 1900 mg at T1 (range 1200–2800 mg), 2100 mg at T4 (range 1600–2800 mg). Mean sodium levels were 132 mM at T0, T1 and T2 and remained between 132 and 134 mM later on. In 9/19 patients medication with ESL was ceased.

Conclusions: In this patient subgroup with a tendency to hyponatremia under treatment with doses of 1050–2850 mg OXC, a switch to a similar dose of ESL did not have an effect on sodium levels. This suggests that off-label treatment with ESL at higher dosages than approved bears a similar risk to hyponatremia as treatment with OXC.

Poster session: Drug therapy II
Tuesday, 30 August 2011

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A CLINAL-EEG STUDY IN PHARMACORESISTANT EPILEPSY PATIENTS TREATED WITH LACOSAMIDE

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Purpose: Lacosamide (LCS) has been recently approved as add-on antiepileptic drug (AED) for pharmacoresistant epilepsy. The aim of this study was to evaluate the EEG and clinical modifications induced by LCS as add-on therapy in a cohort of epileptic patients.

Method: We evaluated 10 patients (6 M/4 F; age 48.2 ± 14.9 years) affected by focal pharmacoresistant epilepsy (symptomatic in 5/10, probably symptomatic in the remaining ones). LCS was added to the pre-existing AED therapy (1–4 AEDs per patient, which in nine patients included AEDS acting on voltage-gated Na^+ channels). LCS daily dosage was titrated slowly up to 100–400 mg (mean 250 ± 81.65) depending on patients' features; the remaining AED therapy was left unmodified. Video-EEG recording was performed before (t0) and at 6 months (t1) after beginning LCS, as well as routine blood tests, AEDs levels assay, and Depression and Anxiety questionnaires (Beck Depression Inventory, Stay 1 and 2). In the EEG traces we performed a quantitative analysis of interictal abnormalities (IIAs), and power spectrum analysis of epochs without IIAs or artifacts (24 2.5 s long epochs for each patient).

Results: LCS induced a significant reduction of seizure frequency (−39.6 ± 27.8% vs t0). In four patients we showed a seizure reduction >50% (one case seizure-free). EEG analysis showed 19.3 ± 17.4% IIAs reduction, without concomitant changes in EEG background. In five patients mood improved. It was not necessary to withdraw LCS in any patients due to adverse events; four patients experienced dizziness, which disappeared by slowing the titration rate. LCS did not affect AEDs levels nor routine blood tests.

Conclusion: In this small cohort of patients we confirmed LCS efficacy and tolerability; furthermore we observed a reduction of IIAs, without a significant modification of EEG background.

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EFFICACY AND TOLERABILITY OF LACOSAMIDE AS ADJUNCTIVE THERAPY IN ADULT PATIENTS WITH DRUG-RESISTANT FOCAL EPILEPSY

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Purpose: Lacosamide (LCS) is a new antiepileptic drug (AED) approved for add-on therapy of epilepsy. The aim of this study was to assess the efficacy and safety of LCS in adult patients with inadequately controlled focal seizures.

Method: All clinical charts of drug-resistant patients referred to our Epilepsy Centre treated with LCS for ≥3 months during the last year were reviewed.

Abstracts

Efficacy was assessed by seizure frequency modification during LCS therapy, and safety was evaluated by adverse events (AEs), based on physicians' notes and patients reporting.

Results: Forty-two patients (25 F, 17 M) aged between 16 and 65 years (mean 38.5 ± 12.7 years) were started on LCS treatment with a daily dose of between 100 to 600 mg (mean daily dose of 334.5 mg/day). Mean follow-up time was 5.5 months (range 3–15). Patients were treated with one to three concomitant AEDs (mean 1.7). All the patients suffered from focal epilepsy: 30% had cryptogenic and 70% had symptomatic epilepsy.

After LCS introduction, 62% of patients presented a clinical improvement: three patients (7%) became seizure-free, 11 patients (26%) experienced a seizure reduction >75%, 12 patients (29%) experienced a seizure reduction >50%. On the other hand, 14 patients (33%) remained unchanged, and two patients (5%) worsened their seizure frequency. Nine patients (21%) discontinued LCS (eight because of inefficacy, one for AEs). AEs included dizziness (23%), nausea (14%), diplopia (12%), headache (5%) and sedation (5%). Twenty-seven patients (64%) did not refer any AEs.

Conclusion: Adjunctive LCS therapy demonstrated good efficacy and was generally well tolerated in adult epilepsy patients.

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EFFICACY AND TOLERABILITY OF LACOSAMIDE AS ADJUNCTIVE THERAPY IN PATIENTS WITH PHARMACORESISTANT FOCAL EPILEPSY

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Purpose: To evaluate safety, tolerability and efficacy of lacosamide (LCM) in a pediatric, adolescence and adult population with partial-onset seizures.

Method: Nineteen patients aged 7–34 years (mean 20) were included. The longer follow up is 9 month (mean 6 months). All patients presented partial seizures, eight with secondary generalization. 6/19 patients presented interictal frontal EEG activity with bisynchronism and two of them underwent callosotomy. LCM was administrated at 300–400 mg/day (given bid). LCM was administrated intravenous in 3/19 patients (age <16 years old). Concomitant AEDs were held stable. Efficacy was evaluated by seizures frequency at the baseline and at last follow up. Safety and tolerability were estimated with adverse events (AEs) that included dizziness, nausea, fatigue, ataxia, diplopia and nystagmus, and considering the number of patients who withdrawal the therapy. The AEs were related to the concomitant AEDs.

Result: In 14 patients the median percentage reduction in seizure frequency was 30–40%. Five patients discontinued therapy: two for dizziness and diplopia, the other three, all with EEG bisynchronism, for ''absence'' seizures aggravation. Of the other three patients with bisynchronism, two had undergone callosotomy and one resolved the increase of absence seizures reducing dosage.

Conclusion: Lacosamide may be an advantageous option for the treatment of partial-onset seizures. The iv administration is well tolerated still in pediatric patients. EEG bisynchronism may be a predictor factor of worsening of ''absence'' seizure. Dizziness is the most important side effect.

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ADJUNCTIVE THERAPY WITH *VINPOCETIN* IN CHILDREN WITH REFRACTORY PARTIAL EPILEPSY: A PILOT STUDY IN MEXICO

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Vinpocetine is a synthetic product related with vinca alkaloid, was used in seizures disorder in adults. A mexican investigators team showed a potent antiepileptic effect under sodium channels in animal models.

Purpose: We studied in a pilot research the potential antiepileptic effects in a group of children with partial epilepsy.

Method: We select children (5–14 years old) with partial epilepsy who received high-dose at least for 4 months with valproic acid (VPA) or carbamazepine (CBZ) monotherapy without seizure control. The patients were random to receive: CBZ-VPA (control group) or add vinpocetine (VPC) to the basal treatment (CBZ-VPC, grup II or VPA-VPC, group III). The vinpocetine dose was increase progressively during a 6 weeks period, from 15 to 45 mg/day or 2 mg/kg/day (60 kg or less). The patients were observed under EEG, clinical and blood monitoring every 3 weeks. Efficacy was evaluate at the 6 and 12 weeks.

Result: Seventeen patients were included, nine with vinpocetine (four previously received CBZ and five VPA) and eight with combinations of CBZ and VPA (control group). The vinpocetine group (n = 9) reduced the frequency of seizures from 6.6 ± 11 to 2.2 ± 4 per week, whereas the control group (n = 8) from 5.4 ± 6 to 2.3 ± 3 (without differences). Five patients of the vinpocetine and control groups reduce significantly the frequency of seizure (less of 50%), without differences between groups, and three patients in every group showed complete control.

Conclusion: The vinpocetine is an old drug, but may have new antiepileptic utilities in children and may equals the effectiveness of the traditional AED.

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LONG-TERM TREATMENT WITH LACOSAMIDE

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Purpose: Lacosamide is a new antiepileptic drug for add-on treatment of focal epilepsies, which is available in Germany since 2008. The aim of this study was the evaluation of patients under treatment up to 12 month with Lacosamide with regard to seizure control and side effects.

Method: Fifty consecutive patients suffering from focal epilepsies who started add-on therapy with lacosamide before December 2009 were analyzed. Maximum evaluation period was 12 months of treatment. Patients suffering from a progressive disease, taking part in another treatment study or undergoing epilepsy surgery during the evaluated period were not included. Demographic data, etiology of epilepsy, retention rates, treatment response, comedication and side effects were recorded.

Result: Twenty-eight men and 22 women of median age 43 (21–72) were included. *Titration*: first week: 100 mg/day, second week: 200 mg/day, third week: 300 mg/day. *Main etiologies*: 30% cryptogenic, 12% hippocampal sclerosis, 10% cerebral malformation, 8% each: encephalitis, perinatal infarction, focal cortical dysplasia. *Retention rates:* 57%/48% after 10/12 months. *Responder rates (ITT)*: 6% seizure-free, 12% seizure reduction (SR) between 75% and 99%, 16% SR between 50% and 74%, 62% SR below 50%, worsening in 4%. *Main comedications*: 32% levetiracetam, 26% oxcarbacepine, 24% lamotrigine. *Main side effects*: 24% dizziness, 8% tiredness, 6% nausea. Temporary or persistent side effects were found in 32% of the patients. In none of the patients lacosamide was tappered because of side effects alone—there was always a lack of treatment response, too. We did not find a significant difference in the retention rates with regard to comedication with versus without Na^+ channel blockers.

Conclusion: Due to the main etiologies most of our patients suffered from a difficult to treat epilepsy. They showed a responder rate (ITT, seizure reduction >50%) of 34%. Tolerability was good, lacosmide was tappered in no patient because of side effects alone. Our results from a

naturalistic treatment setting are well compareable to other add-on studies and confirm that lacosamide is a good therapeutic option in focal epilepsies.

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IMPROVEMENT OF LACOSAMIDE EFFICACY BY OPTIMIZED COMEDICATION: PRELIMINARY RESULTS FROM A PROSPECTIVE OPEN-LABEL INVESTIGATION

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Purpose: Lacosamide (Vimpat) was approved in Germany for adjunctive treatment of focal epilepsies in September 2008. Retrospective analysis of data from three pivotal studies regarding the effect of adjunctive lacosamide treatment showed superior efficacy and tolerability in patients without traditional sodium channel blocking AEDs in their background medication (Sake JK et al. *CNS Drugs* 2010; 24:1055–1068). We investigated whether modification of background medication containing sodium channel blocking AEDs could amplify the effect of lacosamide treatment in individual patients.

Method: Twelve consecutive patients with focal epilepsies and traditional sodium channel blocking AEDs in their background medication were included in a prospective open-label investigation. All patients included showed response to adjunctive treatment with lacosamide, but seizure freedom could not be achieved. Background sodium channel blocking AEDs were replaced by either levetiracetam, valproic acid, topiramate, benzodiazepines or barbiturates at the discretion of the investigator. Efficacy was calculated comparing the mean seizure frequency before and after the modification of background treatment. Assessment of tolerability was derived from patient reports of side effects and neurological examinations.

Result: Five of the 12 patients had improved seizure control as a consequence of optimized background medication, with additional seizure reduction in the range of 50–90%. None of the patients reported worsening of side effects.

Conclusion: These preliminary results of an ongoing prospective investigation are in line with recent retrospective analyses of pivotal trial data. Replacing sodium channel blockers by AEDs with different mechanisms of action may improve the seizure situation in individual patients.

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INTRAVENOUS LACOSAMIDE IN REFRACTORY STATUS EPILEPTICUS (SE)

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Purpose: Many patients present with refractory status epilepticus (SE) despite multiple traditional antiepileptic drugs (AEDs). Lacosimide (LCM) was recently approved as an adjunct AED with intravenous (IV) formulation for partial-onset seizures. It has a unique mechanism of modulating voltage-gated sodium channels by enhancing their slow inactivation with minimal drug–drug interactions. LCM has demonstrated efficacy in animal models of pharmacoresistant seizures. We report our experience with IV lacosimide in patients with SE.

Methods: Pharmacy records were retrieved to identify patients with SE who received IV LCM in our institution. Data on demographics, seizures, response to therapy and adverse effects/outcomes were analyzed. All patients had undergone continuous EEG monitoring.

Result: Ten patients (four men, six women), ages 16–90 years with refractory SE were given LCM. Eight patients were in focal nonconvulsive SE, two were in generalized nonconvulsive SE. The etiologies included anoxic brain injury, idiopathic, encephalitis, tumor, PRES, stroke, and AVM. IV LCM was added after traditional AEDs, including drug-induced coma in some patients, failed to control the SE. All but one patient with focal SE gained seizure freedom upon discharge.

Conclusions: LCM is a useful adjunct in refractory SE. The IV formulation allows prompt administration in the intensive care unit setting. Response was seen especially in focal SE. Response was poor, similar to other AEDs, in patients with postanoxic injury. Our data is limited by the small number of patients. Larger controlled studies are necessary to accurately assess the efficacy of IV LCM as an early treatment of SE.

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EFFICACY AND TOLERABILITY OF ZONISAMIDE AS ADJUNCTIVE THERAPY IN THE TREATMENT OF REFRACTORY EPILEPSY IN AGE OF DEVELOPMENT

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Purpose: To evaluate short-term efficacy and tolerability of zonisamide (ZNS) as add-on therapy of refractory epilepsy in children.

Method: Our prospective, open-label study included 22 patients, with refractory epilepsy, mean age 11.9 years. Ten patients had focal epilepsies, nine epileptic encephalopathies, two Dravet syndrome and one undetermined epilepsy. All the patients were inadeguately controlled on 1–3 AEDs. We used a dose of ZNS of 6–8 mg/kg/die, in two doses. Before the beginning of the treatment and at the end of the follow-up patients underwent the following exams: clinical examination, review of clinical report of the seizures referred to the last 3 weeks, video-EEG, laboratory tests. Duration of treatment and follow-up: 3 months–3 years. At the end of follow-up we evaluated reduction in seizures frequency and side effects.

Result: We found a reduction in seizures frequency ≥75% in seven patients and ≥50% in eight patients; seven had no reduction in seizures frequency. Eleven patients are still on treatment. In three patients we observed a loss of efficacy after 1–2 years. Seven patients discontinued the treatment for inefficacy at three months, one had to discontinue for adverse events. None had a severe adverse event but two patients reported a weight loss and three had drowsiness; one had a cutaneous rash, resolved with the reduction of ZNS dose.

Conclusion: Our preliminary data suggest that ZNS is well tolerated in young patients with focal epilepsy and can be used as an add-on therapy to reduce seizure frequency.

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CLINICAL EXPERIENCE WITH LACOSAMIDE IN PATIENTS WITH PHARMACORESISTANT PARTIAL EPILEPSY: AN AUDIT IN EPILEPSY CLINICS FROM THE SOUTHEAST OF ENGLAND

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Purpose: To evaluate clinical variables, efficacy and tolerability of add-on lacosamide in a outpatient epilepsy clinics setting.

Method: We performed a retrospective case note audit on 88 adult patients (38 male) with refractory epilepsy in whom lacosamide have been prescribed for refractory epilepsy attending five hospitals.

Result: Almost all patients were concurrently receiving one to four antiepileptic drugs (AEDs), eight patients were having four, 30 had three, 26 had two, and 22 had one. Mean of maximum daily doses reached was 200 mg (range 25–500 μg) and mean follow-up for those patients who remained on treatment was 7 months (range 1–24 months).

Of those patients who remained on lacosamide, 35 reported improvement in seizure frequency. Among those 35 patients, 23 have seizure reduction >50%, nine improved by <50%. Two patients reported decrease in seizure severity without change in seizure frequency and one patient remained seizure-free for 14 months. In six patients that improved other AEDs were reduced: two phenytoin, one phenobarbitone, one carbamazepine, one levetiracetam and one primidone. In another two patients that improved other drugs were removed: one levetiracetam and one sodium valproate. No patient was moved to monotherapy.

Side effects were reported by 17 patients: seven reported sedation, five dizziness, four nausea, three headache, two unsteadiness, two gastrointestinal disturbance, one double vision, one panic sensation, one itchiness and one tiredness.

In addition, side effects were reported on 28% of patients who were concurrently taking any sodium channel AED compared to 17% on those who were taking any other no sodium channel AEDs.

Nineteen patients discontinued treatment, among those: 12 presented intolerable side effects (two nauseas, two gastrointestinal disturbances, two sedation, one panic sensation, one itchiness, one dizziness, one headache, one tiredness, and one double vision), four lack of efficacy, and three had increase in seizure number.

Conclusion: Lacosamide appears to be an effective and very well tolerated AED when used as add-on therapy with few side effects mostly sedation.

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THE EFFECTIVENESS OF TOPIRAMATE IN MIGRAINE PREVENTION

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Purpose: Topiramate is a drug that successfully prevent migraine attacks in adults. The present analysis of pooled data from those three trials was performed to characterize the efficacy and adverse events of topiramate for migraine prevention in subjects who had used other migraine preventive medications.

Methods: We were analyzed patients with migraine, who had used migraine preventive medications (tricyclic antidepressants, beta-blockers or neurostabilizers other than topiramate) within approximately 8 months period. Patients with a history of glaucoma, kidney stone were excluded. Patients were admitted to the Department of Neurology in Nis, after observing their miagraine atack, during the period January–December 2010. After the admittion, all of the patients have been diagnostically examend by: thorough physical examination, neurological evaluation, laboratory diagnostics, as well as complementary examinations such as interictal EEG, head CT, MRI, MRA angiography. We analyzed monthly migraine frequency from baseline period to end point. We compared different dosage of topiramate, so as the presence of adverse events. We started with 25 mg/day od topiramate and this lasted for 7 days and we increased dosage of topiramate 25 mg/week. Maximum dosage was 200 mg/day.

Result: Of sum of 167 patients, 96 (57.48%) female, aged between 21 and 59 years (mean age 39.2) were recruited. Subjects were treated with topiramate (50, 100 or 200 mg/day). More subjects on topiramate 50 mg/day (41%), 100 mg/day (63%) and 200 mg/day (54%) exhibited ≥50% reductions in monthly migraine frequency. Most common adverse event was paresthesis; incidence was 11%, fatigue 3%, nausea 2%. Mean duration of paresthesia was 19 days. Cognitive symptoms were registered only in two patients. Anorexia, glaucoma, and kidney stone were not registered.

Conclusion: In subjects who had previously taken other migraine preventives, treatment with topiramate100 and 200 mg/day significantly reduced mean monthly migraine frequency. In our study, the lower dose of topiramate exhibited similar efficacy. Adverse events is rarely and most frequent is paresthesia which disappears in 3 weeks.

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LONG-TERM MAINTENANCE OF EFFICACY AND TOLERABILITY WITH RETIGABINE (EZOGABINE) 600–1200 MG/DAY OVER 24 MONTHS

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Purpose: To assess the long-term efficacy and tolerability of retigabine (RTG; ezogabine in the US and Canada) as adjunctive therapy for adults with partial-onset seizures. RTG 600–1200 mg/day improved seizure control and was generally tolerated in two Phase III double-blind, placebo-controlled trials (Studies 301/302).

Method: Studies 303/304 (NCT00310375/NCT00310388) are ongoing long-term open-label extensions (OLEs) of Studies 301/302. During transition to the OLEs, RTG was adjusted to, or maintained at, 900 mg/day (Study 304) or 1200 mg/day (Study 303). Thereafter, dosages of RTG (600–1200 mg/day) and background antiepileptic drugs could be modified according to individual efficacy/tolerability. Studies 303/304 are ongoing. Responder rates (≥50% reduction in 28-day partial-seizure frequency) and percent change in 28-day total partial-seizure frequency are reported here.

Result: The safety population as of 2 October 2009 included 181 and 375 patients from Studies 303 and 304, respectively. At Month 24, for patients exposed to ≥24 months of RTG (Study 303, n = 69; Study 304, n = 114), the responder rate was 68.9% (Study 303, 69.6%; Study 304, 68.4%), and the median percent reduction in seizure frequency was 64.8% (Study 303, 62.6%; Study 304, 66.1%). The responder rates and median percent reductions in seizure frequency were stable over 24 months of treatment with RTG. The frequency and severity of TEAEs did not change during long-term treatment.

Conclusions: In this integrated analysis of patients who remained on treatment with RTG for ≥24 months, RTG maintained efficacy and was generally tolerated during open-label, adjunctive therapy in adults with partial-onset seizures.

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PHARMACOLOGICAL EFFECTS OF RETIGABINE (EZOGABINE) ON BLADDER FUNCTION

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Purpose: Retigabine (RTG; ezogabine in the US and Canada), a potassium channel opener, has been shown in preclinical studies to inhibit urinary bladder contraction, leading to possible inability to empty the bladder. The safety of RTG with respect to bladder function is evaluated herein from an integrated dataset of Phase II/III clinical studies.

Method: Urinary safety data were assessed in RTG-treated patients from seven completed Phase II/III trials and six long-term open-label

extensions. Adverse events (AEs) related to urinary retention/voiding dysfunction, American Urological Association Symptom Index (AUA SI) scores and postvoid residual (PVR) volume were assessed.

Result: One thousand three hundred sixty-five patients were exposed to RTG (median total exposure, 261 days). Voiding dysfunction and urinary retention-related AEs were reported by 118 (8.6%) patients, including urinary hesitation (3.1%), urinary retention (1.9%), and residual urine volume (1.2%). Four patients reported serious AEs of urinary retention and required urinary catheterization. Urinary hesitation and retention led to discontinuation in 1 (<0.1%) and 6 (0.4%) patients, respectively. Urinary symptoms generally remitted following discontinuation of RTG. AUA SI scores generally remained consistent and low. PVR values of potential clinical concern (PCC) were reported by 53 of 624 (8.5%) patients. Nine patients had PCC values at baseline and postbaseline.

Conclusions: RTG exerts a pharmacological effect on bladder function as evidenced by voiding dysfunction and urinary retention-related AEs and a slight but reversible increase in PVR volume. The majority of AEs were mild, with most patients able to continue treatment.

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ANTIEPILEPTIC DRUG TREATMENT STRATEGY IN CHILDREN WITH EPILEPSY: A RETROSPECTIVE STUDY

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Purpose: To evaluate antiepileptic drug (AED) treatment strategy over time in a cohort of children with newly diagnosed epilepsy treated since 2000 in our hospital (UMCG), a secondary and tertiary epilepsy referral centre.

Methods: We retrospectively studied AED prescription in a series of consecutive patients by collecting clinical data from the electronic patient record system including seizure type and epilepsy syndrome; changes in prescription, comparing conventional and second-generation AEDs (registered after 1995); treatment success rates of the different AEDs defined as number of children becoming seizure-free on an AED plus number of children continuing this AED at the end of follow-up without being seizure-free.

Result: Four hundred eighty-nine Children (median age at onset 3.4 years [range 0–17]; 23% idiopathic, 53% symptomatic, 24% cryptogenic) were included. Valproic acid (VPA) was most often prescribed, followed by carbamazepine (CBZ) and lamotrigine (LTG). VPA was the most often prescribed first-choice AED for almost all age groups, seizure types and syndromes. Over time, a significant increase in prescription of second-generation AEDs as first choice AED was observed ($p = 0.016$), especially of LTG ($p = 0.024$). Furthermore, VPA was significantly less often prescribed over time as first choice AED ($p = 0.006$). Success rates were highest for LTG, levetiracetam (LEV), and VPA, respectively.

Conclusion: Our results are in line with those of previous European studies. Second-generation AEDs were more often prescribed over time, with good success rates for especially LTG and LEV.

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DOES THERAPEUTIC STRATEGY HAVE IMPACT ON QUALITY OF LIFE IN PATIENTS WITH COMPLEX PARTIAL EPILEPSY FAILING ON A SINGLE DRUG?

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Purpose: To evaluate the quality if life (QOL) in patients with complex partial epilepsy, assigned to adjuvant versus alternative monotherapy after failing on a single drug.

Method: Cross-sectional study of 29 consecutive patients with complex partial epilepsy epilepsy refractory to single antiepileptic drug (AED). Inclusion criteria were: (1) age ≥18 years; (2) diagnose of complex partial epilepsy set by standard clinical, electrophisiologicaly and neuroradiology protocol; (3) same therapy during last 2 months; (4) ability to give consent and to fill in the questionnaire with minimum help; and (5) absence of chronically disease or use of medicine with potential for side effects, (6) no previous use of combinational therapy. Physician was independent in choice of strategy, drugs, and doses, according to clinical response. QOL was accessed with validated translation of the QOLIE-31 questionnaire. Scores are obtained according to original manual. Mann-Whitney test ware performed for alpha = 0.05.

Result: Results show significant higher total scores of QOL ($p = 0.012$) as well as higher scores on subscales for social function ($p = 0.44$), cognitive effects ($p = 0.04$), energy/fatigue ($p = 0.027$) and seizure worry ($p = 0.21$) in patients assigned to alternative monotherapy ($n = 14$) in comparison to group with adjuvant therapy ($n = 15$).

Conclusion: Results of this study could highlight alternate monotherapy as preferred option in patient with complex partial epilepsy failing on single drug. Further studies with greater sample size and control of confounding variables are warranted.

Keywords: Epilepsy, antiepileptic drugs, quality of life, monotherapy, politherapy.

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CAUSES OF TREATMENT GAP IN A RURAL INDIAN POPULATION IN THE YEAR 2011: SHOULD WE CONTINUE TO BLAME IT ON LACK OF AWARENESS?

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Purpose: Several authors have reported an epilepsy treatment gap of up to 90% from rural India. This is often attributed to several factors but lack of awareness amongst patients and caregivers is often cited as one of the primary reasons. With the recent strides in information technology and facilitation of communication through mobile phone penetration, current assumptions about low levels of awareness amongst people living even in remote, rural regions, may not be correct. We conducted a survey in one such remote Indian village to explore factors that may influence treatment-seeking behavior in rural patients with epilepsy (PWE).

Method: This data is part of an ongoing epilepsy outreach program. We used a mobile epilepsy clinic to reach a very remote rural region in the Bihar state of India. Using rigorous door-to-door public announcements, we requested PWE to visit our epilepsy clinic. Using a structured, validated questionnaire in Hindi, we asked for reasons that could be responsible for the treatment gap in this population. Parents or caregivers were questioned when the PWE was unfit to be administered our questionnaire.

Result: There were 48 females amongst the 144 PWE who visited our clinic and the mean age was 24 years. All 144 PWE or their caregivers understood that epilepsy was a medical disease and that it would respond to treatment. Ninety-seven percent PWE favored allopathic treatment while 3% felt homeopathy worked for epilepsy. Ninety-three percent PWE said they would seek treatment if they had easy access to a doctor

while 59% felt that they would be able to buy medicines if a doctor prescribed it for them.

Conclusion: Strategies for narrowing treatment gap in rural India need a fresh look. It is more a lack of health infrastructure and doctors rather than a lack of awareness amongst PWE that may be worth targeting.

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INFLUENCE OF GENETIC VARIANTS IN EPHX1 GENE ON THE CBZ DOSES IN THE PATIENT FROM R. MACEDONIA

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The pharmacokinetics of carbamazepine (CBZ) is predominantly determined by drug-metabolizing enzymes such as cytochrome P450 (CYP), uridine 5'-diphosphate-glycosytransferase (UGT), and microsomal epoxide hydrolase (mEH). The mEH, is a biotransformation enzyme that metabolizes numerous reactive epoxide intermediates to more water-soluble transdihydrodiol derivatives. Two variants in the gene encoding mEH have been described; a "slow" variant, EPHX1 337 T>C or Try113His (rs1051740) which operates at 50% of wild-type capacity and a "fast" EPHX1 417A>G or His139Arg (rs.2234922) variant which has 25% faster capacity than the wild type version. Several recent studies have suggested that these variants have a strong bearing on carbamazepine 10,11-epoxide clearance to the inactive diol and that their determination would be useful in CBZ dosage estimation. We analyzed the allelic frequency and genotype distributions of these two variants using TaqMan assay in 111 patients treated with different doses of carbamazepine. Our results show that patients with a haplotype for two high activity variants (homozogotes for 337T and 427G) require the highest maintenance dose of CBZ (583 mg) in comparison to patients with a haplotype with two low activity variants (337C and 417A) who were maintained at 400 mg CBZ. Consistently, patients with one high and one low activity variant (337T and 417A) required intermediate maintenance doze of CBZ of 438 mg. Our results indicate that inherited capacity for CBZ hydroxylation is important determinant for estimation of CBZ doze in patients with epilepsy.

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BROMIDE IN PATIENTS WITH *SCN1A* MUTATIONS MANIFESTING AS DRAVET SYNDROME AND ITS BORDERLINE VARIANTS

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Objective: Bromide is the oldest antiepileptic drug that nowadays is still but rarely used. We analyzed effectiveness and tolerability of bromide in patients with Dravet syndrome and *SCN1A* mutations.

Methods: Retrospective analysis on the basis of patients' histories and structured interviews of parents in 32 patients aged 4–24 years (mean age 12.4 years) with *SCN1A* mutations. The patients suffered from typical Dravet syndrom or its borderline variants.

Result: After 3 months, 26/32 patients (81%) treated with bromide showed an improvement of seizures with a reduction of >50% (>75%) in 18 (12) patients. Four patients did not improve, in two patients treatment had to be stopped because of intolerable side effects. No aggravation of seizures was observed.

To date, 18 patients (56%) still receive bromide (follow up: 9–159 months, average 60 months; mean dose 38.5 mg/kg). Reasons for discontinuation in the other 14 patients (after 3 months–6 years, mean 3.1 years) were: side effects (5), loss (2) or lack (5) of effectiveness, others (2). As side effects drowsiness (n = 6), acneiform skin eruptions (n = 4), aggressiveness (n = 3), and gastrointestinal (n = 2) or motoric symptoms (n = 2) are reported.

Discussion: Bromide showed a clear and often long lasting effectiveness in patients with *SCN1A* mutations. Adverse reactions were mainly mild or moderate leading to treatment termination in 5/32 patients. We conclude that bromide holds promise in epilepsy patients with *SCN1A* mutations and intractable seizures.

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TREATMENT OF EPILEPSY IN ADULTS: EXPERT OPINION IN CHINA

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Purpose: To survey a group of epileptologists in China regarding the treatment of epilepsy.

Method: We sent a questionnaire on the treatment of adolescent and adult epilepsy syndromes to a group of opinion leaders in the field of epilepsy.

Result: Of the 50 experts to whom the survey was sent, 49 (98%) responded, with a mean of 17.9 years in practice. For initial monotherapy for IGE, valproate was rated as treatment of choice. In SLRE-SPS and SLRE-CPS, carbamazepine and oxcarbazepine were treatments of choice, with lamotrigine, topiramate and levetiracetam also usually appropriate. In SLRE-SGTC, carbamazepine, lamotrigine and oxcarbazepine were treatments of choice, while lamotrigine, topiramate, levetiracetam and valproate were also usually appropriate. Valproate was selected as treatment of choice when combined with other AEDs in IGE. For SLRE, combination/add-on therapy of carbamazepine (oxcarbazepine) + topiramate, carbamazepine (oxcarbazepine) + levetiracetam, carbamazepine (oxcarbazepine) + valproate, valproate + lamotrigine were considered as treatment of choice. For women who are pregnant or trying to conceive, lamotrigine was treatment of choice for both IGE and SLRE. For patients with school-age, lamotrigine was treatment of choice for IGE, with oxcarbazepine and lamotrigine for SLRE. In persons with epilepsy and hepatitis B, whether liver function was normal or not, topiramate and levetiracetam were treatment of choice for IGE; Valproate and levetiracetam were treatment of choice for seizures in the emergency department.

Conclusion: The expert consensus method concisely summarizes expert opinion, and this opinion may be helpful in situations in which the medical literature is scant or lacking.

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THE CONSENSUS ON THE APPLICATION OF ANTIEPILEPTIC DRUGS BEFORE AND AFTER EPILEPSY SURGERY

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Purpose: To solve the important issue of regulating AEDs pre and post epilepsy surgery, to ensure the effects of epilepsy surgery and to promote the development of epilepsy surgery in China.

Method: To collect the opinions of domestic senior epileptology experts through expert seminars and questionnaires.

Result: "The consensus on the application of AEDs before and after epilepsy surgery" drafted by an expert group and then discussed repetitively on different groups, revised according to available domestic and foreign literature reports, was finally formed and adopted by the expanded meeting of experts in 2010.

Conclusion: The consensus includes: (1) Basic Principles; (2) Reviewing AED and medical history before surgery; (3) Application and adjustment of AEDs during the preoperative assessment; (4) AED application on the day of surgery and within four weeks after surgery; (5) AED reduction and withdrawal after surgery.

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INVESTIGATE THE EFFECT OF CONTINUOUS SEDATION FOR REFRACTORY EPILEPTIC STATUS IN CHINA

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Purpose: To identify clinical feature, EEG pattern and therapeutic regimes for patients with refractory epileptic status who need continuous sedation in China.

Method: From March 2010 to March 2011, we received six patients with refractory epileptic status who need continuous sedation in Neuro ICU. The diagnosis, imaging, important laboratory tests, routine treatment, antiepileptic drug regimens, continuous EEG monitoring and the average medical expense daily were reviewed.

Result: The mean age of the six patient was 27.5 (16–44 years old), the duration of hospitalization were from 2 days to 4 months. Four patients were diagnosed with viral encephalitis; one patient became epileptic status after neurosurgery; one patient was abstinence syndrome. Except for the patient with neurosurgery, CT or MRI scans were normal or a little edema. The lab tests were normal for all the patients. Besides routine treatment were given, including etilogical treatment, incision of trachea, tube-feeding, all patients need large-dose sedation continuously such as midazolam or propofol even both to suppress the SE. Although sufficient dosage and various AED regimens that were written in guideline or literatures were given, all the patients still need intravenous sedations to control seizure persistently. Continuous EEG revealed spike rhythm at the beginning, and even large dose sedation can't suppress it. But after a period of therapy, the background and ictal on EEG, and the ictal behavior changed. None the patients regained consciousness or successfully took off intravenous sedation when discharge.

Conclusion: Refractory epileptic status that need continuous sedation usually takes place in relatively young and healthy people. It's a tough problem both for doctors and his (her) relatives to handle and decision.

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EVALUATION OF DIFFERENT ANTIEPILEPTIC DRUGS STRATEGY FOLLOWING EPILEPSY SURGERY: A RETROSPECTIVE STUDY

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Purpose: This study aimed to explore the most appropriate antiepileptic drugs (AEDs) strategy after epilepsy surgery.

Methods: A total of 131 refractory epilepsy patients who underwent epilepsy surgery from January 2005 to December 2008 in the Department of Neurosurgery, West China Hospital were retrospectively reviewed. Patients were divided into three groups (monotherapy, duotherapy and polytherapy) according to drug combinations immediately after epilepsy surgery. Seizure outcomes were followed up at 6 months, 2 years and 5 years. Engel classification was used to evaluate seizure outcomes.

Result: The mean postoperative follow-up period was 3.7 ± 1.0 years (Range, 2–5.8 years). Preoperative baseline data among three groups was of homogeneity. Seizure-free patients tried to start AEDs tapering more than 6 months after operation. Seizure recurrence rate in monotherapy was obviously higher than other groups (34.1% vs. 15.1%, 7.1%) at 6-month follow-up, which showed statistically significant difference ($p = 0.02$). Final seizure outcome for 2 years were assessed by Engel classification. In the duotherapy group, rate of Engel class ? was definitely higher than other two groups (69.9% vs. 47.7, 42.9%), and the difference was great meaningful ($p = 0.01$).

Conclusion: Monotherapy is not sufficient to control seizures completely. It appears to have a higher risk when considering drug reduction. Duotherapy would be more effective and safety. Multitherapy may bring some potential problems (poor compliance, economic burden or psychological stress et al).

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ANTIEPILEPTIC DRUG USE IN AUSTRIAN NURSING HOME RESIDENTS

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Purpose: Currently around 30% of all newly developed seizures are diagnosed in persons older than 65 years. Five to seventeen percent of nursing home-residents take antiepileptic drugs. Data on the prescribing behavior for antiepileptic drugs in Austrian nursing homes are missing. The aim of our study was to analyze the type and frequency of prescribed antiepileptic drugs, as well as their indication, comorbidities and co-medications in a population based setting in the elderly.

Method: This was a population based retrospective cross-sectional study, which included all residents of the seven public nursing homes in Innsbruck. The data of the 828 probands were maintained anonymously and have been taken directly on site from the clinical records. The data collection was followed by descriptive statistics. The necessary calculations for this have been carried out with program SPSS 18.0.

Result: Seventy of the 828 (8.5%, 26M/44F of 192M/636F) residents took at least one antiepileptic medication on the reported date. In 51.5% the reason for prescription were epileptic seizures – in this way epilepsy prevalence rate of 4.5% can be indirectly calculated. 20% had no clear indication. The most often used antiepileptic drugs were gabapentin (37%), levetiracetam (24%) and valproate (18.5%). The three most common comorbidities were arterial hypertension (49%), ischemic stroke (36%) and other angiopathies (29%). Six to nine comedications were prescribed in 41% and 26% had more than 10 additional drugs. Overall 141 prescriptions were considered as proconvulsive (average value 2, SD 1.38).

Conclusion: Compared internationally, the study shows that in Austrian nursing homes antiepileptic drugs are not as often used as they are in Americans or Irish, but still more frequently than in German homes. By contrast with prescribing policy in the Anglo-American world, Austrian nursing home residents are mainly treated with newer antiepileptic drugs.

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HOW DO NEW ANTIEPILEPTIC DRUGS IMPACT THE THERAPY OF REFRACTORY EPILEPSY AT THE MUNICIPAL HOSPITAL IN SAKAI?

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Purpose: New antiepileptic drugs (GBP, TPM, and LTG) have been available in Japan during recent years and more than 1 year have elapsed. We aimed to assess efficacy of new AEDs in the hospital base retrospectively.

Method: The investigation includes records of patients who regularly visited the epilepsy outpatient clinic from April 1, 2009 to August 31, 2010. The collected clinical data were age, sex, epilepsy syndrome, prescription of newAEDs, numbers of continuous usage of new AEDs and responder rate of new AEDs.

Result: Ninrty-nine patient visited outpatient clinic during the investigated period. Seventy-nine patients were classified symptomatic laocalization-related epilepsy. Mean number of AEDs were 1.9. New AEDs were administered to 41 epilepsy patients as the add-on therapy. Seven of 15 patients continued the add-on therapy of GBP (47%). Eighteen of 29 patients was in case of TPM (62%), and 10 of 16 patients was in case of LTG (62%). Responder rate of GBP, TPM, and LTG were 26%, 66%, and 50% respectively. The add-on therapy with new AEDs resulted in success of half reduction of seizure frequency in 19 of 29 refractory epilepsy patients.

Conclusion: New AEDs were very effective for refractory epilepsy patients treates classical AEDs in hospital base. The low ratio of treatment failure inidicated new AEDs were tolerable for the add-on therapy.

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COMPARATIVE EFFICACY OF COMBINATION DRUG THERAPY IN REFRACTORY EPILEPSY

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Purpose: We sought to determine whether any antiepileptic drug (AED) combination, produced superior efficacy in medically refractory epilepsy by retrospectively analyzing an extensive database of AED therapy of severely developmentally disabled adults with epilepsy.

Method: We obtained records charting monthly seizure frequency and AED treatment for 168 refractory epilepsy patients at two institutions in Washington State, USA. On the average we analyzed 140 ± 5.8 (mean ± SEM) months of data for each patient and found the average seizure frequency during each unique AED regimen consisting of 1, 2, or 3 drugs in combination from a list of eight consisting of (in order of frequency of exposure using standard acronyms): LTG, VPA, CBZ, PHT, TPM, LEV, GBP, and ZNS. We then made within-patient comparisons of the ratio of seizure frequencies under different regimens.

Result: For patients exposed to both mono- and duotherapy (two drugs at a time), average seizure frequency on duotherapy was 0.81 [95% CI: 0.68, 0.98, p = 0.03) that of monotherapy, a 19% decrease. However seizure frequency with three drugs at a time was 1.07 times that on duotherapy, demonstrating no benefit of adding a third drug on the average.

In comparison of individual AED regimens against a aggregate average of all other regimens to which a patient had been exposed, only the combination of LTG/VPA showed superior efficacy (seizure frequency 0.52 [0.40, 0.66, p = 4e–6] of the aggregate average) out of 32 regimens with at least n = 5 exposures. In head-to-head comparisons, LTG/VPA was superior to six other regimens, constituting the largest number out of 10 statistically significant head-to-head comparisons.

Conclusion: These results suggest that LTG/VPA shows superior efficacy in medically refractory epilepsy. Also, while improved efficacy was seen in adding a second AED to prior monotherapy, there was no benefit on the average when adding a third drug. These results may suggest future prospective trials to confirm the superiority of LTG/VPA, and to better understand the underlying mechanisms of its action.

Poster session: Drug therapy IV
Tuesday, 30 August 2011

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EFFECTS OF ESLICARBAZEPINE ACETATE, ESLICARBAZEPINE, CARBAMAZEPINE AND OXCARBAZEPINE IN THE MAXIMAL ELECTROCONVULSIVE SHOCK TEST IN THE MICE

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Purpose: In contrast with other voltage-gated sodium-channel blockers (carbamazepine, CBZ and oxcarbazepine, OXC), eslicarbazepine acetate (ESL) delays kindling-induced epileptogenesis and inhibits seizure initiation. The present study determined the effect of ESL and its active metabolite eslicarbazepine, CBZ and OXC on the mouse maximal electroconvulsive shock (MES) model and estimated protective-index.

Method: Male NMRI mice (n = 12 per group) were administered MES (50 mA, rectangular current: 0.6 ms pulse width, 0.4 s duration, 50-Hz) via corneal electrodes connected to a constant current shock generator. The rotarod-test was conducted in mice trained to hold onto the rotarod apparatus until they maintain equilibrium for 3 min while rotating at 15 rpm. Tests were conducted 60 min after oral administration of ESL, eslicarbazepine, CBZ and OXC at different doses.

Result: ESL and eslicarbazepine demonstrated a dose-dependent decrease in MES-induced seizures (with ED_{50} values of 23.0 ± 1.9 and 27.8 ± 3.2 mg/kg, respectively), effects being significant ($p < 0.05$) at 25, 50, 100 and 150 mg/kg. CBZ and OXC dose-dependently decreased MES-induced seizures with ED_{50} values of 13.5 ± 2.1 and 13.8 ± 1.6 mg/kg, respectively. The TD_{50} values (mg/kg) for ESL and eslicarbazepine (313.7 ± 14.2 and 348.3 ± 18.8, respectively) were greater than those for CBZ (110.2 ± 64.4) and OXC (100.0 ± 21.0). The protective index (TD_{50}/ED_{50}) for ESL, eslicarbazepine, CBZ and OXC was 13.8, 12.5, 8.2 and 7.3, respectively.

Conclusion: In this analysis, although the anticonvulsant effects of ESL and eslicarbazepine occurred at slightly higher doses than that observed with CBZ and OXC, these doses were characterized by a wider protective-index, suggesting that ESL may be better tolerated than CBZ and OXC.

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EFFECTS OF ESLICARBAZEPINE ACETATE, ESLICARBAZEPINE, CARBAMAZEPINE AND OXCARBAZEPINE IN THE 6-HZ PSYCHOMOTOR SEIZURE MODEL IN THE MICE

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Purpose: The present study was designed to evaluate the effects of eslicarbazepine acetate (ESL), its main metabolite eslicarbazepine, and two other voltage-gated channel blockers, carbamazepine (CBZ) and oxcarbazepine (OXC) on the mouse 6-Hz psychomotor seizure model.

Method: Male NMRI mice (15 per group) were administered currents (rectangular pulse: 0.2 ms, 6-Hz, 44 mA for 3 s) via corneal electrodes. The rotarod-test was conducted in mice trained to hold onto the 3-cm diameter neoprene-rubberized cylinder until they maintain equilibrium for 3 min while rotating at 15 rpm. Drugs were tested 60 min after oral administration at different doses.

Result: ESL and eslicarbazepine exhibited a dose-dependent decrease in forelimb seizure scores (ED_{50} values of 15.9 ± 3.2 and 12.1 ± 1.0 mg/kg, respectively), with effects being significant ($p < 0.05$) at 50, 100 and 150 mg/kg. CBZ and OXC exhibited a dose-dependent decrease in forelimb seizure scores with ED_{50} values of 9.5 ± 2.4 and 9.1 ± 2.7 mg/kg, respectively. Diazepam (4 mg/kg), tested under the same experimental conditions, completely suppressed forelimb seizures. The TD_{50} values (mg/kg) for ESL and eslicarbazepine (313.7 ± 14.2 and 348.3 ± 18.8, respectively) were greater than those for CBZ (110.2 ± 64.4) or OXC (100.0 ± 21.0). The corresponding protective index (TD_{50}/ED_{50}) for ESL, eslicarbazepine, CBZ and OXC was 19.7, 28.7, 11.7 and 10.9, respectively.

Conclusion: In this analysis, although the anticonvulsant effects of ESL and eslicarbazepine occurred at slightly higher doses than that observed with CBZ and OXC in the 6-Hz psychomotor test in mice, these doses were characterized by a wider protective-index, suggesting that ESL may be better tolerated than CBZ and OXC.

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EFFECTS OF ESLICARBAZEPINE, R-LICARBAZEPINE, OXCARBAZEPINE AND CARBAMAZEPINE ON GLYCINE GLYRA3 RECEPTOR-MEDIATED INWARD CURRENTS

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Purpose: Glycine serves as an important mediator of synaptic inhibition, and can evoke inhibition of the neuronal activity by activating glycine GlyRα3 receptor. Altered glycine-mediated neurotransmission may play a role in chronic experimental and human epilepsy. Eslicarbazepine acetate (ESL) is a novel once-daily antiepileptic drug approved in Europe for use in adults as adjunctive therapy for refractory partial-onset seizures. ESL undergoes rapid and extensive first pass hydrolysis to eslicarbazepine, its major active metabolite. This study determined the effects of eslicarbazepine, R-licarbazepine (minor metabolite of ESL), oxcarbazepine (OXC) and carbamazepine (CBZ) on submaximal glycine GlyRα3 receptor-mediated inward currents.

Method: Chinese-hamster ovary cells were stably transfected with recombinant glycine receptor cDNA that encode GlyRα3 receptors. The modulatory effects of eslicarbazepine, R-licarbazepine, OXC and CBZ (25–1000 μM, n = 3–5 cells) on submaximal GlyRα3 receptor-mediated inward currents (short application of 150 μM glycine) were measured in patch-clamped cells at a holding potential of −80 mV; 0.4% DMSO was used as vehicle.

Result: Eslicarbazepine, R-licarbazepine, OXC, and CBZ inhibited glycine GlyRα3 receptor-mediated inward currents with IC_{50} values of 1616, 1186, 380 and 888 μM, respectively. Strychnine, a glycine channel blocker, reduced the GlyRα3 inward currents with an IC_{50} value of 52 nM.

Conclusion: The reduced potency of eslicarbazepine in inhibiting glycine GlyRα3 receptor-mediated inward currents, when compared with OXC and CBZ, may translate into a better safety profile for ESL.

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EFFECTS OF ESLICARBAZEPINE ACETATE ON ACUTE AND CHRONIC LATRUNCULIN A-INDUCED SEIZURES AND EXTRACELLULAR AMINO ACID LEVELS IN THE MOUSE HIPPOCAMPUS

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Purpose: Latrunculin A microperfusion of the hippocampus induces acute epileptic seizures and long-term biochemical changes leading to spontaneous seizures. This study tested the effect of eslicarbazepine acetate (ESL) on latrunculin A-induced acute and chronic seizures, and changes in brain amino acid extracellular levels.

Method: Swiss mice hippocampus was continuously perfused with a latrunculin A solution (4 μM, 1 μl/min, 7 h/day) with continuous EEG and videotape recording for three consecutive days. Microdialysate samples were analyzed by HPLC and fluorescence detection of taurine, glycine, aspartate, glutamate and GABA. Thereafter, mice were continuously video monitored for 2 months to identify chronic spontaneous seizures or behavioral changes. Control EEG recordings (8 h) were performed in all animals at least once a week for a minimum of 1 month.

Result: ESL treatment (100 mg/kg), previous to latrunculin A microperfusion, completely prevented acute latrunculin A-induced seizures as well as chronic seizures and all EEG chronic signs of paroxysmal activity. Hippocampal extracellular levels of taurine, glycine and aspartate were significantly increased during latrunculin A microperfusion, while GABA and glutamate levels remained unchanged. ESL reversed the increases in extracellular taurine, glycine and aspartate concentrations to basal levels and significantly reduced glutamate levels. Plasma and brain bioanalysis showed that ESL was completely metabolized within 1 h after administration to mainly eslicarbazepine, its major active metabolite.

Conclusion: In this analysis, ESL treatment prevented acute latrunculin A-induced seizures as well as chronic seizures and all EEG chronic signs of paroxysmal activity, supporting a possible antiepileptogenic effect of ESL in mice.

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STIRIPENTOL EXHIBITS HIGHER ANTICONVULSANT PROPERTIES IN IMMATURE BRAIN

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Purpose: Stiripentol (STP) has demonstrated efficacy in Dravet Syndrome. It has been shown in in vitro studies that STP directly acts on $GABA_A$ receptors exhibiting a higher chloride influx when containing a α3 subunit usually expressed in immature brain. Here, we explored the efficacy of STP comparing its anticonvulsant effect in P21 relative to adult rats.

Method: P21 and adult rats received vehicle, 150, 250 or 350 mg/kg of STP i.p. 1 h before: (1) blood and brain samples; (2) a subcutaneous injection of pentylenetetrazol (PTZ; 100 mg/kg); and (3) lithium-pilocarpine status epilepticus model. STP levels were assessed in blood and in brain. Using video-EEG recording, we evaluated the delay and the severity of induced-seizures in these models.

Result: No differences in STP levels (blood and brain) were observed between P21 and adult rats. In the PTZ model, the occurrence of generalized seizures was suppressed in 5/13 P21 animals at 350 mg/kg compared to 0/9 in the vehicle group ($p = 0.05$). This effect was not observed in adult rats (0/9 in vehicle group vs. 2/12 at 350 mg/kg; $p = 0.31$). In the SE model, SE did not occur in 6/12 P21 animals at 350 mg/kg, but occurred in all animals (12/12) in the vehicle group ($p = 0.01$). This effect was not elicited in adult rats (0/12 in vehicle group vs. 4/12 at 350 mg/kg; $p = 0.1$).

Conclusion: Our data suggest that STP may be more effective in immature brain compared to mature brain, consistent with its affinity for the α3 subunit.

Abstracts

p378
INCIDENCE OF VALPROIC ACID–INDUCED HYPERAMMONEMIC ENCEPHALOPATHY

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Purpose: Valproic acid–induced hyperammonemic encephalopathy (VHE) is an uncommon complication in idiosyncratic drug reactions, probably underdiagnosed, it consists of the existence of mental confusion and bradypsychia, and there may be focal neurological deficits and vomiting, and decreased level of consciousness, which can range from drowsiness to stupor or coma, even increased seizures, so it may tend to increase doses of the drug.

Although nearly all reported cases have been with the oral form, has also been observed with the intravenous form. In some cases, valproic acid (VPA) levels are normal, even suboptimal, ruling out a dose-dependent effect.

Method: We reviewed patients with hyperammonemia from January 2007 to March 2011. One hundred twenty-seven patients were found, ruling out those patients with hyperammonemia secondary to other causes (hepatic impairment, cytostatic treatment.). We found 16 patients (6 M/10 F) with hyperammonemia on VPA treatment.

Result: Two patients were treated orally, rest intravenously and 12 of them with continuous infusion. The mean dose of drug was 1600 mg/day. VPA blood levels were within normal range, even suboptimal, except two patients had high levels of VPA (107.5 and 102.5). There was clinical improvement and normalization of ammonia levels after discontinuation VPA.

Conclusion: VHE found that a relatively common complication in patients who were treated with intravenous VPA, with increased incidence in patients treated with continuous infusion. Patients with altered mental status and treatment with valproic, VHE should be suspected, because the reversibility of the incident without sequelae.

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ADVERSE EVENTS OF ANTIEPILEPTIC DRUGS, ACROSS INDICATIONS: CAN RANDOMIZED CONTROLLED TRIAL DATA FROM NONEPILEPSY INDICATIONS BE INCLUDED IN META-ANALYSIS FOR AEDS USED IN EPILEPSY?

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Purpose: To determine if adverse event (AE) outcomes from randomized controlled trials (RCTs) of antiepileptic drugs (AEDs) across nonepilepsy indications (neuropathy or migraine) can be meta-analyzed with data from epilepsy trials.

Method: We searched databases for RCTs meeting inclusion criteria. AEDs included were topiramate, gabapentin, valproate, oxcarbazepine, lacosamide, lamotrigine, carisbamate, zonisamide and pregabalin. Extracted data was analyzed using meta-analysis software RevMan V5.0. Common AEs analyzed were; dizziness, ataxia, headache, fatigue, nausea, somnolence, withdrawals due to AE and any AE. Summary statistics of effect size were calculated using the Mantel-Haenszel method. Statistical heterogeneity was assessed using a random effects model. To test between indications we used a fixed effects model and calculated an I^2 statistic.

Result: We included 106 RCTs in epilepsy, neuropathy and migraine. Effect sizes varied with drug and outcome. When dizziness was analyzed, test between indications showed no statistical heterogeneity ($I^2 = 0\%$) for gabapentin, topiramate, lacosamide and lamotrigine. However, heterogeneity was significant ($I^2 = 59\%$) for trials of oxcarbazepine. Similarly when fatigue was the AE outcome, there was no statistical heterogeneity ($I^2 = 0\%$) when we analyzed data for gabapentin, lamotrigine, lacosamide, oxcarbazepine and topiramate. When somnolence was the AE outcome, heterogeneity was insignificant for oxcarbazepine ($I^2 = 8\%$), lacosamide ($I^2 = 0\%$) and topiramate ($I^2 = 0\%$), but significant for gabapentin ($I^2 = 56\%$) and lamotrigine ($I^2 = 60\%$). When nausea was analyzed there was no heterogeneity ($I^2 = 0\%$) for lacosamide, oxcarbazepine and topiramate, but significant heterogeneity existed for gabapentin ($I^2 = 41\%$) and lamotrigine ($I^2 = 40\%$). In instances where there was significant heterogeneity, the size of relative risk was greater in the nonepilepsy indications.

Conclusion: AEs of AEDs from nonepilepsy trials could be used in meta-analysis given the absence of statistical heterogeneity for some interventions and outcomes. Nevertheless this was not the case in all AEDs or outcomes. Effect sizes were larger in the nonepilepsy indications overall. Further meta-regression would unmask any dose effect on heterogeneity and effect size.

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NONEPILEPTIC SEIZURES INDUCED BY PHARMACOLOGICAL OVERTREATMENT IN PATIENTS WITH REFRACTORY EPILEPSY

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Purpose: It is known that antiepileptic drugs (AEDs) may induce adverse events such as paradoxical worsening of seizures or movement disorders or psychotic episodes.

Method: Two cases of nonepileptic seizures induced by AEDs are reported.

Result: Case 1. A female (SD) 34-year-old, affected by left mesial temporal lobe epilepsy with mesial temporal sclerosis has complex partial seizures (about 10 per month) refractory to multiple AEDs in mono- or polytherapy. She started topiramate (TPM) in add-on to carbamazepine and valproate. At a dose of 200 mg she began to signal the onset of seizures of longer duration, accompanied by eyelid myoclonus, and incongruous verbalization, symptoms not present before; with increase of TPM (300 mg) appear multiday episodes characterized by: duration of 2–4 min, drop of the head, preserved consciousness with correct verbal response but weak and slowed speech. A video-EEG recorded four episodes in 2 h, not associated with ictal discharge, or other variations of the interictal EEG. The symptoms ceased after discontinuation of TPM. Case 2. D.L., female 22-year-old, has partial epilepsy symptomatic of right hemispheric lesion consequence of perinatal anoxia. The ictal symptoms are dystonia of the upper left arm and short disturbance of consciousness (few seconds), refractory to numerous attempts with AED. The addition of TPM involves a change in the critical symptoms: after the usual dystonic onset, follow bizarre symptomatology that lasted for about 2 min associated with persistent dystonia, disorder of consciousness, automatism in the upper right arm, in the absence of critical EEG discharge. The first symptom is intermittent and repetitive vocalization imitating the clucking of the hen; then appear rhythmic movements of the trunk accompanied by singing a popular dance (macarena, macarena). There are not interictal psychopathological symptoms. The bizarre seizures ceased suspending the TPM.

Conclusion: Two female patients affected by refractory partial epilepsy experienced nonepileptic seizures of possible psychogenic origin, while receiving a standard dosage of topiramate in add-on.

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GENDER SPECIFIC ASSOCIATION OF DECREASED BONE MINERAL DENSITY (BMD) WITH EPILEPSY

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Purpose: Patients with epilepsy are at increased risk for low bone mineral density. This case-controlled study explored the relationship between bone mineral density (BMD) and long-term treatment with antiepileptic drugs (AEDs) in adults with epilepsy.

Method: The BMD at lumbar spine (L2–L4), total hip and femoral neck was measured in consecutive adult epileptic patients receiving long-term antiepileptics by dual energy x-ray absorptiometry (DXA). Patients were matched for age, sex and BMI with individual controls.

Result: A total of thirty-seven patients (mean age 38.5 ± 12.3 years, mean duration of therapy 13.5 ± 11.3 years) and seventy-one controls were studied. Male patients had significantly reduced bone density while there was no significant differences in females. Duration of treatment and type of AED were independent factors for reduction in BMD in males.

Conclusion: This study supports the hypothesis that long-term AED therapy is an independent risk factor for reduced BMD in epileptic patients. However gender, years of treatment and type of AED are additional and modified risk factors, with the newer antiepileptic agents causing the highest BMD reduction in males. As a conclusion male adults receiving a long-term antiepileptic treatment are at higher risk of osteoporosis and should be offered bone densitometry.

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POLYPHARMACY AND GENERALIZED DSYTONIA: A CASE REPORT

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Among the side effects attributed to valproic acid administration, the production of dystonia is very rare.

Dystonia is a syndrome of involuntary, repetitive (or sustained) muscle contractions of opposing muscles, which may result in torsions and abnormal postures.

We present a case under multiple pharmacologic treatment who developed dsytonia shortly after the adjunct of valproic acid and carbamazepine to lamotrigine. Generalized dsytonia occurred on the first week of this combination treatment.

These symptoms included sustained muscle contractions of opposing muscles of arm and leg which may result in torsions and abnormal postures.

Discontinuation of valproate resulted relief of dsytonic symptoms.

p383
METABOLIC SYNDROME AMONG OVERWEIGHT OR OBESE EPILEPTIC PATIENTS TREATED WITH VALPROATE: A CROSS-SECTIONAL STUDY

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Purpose: This study aims to evaluate metabolic syndrome (MetS) among overweight or obese epilepsy patients using valproate (VPA). In addition, we describe characteristics of MetS in our studied cohort.

Method: A cross-sectional study was carried out in our Outpatient Department of Neurology. Overweight or obese epilepsy patients with VPA monotherapy who met the inclusion criteria were included. Anthropometric parameters and blood samples were obtained after an overnight fasting, then an oral glucose tolerance test were performed for each participant.

Result: A total of 23 overweight and 11 obese epilepsy patients monotherapied with VPA were enrolled in this study. Among those patients, 14 (41.2%) cases satisfied the diagnostic criteria of MetS, broken down as 18.2% of the overweight and 52.2% of the obesity group. The presence of no more than one, two, three or more than three diagnostic components associated with MetS was 41.2%, 17.6%, 29.4% and 11.8% respectively. Over waist circumference (100%), elevated plasma TG (78.6%) and high blood pressure (85.7%) were the most common components in patients with MetS, disturbance of glucose metabolism was rarely relative speaking.

Conclusion: Overweight or obese patients treated with VPA might be at high risk for developing MetS or candidates of MetS, especially among obese patients. Abdominal obesity, hyperglyceridemia and hypertension consist the main characteritics of MetS among this population. Thus we should pay more attention to the early identification and intervention of MetS related with VPA using.

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BONE MINERAL DENSITY IN AN OUTPATIENT POPULATION RECEIVING ENZYME-INDUCING ANTIEPILEPTIC DRUGS

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Purpose: Antiepileptic drugs (AEDs), particularly CYP450 inducers, are associated with adverse bone effects. We tried to estimate a relationship between bone mineral density (BMD) and some biochemical markers in patients receiving enzyme-inducing AEDs (EIAEDs).

Method: In 99 adult outpatients (58 women) treated with EIAEDs for at least 3 years, lumbar spine and total hip BMD was assessed using dual-energy x-ray absorptiometry. Serum calcium, phosphate, magnesium, alkaline phosphatase (ALP), 25-hydroxycholecalciferol (25(OH)D), parathyroid hormone (PTH), dehydroepiandrosterone sulfate (DHEA-S), total and free testosterone, and sex hormone-binding globulin (SHBG) were measured. Spearman rank correlation was calculated.

Result: In women, spine BMD was only normal in seven patients (i.e. 12%), while osteopenia was found in 39 (67%), and osteoporosis in 12 patients (21%). Hip BMD was normal in five patients (9%), osteopenia was seen in 49 (84%), and osteoporosis in four patients (7%). In men, spine and hip BMD was only normal in 1 (2%) and 2 (5%), respectively, osteopenia was observed in 36 (88%) and 39 (95%), and osteoporosis in 4 (10%) and none, respectively. No association of BMD with 25(OH)D and PTH was found in either sex. In women, BMD in both sites was positively correlated with DHEA-S, and negatively with age, menopause duration, number of AEDs used, and ALP. In men, the only positive association was found between hip BMD and both total and free testosterone; there also was a negative correlation with ALP.

Conclusion: BMD in EIAEDs users is commonly abnormal, and associated with sexual hormones, rather than 25(OH)D and PTH.

Poster session: Pediatric epileptology VI
Tuesday, 30 August 2011

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BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES: COGNITIVE, EMOTIONAL AND BEHAVIORAL COMORBIDITIES, AND THE QUALITY OF LIFE

Abstracts

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Purpose: To assess the cognitive profile, emotional and behavioral comorbid disorders and the quality of life in children of benigh childhood epilepsy with centrotemporal spikes (BECTs).

Methods: Fifty-nine BECTs children aged 9.7 (SD = 1.9) years and 59 age- and gender-matched normal children were assessed by a battery of seven cognitive tasks on Reven's progressive matrices, selective reaction time, number comparison, 3-dimentional mental rotation, word rhyming. Fifty-nine children with BECTs underwent neuropsychological assessment with the Depression Self-rating Scale for Children, the Screen for Child Anxiety Related Emotional Disorders and the ADHD Rating Scale-IV, an 18-items parent-rated questionaire based on the diagnostic criteria for ADHD, the quality of life was measured by the Quality of Life in Epilepsy Inventory (QOLIE-31).

Result: (1) Compared to normal children, children with BECTs showed poorer performance on Reven's progressive matrices, selective reaction time, as well as number comparison, $p < 0.05$. However, no difference on the 3-dimentional mental rotation and word rhyming performences was found, $p > 0.05$. (2) Emotional and behavioral disorders were found in 22 out of 59 children with BECTs, at the rate of 37.3% and the frequency of depression disorder, anxiety disorder and ADHD was 13.6%, 22% and 10%, respectively. The suicidal ideation occurred in 3.4% cases, but no suicidal action was found. (3) The emotional and behavioral comorbidities were associated with low quality of life, which was significantly lower in epilepsy children comorbid psychiatric disorder. There was negative impact on the total score of quality of life and four subitems such as overall quality, emotional well-being, cognitive and social function, $p < 0.001$. There also were statistical differences between the two groups in the other three subitems including seizure worry, energy/fatigue and medication effects, $p < 0.05$.

Conclusion: BECTs is associated with cognitive impairments and psychiatric disorders, the frequencies of depression, anxiety disorder and ADHD is considerably high in children with BECTs. Emotional and behavioral comorbidity is one of the negative factors to the quality of life in BECTs patients. To treat BECTs to achieve seizure freedom, the neuropsychological estimate should be done.

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COGNITIVE EFFECTS OF INTERICTAL EPILEPTIFORM DISCHARGES IN CHILDREN

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Purpose: Frequent interictal epileptiform discharges (IEDs) may have momentary and chronic effects on brain function. Children with developing neuronal networks could be at risk for poor cognitive development when IEDs are abundant. We tried to find a relationship between the amount of IEDs and cognitive impairment in children.

Methods: We analyzed a group of 184 children aged 6–12 years old with different epilepsy syndromes with a 24-h ambulatory EEG and cognitive tests both applied within two weeks. IED index in wake and sleep were categorized and correlated to cognitive test results and epilepsy characteristics.

Result: The group of 19 patients with diurnal IEDs in at least 10% of the time showed impaired central information processing speed, verbal memory and visual-motor integration when compared to patients with less IEDs. This effect was seen independently from other EEG- and epilepsy-related characteristics and independently from the epilepsy syndromal diagnosis. The impact of the nocturnal IEDs was of less importance, it only contributed partially to the slowing of central information processing speed in a further regression analysis.

Conclusion: We conclude that children with frequent IEDs in the wake EEG (in more than 10% of the time, which is ≥1 spike [-wave] per 10- second EEG page) could be at risk for poor cognitive development. Whether or not children with high diurnal spike frequency and low seizure frequency can benefit from antiepileptic treatment should be examined in controlled trials.

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VARIOUS SUPPRESSION-BURST EEG PATTERNS SEEN IN EPILEPTIC ENCEPHALOPATHIES AND OTHER CONDITIONS

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Purpose: The most characteristic EEG feature peculiar to the syndrome is suppression-burst pattern (SBP). SBP is seen in various conditions in the pediatric field, such as Ohtahara syndrome (OS), early myoclonic encephalopathy (EME), SSPE, serious brain damage in neonates or during barbiturate coma therapy. Although this EEG pattern seen in OS or EME has been described in some literatures, there is no precise agreed definition. We will highlight our recent experience of epileptic encephalopathies (EEs) and also propose a precise definition for SBP which has not correctly been identified in the literatures.

Method: Some epileptic syndromes starting in the neonatal period such as EME, OS, or migrating partial seizures in infancy are categorized as EEs. There are several different EEG SBPs in different conditions and we showed several representative types of EEG SBPs in EEs and in neonates with serious brain damage or other conditions. We also clarified the SBP in EEG seen in definite OS.

Result: We propose the characteristics of SBP in OS as follows. The bursts must consist with high amplitude nonsynchronized paroxysms like hypsarrhythmia and continue for 2–6 s. The suppression phase must show <10 μV or flat tracing and continue for 3–5 s. Suppression and burst phases must appear alternately and regularly every more than 5 s. SBP in OS should be seen in both during sleep and awake states and should not change according to the sleep-wake cycle and the burst phase is longer with shorter periods of suppression phase than EME. This pattern in OS usually disappears within the first two or three months.

Conclusion: OS is a very rare syndrome and cases reported as OS in the literature may include doubtful cases. SBP seen in EEGs does not always indicate OS. EEs with SBP in neonatal period are known to evolve into relatively few types of epileptic syndromes.

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PARENTAL REACTIONS AND NEEDS IN BENIGN CHILHOOD FOCAL SEIZURES

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Purpose: To detail evidence that despite the fact that benign childhood focal seizures (BCFS) are of excellent prognosis parents of BCFS have significant and unmet needs.

Method: My personal interest started 10 years ago (2000) when speaking extensively with parents of children with BCFS I realized that they were concerned for many more issues than the seizures themselves and other than those that they were discussing with their physician. They had dramatic experiences and many unanswered questions and anxieties. Consequently I have initiated an ongoing study with a purposefully

designed questionnaire aiming to define and analyze the psychosocial effects of BCFS on parents and children, their attitude about epilepsy, their reactions, concerns about the prognosis, necessity of evaluation and needs. This was distributed to 22 parents.

Result: Most of the parents expressed that they felt panic, fear, anxiety, shoc, terror and had thoughts about death. Their sleep and the quality of their work was affected. Few were in denial and few felt secure under the doctor's care. Half of the parent's behavior towards the child has changed. Most of the parents expressed the need for education on epilepsies, psychological support for the child, and themselves. They also expressed the need to participate in groups of parents with the same problem.

Conclusion: There is a need for family management, education, psychological support and specific instructions about emergency procedures. That should be properly addressed from the time of first diagnosis and thus eliminate anxiety and improve the quality of life of the child and family.

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IMPAIRED LANGUAGE PERFORMANCE AS A PRECURSOR OR CONSEQUENCE OF ROLANDIC EPILEPSY?

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Purpose: A correlation between language impairment and rolandic epilepsy is frequently reported. It is unknown whether this language impairment develops gradually as a consequence of rolandic epilepsy or precedes the onset of seizures. In the latter case both language impairment and rolandic epilepsy may be symptoms of an underlying syndrome or both develop during the process of epileptogenesis.

Method: Noncomparative clinical cohort study of 48 children with Rolandic epilepsy (children's mean age is 9 years, and 7 months; SD is 1 year, and 8 months). They were screened for previous and current language impairment and their reading skills were examined.

Result: Twenty-three percent of children with rolandic epilepsy had speech therapy in the past and 35% repeated a year on primary school, which is more often compared to the Dutch population of children. Their results on a reading task revealed lower scores.

Conclusion: Language is impaired in children with rolandic epilepsy. In some children this impairment of language may even be a precursor, for the rolandic epilepsy. It is undecided however, whether the language impairment develops gradually after the onset of epilepsy, whether rolandic epilepsy and language impairment are both symptoms of an underlying syndrome or both develop during the process of epileptogenesis as we observed in some children the onset of language impairment before the onset of epilepsy.

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NEUROPSYCHOLOGICAL OUTCOME FOLLOWING BENIGN MYOCLONIC EPILEPSY OF INFANCY

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Purpose: Since its description in 1981, only 127 cases of benign myoclonic epilepsy of infancy (BMEI) had been reported by 2005. Although termed ''benign,'' the risk of adverse neuropsychological outcome may be higher following BMEI despite adequate seizure control.

Method: We retrospectively reviewed our patients with BMEI, who were neurodevelopmentally normal at the time of diagnosis. All eight patients had the diagnosis confirmed with generalized spike-waves or polyspike-waves, together with epileptic myoclonic jerks that were recorded on video-EEG and surface muscle electrodes, in the presence of normal background for age.

Result: The onset of seizures was between 8 months and 3 years. One patient had prior history of febrile seizure. Two had family history of epilepsy. Seizure control was achieved with monotherapy using valproic acid in six patients. Two others required the addition of levetiracetam to achieve seizure remission. Out of four children who are still on medication, one child has speech and fine motor delay, and one has hyperactivity with poor social skills. In four children who were successfully weaned off all medications for at least 6 months duration, one child has attention deficit, one has dyslexia, and one has central auditory processing deficit.

Conclusion: Although BMEI is generally associated with good prognosis, the neuropsychological and behavioral outcome may be less favorable, as is suggested by our case series. This may occur despite early treatment and good seizure control, indicating that other factors play important roles affecting the neuropsychological outcome.

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EPILEPSY AND ADHD IN CHILDREN: PSYCHOSOCIAL ASPECTS AND BEHAVIOR PROBLEMS

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Purpose: Attention deficit and hyperactivity disorder (ADHD) occurs in 13–31% of all children with epilepsy. The incidence of the ADHD in patients with epilepsy, and the correlation with psychosocial aspects and behavior problems are not completely clear. The aim of this study was to verify psychosocial aspects and behavior problems in a group of patients with epilepsy and ADHD.

Method: This was a transversal study. Eighty-five patients (ages ranging from 6 to 16 years old) were interviewed with a structured questionnaire. Sixty patients were diagnosed with epilepsy with presumably genetic etiology without epileptic encephalopathy (group I) and 25 patients were diagnosed with epilepsy with structural/metabolic etiology (group II). All patients of group I had normal MRI. We used the MTA-SNAP IV Teacher and Parent Rating Scale, Vineland Adaptive Behavior Scales and the Conner's Rating Scales – Revised. No patients had IQ scores under 79.

Result: ADHD occurred in 8/60 patients of group I (13%) and in 12/25 patients of group II (48%). ADHD was significantly more frequent in patients of group II than patients of group I ($p = 0.02$). Patients with ADHD in group II had significantly more seizures ($p = 0.01$), not well controlled ($p = 0.025$), and lower scores ($p = 0.036$) in Vineland Scales (communication domain) than patients in group I.

Conclusion: The incidence of ADHD is higher in patients with determined etiology when compared with patients with genetic etiology. Our data showed that psychosocial aspects and behavior problems follow the same rule.

Keywords: Epilepsy, childhood, ADHD, behavior

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THE SLEEP AND BEHAVIORAL PROBLEMS IN TREATED AND UNTREATED CHILDREN WITH BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES

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Purpose: To evaluate the types of sleep problems and their relationships with behavioral problems in children with benign childhood epilepsy with centrotemporal spikes (BECTS). The difference between treated and untreated patients was also measured.

Method: Eighteen newly diagnosed not medicated and 18 treated patients with BECTS and 14 controls aged 6–2 years, equally distributed for age and gender attending regular schools were investigated. Evaluation was made using the Lithuanian version of Child Behavior Checklist (CBCL) and The Sleep Disturbance Scale for Children (SDSC). We also investigated the schooling, clinical and EEG parameters. Vilnius Regional Biomedical Research Ethics Committee approved this study.

Result: Untreated children with BECTS had significantly higher subscale scores in disorders of initiating and maintaining sleep (66.72 ± 15.85 vs. 56.62 ± 7.05, p = 0.022), sleep- wake transition disorders (68.50 ± 17.56 vs. 55.07 ± 11.70, p = 0.013), disorders of excessive somnolence (62.89 ± 15.85 vs. 52.23 ± 9.67, p = 0.028) and sleep-disordered breathing (56.17 ± 13.1 vs. 47.62 ± 5.83, p = 0.022), compared with controls. Treated children with BECTS had higher scores only in sleep-disordered breathing subscale (60.39 ± 14.76 vs. 47.61 ± 5.84, p = 0.003), compared with controls. Treated and untreated patients did not differ significantly in duration of epilepsy and seizure ratio, schooling, EEG parameters. Higher disorders of excessive somnolence subscale scores were associated with higher difficulties of concentrating attention scores in CBCL (p = 0.003).

Conclusion: These results suggest that in untreated patients with BECTS sleep problems are at least partially due to epilepsy impact on sleep.

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READING PERFORMANCE IN CHILDREN WITH ROLANDIC EPILEPSY CORRELATES WITH NOCTURNAL EPILEPTIFORM ACTIVITY, BUT NOT WITH EPILEPTIFORM ACTIVITY DURING WAKE

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Purpose: An association between language impairment and rolandic epilepsy is frequently reported. This could be correlated with the amount of nocturnal epileptiform activity.

Method: We retrospectively analyzed 26 children with rolandic epilepsy and/or rolandic spikes (mean age 112 months, SD 18.8). All children had had a 24-h electroencephalogram and a neuropsychological assessment within 2 weeks. Reading performances were measured by the skills of reading words and sentences. Intelligence was measured by WISC-III or WISC-RN.

Result: In children with rolandic epilepsy, there was a significant negative correlation between the amount of nocturnal epileptiform activity and the performance of reading sentences of −0.525 (p = 0.008). There was a trend in this correlation between the percentage of nocturnal epileptiform activity and the performance for reading words of −0.398 (p = 0.054). No significant correlation was found between the reading performances and the amount of epileptiform activity during wake. Furthermore we found a negative correlation between the amount of nocturnal epileptiform activity and verbal IQ (R = -0.51 p = 0.08).

Conclusion: Reading performance is impaired in children with rolandic epilepsy. The higher the amount of nocturnal epileptiform activity, the more the reading skills are impaired. Reading sentences (semantic language skills) is more impaired than reading words (morphological language skills).

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LANGUAGE AND AUTISTIC REGRESSION ASSOCIATED WITH EEG EPILEPTIFORM ABNORMALITIES: IMPROVEMENT AFTER PHARMACOLOGICAL TREATMENT

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Purpose: It is still debated whether EEG abnormalities per se can trigger language and autistic regression.

Aim of this study is to describe clinical course and response to pharmacological treatment of a 2-year-old child after the first language regression episode associated with persistent epileptiform EEG abnormalities.

Method: MF, male, presented at 25 months a dramatic regression of language, auditory inattention and autistic-like features. Sleep EEG showed persistent focal epileptiform activity over the left centro-parietal and vertex areas never associated with clinical seizures. He was started on ACTH (40 u/day, for 3 months). At 36 months, a second language and autistic regression fitting diagnosis of Pervasive Developmental Disorder Not Otherwise Specified, prompted a second course of ACTH.Data on the regressions was obtained through parental interviews, reviews of family videos, standardized questionnaires on language development, autism rating scales, formal language and cognitive testing extended into adolescence.

Result: A striking improvement in language and, to a lesser degree, of autistic behavior was documented coinciding with ACTH therapy and suppression of EEG discharges at both regressions. Later course revealed milder fluctuations/regressions in behavior and communicative abilities, in phase with recrudescence of EEG abnormalities prompting additional ACTH courses.

Conclusion: Early referral, detailed standardized assessment, coupled with EEG and therapeutic trials, allowed for a timely documentation of regression episodes suggesting an ''atypical'' autistic phenotype characterized by early isolated language regression antedating autistic regression, striking therapy-induced improvement especially in language skills, fluctuation of symptomatology over time, which could be subsumed by persistent EEG abnormalities.

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DIFFUSION-WEIGHTED IMAGING MEASURES DO NOT DISTINGUISH EPILEPTOGENIC TUBERS IN CHILDREN WITH TUBEROUS SCLEROSIS AND EPILEPTIC SPASMS

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Purpose: To investigate the previously reported ability of fractional anisotropy (FA) and apparent diffusion coefficient (ADC) indices to distinguish epileptogenic tubers, using more accurate tuber delineation and seizure localization techniques.

Method: Seven children (four boys, median age 2.1 years) with tuberous sclerosis (TS), intractable epilepsy with spasms and developmental delay underwent preoperative 3-Tesla MRI and DTI (b value = 3000 s/mm^2, 60 directions), prior to intracranial-EEG localization of seizures. FA and ADC were calculated from regions of interest drawn around tubers on T_2-weighted images coregistered to FA maps. Subdural implantations (unilateral in two, bilateral in five) utilized grids, strips and/or depth electrodes (median 60 contacts per patient). Tubers covered in each child ranged from 4 to 1 (median 7, total 53), in the frontal (16), temporal (22), parietal (14) and occipital (1) regions. Epileptogenic tubers were those showing discrete ictal onset patterns confined to tubers (i.e. not seizure spread patterns or interictal abnormalities only).

Result: Median FA for epileptogenic (23/53) and nonepileptogenic (30/53) tubers were 0.12 (0.08–0.19) and 0.13 (0.08–0.20) respectively (p = 0.664). Median ADC for epileptogenic and nonepileptogenic tubers were 0.00111 mm^2/s (0.00084–0.00125 mm^2/s) and 0.00112 mm^2/s (0.00092–0.00135 mm^2/s) respectively (p = 0.904). In only one child, the tuber with the lowest FA and highest ADC was one of the epileptogenic tubers.

Conclusion: In young children with TS and intractable epilepsy with spasms, measures of anisotropy and diffusivity of tubers are poor markers of epileptogenicity.

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KCNQ2 AND KCNQ3 MUTATIONS AND DELETIONS IN BENIGN FAMILIAL NEONATAL SEIZURES

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Purpose: Benign familial neonatal seizures (BFNS) is an autosomal dominant idiopathic epilepsy of the newborn associated with mutations in KCNQ2 or KCNQ3 genes. Recently, deletions have been added to molecular mechanisms of BFNS patients.

Method: We studied 40 BFNS patients by sequencing for mutations KCNQ2 and KCNQ3. Patients who tested negative were tested for deletions by MLPA (multiplex ligation-dependent probe amplification).

Result: All newborns presented with seizures in the first 9 days of life and were followed for a mean of 8.5 years. All had a normal psychomotor development. Mutations involving KCNQ2 were found in five patients (12%). Two had focal status epilepticus (SE), two had generalized seizures and one had focal and generalized seizures. Four out of five were acutely treated with AEDs. Three patients relapsed in the first 3 months of age. One had febrile seizures (FS) at 14 months. None of them developed epilepsy later in life. Deletions were detected in seven patients (18%), all but one involving KCNQ2. Four patients had focal seizures, two had generalized seizures and SE, and one had focal and generalized seizures. Three of them were treated acutely with monotherapy, the others requiring more than one AED. One patient relapsed at 6 months, and one had FS at 8 months. The child with KCNQ3 deletion developed rolandic epilepsy at three years. 28/40 (70%) of BFNS patients tested negative for both mutations and deletions.

Conclusion: MLPA should be performed in BFNS when sequencing is negative, as deletions may be as frequent as mutations. In children testing negative for both, mutations in the promoter or introns of KCNQ2/3, or additional genetic factors could be involved.

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RETROSPECTIVE RECORDS REVIEW OF EUROPEAN PEDIATRIC PATIENTS RECEIVING VAGUS NERVE STIMULATION (VNS) THERAPY FOR 12 MONTHS OR MORE

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Purpose: Pediatric patients with drug-resistant epilepsy have had access to adjunctive VNS Therapy since its European approval in 1994. However, there is limited information regarding the long-term outcome of VNS Therapy for specific types of seizures among pediatric patients.

Methods: Patients with refractory epilepsy under 18 years of age were enrolled from 11 European centers. Medical records were reviewed with a minimum of 3 months of data before implantation and a minimum of 1 year of follow-up data. Data included changes in seizure frequency, type, severity, adverse events, antiepileptic treatments, VNS parameter settings, and magnet use. Data were collected at baseline, and 6, 12, and 24 months after implantation and at the most recent follow-up visit.

Result: Of the 181 patients enrolled as of March 1, 2011, most are male (101M/75F). Mean age at epilepsy onset was 2.5 ± 2.8 years. Mean age at first VNS implant was 10.8 ± 4.5 years. The predominant seizure type was partial without secondary generalization (31.5%; n = 57), followed by tonic–clonic (21.0%; n = 38), and partial with secondary generalization (15.5%; n = 28). The response rate after 1 year was 39.7% (n = 71), with seizure freedom reported in 6.1% of patients (n = 11). The 2-year response rate was 45.5% (n = 46), with seizure freedom reported in 6.9% of the patients (n = 7).

Conclusion: Results per seizure type and epilepsy syndrome (focal epilepsies, epilepsies with myoclonic-astatic seizures, Lennox-Gastaut syndrome, drug-resistant absence epilepsies) and adverse events will be presented.

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EEG CHARACTERISTICS PREDICT SUBSEQUENT EPILEPSY IN CHILDREN WITH FEBRILE SEIZURE

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Purpose: The role of EEG in the workup of febrile seizure (FS) remains controversial. The meaning of the relationship between seizure number, the risk factors for subsequent epilepsy, and EEG characteristics remains unclear. We investigated the importance of EEG characteristics, especially the localizations of paroxysmal discharges, as a predictor for subsequent epilepsy.

Method: The study included 26 children with FS presenting with paroxysmal abnormalities. Patients were referred from the outpatient department for EEG within 7–20 days after the seizure. The EEGs were classified as paroxysmally abnormal as characterized by spikes, sharp waves, or spike-wave complexes whether focal or generalized, considered abnormal for age and state.

Result: Of 26 patients with paroxysmal abnormality, six (23.1%) developed to epilepsy. Of ten patients with generalized paroxysmal spike and wave activity, one (10%) developed to epilepsy. Of seven patients with rolandic discharge (RD), two (28.5%) developed to epilepsy. Of four patients with paroxysmus at frontal region, three (75%) developed to epilepsy. Of five patients with paroxysmus at occipital region, none developed to epilepsy.

Conclusion: These findings suggest that FS presenting with frontal paroxysmal EEG abnormalities may be a clear risk factor for epilepsy. In the patients with frontal paroxysmal EEG abnormalities, serial EEG should be performed even though it does not contribute to treatment.

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HIGH-FREQUENCY OSCILLATIONS IN BENIGN PARTIAL EPILEPSY OF CHILDHOOD

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Purpose: We explored high-frequency oscillations (HFOs) in scalp sleep EEGs of benign partial epilepsy (BPE) of childhood in order to obtain a better understanding of the pathological mechanisms underlying BPE.

Methods: The subjects were 45 patients, including 32 with benign childhood epilepsy with centrotemporal spikes (BCECTS) and 13 with Panayiotopoulos syndrome (PS). A total of 136 EEG records were investigated through temporal expansion and filtering of traces and time-frequency spectral analysis.

Result: HFOs with frequency of 93.8–152.3 Hz (mean 126.2 ± 13.6 Hz) in the band of ripples were detected in association with benign spikes in 97 records (71.3%).

Time from last seizure to the EEG recording was significantly shorter in the EEGs with spike-related HFOs than in the EEGs with spikes without HFOs ($p = 0.006$). Although time from last seizure reflects age, age at the time of recording was not significantly different between EEGs with and without HFOs. Peak-power values of the high-frequency spots in time-frequency spectra were significantly negatively correlated with time from last seizure ($R^2 = 0.122$, $p < 0.001$) but not with age at the time of recording. Peak frequencies of the high-frequency spectral spots were not significantly correlated with age at the time of recording or with time from last seizure.

Conclusion: The close relationship between the generation of spike-related HFOs and the period of active seizure occurrence indicated that HFOs may tell us more about epileptogenicity in BPE than the spikes themselves. Spike-related HFOs may be prognostic indicators.

p400
CORRELATION BETWEEN PATTERNS OF FOCAL EPILEPTIFORM DISCHARGES AND BRAIN LESION IN CHILDREN WITH FOCAL EPILEPSY

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Purpose: To evaluate of a correlation between patterns of focal epileptiform discharges (ED) and brain lesion diagnosed by MRI in the children with focal epilepsy.

Method: We retrospectively reviewed the routine scalp EEGs, medical records and the result of brain MRI findings of 149 children who were diagnosed as epilepsy with only focal epileptiform discharges in our hospital between 2008 and 2010. We classified the patterns of focal ED into spikes, sharp waves or polyspikes. The EEG finding with homogenous pattern of ED was termed as single-form ED and heterogenous pattern of ED was named as multiform ED. We evaluated the relationship between the specific patterns of focal ED and brain lesions in pediatric epilepsy.

Result: We identified 149 patients with only focal ED and all of them underwent brain MRI scan. Fifty-six of 149 (37.6%) patients had brain lesion in brain MRI. Number of patients with single-form ED were 101 (67.8%, 101/149) and number of patients with multiform ED were 48 (32.2%, 48/149). Thirty of 48 patients (62.5%) with multiform ED showed brain lesion, which was higher incidence than those of patients with single-form ED (25.7%, 26/101) ($p < 0.001$). Number of patients with polyspikes were 41 (27.5% 41/149). Twenty-five of 41 patients (61.0%) with polyspikes had brain lesion, which was higher frequency than those of patients without polyspikes (28.7%, 31/108) ($p < 0.001$). And 19 of 82 patients (23.2%) with single-form ED of only spikes had brain lesion on brain MRI, which was significantly lower than those of remaining patients (55.2%, 37/67) ($p < 0.001$).

Conclusion: We suggest that heterogenous pattern of ED or polyspikes have higher incidence of brain lesion in children with focal epilepsy.

p401
REFRACTORY AND SEVERE STATUS EPILEPTICUS IN A PATIENT WITH RING CHROMOSOME 20 SYNDROME

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Purpose: Ring chromosome 20 syndrome is characterized by mild to moderate mental impairment, behavioral problems, and refractory epilepsy, without significant dysmorphism. We report an adolescent girl with this syndrome who experienced refractory and severe status epilepticus.

Method: We retrospectively reviewed the clinical chart, EEGs findings, and all available neuroimagings. Subject: The patient was a 14-year-old girl with ring chromosome 20 syndrome.

Result: She was born uneventfully to healthy, unrelated Japanese parents. She achieved normal developmental milestones until 7 years of age, except for having a simple febrile seizure at 2 years and 4 months of age. From 7 years of age, she experienced nocturnal complex partial and generalized tonic–clonic seizures refractory to antiepileptic drug treatment, which gradually increased in frequency from a weekly to daily basis. The EEG showed runs of high-amplitude diffuse rhythmic slow wave or spike-and-wave activity at 2–3 Hz with a clear bifrontal predominance. At 11 years of age, she received a diagnosis of ring 20 syndrome based on a chromosomal study. At 13 years of age, short-lasting generalized tonic seizures appeared frequently during sleep, and finally evolved into unremitting tonic status epilepticus requiring pentobarbital anesthesia for nearly 1 year. She was left with severe neurological sequelae, requiring artificial respiratory assistance and heavy antiepileptic medication.

Conclusion: Patients with ring chromosome 20 syndrome may experience severe and lethal status convulsivus refractory to all available treatment. An early diagnosis of this syndrome is important to predict the risk of such a catastrophic complication.

p402
EPILEPSY ONSET RELATED WITH INFECTION IN A GIRL WITH RING CHROMOSOME 20

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Purpose: Although epilepsy in patients with chromosome 20 is intractable, pathophysiology of the epilepsy is not unveiled.

Method and Result: The patient had shown mild intellectual disability until the onset of epilepsy at 7 years old. Several days after the common cold, she became to show ascending sensation accompanied with holding her mouth with her hand. Subsequently, in her seizures, consciousness became to be impaired, and rigid contraction of whole body became to join, and seizures increased to the levels of a few times a day, in spite of several AEDs. Seizures frequencies increased with febrile infection. Ictal EEG showed high-amplitude slow-waves dominantly in the bilateral frontal region, followed by diffuse spike and slow-waves. After the onset of epilepsy, FSIQ decreased from 83 to 60, and behavior became impulsive. MRI was normal and chromosomal examination revealed ring chromosome 20. Antibodies to GluR epsilon2 (NR2B) were found in sera and CSF, and granzyme B and IL-17 were increased in CSF.

Conclusion: Possible relationship between the onset of epilepsy and immunological mechanisms was suggested in a patient with Ring chromosome 20 syndrome, which is genetically determined epilepsy.

p403
CLINICAL AND EEG STUDY OF ABSENCE SEIZURES IN DRAVET SYNDROME

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Purpose: We studied clinical and EEG manifestations of absence seizures (AS) in children with Dravet syndrome to clarify their characteristic features and differences from those of typical AS.

Method: We retrospectively analyzed the focality of initial discharge, duration, frequency, regularity and organization, and postictal changes of ictal EEG. The clinical AS manifestation was assessed by video/EEG.

Subjects: Eleven children with Dravet syndrome were enrolled in this study. The ictal EEG and video/EEG were recorded in 11 and 6/11 patients, respectively.

Result: The age at onset of AS and at the study ranged from 10 to 33 months (mean = 16), and 17 and 80 months (mean = 40), respectively. AS in three children were provoked by photic and pattern stimulations. The number of ictal EEG and video/EEG available for analysis ranged from 3 to 21 (n = 90; mean = 8), and from 5 to 19 (n = 67; mean = 11), respectively. Ictal EEG showed the focality of initial discharge in 46/90 (51%), AS duration ranging from 1 to 180 s (median: 4 s), AS frequency ranging from 2 to 4 Hz (mean = 3.0 Hz), and the irregularity and disorganization of morphology in 63/90 (70%). Postictal EEG were irregular in 66/90 (73%) seizures. In the video/EEG, AS manifested with eyelid-myoclonus and generalized myoclonus in 6/50 (50 available for facial analysis: 12%) and 31/67 (46%), respectively.

Conclusion: AS in Dravet syndrome were characterized by an early onset, relatively shorter duration, mild irregular and disorganized EEG morphology and an approximately 3 Hz EEG pattern as well as an association with frequent generalized myoclonic movement.

p404
MUTATION IN *CDKL5* GENE (CYCLIN-DEPENDANT KINASE-LIKE 5): RETROSPECTIVE ANALYSIS OF ELECTROCLINICAL (VIDEO EEG) AND DEVELOPMENTAL PHENOTYPE IN EIGHT PATIENTS

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Mutations in the *CDKL5* gene (cyclin-dependant kinase-like 5) have been identified in female patients with early onset epileptic encephalopathy with normal initial interictal electroencephalographic records.

Purpose: To characterize the electroclinical and developmental phenotype associated with *CDKL5* mutations in eight patients.

Method: We retrospectively analyzed the electroclinical phenotype of eight patients aged from 4 to 10 years diagnosed with pathogenic *CDKL5* mutations.

Result: The onset of the epilepsy was from 10 days to 12 weeks. The first seizures were clonic (1/8), tonic or "infantil spasm" (6/8), or myoclonic jerk (1/8) and the interictal electroencephalogram was normal.

Two types of evolution are possible.

1. Three patients have tonic frontal seizures without diffuse abnormalities on the electroencephalogram. These patients were seizure-free between 2 and 3 years. The development delay was medium with voluntary prehension at 8 months, walk at 2 years and poor language. During the second year, manual stereotypy appeared.
2. Five patients have several types of seizures (tonic seizure or infantile spasm, myoclonia, absence) with early diffuse abnormalities on the electroencephalogram. They developed refractory epilepsy associated with severe developmental delay and microcephaly.

All patients had normal cerebral magnetic resonance imagery.

Conclusion: Our data suggest two different electroclinical and developmental phenotype.

p405
GEORGIAN CHILDREN WITH EPILEPSY HAVING SLEEP PROBLEMS: A PILOT STUDY

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Purpose: To identify sleep problems among children having epilepsy, that has not been investigated before in Georgia.

Method: A structured sleep-waking questionnaire was developed and designed on the basis of Child Sleep Questionnaire for Parents and the Pediatric Sleep Questionnaire. The complete information concerning sleep-wake habits and sleep complaints was obtained for 153 children (between the ages 1 and 6 years) having epilepsy: 31 were with age according development (AAD), 122 with developmental delay; 68 untreated, 85 treated with AEDs, 95 with ongoing seizures, 58 with clinical remission. Sleep problems were evaluated according to falling asleep difficulty (FSD), nightwakings, snoring and nocturnal breathing difficulties (NBD). These findings were compared to data obtained from 587 children with AAD, aged 1–6 years, and not having epilepsy (AADNE).

Result: In overall sleep problems were more prevalent in children with epilepsy in comparison to the AADNE children (50.4% vs. 29.3%), particularly NBD (23.5% vs. 5.3%). Distribution of FSD (19.6%) and nightwakings (16.3%) were often found among the children with epilepsy. The frequency of sleep problems was higher in AAD children having epilepsy (40.1%) than in AADNE group (29.3%), and NBD (18.75% vs. 5.3%), in particular. Children with clinical remission had less sleep problems (42.8%) than children with ongoing epileptic seizures (56.2%).

Conclusion: The findings of the present study signify high prevalence of sleep related difficulties in Georgian children with epilepsy. More medical attention is needed to assess problems in sleeping of children in correlation with correct treatment strategy of epilepsy.

Poster session: Pediatric epileptology VIII Tuesday, 30 August 2011

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AMPLITUDE INTEGRATED EEG AEEG IN COMATOSE CHILDREN WITH ACUTE CNS INFECTIONS: A PROSPECTIVE EXPLORATORY STUDY IN A PEDIATRIC INTENSIVE CARE UNIT (PICU)

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Purpose: To examine aEEG patterns in children with acute CNS infections and correlate these with raised intracranial pressure (ICP), cerebral perfusion pressure (CPP) and final outcome.

Method: Consecutive children, admitted with acute CNS infections and a Glasgow Coma Scale Score ≤11 were enrolled after written parental consent and approval by the Institute ethics committee. Children with shock, hypoxemia, and preexisting CNS disease, were excluded. aEEG was recorded for 10 days or till discharge from PICU using cerebral function monitor (CeegraphVision Biologic-Systems). ICP (Codman intraparenchymal microtransducer) and intraarterial blood pressure were monitored. aEEG patterns were assessed using criteria by Toet et al and correlated with survival and neurological outcome at discharge, and at 1, 3 and 6 months postdischarge.

Result: Forty-two children, median age 54 months, range 18–96 months, were enrolled. Patients with normal voltage background patterns (n-22) had 90.9% survival as compared to 14.9% in the rest ($p < 0.001$). All 17 patients having aEEG patterns four and five died, while 91.9%, 88.3% and 14.9% with patterns 1, 2 and 3 respectively, survived ($p < 0.001$). Presence of seizures, status epilepticus or asymmetry was not associated with poor outcome. aEEG patterns corelated significantly with ICP ($r = 0.820$) and CPP ($r = 0.863$). The Pediatric Cerebral performance cateogory scale scores for survivors with pattern 1 at discharge and at 1, 3 and 6 months postdischarge were significantly better as compared to patients with patterns 2 and 3 ($p < 0.001$).

Conclusion: aEEG is useful to predict neurological outcome in comatose children with acute CNS infections; aEEG patterns correlate well with ICP and CPP.

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LEVETIRACETAM ADD-ON THERAPY IN CHILDREN WITH REFRACTORY EPILEPSY

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Purpose: To evaluate the efficacy and tolerability of levetiracetam (LEV), as add-on therapy in children with drug-resistant epilepsy.

Method: Children with intractable seizures despite appropriate medication were placed on LEV as add-on therapy at our institute in the past 4 years (January 2006–December 2009). A retrospective analysis of medical information of these patients including age, six, seizure type, EEG findings, dose of LEV and its efficacy and adverse effect were conducted.

Result: A total of 30 patients, aged 1–18 years, were enrolled. Males were 18 and females 12. The seizures in semiology were partial with or without secondary generalization in 19 (63.3%), generalized in 8 (26.7%) and mixed in 3 (10%). The mean close of LEV was 30.8 (range 10–18) mg/kg/day. The mean period of follow-up was 30 months. Over 50% seizure reduction was observed in 12 patients (40%) including three seizures free. Four patients dropped out, due to no effectiveness at acute stage in three and seizure increase in one. Adverse effects were noted as somnolence in four, poor appetite in one and behavior change in another one.

Conclusion: LEV showed its effectiveness as add-on therapy for children with intractable epilepsy, either partial or generalized. It was well tolerated with minimal adverse effects.

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REFRACTORY STATUS EPILEPTICUS: EXPERIENCE AT A TERTIARY CARE HOSPITAL

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Purpose: Describe and analyze the etiology, pharmacological response and the evolution of refractory status epilepticus (RES) in children at a multidisciplinary tertiary care teaching and referral hospital.

Method: We reviewed 23 medical histories of children admitted at the Pediatric Intensive Care Unit with refractory status epilepticus between July 2006 and March 2011.

Result: The prevalence of RES in the study population was 0.1%. The median of age was 36 months, range 3 month and 17 years, 11 female and 12 boys. The median of permanence in Pediatric Intensive Care Unit was 10 days and the median duration of RES was 15 h. The most common etiology of RES was acute symptomatic. In this group, the most common causes were acute uncertain encephalitis (33%). Viral encephalitis and febrile induced refractory epilepticus status were the second etiology (16% each one. Only 16 patients required more than three anti epileptic drugs to control the RES, 11 of them required pharmacological coma and six ketogenic diet. Six patients with acute symptomatic etiology developed sequelaes 6/12 (50%). Seventeen patients (73.9%) had no new sequelae with a follow up of 6–12 months. One patient died (4.3%)

Conclusion: As reported in other big series, the most common etiology was acute uncertain encephalitis in previously healthy children. The acute sintomanic etiology group developed more neurologic sequelae 73.9% of the patients had no changes in their neurological status. Mortality was 4.3%, lower than reported in other series.

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REVERSIBLE TONIC SEIZURES INDUCED BY MIDAZOLAM IN CHILDREN WITH REFRACTORY STATUS EPILEPTICUS

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Purpose: Drug-induced exacerbation of seizures is a serious clinical problem that may be unrecognized. Paradoxical seizure exacerbation with benzodiazepines has been reported in patients with Lennox-Gastaut syndrome. The aim of this retrospective study is to describe four patients with refractory status epilepticus who developed reversible tonic seizures induced by continuous intravenous Midazolam (cIV- MDZ).

Method: Retrospective review of a cohort of 152 children with status epilepticus identified from' Hospital.

Result: Four patients aged 3–12 years old developed new onset tonic seizures during cIV- MDZ. All had severe epileptic encephalophathies with intractable epilepsy and previous episodes of status epilepticus. The etiology was mithocondrial disease (complex I and IV deficiency) n = 1, Dravet syndrome n = 1, and in two patients the etiology was unknown. Three had convulsive and one nonconvulsive status epilepticus refractory to first and second line therapy. Following cIV- MDZ, they developed tonic seizures which were documented during video-EEG monitoring with electrodecremental or incremental pattern. The clinical manifesta-

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tion was subtle in some patients, with subtle eye movements only. The tonic seizures resolved following discontinuation of midazolam and the addition of nonsedating antiepileptic drugs orally. All patients returned to their baseline neurological status. Induction of tonic status was not dose dependent.

Conclusion: Reversible induction of tonic seizures during treatment of status epilepticus is uncommon but can occur with cIV- MDZ in individuals with epileptic encephalopathies. Video-EEG monitoring is strongly recommended as the clinical signs of tonic seizures may be subtle.

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SEIZURES INDUCED INJURY IN DEVELOPING BRAIN

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Purpose: The effect of seizures on the developing brain is age-specific, and also seizures associate with the induction of brain injury. Neurotransmitter glutamate plays key physiological roles in intercellular communication, plasticity, growth and differentiation, but also triggering neurodegeneration as a result of excessive stimulation of postsynaptic receptors by l-glutamate in epilepsy Glutamate release in high concentration activates several postsynaptic glu receptors (GluRs)/ion channel complexes, leads to Ca^{2+} entry into neurons, activates Ca dependent cytodestructive enzymes including neuronal NO synthase, leading to release of NO. This process may be responsible for the initiation of neuronal damage.

Method: Serum content of autoantibodies (aAB) to GluR, cyclic GMP (reflects the NO concentration), Ca^{2+} was determined in 110 epileptic patients (E) (2 months–16years) and 35 children of control group (CG). aAB were estimated by ELISA, synthetic peptide (analogue of GluR1) was used as antigen. cGMP concentration was measured using the ELISA.

Result: The basic level of aAB in control groups of children was revealed, which is increased depending of age. The lowest level was measured in babies of 2–12 months old. The significant increase ($p < 0.05$) more than by 1, 5–2 times of aAB level in E patients in comparison with CG was revealed. In adults the basic level of aAB was invariable. The decreased level of Ca^{2+} in children with E was measured. The significant indirect correlation between aAB and Ca^{2+} was revealed. The cGMP concentration was in seven times higher in patients of 2–12 months and in four times higher in children of 1–16 years ($p < 0.001$) with E versus CG.

Conclusion: The results showed the involving of GluRs in seizure activity and its alteration. Free-radical processes more expressed in babies of 2–12 months old. $Ca^{2+}$and cGMP play an important role in neuronal and glutamate receptor function. The alteration in glutamate receptor function, Ca^{2+} dependent and Ca^{2+}- free intracellular processes, and downstream cascade reactions lead to the damage of neuronal membranes and receptors.

p411
ELECTRICAL STATUS EPILEPTICUS DURING SLOW SLEEP IN VARIOUS DISORDERS

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Purpose: The aim of this study was to analyze the clinical characteristics, electroencephalografic findings, cognitive outcome and therapeutic response of children with specific language imparment (SLI), pseudo-Lennox syndrome, Landau-Kleffner syndrome (LKS) and continuous spike-waves during slow-wave sleep (CSWS) with electrical status epilepticus during slow sleep (ESES).

Method: Prospectively we analyzed clinical findings, EEG recordings, cognitive outcome and therapeutic response in seven children with SLI, pseudo-Lennox syndrome, LKS and CSWS.

Result: We present seven patients with SLI (1), pseudo-Lennox syndrome (2), LKS (1) and CSWS (3) with strong activation of epileptiform activity during sleep. Valproate, ethosuximide, clobazam and topiramate were used both in seizure controle and amelioration of the continuous epileptiform discharges. Four patients received steroid therapy with variable response. Better cognitive outcome on repetitive testing was associated with disappearance of ESES.

Conclusion: Electrical status epilepticus during slow sleep (ESES) is electroencephalographic phenomena characterized by strong activation of epileptiform activity during sleep. Children with SLI, benign childhood epilepsy with centrotemporal spikes (BCECTS), pseudo-Lennox syndrome, LKS and CSWS, could present with ESES. Depending on clinical presentation various AED's in combination with steroid therapy is recomended.

These very different clinical conditions could overlap in EEG characteristics, inclining that they present very wide spectrum of the same neurobiologic continuum.

p412
CLINICAL PROFILE AND SHORT TERM OUTCOME IN CONVULSIVE STATUS EPILEPTICUS IN INFANCY AND CHILDHOOD

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Purpose: To evaluate clinical profile and short term outcome in convulsive status epilepticus in infancy and childhood.

Method: A prospective analysis of 112 children with convulsive status epilepticus over a period of 2 years from March 2008 to March 2010 was undertaken. Status epilepticus is defined as continuous seizure activity lasting for 30 min or more or two or more seizures lasting 30 min or more without full return of consciousness. All the patients were thoroughly investigated including Imaging, CSF analysis and ABG where ever required. All the patients treated with established treatment guidelines. Diazepam or lorazepam followed by fosphenytoin as first line therapy. Second line consisted of phenobarbitone, midazolam, propofal infusions.

Result: There were 112 children (age 2 days–12 years). Seventy-five Males 37 females. Sixty-one patients were <1 month of age. Ten cases were 1–12 months. Thirty-five cases were between 1 and 5 years. Five cases had neurological abnormalities before presention. Seventy-three cases presented with generalized seizures, 39 simple partial seizures with secondary generalization. The etiological factor in 52 cases was, hypoxic ischemic encephalopathy. Febrile seizures in 49 cases. Thirty-one cases had Respiratory distress of varying severity. Sixty-one cases responded to 1st line drugs. Fifty-one cases needed 2nd line drugs.Only seven cases needed ventilator support. Three cases died due to septicemia and multiorgon dysfunction.

Conclusion: Perinatal insults is one of the major etiology of convulsive status epilepticus in neonatal period. It is an important preventable cause in developing countries. Febrile seizures are common cause after 1 month of age. Short-term outcome is good with early treatment. Addition of phenobarbitone was effective and prevented the need for ventilatory care.

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DESCRIPTIVE STUDY OF CLINICAL PROFILE AND RESPONSE TO TREATMENT WITH METHYL PREDNISOLONE PULSES IN CHILDREN WITH ELECTRICAL STATUS EPILEPTICUS IN SLEEP (ESES)

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Purpose: The objective of this study was to describe the demographic and clinical features of children with ESES and their clinical outcome with high dose methyl prednisolone pulse therapy.

Method: Ten children with clinical diagnosis of ESES and followed up at the Children's Hospital, Colombo, Sri Lanka were evaluated. Threapeutic response to high dose methyl prednisolone (30 mg/kg/day * 3 days followed by one month tail off with prednisolone) was assessed after six cycles of therapy.

Result: Mean age at diagnosis was 7.12 ± 2.5 years. Male: female was 1:1. Nine had symptomatic (MRI proven) etiology. Eight were in stage two of the illness at diagnosis. Mean duration of follow up was 24.6 ± 6.5 months. They had decline in neuropsychological state in all, acquired hemiplegia in two, loss of ambulation in five, severe ataxia in seven, regression/complete loss of speech in six, oro-facial manifestations in four. Two older (>11 years) patients were in the third stage of illness at diagnosis.

Mean age of first seizure was 30.6 ± 14.5 months and were focal motor seizures in all. Mean age to onset of second stage was 50.6 ± 16.1 months. Average time gap between onset and second stage was 20 ± 10.19 months. All except one, completed all six pulses of methyl prednisolone. Best response was in improving seizure frequency (9), improvement of gait (6) and drooling (5). Degree of improvement was perceived as significant by parents in 7. One patient deteriorated immediately after the MPNL on two occasions (9 months apart). The interval between pulses increased with successive doses.

Conclusion: Majority in this group of ESES had an structural abnormality. High dose Methyl prednisolone therapy was tolerated by majority. It was effective for both control of seizures as well as improving associated neruological morbidities seen in ESES.

p414
KETOGENIC DIET IMPROVES REFRACTORY STATUS EPILEPTICUS

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Purpose: Ketogenic diet (KD) has been repeatedly advocated in the treatment of drug-resistant epilepsy. However, its possible role in prolonged status epilepticus has not been well described. This study aimed to report successful use of the ketogenic diet in patinets with multidrug resistant status epilepticus after encephalitis.

Methods: We retrospectively reviewed the medical records of five patients with status epilepticus whom we tried ketogenic diet on from October 2006 to August 2010.

Result: The study group comprised four children (4.1–14.3 years old) and one adult (40.4 years old). All patients presented with status epilepticus associated with viral encephalitis. The seizures were not controlled at all despite of the use of multiple antiepileptic drugs (AEDs). The time from onset of epilepsy to introduction of the diet ranged from 0.5 to 14 months (median: 1 month). On initiatig the KD, we administered the 4:1 ratio of lipid to nonlipid with 70–80% liquid and calories of daily requirement using commercial ketogenic liquid. The median time to seizure improvement more than 50% was 8 days (1–19 days). At 1 month after starting KD, one of them was seizure-free and two others exprerienced more than 90% seizure reduction. The rest two of them improved more than 90% seizures and generalized seizures disappeared remaining partial seizures. In four children, they had been on ventilator care and KD made them possible to be weaned the ventilator with reducing dose of AEDs. The duration of diet ranged from 1 to 16 months. One seizure-free responder had to stop the diet in 1 month because of aspiration penumonia but continued to benefit in terms of decreasing other AED with ventilator weaning. Other complications were gastroesophageal reflux in two patients and constipation in four patients. One patient had hypertriglyceridemia which was controlled by atrovastatin.

Conclusions: The KD can be a valuable therapeutic option for the patients with pharmacoresistant status epilepticus.

Poster session: Pediatric epileptology IX
Tuesday, 30 August 2011

p415
PLASMA LEPTIN, NEUROPEPTIDE Y, GHRELIN AND ADIPONECTIN LEVELS AND CAROTID ARTERY INTIMA MEDIA THICKNESS IN EPILEPTIC CHILDREN TREATED WITH VALPROATE

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Background: Weight gain is a common side effect of valproate (VPA) treatment although the mechanism is not clear. Abnormal weight gain and obesity are associated with dislipidemia, hypertension and atherosclerosis. Common carotid artery intima media thickness (CAIMT) gives a comprehensive picture of early arterial wall alterations and currently is considered as a noninvasive marker of premature atherosclerosis.

Purpose: The aim of the present study was to evaluate blood levels of insulin, leptin, neuropeptide Y (NPY), ghrelin and adiponectin in children with epilepsy treated with VPA, and to evaluate them for early atherosclerosis.

Method: Twenty prepubertal children with idiopathic epilepsy treated with VPA were enrolled. Body mass index (BMI) and fasting insulin glucose ratio (FIGR) were calculated; plasma insulin, leptin, NPY, ghrelin, adiponectin, lipid profiles and CAIMT were measured for all subjects before the treatment and after a follow-up period of 6 and 12 months.

Result: At the end of the 6 and 12 months, the mean BMI values, the mean plasma insulin, FIGR, leptin and NPY levels were increased compared with before treatment. Plasma ghrelin and adiponectin levels, lipid profiles and CAIMT did not change significantly.

Conclusion: These results suggest that weight gain during VPA treatment is related to increase in insulin, leptin and NPY levels. However, there was no increase in the risk for early atherosclerosis as determined by CAIMT.

p416
ASSOCIATION BETWEEN UROLITHIASIS AND THERAPY WITH TOPIRAMATE OR ZONISAMIDE: THERAPY? PROPHYLAXIS?

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Background: A well-known side effect of topiramate (TPM) is the formation of kidney stones with an incidence of 1–5.6% in adult patients. This may increase to 54% in young nonambulatory patients. Under

treatment with zonisamide (ZNS) kidney stones have a prevalence of 1–2%. The concrements are composed of either calcium-phosphate or calcium-oxalate. Pathophysiologically, inhibtion of carboanhydrase activity by TPM or ZNS results in metabolic acidosis, hypocitraturia and elevated urine pH, conditions that favor stone deposition.

Methods: Retrospective analysis of 10 patients with symptomatic or asymptomatic kidney stones (three female, 3–47 years, three nonambulatory) under therapy with TPM (dosage 2–8.5 mg/kg or ZNS (7.5 mg/kg). All patients suffered from difficult-to-treat epilepsies (5/10 on comedication with other AEDs; six symptomatic focal, one Dravet syndrome). Therapy of kidney stones included operations (three), urine acidification (one), urine alkalinasition (one), dose reduction (three), and increase of fluid intake (four). TPM was continued in all patients (9/9), ZNS was stopped (1/1).

Discussion: General information about kidney stones associated with TPM and ZNS should be provided including courses of training about possible appearence of sludge in the diaper and the need for sufficient fluid intake. Urine analysis and kidney ultrasound particularly for children with risc factors (e.g., positive history, urological or metabolic diseases, immobile or multimorbid patients), comedication with other carboanhydrase inhibitors (sulthiame, acetozolamide) or under ketogenic diet should be performed. Dose reduction and change in medication can be an therapeutic or prophylactic option.

p417
SERUM AND CSF ZINC LEVELS IN CHILDREN WITH FIRST FEBRILE CONVULSION ADMITTED IN RASHT 17TH SHAHRIVAR PEDIATRIC HOSPITAL, IRAN

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Purpose: The relationship between neurotransmitters and trace element changes in biological fluids and febrile convulsions has been examined in some studies with conflicting results. The authors aimed to evaluate the relation, if any, of serum and CSF status with first febrile convulsion.

Method: In this case–control study, the authors assessed 30 children with a diagnosis of first febrile convulsion, aged between 6 months and 6 years; the control group consisted of 30 febrile children without convulsion. Serum & CSF zinc levels were measured by atomic absorption spectrophotometry (AAS), and compared between two groups.

Result: The mean serum zinc level was 40.38 ± 20.37 μg/dl in case and 43 ± 20.5 μg/dl in control group, without any statistically significant difference between two groups. The mean CSF zinc level in case and control groups was 16.69 ± 4.2 and 18.03 ± 4.1 μg/l, respectively. There was not any statistically difference between these two groups.

Conclusion: The results of this study suggest that febrile convulsions are not associated with reduction in serum and cerebrospinal fluid zinc concentrations.

p418
MANAGEMENT AND OUTCOME OF EPILEPTIC SPASMS UNDER AGE 3 YEARS: SINGLE CENTER US EXPERIENCE

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Purpose: To describe epileptic spasms (ES) management and outcome in patients younger than 3 years. between 2004 and 2010 at CHB.

Method: Retrospective review of 173 children (104 boys) with ES < 3 years. and minimal 6-month follow-up; assessment of onset/diagnosis ages, hypsarrhythmia, etiology, antiepileptic drugs (AEDs), short (<6 months) and long term (≥6 months) seizure control and development.

Result: Median age (first visit) was 6.8 months. Etiology was found in 62% (107/173, group 1) and unknown in 38% (66/173, group 2). Hypsarrhythmia was seen in 104 (60%). Treatment included ACTH (n = 103), VGB (n = 82), or others (121).

Short Term: Spasm control similar rates were observed with ACTH&VGB, in group 1 (33%, 40%, respectively, p = 0.4) and group 2 (50%, 44%, respectively, p = 0.8); other AEDs presented higher failure rates (71%, both groups). Children with initial developmental delay (DD) presented no differences in spasms control comparing ACTH, VGB or other AEDs, regardless of DD degree or etiology.

Long Term: After 27-month median follow-up DD was present in 83% and persistent seizures in 54%. Group 1: ACTH provided better outcome compared to VGB for development & seizure control (p = 0.02, p < 0.01, respectively); group 2: no differences observed with different treatments. Typical hypsarhythmia was more associated to persistent seizures (p = 0.01) and initial hypotonia, to abnormal development in follow-up (p < 0.01), especially with unknown etiology. No relation between persistent seizures and DD with spasm onset age was found.

Conclusion: Epileptic spasms generally progress to poor development & persistent seizures. Although in patients with known etiology ACTH may be associated with better long-term outcome compared to other drugs, similar spasm control should be expected in children with initial DD. Further studies are needed for consensus on management of spasms.

Support CAPES (Brazil).

p419
INTENSE PHARMACOVIGILANCE IN PEDIATRIC PATIENTS WITH FOCAL EPILEPSY TREATED WITH CARBAMAZEPINE MONOTHERAPY

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Purpose: To identify, evaluate, and propose a strategy of solutions for the effectiveness and security problems that pediatric patients show with focal epilepsy diagnosis and treated with carbamazepine monotherapy.

Method: A descriptive observational cross section study.

Result: One hundred eighty-one medical records were evaluated Gender: 54% (n = 98) of male and 46% (n = 89) female. Age: More than half of patients (59.1%) were adolescents. Sixty-six percent of patients had symptomatic focal epilepsy, 26% with probably symptomatic epilepsy and 8% with primary idiopathic epilepsy. Pharmaceutical form, the study is 61% of the population and 39% simple carbamazepine. Carbamazepine retard, the doses found in this study were between 12 and 23 mg/kg/day with a frequency of administration every 8 h. The assessment is crisis management since the beginning of carbamazepine in eight patients, 60% of crisis management, 53 patients 70% of crisis management, 43 patients 80% of crisis management, 37 patients controlled by 90% and 40 patient seizure-free total seizure control at 100%. Patients with adverse drug reactions (ADRs). The presence of rash was 18%. The most common effect of drowsiness at the beginning and gradual ascent is at a 82% rise seen in cases of rapid, in some cases (promotion every three days or the beginning of high dose and change in presentation.) Regarding the supply problem was found in 77%, 66% adherence, problems in management in 49.7%, stored in 8.8% and 89% drug.

Conclusion: We identified all potential problems and/or actual presented in the drug chain. Found adverse events similar to those reported in the literature and are considered moderate. The doses used are within the range recommended by the international medical literature. Issues such as weight, height, malnutrition, etc. were the most frequent

findings in relation to biological aspects. Social aspects are lack of education groups, the motivation for economic reasons, the need to bring protection to deliver your medicine.

p420
A EUROPEAN REGISTRY OF ANTIEPILEPTIC DRUG USE IN PATIENTS WITH LENNOX-GASTAUT SYNDROME: UPDATE OF CURRENT STATUS

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Purpose: Rufinamide is licensed in Europe for the adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) in patients aged ≥4 years. A postmarketing European registry was established to provide long-term data (≥3 years) on >100 LGS patients initiating rufinamide as add-on therapy and up to 300 LGS patients receiving other antiepileptic drugs (AEDs). An update on the registry's current status is presented.

Method: Since May 2008, the registry has been enrolling LGS patients (age ≥4 years) requiring modification in any AED treatment, including initiation of rufinamide. Its primary objective is to evaluate long-term safety. Effects of treatment on seizure control and health care resource utilization are also being assessed.

Result: Currently, 72 sites in nine countries are actively recruiting patients, or undergoing assessment for study inclusion, and 60 patients from 20 sites have been enrolled. A baseline assessment of the first 50 patients (31 male/19 female) found that mean (standard deviation [SD]) age was 16.1 (11.0) years; mean (SD) time since LGS diagnosis was 6.6 (8.9) years; mean (SD) total seizure frequency/month was 196.9 (224.8); and mean (SD) number of prior AEDs was 7.4 (3.6). Mean (SD) number of AEDs used at baseline was 3.2 (1.2); most commonly, rufinamide (46%), sodium valproate (36%), lamotrigine (34%), levetiracetam (32%) and clobazam (26%). At baseline, 34% of patients used a helmet and 60% a wheelchair; 16% were in residential care, the remaining being supported by parent/carer.

Conclusion: The registry is already providing valuable information on LGS and its management.

Study supported by Eisai.

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p421
EPILEPSY, POVERTY AND CHILDHOOD UNDERNUTRITION IN RURAL ETHIOPIA

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Purpose: The incidence of epilepsy in Ethiopia is high compared with more developed countries, but in most cases the cause of epilepsy is unknown. We performed a case-control study to determine whether epilepsy is associated with poverty and markers of childhood undernutrition.

Method: Patients with epilepsy (n = 112), aged 18–45 years, were recruited from epilepsy clinics in and around two towns in Ethiopia. Controls with a similar age and gender distribution (n = 149) were recruited from patients and relatives attending general outpatient clinics. We administered a questionnaire to define the medical and social history of cases and controls, and then performed a series of anthropometric measurements. The study was approved by the ethics committee at the LSHTM and locally in Ethiopia.

Result: Epilepsy was associated with illiteracy/low levels of education, odds ratio = 3.0 (95% confidence interval: 1.5–6.0), subsistence farming, odds ratio = 2.1 (0.9–5.0) and markers of poverty including poorer access to sanitation ($p = 0.009$), greater overcrowding ($p = 0.004$) and fewer possessions ($p < 0.001$). Epilepsy was also associated with the father's death during childhood, odds ratio = 2.2 (1.0–4.6). Body mass index was similar in cases and controls, but patients with epilepsy were shorter and lighter with reduced sitting height ($p < 0.001$), bitrochanteric diameter ($p = 0.029$) and hip size ($p = 0.003$). Patients with epilepsy also had lower mid-upper arm circumference ($p = 0.011$) and lean body mass ($p = 0.037$).

Conclusion: Epilepsy in Ethiopia is strongly associated with poor education and markers of poverty. Patients with epilepsy also had evidence of disproportionate skeletal growth, raising the possibility of a link between childhood under-nutrition and epilepsy.

p422
ETIOLOGIC FEATURES OF NEWLY DIAGNOSED EPILEPSY: HOSPITAL-BASED STUDY OF 892 CONSECUTIVE PATIENTS IN WEST CHINA

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Purpose: We evaluated data from a large cohort of newly diagnosed epilepsy and epileptic syndromes patients from the biggest epilepsy center in West China to determine the most prevalent etiologic factors in this region.

Methods: From May 2008 to May 2010, clinical data of consecutive patients with newly diagnosed epilepsy were systematically recorded in a database prospectively, and analyzed according to sex, age, seizure type, etiology, and other factors.

Result: This study examined 892 consecutive patients with newly diagnosed epilepsy. Among these patients, 346 (38.8%) were confirmed as symptomatic, with highest occurrence rate in the elderly (63.2%). In this symptomatic group, central nervous system (CNS) infections and traumatic brain injuries (TBI) were the two most common symptomatic etiologies. When analyzed according to age bracket, cortical dysplasia (CD), mesial temporal sclerosis (MTS), and CNS infection were the most frequent causes in young patients (<18 years), while CNS infection and TBI were the two most common causes in patients between 18 and 60 years. Stroke was the most common cause of newly diagnosed symptomatic epilepsy in the elderly (>60 years).

Conclusions: More than 30% of newly diagnosed epilepsy cases were shown to be symptomatic by medical history, and careful clinical and laboratory examination. Detailed assessment for epilepsies is essential to formulate a therapeutic plan and for prognosis. The etiology spectrum found in this large cohort forms a comparative baseline for future studies.

p423
THE TREATMENT GAP OF ACTIVE CONVULSIVE EPILEPSY IN RURAL WEST CHINA

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Purpose: The aim of this study is to determine the treatment gap (TG) and possible affecting factors in our region.

Methods: The survey based on primary health care unit was conducted in seven areas of West China from May 2005 to May 2008 with the aim to screen out active convulsive epilepsies. Data were collected and analyzed focused on TG.

Result: Total 2538 patients with convulsive epilepsy were enrolled into our study. Overall estimate of TG in West China was 65.7%; and TG increased as age proceeded. Patients suffering seizures with the duration of 1–5 years were more likely to seek treatment than <1 year or above 5 years. TG was lager in farmers (than nonfarmers), and females (than males). Further much more adult women (30–50 years) were observed to have failed to be treated than men.

Conclusion: There is a great TG in rural area of China and more attention on potential factors should be paid on a government level in order to achieve an expected outcome against epilepsies.

p424
CASE MANAGEMENT OF EPILEPSY IN RURAL VILLAGES OF MALI, A 3-YEAR COHORT STUDY

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Purpose: To evaluate a case management model of people with epilepsy (PWE) developed at a community based level in Mali, we assessed treatment efficacy and program compliance from 2003 and 2006.

Methods: A network of general practionners in six rural districts was selected for this survey: evaluation and monitoring of all the identified PWE and use of generic phenobarbital and valproate for epilepsy case management. All the PWE participants were included in the database and followed up at 4-month intervals over a period of three years. Seizure frequency, treatment doses and appearance of adverse events were systematically recorded. Efficacy was evaluated in terms of reduction of seizures frequency while noncompliance in terms of time to study withdrawal for any cause.

Result: A total of 1100 PWE were screened and we were able to follow 834 patients (97.6% received phenobarbital and 2.4% valproate). 49.6% of patients completed the 12-months and 5.3% the 36-months follow-up. 53.6% were considered seizure-free at 4 months, 47.8% at 8 months while 45.0% at 12 months. The multivariate analysis shows that presenting partial seizure ($p = 0.03$) or being attended in one out of six areas ($p = 0.0003$) were protective factors to be withdraw at 12-months. Having more than five seizures/month was a predictor of withdrawal at 36 months while having an age <18 years was a risk factor at both 12 ($p = 0.008$) and 36 months ($p = 0.02$).

Conclusion: This survey shows a good efficacy to the treatment. We documented risk factors for high rate of withdrawals.

p425
POSSIBLE REASONS FOR TREATMENT GAP IN A RURAL COMMUNITY IN SOUTH INDIA AND THE IMPACT OF COMPREHENSIVE RURAL EPILEPSY STUDY IN SOUTH INDIA (CRESSI) ON REDUCING THE TREATMENT GAP

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Purpose: Globally treatment gap (TG) for epilepsy is ~85%, most of it in developing countries. The reasons for this TG have not been well studied.

Method: The possible reasons for the TG were studied in a cohort of prevalent people with epilepsy (PWE) in a rural community at the initiation of Comprehensive Rural Epilepsy study in South India (CRESSI). The impact of CRESSI on TG was studied at 7-year of initiation of the program. In CRESSI care provider team includes: neurologist, psychiatrist, epilepsy coordinators, and multipurpose health workers and antiepileptic drugs (AED) are given free of cost once a month.

Result: Of the 462 prevalent cases, 381 (82%) were not appropriately treated for epilepsy on the prevalence day, 78 (17%) were not on any form of treatment. The main reasons for TG included low purchasing capacity (83%), limited access to health care and limited knowledge among local practicing physicians. The mean annual AED cost per patient was INR: 1917.6, 7.8% of per capita GNP. At 7-year of initiation of the program, of the 353 evaluable PWE, 333 were on regular AEDs. The TG has been reduced to 5.7%. The reasons for TG in the remaining 20 PWE included: other systems of medicine in 8 (40%); poor drug adherence (irregular medication) in 8 (40%); and refusal of drug treatment in 4 (20%).

Conclusion: The main reason for TG is nonaffordability of treatment. The CRESSI model of specialist care at the doorstep of PWE can be an effective way to reduce TG in developing countries.

p426
POSTTRAUMATIC SEIZURES IN A NEW RURAL NEUROSURGERY SERVICE: PATTERNS AND RISK FACTORS

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Purpose: Traumatic brain injury (TBI) is a well recognized risk factor for seizures. Whereas TBI is a common occurence in Nigeria, a developing economy, there is paucity of literature on posttraumatic seizures (PTS) in the Nigerian population with TBI. We have recently pioneered a rural neurosurgical service in a Nigerian tertiary health centre in the country. This study provides our preliminary report on the profile and pattern of PTS in TBI patients.

Method: A prospective observational study of TBI patients was carried out between November 2010 and March 2011. Patients demographics, nature of TBI, type of seizure (early or late), seizure semiology and cranial computerized tomography (CT) findings were assessed. Simple descriptive data analysis was done.

Result: Forty-five patients were managed for TBI within the study period. Of these, 39(86.7%) were males while 6 (13.3%) were females. Eight (17.8%) of the patients were children. There were 25 (55.5%), 8 (17.8%), and 12 (26.7%) cases of mild, moderate and severe head injury respectively. Three (6.7%) patients had open depressed skull fracture while 2 (4.4%) had gunshot wound to the head (GSWH). There were 4 (8.9%) cases of early PTS and these were in patients with severe head injury, 3 (75%) of whom had acute subdural hematoma on CT scan while the fourth had GSWH. Seizure occured in three of them within 24 h of trauma while it occured on the 5th day posttrauma in the other. Only two of them required anticonvulsant therapy because of recurrence but none progressed to late PTS. One patient who was managed for mild head injury a year previously presented with late posttraumatic seizures that were well-controlled with anticonvulsant.

Conclusion: Most cases of PTS are associated with severe TBI, acute subdural hematoma and GSWH. Progression of early to late PTS is rare.

p427
BRIDGING THE TREATMENT GAP FOR EPILEPSY IN LAO PDR

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Abstracts

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Purpose: In 2009 an initiative was launched in Laos to bridge the treatment gap for epilepsy that was previously estimated to be over 90%.

Method: In 2010 a national randomized survey evaluated the prevalence and situation of active epilepsy and the relation of epilepsy patients with the health system in all Lao provinces (16). The same year 3 days-trainings of 72 districts' doctors were conducted in 5/17 provinces together with the production of leaflets, daily radio advertising and authorities' advocacy. In 2011 in an attempt to link the health staff with their population of epileptic patients an active screening of patients was conducted in the same districts of trained doctors from March to April 2011with an theoretical objective of 1200 new patients.

Result: Of 180 patients screened during the initial trainings, trained doctors assumed the follow up of <130 new patients 6 months after despite a regular feedback and monitoring in 2010. Of 72 trained doctors only 40 were available to participate to the 2011 survey. The treatment situation of patients screened during the 2011 survey and 3 months after will be presented. Main lessons to improve the treatment gap in this particular context will be discussed.

Conclusion: Treatment gap remains a main challenge that could benefit of strategies adapted to local context.

p428
PUBLIC AWARENESS AND ATTITUDE TOWARD EPILEPSY IN SAUDI ARABIA

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Purpose: No previous data were available about epilepsy awareness in Saudi Arabia. The study was conducted to obtain the baseline information about epilepsy in general public in the capital city, Riyadh.

Method: Using a questionnaire survey in Arabic (native language) that contains 11 items regarding epilepsy, we interviewed, face-to-face, a sample of 750 persons, divert in (age, sex and educational backgrounds), selected randomly in public places, schools and colleges.

Result: Ninety-two percent of respondents had heard about epilepsy, 79% knew someone with epilepsy, 63% believed that epilepsy is an organic disease, 18% believed that it is an evil spirit possession. Epilepsy needs a medical treatment and prayers together according to 47% of them, prayers alone and medication alone in 24% and 19% respectively. About 61% will accept an epileptic patient if he applied for a job but 65% refused marriage to someone with epilepsy.

Conclusion: The majority of public know epilepsy as a term and know someone with epilepsy, but a significant number linked it to evil spirit possession.

Prayers/religious healers were chosen either alone or with medical treatment as a preferred method for treatment by most of them, irrespective to their educational levels.

More education and epilepsy camping is needed in our community to counter act the misconception of epilepsy.

p429
CAUSES AND OUTCOME OF HOSPITAL ADMISSION AMONG PEOPLE WITH EPILEPSY IN A RURAL DISTRICT HOSPITAL IN KENYA

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Purpose: People with epilepsy (PWE) frequently develop complications that require admission to hospital. However, there is limited data on this morbidity in resource-poor settings. We determined the causes and outcomes of hospitalization in PWE admitted in a Kenyan rural district hospital.

Method: We retrospectively reviewed case notes of all children and adults admitted to Kilifi District Hospital between January 2003 and December 2009 who had history of two or more unprovoked seizures and/or regularly used antiepileptic drugs. Chi-square tests were performed to determine the factors associated with death.

Result: Of the 538 admissions eligible for the study, 64% were children. Epilepsy was codiagnosed with other illnesses in 297 patients (55%). Status epilepticus (SE) was the commonest cause of admission (41%) with a mortality of 5.4%. Epilepsy related injuries, such as burns or fractures occurred in 24%, whilst admissions not related to occurred in epilepsy (35%). Patients who were admitted in a postictal coma were more likely to die (Fisher's exact test $p = 0.0265$), but mortality was not significantly associated with SE or burns.

Conclusion: Prolonged postictal coma, SE and burns are the commonest causes of admission to hospital, but only postictal coma is associated with death. These complications can be prevented by better management of epilepsy in the community.

p430
FIRST POPULATION-BASED SURVEY OF EPILEPSY IN GABON, CENTRAL AFRICA

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Purpose: Prevalence of epilepsy in Africa is high (median prevalence: 15‰). However, no data exist in several countries, as in Gabon although seven neurologists are working there. Data are important to sensitize health authorities and allocate specific resources.

Objective: To estimate the prevalence of epilepsy in a semirural area of Gabon (first population-based survey in this country).

Method: Door-to-door survey was done in 2005 in the area of Ntoum, 40 kms west from the capital Libreville. First a screening phase was implemented using the Limoges Questionnaire for Investigation of Epilepsy in Tropical Countries. This questionnaire has been validated in Mauritania leading to a sensitivity of 95% (CI95%: 87–98). Two other sources of information were used: nonmedical source (traditional healers, head of the villages, teachers, religious leaders) and medical source (medical registries, pharmacies). A neurologist examined all suspected cases identified in any of the sources and confirmed or not epilepsy. Epilepsy was defined using epidemiological definition of those of ILAE, 1993. Capture-recapture method was used to estimate the number of people with epilepsy missed by all sources.

Result: Out of 6259 included subjects, 48 people with epilepsy were identified by door-to-door survey leading to a prevalence of 7.7‰ (CI95% 5.7–10.2). Furthermore, 16 people with epilepsy were confirmed by nonmedical source and eight by medical source. In total, 51 cases were confirmed by the three sources. Capture-recapture methods estimated 58 cases in total, then a prevalence of 9.3‰ (CI95% 6.9–11.7). Only 13.8% of the cases were treated for their epilepsy.

Conclusion: Prevalence was slightly lower than expected. Use of several sources of information could be useful as already found in Benin. The treatment gap is huge. Actions will be implemented in Gabon.

Poster session: Epidemiology II
Tuesday, 30 August 2011

p431
FIRST UNPROVOKED SEIZURE 1-YEAR MORTALITY: A MONOCENTRIC PROSPECTIVE COHORT STUDY

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Purpose: To evaluate the 1-year mortality in patients after a first unprovoked seizure in adolescence or adulthood.

Method: A monocentric prospective cohort study was performed on a population of 394 consecutive patients observed with a first unprovoked seizure from January 1, 2006 to December 31, 2009 (age range 14–91 years; male, 220). Follow-up evaluations were performed every 6 months. Population expected deaths were calculated using Modena's County 2006–2009 life tables.

Result: At the last follow-up 107 patients were lost, 50 of which died. Based on the 29 deaths occurred during the first year after the index seizure the population 1-year standardized mortality ratio (SMR) is 6.5 (CI 95% 4.1–8.9). The patients who died within one year were above 50 years at the time of the index seizure. Twenty-eight of the 29 patients who died had a remote symptomatic seizure, while one patient had a cryptogenic one. One-year mortality was higher in patients with a focal remote symptomatic seizure (SMR 9.1 CI 95% 5.7–12.5). No subjects died for SUDEP. No deaths were observed in patients with normal MRI and generalized spikes wave discharges suggesting a generalized idiopathic epilepsy syndrome.

Conclusion: These results suggest that one-year mortality is increased in subjects with a first unprovoked seizure after 14 years of age. Mortality is particularly increased: (1) in patients with a focal remote symptomatic seizure (Loiseau P. 1999); (2) in patients over 50 years, especially in male gender.

p432
MORTALITY IN GEORGIAN POPULATION WITH DIAGNOSED EPILEPSY

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Purpose: To estimate mortality patterns in people with epilepsy in Georgia.

Method: A retrospective cohort study of people with epilepsy attending the Institute of Neurology and Neuropsychology between 2005 and 2008. Survivorship was established through contact with patient, family members, and caregivers. In cases of death possible causes were established through death certificates supplemented by verbal autopsy, and post mortem examination when available. Age-adjusted standardized mortality ratio (SMR) has been calculated through an indirect standardization method. The study was approved by the National Council on Bioethics.

Result: The cohort consisted of 1106 people of whom 77 are known to have died. The observation period consisted of 11,249 person/year. Mean follow up was 9.7 years. The age-adjusted SMR (95% CI) was 1.5 (1.2–1.88). Age-specific SMR (95% CI) for the 15–19 age group was 7.9 (3.3–18.9), for the 20–24 age group was 2.8 (1.05–7.4) and for the 25–29 age group- 3.3 (1.5–7.4). Main causes of death were: Stroke 23%; Brain tumors 20%; accidental death 8%, possible sudden unexpected death in Epilepsy 1%.

Conclusion: This study is ongoing. An additional thousand cases are planned to be followed and final results will be provided. Preliminary data suggests that mortality rate in Georgian population with epilepsy is about 1.5 times higher compared to general population. Increased mortality among young patients is a matter of special concern.

p433
DRUG-RESISTANT EPILEPSY AFTER A FIRST UNPROVOKED SEIZURE IN ADOLESCENCE AND ADULTHOOD: A PROSPECTIVE COHORT STUDY

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Purpose: To identify the short-term frequency of drug-resistant epilepsy (DRE) in patients with a first seizure in adolescence or adulthood. Early identification of DRE can provide rational combinations of antiepileptic drugs or lead to early epilepsy surgery.

Method: A monocentric prospective cohort study was performed on a population of 394 consecutive patients with a first unprovoked seizure evaluated from January 1st 2006 to December 31st 2009. Follow-up evaluations were performed every 6 months. Drug resistance was determined using two different definitions: (1) Berg, 2006 (Berg et al, 2006); (2) ILAE, 2010 (Kwan et al, 2010).

Result: At last follow-up (12–60 months) 107 patients were lost, including 50 due to death (14.8%). In the remaining population (n = 287), ILAE DRE patients are 18 (6.5%), Berg DRE patients are 10 (4.5%). Fifteen patients have focal epilepsy: 12 with symptomatic etiology, three with cryptogenic etiology; two patients have an idiopathic generalized epilepsy, one cryptogenic generalized epilepsy. Seven patients reported history of seizures before the index seizure, three patients starting with status epilepticus. All DRE patients had the second seizure within three months from the index one.

Conclusion: These results suggest that (1) the percentage of patients who develop DRE after a first critical event in adolescence/adulthood is relatively low (4–7%); (2) these patients quickly became drug-resistant, supporting the concept of DRE as an expression of an intrinsic severity of the disease (Sillanpaa et al, 2009). Early detection of these patients can lead to early epilepsy surgery.

p434
VALIDATION OF A NOVEL DIGITAL ANIMATION SEIZURE-SCREENING QUESTIONNAIRE SUITABLE FOR POPULATION-BASED RESEARCH

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Purpose: The conventional research method to screen for epilepsy is with a written questionnaire administered door-to-door (WQ). Although this enables comprehensive capture of undiagnosed and untreated cases, it is resource intense, insensitive to nonconvulsive seizures and inefficient for large-scale case ascertainment. Our aim was to ''field test'' a novel digital animation seizure-screening questionnaire that may be more suitable for community-based recruitment.

Method: We developed a series of five high-resolution digital animations depicting visual sequences of young people with seizures (AQ) consisting of: tonic–clonic, simple partial motor, complex partial temporal lobe, absence and myoclonic. Following each scene respondents are asked: ''Has this ever happened to you in your life?'' In addition, if respondents affirm to the tonic–clonic seizure, they are also asked about tongue- biting and urinary incontinence. Finally questions regarding ''prescribed antiepileptics ever'' and ''diagnosed epilepsy ever'' are asked. We aimed to administer AQ to 500 primary and secondary school students aged 5–18 years. Secondary school students completed AQ

face-to-face, in their class groups, with one parent completing AQ via the internet. Only primary school parents completed AQ. Administration to parents was by a specially constructed study Website www.sparks.org.au. Families without access to broadband internet (>128 kbs) were offered a DVD version of AQ. Screen positive students underwent epilepsy specialist assessment (ESA) including EEG, to confirm the diagnosis of epilepsy. AQ was repeated on 100 randomly selected students and parents after first completion, to estimate AQ repeatability. In addition, 100 randomly selected screen negative cases underwent blinded ESA to estimate AQ sensitivity and specificity.

Results: To date, 49 students have undergone AQ administration with the remaining students anticipated to complete AQ over the next few months.

Conclusion: If AQ demonstrates similar validity to WQ, it may be a more effective population screening instrument, as it can potentially reach larger numbers of individuals in the community through the internet, DVD and the next generation of mobile phones incorporating video streaming.

p435
IMPLEMENTATION OF THE NEW ILAE CRITERIA FOR AED RESISTANCE IN CURRENT PRACTICE: OBSERVATIONAL STUDY AMONG FRENCH AND SPANISH NEUROLOGISTS (ESPERA)

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Purpose: In 2009, the International League Against Epilepsy (ILAE) has proposed new criteria to define pharmacoresistant epilepsy. ESPERA study investigates the implementation of these criteria by French and Spanish neurologists in current practice, in patients on polytherapy for focal epilepsy.

Method: A European observational, cross-sectional study was conducted in France and Spain in 2010. A random sample of neurologists enrolled prospectively adult patients treated with at least two antiepileptic drugs (AED) in combination for partial epilepsy. The investigators classified their patients according to the new ILAE criteria. The classification was then reviewed by two independent experts.

Results: Seventy-one French neurologists collected analyzable data on 405 patients. Among them (three nonclassified patients), 240 (59%) were classified as drug resistant, 150 (37%) as responsive and 12 (3%) as undefined. Following the experts review, 73 patients (18%) were considered wrongly classified: 61 responsive patients (84% of all discrepancies) were considered resistant in 43 cases and undefined in 18 cases, five resistant patients were considered undefined and seven undefined status patients were considered resistant in six cases and responsive in one case. Misclassifications of the 61 patients wrongly classified as AED responsive were mainly due to an erroneous interpretation of the reduction in seizure frequency as responsiveness criteria. Around 250 patients were enrolled in the Spanish analysis: the results will be available for the final communication.

Conclusion: Because of their complexity, the utilization of the new ILAE criteria needs to be supported by relevant information and training to be adequately applied by neurologists.

p436
INCIDENCE AND RISK FACTORS FOR SUDDEN UNEXPECTED DEATH IN EPILEPSY (SUDEP): A TYROLEAN CASE-CONTROL STUDY

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Purpose: Sudden unexpected death in epilepsy patients (SUDEP) accounts for up to two-thirds of fatalities in patients with drug resistant epilepsy. Incidence rates vary between 0.3 and 10/1000 person years (PY). We aimed to analyze incidence rate and risk factors of SUDEP in a hospital based cohort in Tyrol.

Method: All patients with epilepsy (n = 3334) treated at the outpatient epilepsy clinic Innsbruck, between 1–1970 and 12–2000 were included. Epilepsy diagnosis was based on the classification of the ILAE. Patients were followed until death or 12–2006. A total of 48.595 person years were recorded. All dead patients with ICD-10 codes G40.0-G41.9 (i.e. ''epilepsy'') were analyzed in detail (n = 43). We classified SUDEP cases as definite, probable, possible and non SUDEP. We calculated incidence rates, proportional mortality and compared potential risk factors in SUDEP cases and in three controls, which were living epilepsy patients matched for age and sex. They were selected from the same cohort and for each SUDEP case.

Result: We identified 34 (median age 44.6 years, range 19–94, M24/F10) patients with SUDEP (five definite, seven probable and 22 possible). Eight patients had non-SUDEP; one near-SUDEP case was excluded from the study population. Incidence rate of SUDEP was 0.2/1000 PY. SUDEP accounted for 1.8% (12/648) of all deaths caused by epilepsy in Tyrol. Seizure frequency (>15 seizures/year) was the factor most strongly associated with an increased risk of SUDEP (odds ratio [OR]: 19.8, CI: 5.2–77).

Conclusion: In this hospital based study, incidence of SUDEP was as low as in previous population based studies on SUDEP, reflecting the big catchment area of our center. Further this work supports the idea that SUDEP is a seizure related event.

p437
ACCURACY OF EPILEPSY SURVEY BY TRAINED MEDICAL RECORD ADMINISTRATORS

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Purpose: To perform a nationwide epidemiologic study for treated epilepsy, we trained the professional medical record administrators (MRAs) to review the record associated with epilepsy with a structured case record form (CRF). In this study, we purposed to validate the medical record survey by trained MRAs.

Method: Subjects for survey were the 80 patients who were prescribed anticonvulsants for 1 year in 2009 at two tertiary hospitals. The contents of CRF were demography, anticonvulsants, diagnosis, disease activity, type of seizure, cause and classification of epilepsy, and results of the electroencephalography and brain imaging. The CRF consists of two

parts, MRAs' documentation and epileptologists' interpretation after checking on the documentation collected by MRAs. For the validation, two MRAs and one epileptologist of own hospital documented the medical records of same patients independently. Interpretation was done by unrelated epileptologist for MRAs' documentation. We assessed the accuracy, sensitivity and specificity of the results by MRAs, using those by the epileptologist of own hospital as standard.

Result: The accuracy of the survey by trained MRAs was 95–100% for the diagnosis and disease activity and 85–100% for the cause and classification. The sensitivity are 90.9–100% for diagnosis and 100% for disease activity. The specificity is 100% in diagnosis and activity.

Conclusion: Our structured CRF was appropriate for epilepsy survey using medical records, and trained MRAs were not inferior to epileptologist for collecting the information associated with epilepsy. This method is useful for large scaled epidemiologic study of epilepsy.

p438
THE FRENCH SENTINEL NETWORK ON THE EPILEPSY-RELATED MORTALITY

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Purpose: It is reliably established that mortality is increased in persons with epilepsy. The French network on epilepsy-related mortality named Réseau Sentinelle Mortalité Epilepsie (RSME) aims to describe causes and circumstances of deaths related to epilepsy in France. The secondary objectives are to evaluate the expectations and needs of bereaved families and to create a national database for future research programs.

Method: This register is based on networks of epileptologists and neuropediatricians from each region and representatives of bereaved families. During the registration period (January 2010–January 2012), information about dead patients will be reported by neurologists with a standardized form and completed by an interview with bereaved families.The study protocol was approved by the Ethics Committee of Lyon.

Result: Twenty-seven cases of death related to epilepsy have been reported, 61% of them were male (n = 16). Median age of death was 26.5 years (Interquartile: 19–37). SUDEP accounted for 92% (n = 24) of deaths, six of them were autopsied. Within the SUDEP group, all the type of epilepsy were represented (idiopathic 17%, symptomatic 33%, cryptogenic 33%) and 80% had drug-resistant epilepsy (n = 20). Three-quarters (n = 18) of the SUDEP cases died while sleeping and 43% experienced a treatment modification during the three last months.

Conclusion: While the exhaustivity must be improved, this study will permit to promote informations concerning epilepsy-related mortality and to propose adequate support to bereaved families. SUDEP deaths will be part of a future case control study to identity risk factors.

Poster session: Epidemiology III
Tuesday, 30 August 2011

p439
LONG-TERM OUTCOME IN EPILEPSY: 25 YEAR FOLLOW-UP OF A GENERAL POPULATION COHORT WITH INCIDENT EPILEPSY

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Purpose: The National General Practice Study of Epilepsy was set up in the 80s and is one of the longest established general population-based studies of epilepsy in existence. It aims to follow-up a large incident cohort of people with newly suspected or diagnosed epileptic seizures in the community, as most previous studies have been performed in clinic-based cohorts, which may provide a biased view of prognosis.

Method: One thousand X twelve people including 792 patients with definite or probable epilepsy and 220 with febrile seizures were notified to the study by their general practitioners (GPs) and they 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 have ascertained the outcome of the cohort in 2009–10 in regards to survivorship, seizure and seizure outcome.

Result: Of the original cohort of 1012 people, 301 (28%) have died. Long-term follow-up was obtained in 552 people. Over 80% of those with definite and probable epilepsy are currently in terminal remission (TR) (5 years or more seizure-free) on or off AEDs at last follow-up. Less then 10% of those who attain TR subsequently relapsed. The only factors found to influence long term prognosis were seizures before the index seizure and etiology.

Conclusion: The long-term data from this incident cohort suggests that the often cited maxim that one-third will have refractory epilepsy may be overly pessimistic. Further long-term prospective studies are needed to verify this finding.

p440
THE DECISION OF AN AUSTRALIAN EPILEPSY NGO TO INVEST IN EPIDEMIOLOGY RESEARCH

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Purpose: To describe the process undertaken and factors influencing Epilepsy Action Australia's (EAA) decision to invest in epidemiology as a strategy to develop appropriate epilepsy specialist services and influence social health policy in Australia.

Method: Conducted desktop research to understand existing data and gaps; consulted consumers to capture ''the experience'' of living with epilepsy; identified and approached potential strategic partners; and, undertook internal groundwork for financial invest in epidemiology by EAA.

Results: 1. Identified inherent sector weaknesses, being lack of quality Australian NGO research and journal publications
2. Consulted with consumers through advisory group meetings and 32 forums across Australia with 204 participants who identified emotional/social, daily living, information and employment issues
3. Formed strategic partnership with the George Institute for Global Health, and later, Epilepsy Society of Australia, key neurologists and government
4. Supplied initial seed funding and ongoing financial investment which contributed to successful National Health and Medical Research Council Partnerships funding application
5. Hosted initial policy forum with 50 attendees representing a broad cross section of stakeholders with report published in Medical Journal of Australia

Conclusion: Development of appropriate epilepsy services and influencing social health policy remain EAA's primary goals, however there are additional benefits of the decision including the growth and corporate maturity of an NGO. EAA is gaining exposure to and experience with academia, application processes for research grants, liaison with key

clinical experts and with the research project in progress, there are opportunities for the professional development of staff.

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A PROSPECTIVE STUDY EVALUATING THE RECURRENCE OF TAKOTSUBO CARDIOMYOPATHY RELATED TO SEIZURES

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Purpose: Takotsubo cardiomyopathy may occur during acute neurological events such as epileptic seizures. Mild troponin release, ST-segment elevation and transient wall-motion abnormalities characterize this fully reversible but potentially lethal condition. Our aim is to assess the incidence of takotsubo cardiomyopathy related to epileptic seizures, and characterize the clinical features most frequently linked to this pathology. Here we report two cases of takotsubo cardiomyopathy observed after epileptic seizures.

Method: Two case-reports of takotsubo cardiomyopathy diagnosed after systematic troponin assessment among 258 patients presenting with epileptic seizures in our two institutions. Thirty-one patients had elevated troponin levels.

Result: Case 1: this postmenopausal woman (62 years) presented repetitive hypermotor seizures and altered consciousness. Seizures were stopped by benzodiazepine and phenytoin administration. The patient presented few hours later low blood pressure, EKG abnormalities and echographic signs of cardiomyopathy. Coronarography showed no vessel obstruction. The patient recovered fully after cardiac support care. Case 2: This man, aged 58, is ethylic and on the 4th day of alcohol withdrawal, presented two tonic–clonic seizures. He was admitted in the ICU. The EKG revealed ST-T abnormalities with elevated troponin. The cardiac ultrasound showed a dilated left ventricle, reversible and the coronarography no significative coronary lesion. He was treated with valproate.

Conclusion: Cases of takotsubo cardiomyopathy related to epileptic seizures seem rare (42 published cases). The contribution of this condition to SUDEP is unknown. We are currently conducting a similar prospective study to assess the importance and characteristics of takotsubo cardiomyopathy related to epileptic seizures and have already identified these two cases after a few months of monitoring.

p442

INNOVATION IN RESEARCHING THE SOCIAL IMPACT OF EPILEPSY IN AUSTRALIA: A LONGITUDINAL STUDY

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Purpose: In 2006 the Epilepsy Foundation of Victoria established a Research Participant Register (RPR) for applied social and behavioral research. This RPR now includes research participants from all Australian states. This register is unique as it specifically studies the social impact of epilepsy. The Research Working Group of Epilepsy Foundation of Victoria which oversees the RPR received full HREC approval to conduct a longitudinal study to demonstrate the social impact of epilepsy across the whole of people's lives in Australia. Two surveys or 'waves' have now been conducted in 2007 and 2010. Here we present results from the Wave 2 data (Wave 1 presented Xiamen 2008) and discuss some of the challenges of conducting a longitudinal survey.

Method: Data are collected by self-administered questionnaires to the whole of the RPR. The questionnaire for Wave 2 is very similar to that of Wave 1. Some questions were modified in order to improve the quality of the collected data. SPSS is used to analyze data.

Result: We present results of Wave 2 in the areas of education, income, employment, housing, medicine usage and adherence.Longitudinal surveys are conducted as ''waves'' and require comparable survey tools and analysis. However these require modification over time. RPR participants may die, change addresses or withdraw from the RPR. Additionally new people are added while people already on the RPR may choose not to answer a particular survey. All these issues make comparisons over time and between groups difficult. Protocols are required to ensure comparability; to keep people engaged; engage with new participants and analyze data.

Conclusion: While the challenges of establishing a longitudinal survey are manifold the results show that it is worthwhile since the richness of comparable data over a period of years provides a picture of the quality of lives of people with epilepsy and demonstrates patterns of change in people's lives. These data provide the basis for better planning of services and evidence-based submissions to Government.

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VARIATION OF MONTH AND SEASON OF BIRTH IN AN IRISH EPILEPSY POPULATION

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Purpose: Previous reports from other countries have identified a season of birth affect in epilepsy, but this has not been assessed in an Irish population. it has aslo not been considered in different epilepsy syndromes. We assessed the season of birth in patients attending our service, both overall and for specific epilepsy syndromes.

Method: Using data from an Epilepsy Electronic Patient Record which we have previously validated for clinical use, we reviewed the month of birth for patients attending our service who had details recorded on their epilepsy syndrome. We calculated the statistical significance of the variation in month of birth for the group overall and separately for patients with juvenile myoclonic epilepsy (JME) and temporal lobe epilepsy with mesial temporal sclerosis (TLE). To compare our figures to available national data, we then analyzed the birth pattern by quarter.

Result: At the time of acquisition, data were available for 1308 patients. In the group overall, there was no statistically significant variation in month of birth ($p = 0.6109$), with a peak in births in July and a trough in September. A peak in July was seen in TLE ($p = 0.0928$) and in March in JME ($p = 0.0183$). When analyzed by quarter, the association with JME remained significant ($p = 0.0011$), which could not be accounted for by differences in the population overall.

Conclusion: Some of the results in this Irish cohort are similar to previous reports in other populations. However, seasonality of birth in JME has not been reported before. Our results may point to environmental factors involved in the etiology of JME compared to other epilepsy syndromes, although more formal analysis with larger numbers is needed before this can be confirmed.

p444

HOSPITALIZATION FOR PSYCHIATRIC DISORDERS BEFORE AND AFTER ONSET OF UNPROVOKED SEIZURES

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Purpose: To study hospitalization for psychiatric disorders before and after onset of unprovoked seizures.

Method: In this population-based case-control study, the cases were 1885 persons from Stockholm with new onset unprovoked seizures from

September 1, 2000 until the August 31, 2008. Controls, in total 15080, were randomly selected from the register of the Stockholm County population. Exposure was defined as a hospital discharge diagnosis using ICD codes from the Swedish Hospital Discharge Registry. Odds ratios (OR) were calculated to assess the risk of developing unprovoked seizures before and after a psychiatric diagnosis (depression, bipolar disorder, anxiety disorder or psychosis).

Result: The age-adjusted OR (95% CI) for unprovoked seizures after a hospital discharge diagnosis of psychiatric disorders combined was 2.7 (2.0–3.6), and slightly higher for the subgroup of patients with cryptogenic/idiopathic etiology. The risk of developing unprovoked seizures was highest <2 years before and up to 2 years after a first psychiatric diagnosis. The population attributable risk percent (PAR%) for psychiatric disorders and the risk of developing seizures was 2.4%.

Conclusion: The increased prevalence of psychiatric comorbidity relatively closely preceding and succeeding seizure onset points to a bidirectional relationship and indicates common underlying mechanisms for psychiatric disorders and epilepsy.

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ATTITUDE TOWARD SCHOOL AND SCHOOLWORK IN NORWEGIAN YOUTH WITH EPILEPSY A POPULATION BASED STUDY—THE AKERSHUS HEALTH PROFILE STUDY

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Purpose: We have previously published data showing a higher prevalence of psychiatric symptoms and preliminary data on increased risk taking behavior in youth with epilepsy (YWE) compared to controls. The aim of this presentation was to investigate the attitude towards school and schoolwork in youth with epilepsy (aged 13–19) compared to controls in a Norwegian County.

Methods: The study was cross-sectional and based on questionnaires from youth with epilepsy aged 13–19. 19995 questionnaires were filled in (response rate 85%). Two hundred forty-seven (1.2%) reported having or having had epilepsy. Student's *t*-test and chi square test were used for testing for group differences in selected continuous and categorical variables, respectively. We estimated odds ratios (OR) using multiple logistic regression analysis.

Result: The attitude towards school performance and participation was significantly decreased in YWE compared to controls (i.e. without epilepsy). Twenty-three percent of YWE compared to 12% of controls felt uncomfortable at school ($p < 0.001$). Nineteen percent of YWE compared to 14% of controls were truanting school often ($p = 0.05$). Forty-five percentof YWE reported being stressed by school and schoolwork versus 44% in youth without epilepsy (NS). Having epilepsy was an independent predictor of feeling uncomfortable at school (OR 2.07, $p < 0.001$). Low family affluence, male gender and living in a single parent household were also predictors for feeling uncomfortable at school with OR of 2.25, 1.15, and 1.26 respectively.

Conclusion: YWE selected from a general population report a negative attitude towards school. This finding corresponds well with prior findings from the same population showing increase in psychiatric symptoms, risk behavior, drug use and anxiety among children and youth with epilepsy. This further emphasizes the importance of offering comprehensive care to YWE.

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PERCEPTIONS OF EPILEPSY IN TURKEY, VIEWED IN THE LIGHT OF TWO DIFFERENT CITIES FROM WEST TO EAST

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Purpose: The social exclusion as a result of negative attitudes of others toward people with epilepsy. The stigma, adults may be barred from marriage, and employment is often denied, even when seizures would not render the work unsuitable or unsafe. Religions, beliefs, culture, and tradition contribute to this stigmatization. In our previous study, we investigated the knowledge and perceptions of epilepsy and preferred treatment options of people with epilepsy, their first degree relatives, and healthy individuals in Yuksekova, a city at the south east region of Turkey. Currently, our aim is to compare our previous study results with another study about stigmatization and epilepsy performed in Kutahya, a city at the Aegean region of Turkey which has different cultural, social, economical and educational status. Thus, by evaluating the epileptic stigmatization in Yuksekova, a southeast city that is underdevelopment and in Kutahya, a modern, developed Aegean city with higher socioeconomical status, we would be able to analyze the regional differences in social stigmatization of epilepsy.

Method: We compared the answers of the questionnaires which were filled by the first-degree relatives of PWE in two previous studies held in Yuksekova and Kutahya; cities of two different ethnic origin, social, cultural, economic and educational status. Data were organized in an SPSS Version 15.0 database.Statistical analyses were performed with the χ^2 test. p-values < 0.05 were considered to indicate statistical significance.

Result: When asked if they would permit their healthy child to marry a person with epilepsy, about 15.4% of the participants answered ''yes'' in the Yuksekova group.The rate of the ''yes'' responders was 22.8% in the Kutahya group ($p < 0.05$). ''Should a person with epilepsy have a baby?'' question had been answered as ''yes'' in 70% of Yuksekova group, while the rate of ''yes'' responders was 46% in the Kutahya group ($p < 0.05$). When asked if they would tell other people that they have a relative with epilepsy, 63% of the first-degree relatives of PWE in the Kutahya group would tell their ''closest friends/relatives only,' whereas 80.8% of the Yuksekova group would do so ($p < 0.05$).

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PREVALENCE OF DRAVET SYNDROME AMONG CHILDREN REPORTED WITH A CONVULSION AFTER VACCINATION, IN A NATIONWIDE 10-YEAR COHORT

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Purpose: This study is undertaken to assess the frequency of Dravet syndrome (DS) due to a *SCN1A* mutation, in children reported with a convulsion after vaccination, in a nationwide 10-year cohort (1997–2006), and to analyze which clinical characteristics distinguishes children with and without DS.

Method: Medical data of all children, reported with convulsion(s) after vaccination in the first 2 years of life to the National Institute for Public Health and Environment in The Netherlands, were reevaluated. In children with possible DS, additional medical information was requested. DNA-analysis of *SCN1A* was offered, if not yet performed, to those with a clinical history compatible with DS. The study has been approved by the medical ethics committee of the UMC-Utrecht.

Result: One thousand three hundred one children were reported with 1368 convulsions after vaccination. Median age at initial reporting was 1.3 years. One hundred three (7.9%) children had been diagnosed with epilepsy. Of 239 children (median age 8.4 years) out of 285 children with possible DS, additional medical information could be retrieved. Fifteen children were diagnosed with DS, four as a result of this study, and had a *SCN1A* mutation. Seizures in children with DS occurred at a lower age (4 vs. 11 months), were more often afebrile (64.3% vs. 25.4%) and reoccurred more often after following vaccinations (26.7% vs. 3.9%), than in children without a diagnosis of DS (p-values < 0.01).

Conclusion: At least 1.2% (15/1301) of children with a convulsion after vaccination in the first 2 years of life has Dravet syndrome due to a *SCN1A* mutation.

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HIGHER RISK OF FEBRILE SEIZURES IN BOYS – GENDER DIFFERENCES IN A LARGE DANISH COHORT

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Purpose: To study the gender difference in incidence of febrile seizures taking age, secular trends and genetic predisposition into account.

Methods: The Danish Civil Registration System (CRS) was used to identify all children born in Denmark between 1977 and 2001 (N = 1,655,168 children). The Danish National Hospital Register was used to trace children hospitalized with febrile seizures between 3 months and 5 years of age up to December 31, 2006.

Result: Among all children followed, 50,976 children (3.1%) had been hospitalized with febrile seizures. Among 821,050 boys, 28,508 boys (3.47% [95% CI: 3.43–3.51%]) were diagnosed with febrile seizures and among 783,139 girls, 22,468 girls (2.87% [95% CI: 2.83–2.91%]) were diagnosed with febrile seizures. The cumulative incidence of febrile seizures was more than 20% lower among girls than boys (79.0% [95% CI: 78.5–79.5%]). The risk of febrile seizures was highly age dependant, the incidence peaked at 16 month of age and 90.1% had their fist febrile seizure before the 3 years birthday. The age of onset was remarkably similar between boys and girls. The risk was independent of age of onset, birth month, calendar year, and found in both full and half siblings, and was not explained by differences in recurrence rate of febrile seizures or by length of follow up.

Conclusions: The risk of febrile seizures is higher among boys than among girls.

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CLINICAL, NEUROPHYSIOLOGIC, NEUROPSYCHOLOGICAL FEATURES AND MRS FINDINGS OF A CHINESE PEDIGREE WITH FAMILIAL CORTICAL TREMOR AND EPILEPSY

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Purpose: To investigate clinical, neurophysiologic, neuropsychological features of a Chinese family in which six members in five generations developed nonprogressive adult onset cortical tremor and epilepsy.

Method: Clinical and electrophysiological data of all family members was collected. Proton magnetic resonance (MR) spectroscopy (1H-MRS) was used to detect the neurochemical pattern in patients with FCTE. All affected members underwent a neuropsychological assessment battery designed to evaluate attention performance, executive functions, memory, language, visuaospatial and psychomotor function.

Result: Six members, aged 24–59 years. Suffered from hand tremor and myoclonus, whereas generalized seizures occurred in all patients. The seizures were sporadic in nature and easily controlled by the anticonvulsants. The tremor also responded well to anticonvulsants, but not to β-blockers. Cranial CT and MRI were normal. EEG showed generalized spike and wave complexes in five patients. In the SEP study, all the early cortical componentswere identified in every patient. The average amplitude of N20-P25 was 20.41 ± 12.37, and P25-N30 was 33.01 ± 25.61. Electrophysiologic studies revealed giant somatosensory evoked potentials (SEPs), enhanced long latency reflexes (C-reflex). Compared with healthy subjects, patients with FCTE displayed elevated choline/creatine ratio in the temporal cortex ($p < 0.05$), whereas there was no significant difference for the other ratios. The neuropsychological assessment demonstrated that all the clinically affected members had a psychomotor function impairment.

Conclusion: In summary, familial cortical tremor with epilepsy may not be a rare disorder. Recognition of the EEG abnormalities, or seizures associated with a postural tremor resembling essential tremor, together with a positive familial history, are essential for diagnosis.

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THE NEW ILAE-PROPOSAL FOR A REVISED TERMINOLOGY AND CONCEPTS FOR AN ORGANIZATION OF SEIZURES AND EPILEPSIES: COMMENTS OF THE KÖNIGSTEIN WORKING GROUP OF EPILEPTOLOGY

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Purpose: To present opinions of a German speaking expert group (eight pediatric and seven adult epileptologists supplemented by a psychiatrist and neurophysiologist) on the recently proposed revised terminology and concepts for an organization of seizures and epilepsies (Berg A et al., Epilepsia 2010; 51: 676–85).

Method: Questionnaire study prior to a meeting of the Working Group in March 2011 including 19 items with predefined answers and an open question asking for suggestions to improve the revision.

Result: Positive opinions predominated for the simplified classification of absences (15/17) and for the reintroduction of the term "electroclinical syndrome" (13/17). However, only 7/17 regarded the new proposal in general as improvement in comparison to the classifications of 1981 and

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1989. On a visual analogue scale (1 = useless, 10 = perfect) it was rated with a mean of 5.8 (range 3–8) points. Major points of criticism were the unbalanced representation of ILAE chapters in the commission (16/17) and the rejections to replace ''secondary generalized seizure'' by ''seizure evolving to a bilateral, convulsive seizure (involving tonic, clonic, or tonic and clonic components)'' as well as ''astatic seizure'' by ''atonic seizure'' (13/17 each). Improvement suggestions included to differentiate only between symptomatic epilepsies (structural/metabolic, genetic, or both) and epilepsies of unknown etiology. In addition, there were a number of inconsistencies in the given text (e.g. ''benign'' is abolished in one part of the text, whereas it is still used in the syndrome classification, or rolandic epilepsy seems to be no longer considered a genetic epilepsy). Details of all 19 items will be presented.

Conclusion: There was considerable disagreement with many aspects of the recent ILAE proposal. A more detailed discussion within the international epilepsy community seems to be necessary before final approval.

p451
MYOCLONIC STATUS EPILEPTICUS IN NONEPILEPTIC PATIENTS

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Purpose: Myoclonic status epilepticus (MSE) consists of irregular, generalized myoclonic jerking without interference with consciousness. MSE was usually reported in epileptic patients. There are also few published reports that it may be associated with toxic-metabolic brain diseases or induced by drugs.

Method: We reviewed the clinical features, ictal EEGs and video records in five adults (three men, two women, age range of 53–84 years) with MSE who didn't have prior diagnosis of epilepsy.

Result: Three patients had generalized myoclonia precipitated by drugs. Two of them had been treated with pregabalin for neuropathic pain. The EEGs which showed continuous irregular generalized spike-wave discharges (GSPWD), normalized rapidly after drugs were discontinued. One patient who had been receiving hemodialysis for chronic renal disease, admitted with generalized seizures and myoclonia. Before, he had been treated with sclerotherapy for gastric variceal bleeding and had ceftriaxone prophylaxis postoperatively. EEG showed GSPWD which were photosensitive. One patient with a history of dementia was treated with donezepil and ketiapin. His grandson had juvenile myoclonic epilepsy. One patients' MRI showed subacute ischemic stroke on left frontal lobe and multifocal chronic ischemic lesions. Both patients had generalized myoclonia and GSPWD on EEG. Multifocal jerks disseapeared with levatirecetam in both patients. Consciousness was not impaired during MSE in four of five patients.

Conclusion: Drugs can induce generalized SE and myoclonic SE even in patients who have not epileptic seizures before. Old age, cognitive impairment, renal failure and family history of myoclonia may also predispose to this condition.

p452
X MONOSOMY WITH NONCONVULSIVE STATUS EPILEPTICUS

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Purpose: Deletion of one X chromosome in female (X monosomy) is well known for Turner syndrome (TS). Reports of X monosomy patients with epilepsy are rare, and most of them have cortical malformation. Further there is no clinical report of X monosomy with nonconvulsive status epilepticus (NCSE). We experienced seven TS patients with epilepsy from 1996 to 2010 and three of them had NCSE.

Method: We reviewed the records of patients referred to Shizuoka Epileptic Center, Japan, and identified patients with video-documented.

Result: Three patients with X monosomy were aged 40–51 years. All patients had mosaicism for 45, X, with one or more additional cell lineages (45,X/46,XX/47,XXX, 45,X/46,X). The ages of seizure onset ranged between 1 and 4 years. Interictal EEG showed slowing in background activity and spikes over C, P, or F region, or bilateral spike and waves. All patients had NCSE. One patient manifested simple and complex partial seizures. Another two patients had atypical absences with or without myoclonus and one patient showed secondarily generalized convulsions. Electroclinical investigation of NCSE revealed focal features in one, and generalized ones in the others. MRI of all patients was normal. The seizures were intractable in all patients.

Conclusion: We encountered three patients with X monosomy with mosaicism manifesting NCSE. As there are many important genes relating to neuronal development or myelination in X gene, mosaicism of monosomy/trisomy may introduce an abnormality of the gene dosage leading to complicated gene expression with epilepsy in some, although the reason for NCSE is unknown. Future additional molecular genetic analysis is necessary.

p453
IDIOPATHIC GENERALIZED EPILEPSY WITH PHANTOM ABSENCES: SAME FOCAL AND GENERALIZED EPILEPTIC DISCHARGES IN A BROTHER AND SISTER

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Purpose: Phantom absences (PA) are typical absence seizures with the mildest form of impairment of consciousness, and characterized by a triad of PA, generalized tonic–clonic seizures (GTCS) and absence status epilepticus (ASE). Genetical factors are the only suspicious etiology known. ILAE referred PA to be a result of brain maturation.

Method: We reviewed the clinical features, ictal and interictal EEG recordings of a brother and sister with idiopathic generalized epilepsy with phantom absences (IGE-PA).

Result: A 68-year-old male was admitted with complaint of mild abstraction, dullness, slowing of movements. Ictal EEG recording revealed continue generalized polyspike wave discharges (GPSWD) demonstrating ASE and iv diazepam suppressed EEG discharges and improved conscicousness. Same attacks were described five times at last year. Three days after this recording, his interictal EEG showed only the left temporal FED. He had 5 late-onset GTCS between ages 23 and 31. No myoclonic activity, typical absences or automotor seizures were defined. MRI was normal. Interictal EEG showed 3–4 Hz GPSWD with fragmentation and left temporal localized isolated sharp waves indicating a focal epileptic discharges (FED). GPSWD were provacated by hyperventilation (HV). His sister was a 59-year-old female with a history of 5 GTCS between the age of 15–23, and seizure-free for 36 years. In her interictal EEG fragmented 3–4 Hz GPSWD provacated by HV, and a right temporal FED was detected. Neurologic examination and intelligence were normal in both patients.

Conclusion: IGE-PA is a poorly recognized and hardly diagnosed epileptic subgroup with its only described etiology of genetical background.

p454
PROPAGATION OF GENERALIZED DISCHARGES IN IDIOPATHIC GENERALIZED EPILEPSY: THE IMPLICATIONS

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Purpose: Patients with idiopathic generalized epilepsy show generalized discharges which are assumed to occur synchronously over the entire cortex. Since discharges can quickly propagate along the cortex, we have tested our hypothesis that generalized discharges are in fact propagated by identifying latency differences between spikes recorded at homologous sites between hemispheres at discharge onset.

Method: Scalp EEG recordings from 85 (IGE) patients, that showed generalized epileptiform discharges were critically analyzed to identify small latency differences at discharge onset between spike peaks recorded at different homologous sites.

Result: Eighty-five patients studied showed either synchronous or nonsynchronous generalized spike and wave (GSW), generalized polyspikes and wave (PSW), or mixed GWS + PSW discharges in their EEG traces.

At the onset of generalized discharges, within the first 1–2 s, discharges were synchronous with no latency differences between hemispheres in 29 patients (34%). Discharges were led by the left hemisphere in 17 patients (20%). Discharges were led by the right hemisphere in 16 patients (19%). In 23 patients (27%) the generalized discharges were a mixture of either synchronous or were led by the right or the left hemisphere at discharge onset. The range of latency difference between hemispheres was 5–45 ms (mean latencies 19.2 ms) at discharge onset.

Conclusion: A strong correlation exists between the presence of synchronous discharges in IGE to one seizure type, e.g. absence and the presence of nonsynchronous discharges to multiple seizure types e.g. myoclonic jerks, generalized tonic–clonic seizures and absence (p-value = 0.01).

There is a strong correlation between the presence of synchronous generalized discharges and good response to drug treatment and the presence of nonsynchronous discharges to poor seizure control and poor prognosis (p-value = 0.0001).

p455
LANGUAGE DOMINANCE IN ADULT PATIENTS WHO UNDERWENT FUNCTIONAL HEMISPHERECTOMY

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Purpose: Functional hemispherectomy is a surgical technique used to treat refractory epilepsies in the setting of extensive unilateral hemispheric lesions. There are only a few and small series of adult patients treated with this technique. The aim of this study is to analyze language dominance in adult patients that underwent hemispherectomy.

Method: We studied retrospectively five patients with refractory epilepsy secondary to unilateral hemispheric lesions who underwent functional hemispherectomy. All patients had a complete presurgical evaluation including video EEG, neuropsychological testing and anatomical and functional neuroimaging. We analyzed several clinical variables of the epilepsy of the patients. We study the language dominance by functional magnetic resonance imaging (fMRI) and neuropsychological testing. We also analyzed the seizure outcome after surgery.

Result: In four patients, epilepsy was secondary to a early middle cerebral artery infarction. One patient had Rasmussen encephalitis. Language fMRI showed activation of the healthyhemisphere in four patients (80%). One patient had seizures during fMRI acquisition, so results were invalidated, and a Wada test was performed. Results of fMRI were concordant in the four patients with their neuropsycological testing. After surgery, four patients were seizure-free, and the fifth patient has a reduction of 75% of seizure frequency (range of follow up 8–50 months). Any patient had an aphasic disorder after surgery.

Conclusion: Language fMRI and neuropsychological testing are useful tools to determine language dominance in patients that are going to undergo hemispherectomy. This is an effective surgical alternative in selected patients with severe refractory epilepsy secondary to hemispheric syndromes.

p456
MISSED AIM: PHARMACORESISTANT PARTIAL EPILEPSY TRANSFORMED TO EPILEPSIA PARTIALIS CONTINUA YEARS AFTER EPILEPSY SURGERY

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We present the case of a 42-year-old woman with severe pharmacoresistant epilepsy. She had focal motor seizures associated to a right central non-progressive lesion that, based on video-telemetry, was supposed to be her epileptogenic region. Subtotal removal of the lesion, a combined dysgenetic/ganglyoglioma as well as subpial transsections (according to Morrell's method) of the central region in 2006, resulted in mild left hemiparesis and transient seizure freedom for some months. Then, in spite of continuous antiepileptic treatment, rare focal tonic motor seizures returned. After 2 years' pharmacologic treatment epilepsia partialis continua of her left hand II-IV. Fingers appeared that has continued ever since with gradual worsening of her epilepsy, persistant hemiparesis and mild mental deterioration. Further pahrmacologic treatment and neurostimulation methods are being considered.

We discuss the pathogenesis of epilepsia partialis continua in her case, considering the possible role of the performed Morrell method, the nature of her gangliolyoma as well as possible secondary transformation of her epilepsy e.g. a secondary Rasmussen-like syndrome.

p457
RARE AUTONOMIC SYMPTOMS AS THE PREDOMINANT MANIFESTATION OF EPILEPTIC SEIZURES

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Introduction: The signs and symptoms of seizures may be included in various spheres: sensorial, consciousness, motor and autonomic. Most of the seizures involves symptoms of more than one of these spheres, however the dominance of one of them determines their semiologic classification. Some symptoms and autonomic signs are uncommon and less known, so can hamper an early diagnosis of epilepsy.

Clinical Cases: We present the cases of three patients with a definitive diagnosis of epilepsy and with ictal semiology with predominance of rare autonomic symptoms. In one patient the main manifestation was a sensation of heat upwards from the feet to the malar region, followed by excess salivation. The second patient had only simple partial seizures in paroxisms characterized by urinary urgency and a strange discomfort in the head. The third patient described a sensation of diffuse heat with increase in body temperature and heart palpitations, followed by a partial complex phase with automatisms. Electroclinical seizures were recorded with video-EEG in all patients, localized to the temporal lobes. All patients underwent brain MRI and it was possible to identify temporal lesions in two of them.

Conclusion: The cases described illustrate the importance of conducting video-EEG in confirming the epileptic nature of rarer clinical ictal semiology, allowing an appropriate therapeutic approach.

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CASE OF ICTAL TREMOR WITH TEMPORAL LOBE EPILEPSY

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Purpose: Ictal tremor is a very rarely documented phenomenon. We were able to find just one paper on ictal tremors from 1966 (Harrington, Karnes, Klass, 1966). We would like to present the case of one of our patients with suspected ictal tremor. Three possible alternatives to tremor will be discussed: automatism, RINCH and myoclonus.

Method: Woman, 19 years old. Right-handed; epilepsy since 13 years. No family history; no febrile seizures; pharmacoresistant. MRI: right-sided mesiotemporal sclerosis, PET FDG: considerable hypometabolism on the temporal-right region.

Wada test proved speech dominance of left hemisphere. Interictal as well as ictal semiinvasive video EEG findings is lateralized on right anteromedial area only.

Aura (palpitation, déjà vu, déjà vecu, gastric aura), complex partial seizure with perioral automatisms, extremity automatisms, ictal tremor of right upper extremity, dystonia of left upper extremity, ictal and postictal drinking water.

She had the AMTR epilepsy surgery 12 months ago and she is seizure-free now.

Result: Results supporting the tremor diagnosis:

1. EMG polygraphy proof tremor;
2. Rhythmic character, contrary to automatism;
3. Ipsilateral to the seizure onset zone and the recorded tremor is of a higher frequency than we can usually find in RINCH-movement cases;
4. We did not find cortical potential preceding the followed phenomena in the course of back-averaging examination.

Conclusion: We suppose that our finding is a case of ictal activity which has spread to deep subcortical cerebral structures. On the other hand, we cannot rule out a possible spread of ictal activity to the left side.

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ICTAL WATER DRINKING AS A LOCALIZING SIGN

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Purpose: To report an interesting case presenting with ictal water drinking as a valuable sign that can differentiate right from left temporal lobe origin.

Method: The subject is 37 year-old female with multifocal postencephalic epilepsy. We reviewed and analyzed ictal manifestation of several seizures recorded by video-EEG.

Result: The patients suffered from encephalitis at the age of 22. Since then she has experienced several types of seizures including two types of complex partial seizures (CPSs). In one type of the CPSs, she became confused, called a nurse loudly, took a plastic bottle naturally, unscrewed the lid skillfully, took single swallow of tea, and then screwed the lid back on. She could respond with gesture to some questions during the seizure. On scalp EEG ictal discharges restricted over right temporal region continued through this series of behavior. On the other hand, in another type of her CPSs, she looked frightened with fearful expression and her consciousness was impaired so profoundly that she could not respond to any questions at all. Ictal water drinking could never be recognized even in the same setting as she could easily take a bottle or a cup. EEG demonstrated ictal discharges restricted over the left temporal region throughout the seizure.

Conclusion: Ictal or periictal water drinking is a good indicator for right (nondominant) temporal origin, as reported by Trinka et al. in their series of patients with TLE.

p460
ECSTATIC EPILEPTIC SEIZURES: A POTENTIAL WINDOW ON THE NEURAL BASIS FOR HUMAN SELF-AWARENESS

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Purpose and Method: Epilepsy with ''ecstatic auras'' (Dostoevsky's epilepsy) constitutes a rare form of focal epilepsy, whose frequency is probably underestimated due to the difficulties patients have in describing and discussing it. In prior reports, a temporal lobe origin was suspected, yet no precise localization has ever been demonstrated. We studied five new patients in order to better understand the anatomical correlate of ecstatic seizures.

Result: All patients' descriptions encompassed an emotional dimension of bliss, a physical dimension of enhanced well-being and a heightened self-awareness. Three had a cerebral lesion located within or close to the temporal pole (left, two cases; right, one case). In the two MRI-negative patients, EEG abnormalities were located in the left anterior temporal region. An ictal SPECT using 99mTc-ECD performed in one patient showed increased blood flow maximal in the right anterior insula.

Conclusion: The link between ecstatic seizures and heightened self-consciousness, which was clearly reported by these patients and by Dostoevsky, was not mentioned before in the scientific literature.

It has recently been proposed that the anterior insular cortex has a fundamental role in the feeling of well-being and in self-awareness. In the ecstatic seizures of these five patients is consistent with the functional characteristics of the anterior insular cortex. The descriptions by these patients (coupling of bodily feelings and intense emotional feelings with enhanced self-awareness) together with the neurophysiological and neuroradiological evidence, support a theoretical framework for understanding ecstatic states based on hyperactivation of the anterior insula (''symptomatic zone''), rather than the temporal lobe.

p461
PERIICTAL BED LEAVING IN TEMPORAL LOBE EPILEPSY: INCIDENCE AND LATERALIZING VALUE

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Purpose: The main purpose of our study was to establish the incidence and lateralizing value of ''periictal bed leaving'' (PBL) in patients suffering from temporal lobe epilepsy (TLE).

Method: We analyzed periictal bed leaving (PBL) symptoms in 105 patients with temporal lobe epilepsy (TLE). All patients were classified as Engel I at the 2-year follow-up visit. Histopathological examination revealed hippocampal sclerosis (TLE-HS) in 64 patients and other lesions in 38 patients (TLE-oth); three patients had no lesions. We reviewed 412 seizures. PBL was defined as lateralized leaving of the bed occurring during the seizure or up to 3 min after the end of the seizure.

Result: PBL was observed in 28 out of 105 patients (26.7%), in 45 out of 412 seizures (10.9%). PBL was more frequently present in patients with TLE-HS than in patients with TLE-oth (32.8% vs. 17.1%; $p = 0.058$). PBL was ipsilateral to the seizure onset in 71.4% of patients and 71.2% of seizures ($p = 0.012$; $p < 0.001$). In patients with TLE-HS, PBL ipsilateral to seizure onset was present in 76.2% of patients and 81.2% of seizures ($p = 0.008$; $p < 0.001$). In patients with TLE-oth, PBL ipsilateral to seizure onset was present in 42.8% of patients and 46.1% of seizures.

There were no differences in the incidence and lateralizing value in patients suffering from right and left-sided TLE.

Conclusion: PBL is a relatively frequent periictal sign in patients with TLE. The side of PBL in patients with TLE-HS lateralizes the seizure onset to the ipsilateral temporal lobe.

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TREATMENTS OF LOCALIZATION-RELATED SYMPTOMATIC EPILEPSIES

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Purpose: To evaluate causes of symptomatic localization-related epilepsies (LRE), different treatments and effects.

Method: Sixty patients (pts) aged 13–74 years (ys), female/male ratio 30/30 were diagnosed as symptomatic LRE.

Result: Brain CT/MRI identified different causes: Posttraumatic epilepsy after TBI was found in 16 cases, two underwent surgery, nine were on AED monotherapy (MT), six on polytherapy (PT), 13 were compliant, eight seizure-free, AED was withdrawn in one, reduced in one. Additional 2 pts underwent surgery for subdural hematoma. Both were compliant and seizure-free, one on MT, the other on PT. Brain tumors (TM) were found in 14 cases, eight benign (BG) six malignant (MG), 12 pts underwent surgery. AED was withdrawn in one, in 10 pts MT was used, PT in one, all except one were compliant and seizure-free. Two BG TM pts were seizure-free on MT without surgery. Arteriovenous malformations were found in 3 pts, two underwent embolization, two were on PT, no seizure control, one was seizure-free on MT, all were compliant. Hemangiomas were found in 3, 2 underwent surgery, not seizure-free, on PT/MT. One patient was only on AEDs, relapsed on MT. Poststroke epilepsy was found in 9 pts, hemorrhagic in 4, 3 underwent ruptured aneurysm surgery, three were on MT, seizure-free, one on PT, no seizure control. Five pts with ischemic stroke were compliant, no seizure control in 2, PT in two MT in 2, AED was withdrawn in one. Postencephalitic epilepsy was found in 4, one underwent cerebral abscess surgery. All were compliant, three on PT, one MT, two seizure-free. Refractory on PT were three tuberous sclerosis pts, one Sy Sturge-Weber and one polymycrogyria. Sclerosis multiplex was found in two, sarcoidosis in one and hydrocephalus in one patient. All were compliant, two on MT, one seizure-free.

Conclusion: LR symptomatic epilepsies require comprehensive diagnostic and treatment approach for better patient's quality of life.

p463
MULTIPLE ORGAN DYSFUNCTION SYSTEM IN 195 ADULT PATIENTS WITH CONVULSIVE STATUS EPILEPTICUS

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Purpose: To investigate the incidence, the risk factors of multiple organ dysfunction syndromes (MODS) caused by convulsive status epilepticus (CSE), to evaluate the efficacy of Sequential Organ Failure Assessment (SOFA) and the organ system failure score in predicting prognosis.

Method: One hundred ninety-five patients with CSE from January 1996 to October 2007 were investigated respectively. Clinical factors were analyzed by univariate and multivariate regression to determine clinical features associating with MODS. SOFA and the organ system failure score were used to evaluate the relationship of severity of MODS with prognosis.

Result: Fifty-three of 195 cases developed MODS. The incidence of MODS arrived at 27.2%. Twenty-nine patients died (14.9%), among them, 23 patients died from MODS. Univariate and multivariate logistic analysis identified age (OR 1.055, 95%CI 1.03–1.081, $p < 0.01$) and SE duration after admission (OR 1.034, 95%CI 1.014–1.054, $p < 0.01$) were risk factors of MODS in patients with CSE. Scoring assessment of MODS revealed higher SOFA scores associating with poor prognosis. The respiratory system was the most frequent extrabrain organ involved in MODS due to CSE.

Conclusion: The poor prognosis associating with development of MODS in patients with GCSE and higher SOFA score should be noted. Prompt life supporting and antiepilepsy therapy should be emphasized before irreversible organs injury and metabolic disturbances occur, especially in patients with older age or with long term duration of GCSE.

p464
PLASMA N-TERMINAL BRAIN-TYPE NATRIURETIC PEPTIDE LEVEL CAN DISTINGUISH SEIZURE FROM SYNCOPE IN ADULTS

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Purpose: To explore the clinical feasibility of plasma N-terminal brain-type natriuretic peptide (pro-BNP) level to differentiate the two major causes of transient unconsciousness, seizure and vasovagal syncope (VVS) in adult patients.

Method: We assessed pro-BNP levels within 24 h following attack in 52 consecutive patients who experienced a transient episode of unconsciousness. For confirmatory diagnosis, we thereafter reviewed prior history of attacks and performed clinical investigations including electroencephalography and cerebral imaging and tilt-table test where history is suggestive of VVS, as a part of usual clinical approach.

Result: According to various relevant evaluations, 28 patients were diagnosed as seizure (age, 48.2 ± 16.6 years) and 24 patients were VVS (age, 38.1 ± 17.1 years). Plasma concentrations of pro-BNP was significant higher in postseizure group (median 47.6, IQR 44.3–174.5 pg/ml) than those in post-VVS group (median 32.3, IQR 8.9–77.4 pg/ml) ($p = 0.01$). We could deduce the cutoff value for a diagnosis of seizure using ROC curve, which was 41.1 pg/ml (sensitivity 78.6%, specificity 58.3%). All 12 patients whose level was over 110 pg/ml turned out to be postseizure group. However, pro-BNP levels were not associated with the sampling times within 24 h after the episodes.

Conclusion: The elevation of plasma pro-BNP level may help us to infer seizure rather than VVS attack about the unrevealed transient unconsciousness. The more validated results with a large population should be needed in future studies to apply it in clinical circumstance.

p465
HEMOSTATIC PARAMETERS OF NEWBORNS FROM MOTHERS WITH EPILEPSY

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Purpose: To analyze features of hemostasis system and frequency of thrombohemorrhagic complications in newborn from mothers with epilepsy, who receive antiepileptic drugs for prolonged period.

Method: We observed 187 newborn babies, who were born from mothers who received antiepileptic therapy. Valproate and carbamazepine were the prevalent drugs.

Hemostatic parameters were investigated in sixty term infants who were included into study group. Twenty term infants whose mothers didn't receive antiepileptic treatment formed the control group.

Clinical examination (anamnesis, evaluation of clinical status), hemostasiologic.

Hemostasis system was analyzed by reagents of Dade Behring, on the device Amelung ÊÑ 10 À. It was taken 9 ml of funic blood for analysis. We analyzed the activity of factors of prothrombin complex, APTT, antithrombin system – AT III, the containment of endogenous heparin, Anti-FX a activity. Functional platelets activity was evaluated on aggregometer of company Crono-Log.

Result: Clinical examination revealed that there were no thrombohemorrhagic complications in all of 187 cases. The examination of hemostasis revealed the decrease of procoagulants and physiological anticoagulants, and the increase of Willebrands factor both in study group and in control group.

Conclusion: There was no significant difference between study group and control group, and the received values of hemostasis system were equal to those received in other studies of healthy term infants.

p466
INFLAMMATORY RESPONSE INDUCED BY SEIZURE

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Purpose: Seizure activity can produce systemic physiologic changes. Particularly fever is frequently accompanied with seizure, which arouses the concern about infection. We purposed to describe the seizure induced inflammatory response and find the way to differentiate the seizure induced changes from the infection.

Method: We prospectively investigated 148 consecutive patients who visited emergency room because of seizure between January, 2007 and December, 2008. We checked the clinical factors including semiology and duration of seizure, neurologic status at visit, vital sign, use of antibiotics or antipyretics, outcomes, laboratory tests including blood cell count, C-reactive protein (CRP), chest x-ray, and urine analysis in all case, and other tests to evaluate the infection in some case. We reviewed whether the patients had infection or not after discharge.

Result: Among 148 patients recruited, 102 patients (68.9%) had fever, leukocytosis or elevation of CRP. In 23 patients, there were symptoms suggesting infection such as cough, sputum, voiding difficulty, diarrhea, abdominal pain or radiologic or micobiologic evidence of infection. In the other 79 patients, there was no evidence of infection and spontaneously improved without treatment. The duration of hyperthermia was varied from 1 to 8 h. There was a peripheral leukocytosis in 36 patients (45.6%), ranging from 10,300 to 19,800. We cannot find abnormal cell contents in CSF but high protein concentration up to120 mg/ml in three of 13 patients. An elevated CRP was seen in 31 case (39.2%), ranged from 0.53 to 5.72.

Conclusion: Seizure frequently induces fever, leukocytosis, elevated CRP in the absence of infection. It is self-limiting usually within a few hours.

p467
CLINICAL PROFILE OF EPILEPSY IN ELDERLY: A STUDY FROM EASTERN INDIA

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Introduction: Worldwide there is increase in elderly population. There is also increasing incidence of epilepsy in elderly population. There are differences in etiology, clinical features and treatment of epilepsy in elderly population.

Aims & Objective: 1. To identify the etiolgy and semiology of epilepsy in elderly.

2. To study the response to treatment.

Materials and Methods: Patient with seizure onset after 60 years, who attended OPD and epilepsy clinic of Bangur Institute of Neurosciences, were evaluated by a group of neurologist by detailed history, clinical exanimation and necessary investigations like EEG, CT Scan of Brain, MRI of Brain.

Inclusion Criteria: Epilepsy patients with seizure onset after 60 years are included.

Exclusion Criteria: Elderly patients with acute symptomatic seizures are excluded.

Result: Sixty-six elderly patients were selected, majority of them had complex partial seizure with or without secondary generalization (66.6%) followed by simple partial seizure (18.18%) and generalized tonic–clonic seizure (12.12%). Most common etiology identified is cerebrovascular diseases (42.42%), CNS infection (18.18%), brain tumor (15.15%), dementias (7.57%). Majority of them responded well to monotherapy and that too with lower dosage of AEDs.

Conclusion: Complex partial seizure is commonest seizure in elderly, cerebrovascular diseases is the commonest cause in elderly. Majority responded well to monotherapy.

p468
NEUROCYSTICERCOSIS: LEADING CAUSE OF FOCAL SEIZURES IN NORTH INDIA

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Purpose: To evaluate the etiological factor in epileptic patients attending neurology OPD in a tertiary care referral hospital under University of Delhi.

Methods: We evaluated the cause of epilepsy in 212 patients with CT or MRI being the most important investigation with additional investigations wherever necessary.

Result: Out of the total 212 patients GTCS were seen in 142 patients (67%) and focal seizures in 70 patients (33%). The CT or MRI was abnormal in 43.4% of the total cases. Among patients with GTCS, CT or MRI abnormality was observed in 35.2% cases as compared to 60% of patients with focal seizures. The most common abnormality in CT or MRI was multiple ring enhancing or calcified lesions consistent with inflammatory granulomas, seen in 51.4% of cases of focal seizures compared to only 28.4% cases of GTCS. Neurocysticercosis was the leading cause as compared to multiple tuberculomas. Normal imaging was seen in 40.8% of cases with GTCS in contrast to only 15.7% of cases focal seizures. In 20% of cases with GTCS and focal seizures, imaging was either being done or the report was not available during the study.

Conclusion: Inflammatory granulomas are the most common identifiable cause of epilepsy in focal seizures though this may not reflect the general population because only difficult or complicated cases may have been referred to our hospital.

p469
LONG-TERM EVOLUTION OF ADULT EPILEPTIC PATIENTS WITH MALFORMATIONS OF CORTICAL DEVELOPMENT

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Purpose: End point is to evaluate clinical features and evolution in adulthood of patients with epilepsy secondary to malformations of cortical development (MCD).

Abstracts

Method: We retrospectively evaluated patients with epilepsy secondary to MCD followed in our Unit of Epilepsy. MCD were diagnosed by magnetic resonance imaging, most in 3 T system. We collected epidemiological, clinical and therapeutic data.

Result: Fifty-five patients were analyzed, 36 women and 19 men. Median age was 40.6 years (range 14–78). Seizure onset median age was 17, with follow-up of 11 years (range 0–39). MCDs described were dysplasia (33), polymicrogyria (5), schizencephaly (4), heterotopia (3), pachygyria (2) and hemimegalencephaly (1); seven patients had mixed MCDs. Damage was unilobar (65.5%, mainly frontal), bilobar (16.3%) or multilobar (18.2%). Physical exam revealed focal deficits in 30.9% and 14.5% showed delayed cognitive development. Drug-resistance was 85.5%, with median of six drugs used (range 0–11). Thirty-four patients (62%) had at least one seizure-free period longer than 1 year (maximum 18 years). Dysplasias affected essentially one lobe (81.9%), associated focal deficits in 18.2% and delayed cognitive development in 3%; frequently were drug-resistant (82%) but with less than one seizure per year in 45.5%. Patients with several MCDs or multilobar damage often evidenced focal deficits (86–80%), delayed cognitive development (43–40%), drug-resistance (100%) and more than one seizure per month (86–60%) respectively.

Conclusion: Adults with epilepsy secondary to MCDs are generally drug-resistant, infrequently associate neurological deficits and can reach long seizure-free periods. Evolution depends on malformation and its spreading over brain: unilobar dysplasia the best, multilobar mixed MCDs the worst.

p470
RECURRENT EPILEPTIC SEIZURES INDUCED BY CRANIAL TRAUMA: A DISTINCT FEATURE OF MEGALENCEPHALIC LEUCOENCEPHALOPATHY WITH SUBCORTICAL CYSTS

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Purpose: Megalencephalic leucoencephalopathy with subcortical cysts (MLSC) is a rare autosomal recessive disease caused by mutations of the MLC1 gene. The first symptom, usually noted in the first year of life, is megalencephaly, followed by progressive ataxia, pyramidal deficits, cognitive impairment and sporadic seizures during childhood. In this condition epileptic seizures have never been described in detail.

Method: Two sisters, aged 43 and 46 years, with MLSC underwent a complete clinical, neurophysiological, neuroradiological and genetic study.

Result: These two sisters, born from a nonconsaguineous marriage,showed megalencephaly since the first 2 weeks of life and developed over the years a progressive cognitive and motor impairment. They were forced to wheel chair since their teens. The seizures, of tonic–clonic type without clear focal symptoms, were sporadic and occurred exclusively after minor cranial trauma. Both patients were on chronic treatment with valproate. No epileptic abnormalities were found on EEGs, performed also during sleep. Cerebral MRI showed extensive alterations in white matter and subcortical cysts in fronto-temporo-parietal regions. Mutations of MLC1 gene were found.

Conclusion: In our patients epileptic seizures were constantly induced by minor cerebral trauma, suggesting that a mechanical insult may cause a transitory derangement of cortical excitability in this condition with severe intracerebral cysts.

p471
EPILEPSY IN PRIMARY CEREBRAL TUMORS: PRELIMINARY RESULTS OF THE PERNO STUDY (PROJECT OF EMILIA ROMAGNA REGION ON NEUROONCOLOGY)

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Purpose: The present study is aimed to define the clinical features of tumoral epilepsy, with special emphasis on the response of seizures to different neurooncological treatments.

Method: This study is a section of the PERNO project – a prospective registry of primary brain tumors (PBT) in Emilia-Romagna Region spanning a three year period (2009–2011). All patients with epileptic seizures were included in the study and followed up on a regular basis. A specific questionnaire aimed to define the clinical, neuroradiological and pathological findings was used for analysis. A consent form was obtained by each patient or responsible guardian.

Result: Out of 610 PBT cases collected over a 2-year period, 114 (19%) had epileptic seizures. Of the 72 (48 male and 24 female) patients with sufficient data for analysis, forty-six (64%) had malignant PBT, mainly involving the frontal (65%) or temporal (43%) lobes. Seizures were the first symptom in 53 cases (74%) and were focal motor (32%), somatosensitive (13%) or tonic–clonic (26%). High seizure frequency at the onset was observed in 32% of the cases and status epilepticus in 11%. Preliminary follow up data (available in 29 cases with glyoblastoma) showed a strong drug-resistance of seizures, which were stopped only by surgical treatment.

Conclusions: In this group of patients, mostly with malignant PBT, the seizures appeared lesion-dependent: they were the initial symptom of the tumor, heralded its relapse and were controlled by surgery.

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p472
DEVELOPMENT OF VASCULAR EPILEPSY IN PATIENTS WITH MALIGNANT STROKE OF MIDDLE CEREBRAL ARTERY (MCA)

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Purpose: Patients with malignant (massive) ischemic stroke of MCA have an increased risk of development of vascular epilepsy. Our aim was to describe the factors associated with evolution to epilepsy in these patients.

We evaluated all 68 patients with malignant MCA ischemic stroke included in our protocol for decompressive craniectomy and/or hypothermia (June 2002 – March 2011). Mean age was 49.9 ± 11 years old. Decompressive craniectomy was performed in 85% (n = 58), 41% of them associated with hypothermia. Twenty-nine percent died within the first days, and only one of them had an acute symptomatic seizure. In total 53.1% showed seizures in their evolution, 8.3% only during the acute phase (≤7 days), 42.9% during the follow-up (''late''), and 4.1% had both early and late seizures. The median time of ''late'' seizures was 6.5 months. Regarding to semiology, most of them had a motor focal seizure with generalization (54.5%), followed by generalized tonic–clonic seizures (22.7%) and simple motor seizures (8.3%). When comparing those patients with and without seizures, the only difference was the time between the stroke and the surgery (65.7 h vs. 47.3 p = 0.069), after a multivariate analysis a time over 33 h was the only factor associated with the development of seizures (OR 5.11; [1.08–24.4]; p = 0.039). Regarding to functional outcome, those patients with seizures did no show a higher disability evaluated with Barthel Index and Rankin scale score. 69.5% were under control using monotherapy. With regard to EEG, we could describe some abnormalities (intensity/distribution), allowing us to establish the chronology of epileptogenic features and predict the development of seizures in these patients.

Conclusion: 53.1% of patients with malignant MCA ischemic stroke developed seizures. Its appearance was related to a longer time in the completion of craniectomy. The performance of serial EEG may help to predict the development of seizures in these patients.

p473

SEIZURE IN PATIENTS WITH ANTI-GAD ANTIBODIES

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Purpose: Anti-GAD (glutamic acid decarboxylase) antibodies are associated with refractory partial seizures and stiff person syndrome (SPS). We examined the clinical features and outcome of patients with anti-GAD antibodies and seizures.

Method: Four patients had anti-GAD antibodies and seizures. Seizure type, clinical features, comorbidity, anti-GAD titer, other autoimmune antibodies, MRI, EMG, EEG, treatment methods and outcomes were evaluated.

Result: All patients were female, had complex partial seizures (CPS) with an average frequency of 4×/month beginning between ages 26–42. One patient with hyperthyroidism and newly diagnosed diabetes (DM) complained of oscillopsia and gait instability. One patient with hypothyroidism and newly diagnosed insulin dependent DM had truncal stiffness; EMG showed SPS. The other two had no comorbidities.

The serum anti-GAD titers ranged from 30 to 236 U/ml. Three patients had elevated thyroperoxidase or thyroglobulin antibody. Malignancy workup was unrevealing. EEG findings were consistent with temporal lobe seizures. MRI revealed mesial temporal sclerosis in two patients and increased hippocampal signal in a third patient.

The patient with oscillopsia failed two anticonvulsants and was seizure-free after IVIG therapy. The patient with SPS failed four anticonvulsants but became seizure-free after steroid treatment for 6 weeks. The third patient who failed six anticonvulsants became seizure-free on lacosamide. The fourth did not respond to immunotherapy and had surgical resection with moderate benefit.

Conclusion: Immunotherapy successfully treats seizures in some patients with anti-GAD antibody syndrome. Patients with the antibody should be evaluated for endocrine disorders and SPS if they complain of stiffness.

p474

PREGNANCY OUTCOMES OF WOMEN WITH EPILEPSY

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Purpose: To analyze the course of pregnancy and its outcomes in 111 women with epilepsy (WWE) with planned and unplanned pregnancy; to evaluate psychomotor and speech development of 30 children born to mothers with epilepsy.

Method: The pregnant women were stratified into two subgroups: subgroup I (n = 57) consisted of women who were prepared for pregnancy by the epileptologist; subgroup II (n = 54) included women with unplanned pregnancy. The management of WWE included: seizures control, serum concentrations of AEDs, analyze of system hemostasis and EEG every trimesters; evaluation of maternal serum alpha fetoprotein, dynamic ultrasound examinations. Psychomotor and speech development of 30 children aged from 6 month to 3.5 years born to mothers with epilepsy were studied.

Result: Seventy-eight percent of WWE from subgroup I had remission of epilepsy during pregnancy comparison 40% of WWE with unplanned pregnancy from subgroup II respectively. Frequency of cesarean section in subgroup I – 38%; in subgroup II – 54%; in control group – 22.5%. There were two major congenital malformations in the 111 pregnancies detected by ultrasound examination. No significant difference was found in the performance on the Bayley-III scales between children born to mothers with epilepsy and children born to healthy mothers (controls) though the scores on the fine motor scale and speech development scale were lower in 3(10%) and 5(16%) children of the index group, respectively.

Conclusion: The comparative study of the pregnancy course in these subgroups revealed that in subgroup I the compliance to treatment was higher and pregnancy and delivery were more successful as compared to subgroup II. Preparing for pregnancy and its planning together with epileptologist allows to control for seizures using minimal doses of AED and decreases pregnancy and delivery complications.

Poster session: Adult epileptology VIII
Tuesday, 30 August 2011

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UNUSUAL OR UNRECOGNIZED SEIZURE TRIGGERS IN PATIENTS WITH REFRACTORY FOCAL EPILEPSY

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Purpose: To identify unusual seizure triggers in patients with refractory focal epilepsy.

Method: In consecutive adults studied in our epilepsy center from February 2009–March 2011, a structured questionnaire focused on seizure triggers was carried out. Patients, family or witnesses were requested for presumed relationship between any kind of stimulus and seizures. A complete set including simple/complex auditory, visual, and cognitive stimulation, and somatosensory stimuli was applied. If possible, particular triggers were used during video-EEG monitoring. We analized epidemiologic/clinical data, structural/functional neuroimaging, and video-EEG monitoring results, including invasive EEG in four patients.

Result: Eighteen patients were recruited, 50% women. Mean age at study: 32-year-old (18–55); mean age at seizure onset: 13.9 (6 month–35-year-old). Most frequent epileptogenic focus was localized in temporal lobe (66.7%). Unusual triggers were identified in 77.8% of patients, ≥2 in 50% of them. They included seeing prisms, faces, animals or cooked food, illusory motion, using iPhone, listening to the clock tic-tac, noises or music, drinking soda, eating, smiling, smelling specific foods, cold/hot sensation, staying at crowded places, and sleep apneas. Many triggers could be documented during video/EEG monitoring because they provoked electrographic/electroclinical seizures. Some patients were not aware of their triggers before this study.

Conclusion: In this series we identified several unusual or unrecognized seizure triggers. They are probably underestimated for lack of physician awareness or insufficient observation by patients/witnesses. Epileptogenic triggers are possibly anywhere and some of them can be difficult to identify. Their recognition can be important in presurgical studies and for therapeutic reasons.

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PATIENTSLIKEME® EPILEPSY COMMUNITY: AN INSIGHT INTO SYMPTOMS AND SIDE EFFECTS REPORTED ONLINE BY PATIENTS WITH EPILEPSY

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Purpose: To describe the symptoms and side effects reported by patients with epilepsy on the free online PatientsLikeMe® platform.

Abstracts

Method: The PatientsLikeMe® platform (launched January 2010 in the USA) allows patients with epilepsy to record, monitor and share their treatments, symptoms and seizure frequency/severity. The platform was built to facilitate entry of predefined symptoms (memory problems, problems concentrating, fatigue, somnolence, headache, insomnia, anxiety, depression, pain) and perceived side effects and to rate their severity (normal-mild-moderate-severe).

Result: By September 2010, 1838 users diagnosed with epilepsy had registered (mean age: 36.5 years; 71.7% female; mean duration since diagnosis: 16.7 years) and 1341 (73.0%) completed the symptoms list.

Of the patients who completed the list of symptoms, 74.4% had AED treatment data available (54.7% on polytherapy; 52.9%, newer AED(s); 17.4%, older AED(s); 29.7%, newer and older combined).

At the first symptom assessment, 88.1% reported ≥1 moderate/severe symptom(s) [36.5% between 1 and 3 symptoms, 36.1% between 4 and 5, 15.5% between 7 and 9]; symptoms most frequently reported as moderate/severe: memory problems (60.5%), problems concentrating (53.4%), fatigue (49.5%), and somnolence (42.5%).

Only 20.6% of the users perceived side effect(s) they associated with treatment; most frequently fatigue and somnolence.

Conclusion: Cognitive problems, fatigue and somnolence were the symptoms most frequently reported as moderate/severe by the PatientsLikeMe® Epilepsy Community members. Use of a predefined list allows a standardized and systematic assessment of important symptoms. It also provides patients with the opportunity to record and follow the main symptoms they experience, which can be taken to their doctor to help guide the consultation.

UCB-Sponsored.

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DEPRESSION EVALUATION OF PATIENTS WITH EPILEPSIA THROUGH BDI-II QUESTION FORM

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Purpose: Introduction and goal of this paper is to demonstrate prevalence, data, method of treatment and risk factors for depression apearance of epilepsy patients.

Method: Ambulatory patients which were checked up regularly during the period of 2 months have filled up two question forms: BDI-II which purpouse is to evaluate existance, severity of depression symptoms and questionary with demographic data, clinical features of epilepsy and medical treatment.

Result: We examined 252 patients: male patients 48.8%, middle age 43 ± 16 years, presence of epilepsia 13.3 ± 11 years). Scores of BDI-II for our examinees are: minimum depression 59%, mild 15%, moderately 14% and severe depression 12%. The procentage of persons which took antidepressives according to categories of depression was: minimum 5.4%, mild 26.3%, moderately 20%, severe 54.8%. In statistic we used hi-quadrat test. Group with moderate and hard depression are consolidated (N = 66) and comparated with rest of examinees (N = 186). That consolidated group (N = 66) took antidepressives more often ($p < 0.01$), they were poor educatated ($p < 0.01$), had epileptic seizures more often ($p < 0.01$), and were older than 40 years ($p < 0.01$). There was not found any larger statistical differences regarding to the lenght of epilepsia, number of antiepileptics used, appearance of generalized convulsive seizures and social categories: marital status, parenthood, employment, ownership of drivers license.

Conclusion: Relatively high percentage of depression at epilepsy patients shows a need for multidisciplinar diagnostic and therapeutic procedures. Some of risc factors for depressive disorder are poor epilepsy controle, eldery age and poor education.

p478
EPILEPTIC AND NONEPILEPTIC PANIC ATTACKS: HOW TO GET THE MOST ACCURATE DIAGNOSIS?

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Purpose: Panic may represent the most relevant finding during an epileptic seizure or a severe anxious syndrome. Distinction between the two different pathologies may not be easy, expecially when seizures and anxiety display similar symptoms mimicking each other in the same patient; moreover, epileptic patients may have a chronic anxious disorder. We analyzed retrospectively a group of epileptic patients showing ictal fear, to identify possible diagnostic criteria.

Method: We studied six patients (four females; age range 17–31 years), showing paroxysmal episodes with panic symptoms; two were suspected to have severe anxious syndrome with panic attacks. Each patient underwent accurate anamnestic interview, long-term video-EEG monitoring, cerebral MRI. Ictal symptomatology was analyzed and discussed with the patients and their caregivers.

Result: In all patients, epileptic seizures were recorded. Two showed only seizures with panic despite of a first diagnosis of psychogenic episodes; four patients revealed both panic attacks and epileptic seizures with fear. Four patients showed right temporal and two left temporal seizures. MRI highlighted mesial temporal sclerosis in three cases, dysplasia of the right amygdala in one case, no abnormality in two cases.

Conclusion: Video-EEG monitoring was crucial to get the right diagnosis. The seizures with panic were all temporal and the majority right temporal.We shared our results with patients and caregivers, obtaining a significant decrease of nonepileptic panic attacks. We suggest a common neuronal circuitery (expecially amygdala and limbic structures) involved in panic emotions, that can be activated either in epileptic and nonepileptic disorders.

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EPILEPSY SINCE ANTIQUITY UNTIL THE PRESENT: A SHORT WALK THROUGH THE HISTORY OF THE "SACRED DISEASE"

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Epilepsy is considered to be one of the most ancient afflictions known within the neurological area of medicine. Epilepsy is a chronic neurological condition and brain disturbance, characterized predominantly by recurrent, unpredictable and unprovoked interruptions of normal brain function called epileptic seizures. This condition is due to excessive discharges from a group of cerebral neurons being associated with a variety of clinical disturbances and laboratory manifestations. Every human being and/or animal can be a potential epileptic. Nowadays approximately 60 million of people are affected by epilepsy worldwide.

Authors of antiquity spoke of epilepsy or of an epileptic fit whenever a person's senses were abruptly suspended or seized and this concept of epilepsy has remained virtually unchanged even today. For many centuries, a cloud of fear, superstition and prejudice have shrouded epilepsies.

The purpose of this presentation is to propose in-depth outline of the history of epilepsy, also known as "Falling sickness" or the "Sacred disease." This presentation also presents a large number of famous or outstanding in their way persons suffering from epileptic seizures and what has been changed in the diagnostic and treatment approaches to epilepsy in the course of successive historical periods from the dawn of human civilization to our days, taking us through Antiquity (the Archaic period, the Classical period, the Hellenistic period, the Roman period), the Middle Ages (the Old period, the First Medieval Period, the Second Medieval Period), the Renaissance until the Modern era and present day efforts.

Diagnosis and treatment methods have been improved but there are still no curative medicines, at least none to be universally effective and while desperation in this area of knowledge still exists, the stigma of epilepsy has generally been diminished to a great extent in the perception of modern communities.

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CLINICAL PROFILE OF PSYCHOGENIC NONEPILEPTIC SEIZURES: A STUDY OF 60 CASES

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Purpose: To study the clinical, video-EEG profile, psychiatric comorbidity and outcome of patients with Psychogenic Nonepileptic Seizures (PNES).

Method: All patients with clinical suspicion of PNES were confirmed by induction during video-EEG monitoring, and evaluated for psychiatric comorbidities. After proper disclosure of diagnosis, nonstructural psychotherapy and appropriate medication follow up was done at 6 and 12 months period.

Result: Among 60 patients, 52 (87%) were females and 8 (13%) males; mean age 28 years (14–55 years), and mean duration of illness 18 months (1 week–12 years). Thirteen percent had coexisting epilepsy, presenting with refractory seizures, 37% had PNES and were on antiepileptic drugs, while 47% were not on any treatment. Duration and frequency of attacks was variable. Patients were divided; Group A—motor attacks, 35%; Group B—limp attacks, 52%, and Group C—limp with motor phenomenon, 12%. Common features were headache 90%, resistant behavior 77%, eyes closure 74%, partial responsiveness 70%, teeth clenching 55%, and waxing-waning pattern in 44% patients. Comorbid depression was seen in 90%, anxiety 58%, and somatoform disorder in 37%. At 6 months, out of 30 patients; 13 were asymptomatic, 13 partially improved while four remained the same. Further followup of 13 asymptomatic patients at 12 months, four remain asymptomatic, while nine patients had relapse. Seven patients were lost to followup while 23 had followup of only 2–3 months.

Conclusion: PNES is common, but frequently underdiagnosed. A high index of clinical suspicion and confirmation by video-EEG is diagnostic. An early diagnosis, identification and treatment of comorbid factors can improve their outcome.

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ICTAL TRIPHASIC WAVES UNMASKED BY GABAPENTIN WEANING MANIFESTING AS INCREASED CONFUSION WITH EMOTIONAL LABILITY: CASE REPORT WITH LITERATURE REVIEW

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Purpose: Antiepileptic drugs (AEDs) are frequently used off-label for the treatment of psychiatric and pain disorders. Weaning AEDs may reveal seizure disorders and underlying EEG abnormalities leading to a clearer understanding of ictal neuropsychiatric presentations. This case addresses off-label gabapentin masking ictal activity.

Method: Case analysis with literature review.

Result: A 78-year-old woman with history of diabetes, peripheral neuropathy, coronary artery disease, hypertension, chronic obstructive pulmonary disease, transient ischemic attacks, recurrent urinary tract infections, lower back pain, and depression presented with altered mental status (AMS). There was no history of epilepsy. Admission Folstein Mini-Mental Status Examination (MMSE) was 25/30. Her outpatient medication regimen was complex and included gabapentin 600 mg twice daily for neuropathy/pain and escitalopram 20 mg daily for depression. Laboratories were unremarkable and did not suggest a metabolic, infectious, or toxic basis for her AMS. CT scan of the head revealed mild small vessel ischemic disease and chronic right thalamic infarction. Routine EEG revealed intermittent triphasic waves. To better ascertain the etiology of her intermittent confusion, the patient was evaluated with video-EEG monitoring and her gabapentin was weaned. Upon weaning, her triphasic waves became continuous and rhythmic at 2 Hz with accentuated sharp components consistent with an ictal pattern. Her confusion worsened and she had increasingly frequent episodes of emotional lability and aphasia, correlating with electrographic findings and suggesting an ictal origin for her neuropsychiatric symptoms. Gabapentin was restarted with electrographic resolution of seizure activity. She was discharged on gabapentin 800 mg three times daily with significant improvement in both her clinical condition and electrographic findings with a MMSE of 30/30.

Conclusion: AEDs are often used off-label for psychiatric and pain disorders. It is important to realize that their use in such circumstances might mask an unusual clinical presentation of seizure activity, as this case demonstrates. Weaning AEDs with concurrent video-EEG monitoring is an important diagnostic tool in these complex cases.

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A PROVABLE DIAGNOSIS OF EPILEPSY BASED ON BOOLEAN LOGIC AND THE INTERNET

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p483
AN APPARENT SYMPTOMATIC FOCAL EPILEPSY IN A PATIENT WITH MALIGNANT INSULINOMA ASSOCIATED TO GLUCAGONOMA

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Purpose: We report a young male patient presenting initially with an apparent seizure disorder and then with bizarre behavior.

Method: Result: After 8 years a large and malignant pancreatic lesion was detected. The MRI finding was a left frontal developmental venous anomaly and the interictal EEG showed a left focal activity with enhanced response to hyperventilation. Initially he was misdiagnosed as symptomatic focal epilepsy and anticonvulsivant therapy revealed not effective. After seven years he developed neuropsychiatric symptoms and a subsequent endocrine evaluation suggested insulinoma. MRI abdomen showed a large mass in the head of pancreas and histopathological evaluation revealed a malignant insulinoma associated with multiple nodules of glucagonoma. After surgical intervention, the patient became seizure-free, neuropsychiatric symptoms disappeared and antiepileptic drugs were progressively stopped. Insulinoma is a rare endocrine disease and commonly it is misdiagnosed because of unspecificity of its symptoms. In this case the association with glucagonoma probably masked altered blood glucose level for a long time.

Conclusion: This case highlights the need for a careful evaluation of all drug-resistant seizures, especially if associated with neuropsychiatric symptoms, even if there are epileptiform discharges on EEG and compatible lesions on neuroradiological imaging.

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SUDEP AFTER EPILEPTIC SEIZURE IN LIMBIC ENCEPHALITIS CAUSED BY ACUTE MYOCARDIAL ISCHEMIA DOCUMENTED BY AUTOPSY

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Purpose: SUDEP is the most common seizure-related cause of death in epilepsy, and usually occurs after convulsive seizures. It has been postulated that SUDEP is the result of respiratory arrest after a seizure although cardiac arrhythmias may be also thought responsible for a proportion of cases. We described a case of SUDEP after epileptic seizure caused by acute myocardial ischemia in a patient with limbic encephalitis.

Method: This 55-year-old male patient with rapidly progressive psycho-organic syndrome, characterized by behavioral changes, memory loss, involuntary movements and drug resistant epileptic seizures, was investigated using EEG, MRI, neuropsychological evaluation, serological tests by cerebrospinal fluid and serum (antibodies to VGKC) and after his sudden death, caused by heart attack following a seizure, by autopsy.

Result: The EEG recordings showed interictal and ictal predominantly left temporal epileptic abnormalities. MRI revealed increased left hippocampal T_2-weighted signal. Neuropsychological evaluation showed widespread cerebral dysfunction (attention, executive functions, verbal and visuo-spatial memory, language) mainly involving the fronto-temporo-parietal areas of the left hemisphere. We detected the presence of antibodies to VGKC (290.60 pM). The autopsy revealed interfibrillar granulocytes aggregates (suggestive of myocardial ischemia) in the territory of the a coronary descendant anterior. The neuropathological findings (perivascular cuffing, with mainly CD8-positive lymphocytes, in the amygdale and hippocampus, basal nuclei and basal telencephalus, moderate reactive astrocytosis, mild neuronal loss in the hippocampus) were consistent with limbic encephalitis.

Conclusion: We would like to discuss the possibility that recurrent drug resistant seizures related to the limbic encephalitis could have provoked a cardiomyopathy (''takotsubo cardiomyopathy'' caused by impaired coronary microcirculation induced by abnormal catecholamine release) with acute myocardial ischemia.

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NO EVIDENCE FOR LACOSAMIDE BINDING TO COLLAPSIN RESPONSE MEDIATOR PROTEIN 2 (CRMP-2)

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Purpose: Lacosamide (LCM, SPM 927, Vimpat) is a new antiepileptic drug recently approved in the USA and Europe as add-on treatment for partial onset seizures. LCM presents a novel mode of action by selectively enhancing sodium channel slow inactivation and was previously reported to bind to CRMP-2. In the present study we investigated the potential binding of LCM to the cloned CRMP-2 protein.

Method: The cloned human CRMP-2 protein was transiently expressed in a variety of mammalian cells and *Xenopus laevis* oocytes. Specific binding of [^{3}H]LCM was assessed on isolated and membrane bound CRMP-2 protein using classical filtration binding assays or scintillation proximity assays. The binding of unlabelled LCM to CRMP-2 was investigated by surface plasmon resonance and x-ray crystallography.

Result: The hCRMP-2 protein was efficiently expressed in membrane fractions from mammalian cells and *Xenopus* oocytes and binding of [^{3}H]LCM was investigated under various experimental conditions. We observed no specific binding of [^{3}H]LCM to the hCRMP-2 protein expressed in membrane fractions or to the isolated tagged hCRMP-2 protein under all experimental conditions tested. Biacore analysis showed that LCM over a concentration range of 0.39–100 μM does not specifically bind to the hCRMP-2 protein. LCM (5 mM) did not cocrystallize with the CRMP-2 protein.

Conclusions: Although the methods used in this study were well suited to measure the binding of LCM to CRMP-2, the results obtained were all negative. In conclusion, the present study does not support the presence of a specific binding site for LCM on the hCRMP-2 protein.

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FIRST OCCURRENCE OF PSYCHOGENIC NONEPILEPTIC SEIZURES DURING PRESURGICAL VIDEO-EEG MONITORING

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Purpose: The coexistence of psychogenic nonepileptic (PNES) and epileptic seizures (ES) is a well-known phenomenon and reported in 5–20% of the ES population. Long-term video-EEG monitoring is the gold standard for differentiating ES from PNES. However, the usefulness of provocation procedures is debatable. We report on six female patients with drug resistant epilepsy who developed PNES for the first time of their life during video-EEG monitoring for presurgical evaluation.

Methods: We reviewed the video-EEG recordings, medical reports, and neuropsychological data of these six patients. We showed the recorded ES and PNES to the patients and their relatives to confirm that the ES were the habitual seizures whereas the PNES never had been observed before.

Result: Age ranged from 17 to 49 years. Five patients had a structural, one a metabolic epilepsy. Clinical features of PNES were definitely different from ES semiology. Simultaneous EEG recording helped clearly to distinguish ES from PNES. All except one patient had psychiatric comorbidities.

Conclusion: The pressure to ''deliver'' seizures in the artificial lab situation represents an enormous stress factor for some patients, which may result in the first and maybe unique occurrence of PNES. Even if our observation comprises only a small series of patients, it indicates that one should be careful with the use of provocation techniques (e.g., intravenous placebo infusion) to induce PNES because the results may be misleading. The precise knowledge of the patient's history and the involvement of eyewitnesses are crucial for the accurate diagnosis.

Poster session: Adult epileptology IX
Tuesday, 30 August 2011

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EPILEPSY IN ELDERLY PATIENTS WITH DEMENTIA

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Purpose: Patients with dementia have an increased risk of newly diagnosed epilepsy. The aim of our study was to characterize seizure type, diagnosis of dementia, EEG, imaging and therapy in elderly patients with epilepsy and dementia.

Method: Patients with epilepsy and dementia referred to our epilepsy centre were retrospectively analyzed. Clinical characteristics, Mini Mental State Evaluation (MMSE), CT scanning or MRI of the brain, EEG, treatment outcome, were extracted from patient chart.

Result: Thirty-one elderly patients (18 females, 13 males) with a mean age of 77.94 years (range: 60–92) were included in the study. The mean MMSE score was 15.58 (range: 10–23). Seventeen patients (54.8%) received a diagnosis of Alzheimer's disease (AD). Eleven patients (35.6%) had complex partial seizures, nine patients (29%) had generalized tonic–clonic seizures, nine patients (29%) had complex partial seizures and generalized tonic–clonic seizures. Fifteen patients (53.6%) had cortical atrophy on CT scan. EEG recording showed epileptiform discharges in 22 patients (71%) and slow waves in nine patients (29%). The antiepileptic drug therapy administered included lamotrigine in 12 patients (39%), levetiracetam in eight patients (26%), carbamazepine in seven patients (22%), valproic acid in three patients (10%), phenobarbital in one patient (3%). Twenty-seven patients (87%) were seizure-free for at least 1 year.

Conclusion: The results of our study indicated that in elderly patients with dementia and epilepsy, complex partial seizures are the most frequent seizure type. AD is the most common diagnosis of dementia and seizures occur few years after the onset of cognitive impairment. The patients may be adequately controlled on AED therapy.

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IMPROVED SLEEP QUALITY IN MEDICALLY REFRACTORY PATIENTS UNDERGOING EPILEPSY SURGERY—A CLINICAL AND POLYSOMNOGRAPHIC STUDY

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Purpose: To evaluate the change in sleep quality in medically refractory patients undergoing epilepsy surgery.

Method: In a prospective cohort study, we recruited medically refractory epilepsy patients (who were to undergo epilepsy surgery) from Intractable Epilepsy Clinic at AIIMS, New Delhi. All the patients were assessed pre- and (3 months) postoperatively with history pertaining to epilepsy and sleep related events and Epworth sleepiness scale (ESS). All patients filled 1 week sleep logs followed by underwent overnight Polysomnography (PSG) pre- and postoperatively.

Result: Among 17 patients [mean age 18 (10–35) years, 11 males], the self reported clinical sleep parameters had significantly improved 3 months following epilepsy surgery [improved total duration of night time sleep, regularity on 7 days sleep log and ESS ($p < 0.05$)].

Patients with good surgical outcome (n = 12) had lower ESS postoperatively and PSG sleep quality also showed a corresponding increase in total sleep time and lower arousal index ($p < 0.05$) postoperatively, with four patients (25%) showing >50% reduction in their postoperative arousal index. While among the patients with poor surgical outcome (n = 7), there was no significant change either in self reported clinical or PSG parameters.

Two out of eight good surgical outcome patients (25%) with ESS >10 (marker of Excessive daytime sleepiness) showed lower ESS (<10) following surgery. Two patients with preoperative apnea-hypopnea index (AHI) >5 (marker of obstructive sleep apnea) had marked reduction in AHI (<5) following surgery, both were lying in good surgical outcome group.

Conclusion: Our results indicate that there is overall improvement in self-reported clinical sleep parameters in all patients who undergo epilepsy surgery. Among the patients with good surgical outcome, there is remarkable improvement in polysomnographically documented night time sleep quality with resulting reduction in excessive daytime sleepiness.

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EYE CLOSURE SENSITIVITY IN A POPULATION OF JUVENILE MYOCLONIC EPILEPSY

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Purpose: "Eye closure sensitivity" (ECS) is a temporary epileptiform change in EEG that immediately follows the eye closure. It lasts <3 s and induces EEG changes mainly generalized, appearing within 2–4 s after closing the eyes and usually lasting 1–4 s.We aimed to study a population with Juvenile Myoclonic Epilepsy (JME) in order to determine the electroclinical features of this phenomenon.

Method: Patients monitored from January 1999 to December 2008, with diagnosis of JME, were screened retrospectively for the presence of ECS. We identified two subgroups: patients with eye closure sensitivity (ECS+) and patient without this condition (ECS−). We compared family history, clinical and EEG data, treatment and outcome of both groups.

Result: We considered 139 JME patients (92 women and 47 men; mean age 32 ± 9.8). Thirteen seven patients (26.6%) had ECS (29 women, eight men; aged 29.9 ± 9.7) and 102 patients had not ECS, (63 women, 39 men; aged 33 ± 9.7). Photoparoxysmal response to intermittent photic stimulation in EEG recording was detected in 54% of ECS+ and in 23.5% of ECS−. The frequency of seizures in ECS+ was higher (monthly in 32.4%) than in ECS− (sporadic in 42.1%). Fifty-four percent of patients with ECS+ were responsive to monotherapy whereas 80% of patients with ECS− were unresponsive.

Conclusion: ECS is presented by 26.6% of JME patients and associated to epileptic events during daily activity. Patients with ECS also presented more frequent seizures than patients without ECS and had a poorer response to monotherapy.

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HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH NOCTURNAL FRONTAL LOBE EPILEPSY COMPARED WITH TEMPORAL LOBE EPILEPSY PATIENTS

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Purpose: To compare health-related quality of life (HRQoL) in nocturnal frontal lobe epilepsy (NFLE) and temporal lobe epilepsy (TLE) patients.

Method: Twenty-eight NFLE patients and thirty-one TLE patients self-administered the 36-Item Short Form (SF-36). The scoring of the eight scales (physical functioning PF; role functioning-physical RP; bodily pain BP; general health GH; vitality VT; social functioning SF; role functioning-emotional RE; mental health MH) and the two overall physical (PCS) and mental domains (MCS) of the SF-36 were calculated. Scale scores were compared with the Italian SF-36 normative data, and the standard scores (z-scores) calculated. Each score equal to the normative mean is equivalent to z-scores of zero, while the positive and negative points are higher or lower than the normative mean respectively.

Result: No SF-36 scales differed between the two groups. The following scales were lower than the values of Italian normative data: RP −0.54 ($p = 0.021$), GH −0.51 ($p = 0.023$), RE −0.59 ($p = 0.019$) in the NFLE

group; RP −0.60 (p = 0.010), VT −0.62 (p = 0.008), RE −0.51 (p = 0.010), MCS −0.56 (p = 0.009) in the in TLE group. According to multivariate linear regression the response to therapy correlated with the PCS and MCS without a ''type of seizure'' effect.

Conclusion: NFLE has some limitations on HRQoL, namely the domains pertaining to the patients' family and social role, and their experience of the illness. No major differences were found with TLE. Response to therapy may play a role in both groups.

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EFFECT OF JUVENILE MYOCLONIC EPILEPSY ON SLEEP: A POLYSOMNOGRAPHIC STUDY

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Purpose: Juvenile myoclonic epilepsy (JME) is an idiopathic sleep sensitive epilepsy in which the effect of seizures on sleep could have therapeutic implications on sleep quality and seizure control. This study analyzed the effect of epilepsy on sleep in JME using polysomnography (PSG).

Method: Twenty-five patients (M: F = 13:12) aged >12 years on valproic acid (VPA) monotherapy and matched controls (M: F = 16:9) were recruited for this prospective, hospital based, case control study. All patients underwent clinical assessment, electroencephalogram (EEG) and neuroimaging, and all subjects underwent PSG.

Result: There were no significant differences between the patient and control group with regard to age, gender and body mass index (BMI). The clinical profile of JME was similar to published literature while the prevalence of EEG abnormalities was less compared to similar studies. A high prevalence of VPA adverse effects was noted. PSG revealed significant alterations in sleep architecture in the JME group in the form of reduced mean sleep efficiency [p < 0.035] and number of patients with reduced sleep efficiency [p = 0.001], increased mean sleep onset latency [p = 0.039] and number of patients with increased sleep latency [p = 0.023], reduced mean stage 2 sleep percentage [p = 0.005] and reduced mean total NREM (non–rapid eye movement) sleep [p = 0.001] and increased mean wake percentage [p = 0.001].The frequency of arousals, involuntary limb movements, and event related arousals in the JME groups was not different from the controls. Patients older than 20 years had reduced total sleep time compared to younger patients (p = 0.012). Patients with seizures for >5 years had reduced NREM sleep percentage (p = 0.042) and those on VPA therapy >1 year had a longer stage 2 (p = 0.03) and stage 3 latency (p = 0.029). Patients on ≤600 mg/day of VPA had a higher prevalence of isolated limb movements (p = 0.010).

Conclusion: Patients with JME have significant sleep disturbances noted on polysomnography, despite adequate medications and good seizure control.

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SLEEP ABNORMALITIES IN JUVENILE MYOCLONIC EPILEPSY: A SLEEP QUESTIONNAIRE–BASED STUDY

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Purpose: Sleep and epilepsy share a complex pathophysiological association. Juvenile myoclonic epilepsy (JME) is a common sleep sensitive epilepsy in which the effect of seizures could have therapeutic implications in terms of sleep disturbances and seizure control. This study aimed to analyze the effect of epilepsy on sleep in patients with JME.

Method: Fifty patients on valproic acid (VPA) monotherapy and age and gender matched controls were recruited into this prospective, hospital based, case control study after informed consent and screening for inclusion criteria. They underwent a detailed clinical assessment, electroencephalogram (EEG) and neuroimaging, and were administered validated sleep questionnaires, which included the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI) and NIMHANS Sleep Disorders Questionnaire.

Result: The patient and control group had identical number of males and females (M: F = 22: 28), without any significant difference in the age and body mass index (BMI). The clinical profile of JME was similar to published literature while the prevalence of EEG abnormalities was less compared to similar studies. The mean ESS and PSQI scores and the number of subjects with abnormal scores on one or both questionnaires was significantly more in patients. Patients had a higher prevalence of sleep disturbances, insomnia and excessive daytime somnolence. No significant seizure or treatment related factors influencing sleep could be identified. A high prevalence of VPA adverse effects was noted.

Conclusion: Patients with JME have significant sleep disturbances characterized by excessive daytime sleepiness and disturbed night sleep, despite adequate medications and good seizure control. The role of VPA in the genesis of these symptoms needs clarification.

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SUBJECTIVE SLEEP DISTURBANCE IN PATIENTS WITH EPILEPSY

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Purpose: To determine the (1) prevalence of sleep disorders, (2) the effects of clinical variables on the sleep disorders, and (3) their impact on QOL in adult patients with epilepsy (PWE).

Method: Data were collected from 181 adult PWE and 157 unselected controls without epilepsy. The Medical Outcomes Study (MOS) Sleep Scale, Epworth sleepiness scale (ESS), Sleep Apnea scale of the Sleep Disorders Questionnaire (SA/SDQ) were used. We measured symptoms of anxiety, depression, and quality of life with Hospital Anxiety and Depression Scale (HADS) and Quality of Life in Epilepsy-10 instrument (QOLIE-10). We also evaluated restless legs symptoms and insomnia.

Result: PWE demonstrated significantly poorer sleep scores than controls in the categories of Disturbance (p = 0.003), Snoring (p < 0.001), Shortness of Breath/Headache (p < 0.001) and other problems index 1 (p = 0.006) and 2 (p = 0.002) in MOS Sleep Scales. Among PWE, having seizures was associated with shortness of breath/headache (p < 0.001), somnolence (p = 0.015) and general sleep problems (p = 0.027) than seizure-free patients; antiepileptic polytherapy was associated with sleep disturbances (p = 0.03) and general sleep problems (p = 0.006). 23.2% (42/181) of PWE and 16.6% (26/157) of controls had elevated ESS scores (p = 0.09). RLS was found in 6.6% (12/181) of PWE and 5.1% (8/157) of controls. Among PWE, RLS was significantly higher in women than men (15 vs. 4, p = 0.015) and those who reported to have restless legs symptoms ''almost always (6–7 times per week)'' were significantly higher in PWE than controls (p = 0.03). Insomnia was reported in 34.8% (63/181) of PWE and 17.2% (27/157) of controls. It was significantly higher in PWE than controls (p < 0.001), especially in difficulty initiating (p = 0.01) and maintaining (p = 0.03) sleep. Poorer QOL was shown in PWE with poorer MOS sleep scores (p < 0.001) and elevated ESS score (p = 0.001).

Conclusion: Sleep disturbances are frequent in PWE and are associated with impaired QOL. Sleep should be evaluated and any disturbance should be treated as a part of epilepsy management.

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DOES AGE AT SEIZURE ONSET INFLUENCE THE NATURAL HISTORY OF JUVENILE MYOCLONIC EPILEPSY?

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Purpose: Juvenile myoclonic epilepsy (JME) is considered as an IGE syndrome with life-long duration. However, recent reports and a previous study from our clinic have stressed the variability in the natural course of JME, even suggesting the existence of patients who may achieve long-term remission. We aimed to explore the predictable role of the age at onset of seizures on the natural history of JME.

Method: We studed retrospectively all JME patients attending our epilepsy clinic since 1989. Included patients had to have a definite diagnosis of JME based on myoclonic jerks (MJ ± GTCS, ± typical absenses (TAs), EEG and/or video-EEG recordings showing generalized 3–6 Hz sw discharges, normal intelligence/neuroimaging. We performed correlations between age at onset of seizures and outcome.

Result: Inclusion criteria for JME were met by 170 (106 women) consecutive patients. Their mean ± SD age is 31.0 ± 9.9 (range: 14–72) years. Mean ± SD follow-up has been 7.3 ± 4.7 years, with 110 patients being followed for ≥5 years. Three patient groups were identified: (1) a ''classical'' group (155 patients) with good response to treatment, (2) a ''resistant'' group (six patients) with persisting seizures despite AED polytherapy, and (3) a third group ''in-remission'' (nine patients), showing long-term seizure freedom (mean: 13 years) despite AED discontinuation. No significant differences were found between age at MJ onset among the three patient groups (15.1: 14.1: 12.7 years of age respectively). GTCS usually started around the same age as MJ and were present in 142 patients of group (a), five patients of group (b), and five patients of group (c). TAs, although present in 26% in group (a), were persistent in the ''resistant'' group, and rarely seen (one patient) in the group ''in-remission.''

Conclusion: Age at seizure onset does not seem to be prognostically related to the evolution of JME. However, other factors, like predominant seizure type may be significant, as absence of GTCS and TAs was observed in patients with favorable outcome with long-term seizure freedom (pure myoclonic form?).

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ANALYSIS OF DAYTIME SLEEPINESS AND SLEEP QUALITY IN REFRACTORY TEMPORAL LOBE EPILEPSY PATIENTS

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Purpose: To evaluate excessive daytime sleepiness and sleep quality in a cohort of patients with refractory temporal lobe epilepsy in an epilepsy comprehensive center.

Method: Fifty-one consecutive patients with diagnosis of epilepsy according to the ILAE criteria were evaluated with a questionnaire including clinical-demographic variables, the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS) and the Stanford Sleepiness Scale (SSS). The data were compared to a control group (n = 44), matched by gender, age, handedness and socioeducational level. The scores were analyzed according to antiepileptic drugs (AED) in use and seizure frequency.

Result: All the patients had the diagnosis of mesial temporal lobe epilepsy, 96% associated to hippocampal sclerosis and 57% were in monotherapy. Seventy-two percent of patients were taking carbamazepine. Patients with epilepsy (PWE) presented higher ESS scores compared with normal controls (p = 0.02). Regarding sleep quality (PSQI), PWE presented higher scores in the ''daytime dysfunction'' domain (p = 0.004). No correlation was found between the scores and AED class, number of drugs in therapy and seizure frequency.

Conclusion: PWE present daytime sleepiness and sleep quality impairment.

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A LONG-TERM FOLLOW-UP STUDY OF 100 PATIENTS WITH NOCTURNAL FRONTAL LOBE EPILEPSY (NFLE)

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Purpose: This study analyses the clinical and prognostic features of 100 patients (pts) with NFLE after a long follow-up.

Method: We selected 100 pts with NFLE according to this criteria: a history of nocturnal seizures suggesting frontal lobe involvement, video-polysomnographic recording of at least one major episode (hypermotor or tonic seizures) or two stereotyped paroxysmal arousals, a follow-up period longer than 5 years and last visit within the last 24 months. All pts underwent a clinical, neuroradiological and neurophysiological examination. On the basis of seizure frequency at the last visit our population was divided into two groups: Negative Evolution (NE- seizure varying from daily to pluri-yearly) and Positive Evolution (PE- seizure-free for at least 1 year or with sporadic seizure).

Result: The final population of 100 pts (62 males) had a mean age at onset of epilepsy of 13.3 ± 10.4 years; the mean of follow-up was 12.9 ± 6.9 years. Most pts (64%) presented hypermotor seizures, 28% presented tonic asymmetric seizures, and 6% both. Among NE pts the mean age at onset of epilepsy was slightly lower than in PE pts (p = 0.049). No significant differences were observed in seizure type, personal history of febrile convulsions (FC), family history of FC, family history of epilepsy and parasomnias, status epilepticus, secondary generalization, seizures also in wakefulness or interictal epileptiform abnormalities.

Conclusions: These data show significant differences between NE and PE pts only for earlier age at onset and high seizure frequency at onset in the NE group, that seems to be a negative prognostic factor.

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RECIPROCAL RELATIONSHIP OF AN OVERLOOKED COMORBIDITY: OSAS AND EPILEPSY

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Purpose: To retrospectively determine OSAS's comorbidity in epilepsy analyzing clinical and demographic characteristics. To study possible correlations among OSAS, seizures frequency, BMI, AEDs and daytime somnolence. To prospectively evaluate effects of OSAS treatment with CPAP on seizures frequency.

Method: Database of the Epilepsy Centre of Policlinico Tor Vergata was retrospectively reviewed (2002–2009) in order to identify patients affected by both diagnosis of epilepsy and OSAS meeting ILAE and AASM criteria. Epilepsy (seizure frequency, AEDs) and OSAS characteristics (BMI, daytime somnolence evaluated by means of Epworth sleepiness scale, polysomnographic parameters) were collected. Finally,

the effects of CPAP ventilotherapy on seizure frequency were prospectively evaluated.

Result: Of 847 epileptic patients, 8% (68 pts, 38 M, mean age 53.03 ± 16.02) were affected by OSAS. Mean BMI was significantly higher in females than males. Mean Apnea/Hypopnea Index (AHI) was 21.85 ± 20.29/h, higher in males than in females. OSAS was severe in 26.6% patients, moderate in 20.3%, mild in 53.1%. Pathological daytime somnolence was evident in 29.4% patients. Seizure frequency was high in 47%. VPA treatment significantly affect BMI other than AHI. CPAP treatment was prescribed in 34/68 patients. Of 26 patients utilizing CPAP with good compliance, 46.15% were seizure-free and 15.4% responders at follow-up ranging from 6 months to 5 years.

Conclusion: The prevalence of OSAS observed in our unselected epilepsy population is 8%, higher than expected value. Male-female ratio in our sample is 1.7:1, lower than OSAS disease, suggesting that epileptic patients per se, in a gender-independent manner, exhibit a predisposition to OSAS. Only 29.4% of patients showed daytime somnolence confirming that such symptom does not predict OSAS in epilepsy. Prospectively, we observed positive effects in 61% of patients treated with CPAP ventilotherapy. Despite several hypothesis formulated, underlying mechanisms are not yet understood.

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CLINICAL CHARACTERISTICS OF ICTAL ASYSTOLE IN TEMPORAL LOBE EPILEPSY

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Purpose: The aim of the study is to clarify the clinical characteristics of ictal asystole.

Method: We searched the patients who had the diagnosis of ictal asystole in 900 consecutive patients who attended the epilepsy center at our institution. The diagnostic criteria for the ictal asystole is confirmation of the ictal cardiac arrest by video/EEG monitoring and/or long term implanted loop recorder for heart beat.

Result: There were three patients identified. Thus, the prevalence of the ictal asystole was 0.3% in patients with epilepsy. All had temporal lobe epilepsy. Patient 1 is 36-year-old man who underwent cardiac pacemaker implantation for syncope. After the failure of the complete control of the syncope, EEG recording revealed temporal lobe epilepsy. Patient 2 is a 80-year-old woman who has been treated for temporal lobe epilepsy for 15 years. Video/EEG monitoring was conducted for her intractable epilepsy, which revealed ictal bradycardia/asystole. Implantation of the cardiac pacemaker did not abolish the loss of consciousness as the complex partial seizure persisted. Patient 3 is 72 year-old man who underwent ECG with implantable loop recorder for his syncope. Asymptomatic frequent nocturnal cardiac arrest triggered the cardiologist to suspect the presence of epilepsy. EEG showed frequent temporal spikes and treatment with carbamazepine completely abolished the asystole and symptoms.

Conclusion: The ictal asystole in temporal lobe epilepsy is rare. The prevalence was 0.3% in patients with epilepsy. The diagnosis is often delayed. The clinical presentation could be syncope or complex partial seizures.

Poster session: Adult epileptology X
Tuesday, 30 August 2011

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KONQUEST: KEPPRA VERSUS OLDER AEDS AND NEUROPSYCHIATRIC, NEUROCOGNITIVE AND QUALITY OF LIFE OUTCOMES IN TREATMENT OF EPILEPSY AS SUBSTITUTION MONOTHERAPY

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Purpose: To compare a broad range of epileptic and psychological outcome measures in patients who had substitution monotherapy with levetiracetam (LEV) versus one of two older antiepileptic drugs (AEDs), carbamazepine (CBZ) or valproate (VPA).

Method: KONQUEST was a single-centre, randomized, open-label study. Participants had partial epilepsy on monotherapy which had "failed" either due to lack of efficacy or adverse effects. Based on baseline depression score, participants taking phenytoin (PHT) or CBZ were randomized to either LEV or VPA, and participants taking VPA were randomized to LEV or CBZ. Assessments were performed at baseline, 3, and 12 months using questionnaires measuring seizure control, anxiety and depression (HADS), psychiatric distress (Symptoms Checklist 90 – SCL 90), Quality of Life in Epilepsy (QOLIE 89), adverse effects (Liverpool Adverse Effect Profile – LEAP) and, neurocognitive performance (IntegNeuro). Outcomes analysis was performed on the basis of intention to treat.

Result: Ninety percent (89/99) of enrolled patients completed the study: 46 in the LEV and 43 in the older AED groups (VPA, n = 25, CBZ, n = 18). All assessments improved from baseline at both 3 and 12 months; however, we found no differences between the LEV and older AED treatment groups in terms of seizure control, adverse drug effects, retention rates or any of the psychiatric, neurocognitive or quality of life measures.

Conclusion: Switching to a different AED in patients who are experiencing ongoing seizures or adverse effects to their first AED is associated with improvement on a wide variety of epilepsy and psychosocial measures. This effect is similar for both LEV and the older AEDs.

Disclosure: KONQUEST was an investigator-initiated study funded by UCB Pharma.

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EFFECTIVENESS OF RITUXIMAB IN A CASE OF AUTOIMMUNE ENCEPHALITIS

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Purpose: To describe the effectiveness of rituximab in a case of refractory status epilepticus in a patient diagnosed of probable autoimmune encephalitis.

Method: We report the case of a 33-year-old patient who was admitted to our hospital with fever, behavioral disturbance and headache. After 24 h he had a tonic–clonic seizure, followed by focal motor seizures in the next days till he finally presented a refractory status epilepticus, requiring mechanical ventilation and the use of anesthetics.

Result: A lumbar puncture was performed, showing mild pleocitosis (21/mm^3) and slightly elevated protein concentration (45 mg/dl) with normal glucose concentration. Cranial CT scans and MRI were normal and EEG showed right temporal sharp waves. He was treated firstly with antiepileptic drugs without response and empiric acyclovir. Corticoids and immunoglobulin were tried but electrical paroxysms remained in the EEG and we were unable to drop out barbiturates. Analyses for autoantibodies including Hu, amphiphysin, NMDA receptor, K channel, AMPA, and GABA(B) were all negative. Neither teratoma nor other tumors were found despite comprehensive tumor screening. Given the lack of

improvement, four doses of rituximab (375 mg/m^2 per week) were administered and the patient recovered consciousness and was seizure-free after the second dose.

Conclusion: Immunological therapy should be considered in patients with refractory status epilepticus of uncertain origin but suspected autoimmune etiology. We propose rituximab as a safe and effective treatment in those cases.

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FOCAL REFRACTORY EPILEPSY: SHOULD VALPROIC ACID–LAMOTRIGINE COMBINATION BE TESTED PREVIOUS TO ESTABLISHING DIAGNOSIS?

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Purpose: Refractory epilepsies (RE) are characterized by the persistence of seizures despite the use of two or more appropriately used and well tolerated antiepileptic drugs (AED). These epilepsies are associated with poor prognosis.

The purpose of this study is to evaluate the effect of different AED on seizure frequency in patients with RE and identify effective pharmacological combinations.

Method: This transversal study has a retrospective first phase and a subsequent prospective follow-up. All patients with diagnosis of RE (according to ILAE definition) were included. They were classified into three groups; (1) Seizure freedom, (2) Reduction of seizure frequency in more than 50%, (3) No significant change in seizure frequency.

We identified the therapeutic combinations that reduced the seizure frequency.

Result: We included 60 patients with focal RE with no response to an average of four AED. At 1 year follow-up, 21 patients (35%) were seizure-free and 10 patients (17%) had a >50% decrease in seizure frequency. Among the patients who were seizure-free, 70% received valproic acid–lamotrigine combination. No other AED combination showed a consistent effect on seizure control.

Conclusion: These results are encouraging as 35% of patients considered to be drug-resistant responded to therapy. The great majority of them were treated with valproic acid–lamotrigine combination. These findings suggest that this combination should be tested, whenever possible, previously to making a definite diagnosis of focal refractory epilepsy.

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THE DESIGN OF A DOUBLE-BLIND, RANDOMIZED, HISTORICAL CONTROL STUDY OF THE SAFETY AND EFFICACY OF ESLICARBAZEPINE ACETATE MONOTHERAPY IN SUBJECTS WITH PARTIAL EPILEPSY NOT WELL CONTROLLED BY CURRENT ANTIEPILEPTIC DRUGS

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Purpose: Based on the safety and efficacy demonstrated in clinical trials of once-daily (QD) eslicarbazepine acetate (ESL) as adjunctive therapy in adults with partial-onset seizures, ESL may also be a safe and effective agent in monotherapy. This phase III, randomized, double-blind study aims to evaluate the safety and efficacy of ESL as monotherapy treatment for subjects with partial-onset seizures not well controlled by current antiepileptic drugs (AEDs).

Method: Multicenter study based on the French J et al. (Epilepsia 2010;51:1936–1943) historical control monotherapy design. Projected enrollment of approximately 170 male or female subjects aged 16–70 years (inclusive) receiving 1–2 AEDs in a stable dose regimen for 28-days prior to screening. Subjects experiencing ≥4 partial-onset seizures during the 8-week baseline period with no 28-day seizure-free period will be randomized in a 2:1 ratio into two treatment arms: ESL 1600 mg QD (116 subjects) or eslicarbazepine acetate 1200 mg QD (58 subjects). The 18-week treatment period includes a 2-week titration period, a 6-week AED taper/conversion period, and a 10-week double-blind monotherapy period. The control group is external to the study based on the historical control.

Result: The study is expected to be completed by the end of 2012.

Conclusion: This study aims to evaluate ESL 1600 and 1200 mg QD as monotherapy for subjects with partial-onset seizures not well controlled by current AEDs.

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LONG-TERM SAFETY AND EFFICACY OF LACOSAMIDE AS ADJUNCTIVE THERAPY IN PATIENTS WITH UNCONTROLLED POS: RESULTS FROM A PHASE III OPEN-LABEL EXTENSION TRIAL

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Purpose: Long-term (≤5.5 years exposure) safety and efficacy were evaluated from a completed open-label extension trial (SP756; NCT00522275) of the antiepileptic drug (AED) lacosamide.

Method: Patients entering the open-label extension (institutional review board-approved) after completing a double-blind trial of adjunctive lacosamide in partial-onset seizures (SP754; NCT00136019; Chung et al, Epilepsia 2010; 51: 958–67) had transitioned to 200 mg/day lacosamide. Dosage adjustment of lacosamide (100–800 mg/day) and/or concomitant AEDs was allowed to optimize tolerability and seizure reduction. Treatment-emergent adverse events (TEAEs), vital signs, body weight, clinical laboratory data, electrocardiograms, and seizure frequency from subject diaries were evaluated.

Result: Of 308 patients exposed to open-label lacosamide (median modal dose 500 mg/day), 75%, 63%, 54%, and 29% had >1, >2, >3, or >4 years lacosamide exposure, respectively. Primary reasons for discontinuation were lack of efficacy (26%) and AEs (11%). Common TEAEs (≥15%) were dizziness, headache, contusion, nausea, convulsion, nasopharyngitis, fall, vomiting, diplopia. TEAEs that led to discontinuation in ≥1.0% of patients were dizziness (1.6%) and convulsion (1.0%). Median 28-day seizure frequency was 13.0 at Baseline of SP754; median percent reduction from Baseline across Treatment was 48.5%, and was 53.4%, 55.2%, 58.1%, and 62.5%, respectively, for 1-, 2-, 3- and 4-year completers. The ≥50% responder rate was 48.2% across Treatment, and was 52.8%, 56.5%, 58.7% and 62.5% for 1-, 2-, 3- and 4-year completers, respectively. Of patients exposed to lacosamide ≥2 years, 3.1% remained seizure-free through ≥2 years.

Conclusion: Long-term lacosamide treatment was generally well tolerated and associated with seizure reduction and maintenance of efficacy.

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STABLE AND UNSTABLE TREATMENT PATTERNS IN EPILEPSY AND THEIR DIRECT COST IMPACT: PHARMETRICS ANALYSIS OF AED ADD-ON THERAPY, SWITCHES, AND DISCONTINUATIONS

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Abstracts

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Purpose: Average annual health care costs of managing epilepsy are estimated at US$ 11,664/patient. The aim of this study was to determine whether patients on stable AED treatment have different characteristics and health care costs compared to those experiencing unstable AED treatment.

Method: A retrospective cohort study was conducted using a U.S. claims database, following patients with epilepsy taking ≥1 AED over a 2-year period. Demographic features, baseline characteristics, and annual total health care costs were stratified by AED treatment pattern category during the 24-month observation period: stable (no change in treatment regimen) versus unstable (switch, add-on, or discontinuation of treatment).

Result: Of 12,178 patients included, 53% had unstable AED therapy during the study (22% add-on, 6% switch, 25% discontinuation). Eighteen percent of patients with stable treatment had been diagnosed ≤1 year prior to baseline compared to 28% with unstable treatment (add-on: 739/2690 [28%], switch: 238/733 [33%], discontinuation: 799/3022 [26%]). Greater health care costs were associated with unstable AED treatment. Overall health care cost for patients with an AED switch ($28,732) or add-on ($31,321) were >2-fold higher than the overall health care costs for patients on stable treatment ($11,505). Emergency room costs for patients with unstable AED treatment (add-on: $9240, switch: $6392, discontinuation: $3012) were approximately 3–8-times higher than for those on stable therapy ($1176).

Conclusion: These data reinforce the importance of fast and sustained control of epilepsy for the benefit of both the patient and society.

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LONG-TERM ADJUNCTIVE LACOSAMIDE IN PATIENTS WITH UNCONTROLLED PARTIAL-ONSET SEIZURES: RESULTS FROM THE SP774 PHASE III OPEN-LABEL EXTENSION TRIAL

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Purpose: Long-term (≤5.5 years exposure) safety and efficacy were evaluated from a completed open-label extension trial (SP774; NCT00515619) of the antiepileptic drug (AED) lacosamide.

Method: Patients entering the open-label extension (institutional review board-approved) after completing a double-blind trial of adjunctive lacosamide in partial-onset seizures (SP755; NCT00220415; Halász et al 2009) had been transitioned to 200 mg/day lacosamide. Dosage adjustment of lacosamide (100–800 mg/day) and/or concomitant AEDs was allowed to optimize tolerability and seizure reduction. Treatment-emergent adverse events (TEAEs), vital signs, body weight, clinical laboratory data, electrocardiograms, seizure frequency, responder rates (percentage of patients with ≥50% or ≥75% seizure frequency reduction from Baseline of the double-blind trial), and seizure-free status from subject diaries were evaluated.

Result: Of 376 enrolled patients, 75% had >1-year and 53% had >3-years lacosamide exposure. Median lacosamide modal dose was 400 mg/day. Common AEs (≥10%) were dizziness (24%), headache (14%), diplopia (14%), and nasopharyngitis (14%). Discontinuations due to AEs were 9%; only dizziness (1.3%) led to discontinuation in >1% of patients. The overall median percent seizure reduction from Baseline of Trial SP755 over the SP774 Treatment Period was 49.9%, and was 55.4% and 62.3%, respectively, for 1-year (n = 279) and 3-year completers (n = 200). The ≥50% responder rate was 50.0% over the Treatment Period and was 55.9% and 63.0% for 1- and 3-year completers, respectively. Of patients exposed to lacosamide for ≥1 year, 3.2% remained seizure-free for ≥1 year.

Conclusion: In patients choosing to enter the long-term extension trial, lacosamide was generally well tolerated and associated with seizure reduction and maintenance of efficacy.

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LACOSAMIDE: LONG-TERM SAFETY AND EFFICACY IN PARTIAL-ONSET SEIZURES

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Purpose: Long-term (≤8 years exposure) safety and efficacy of the antiepileptic drug (AED) lacosamide were evaluated from a completed open-label extension (SP615; NCT00552305) in partial-onset seizures.

Method: Patients enrolled following double-blind or open-label lacosamide trials. Dosage adjustment of lacosamide (100–800 mg/day) and/or concomitant AEDs occurred to optimize tolerability and seizure reduction. Treatment-emergent adverse events (TEAEs), vital signs, body weight, clinical laboratory data, electrocardiograms, and seizure frequency from subject diaries were evaluated.

Result: Of 370 enrolled patients, 77%, 51%, and 39% had >1, >3, or >5 years lacosamide exposure, respectively (median modal dose 400 mg/day). Common TEAEs (≥15%) were dizziness, headache, nausea, diplopia, fatigue, upper respiratory tract infection, nasopharyngitis, contusion, and coordination abnormal. Discontinuations due to TEAEs were 12.7%; only dizziness and convulsion led to discontinuation in ≥1% of patients. Median 28-day seizure frequency was 12.0 at Baseline of previous trials; median percent reduction from Baseline was 50.8% across Treatment, and was 47.3%, 56.8% and 65.2%, respectively, for 1-, 3- and 5-year completers. The ≥50% responder rate was 51.2% across Treatment, and was 48.8%, 57.2% and 63.4% for 1-, 3- and 5-year completers, respectively.

Conclusion: Long-term adjunctive lacosamide treatment was generally well tolerated, reduced seizure frequency and maintained efficacy.

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AN ONGOING POSTMARKETING STUDY EVALUATING LACOSAMIDE AS ADJUNCTIVE THERAPY TO ONE BASELINE ANTIEPILEPTIC DRUG IN EPILEPSY PATIENTS: SP0973 VITOBA STUDY (VIMPAT ADDED TO ONE BASELINE AED)

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Purpose: Lacosamide (Vimpat) is an approved antiepileptic drug (AED) for the adjunctive treatment of partial-onset seizures (POS). Results from a post hoc analysis of three pivotal studies evaluated efficacy and tolerability of adjunctive lacosamide based upon inclusion or noninclusion of a traditional sodium channel blocking AED. (Sake JK et al. *CNS Drugs* 2010; 24: 1055–1068). Unlike the previous analyses that included patients with up to three concomitant AEDs, this ongoing study will assess efficacy and tolerability in single AED combinations to better evaluate the potential for additive or synergistic effects without the confounding factor of multiple concomitant AEDs.

Method: Planned enrollment for this 6-month prospective, noninterventional study is 500 evaluable POS patients. The adjunctive AED will be chosen independently of study protocol by the treating physician. Main outcome variables include change in seizure frequency and AED dose and adverse events. Statistical analysis will be descriptive for the enrolled study population and grouped by baseline AED.

Result: As of March 26, 2011, 264 patients have been enrolled. Patient baseline AED distribution includes levetiracetam (30%), lamotrigine (22%), valproic acid (16%), carbamazepine (15%), oxcarbazepine (9%), topiramate (5%) and other AEDs (3%). Forty-eight percent of patients were taking ''traditional'' sodium channel-blocking baseline AEDs.

Conclusion: These data will provide insight into patient outcome in a real life clinical setting. Ongoing data collection will allow a mechanism-based analysis of lacosamide in combination with a single ''sodium channel'' or ''non–sodium channel'' AED.

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ADJUNCTIVE ZONISAMIDE IN CLINICAL PRACTICE: RESULTS FROM THE NONINTERVENTIONAL ZADE STUDY

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Purpose: To evaluate efficacy, tolerability and quality of life (QOL) effects of adjunctive zonisamide (ZNS) in patients with partial seizures treated in everyday clinical practice.

Method: ZADE (Zonisamid im Alltag der Epilepsiepatienten; German acronym) was a binational (Germany, Austria), multicenter, noninterventional study, enrolling adult patients with inadequately controlled partial seizures receiving ≥1 antiepileptic drugs (AEDs) at baseline. ZNS dosing was based on SmPC with schedules prepared on an individual patient basis. Efficacy was evaluated over 4 months by assessing seizure frequency during last 8 weeks of observation vs. baseline (last 8 weeks prior to ZNS initiation). Tolerability assessments included incidence of adverse events (AEs). QOL was assessed using the QOLIE-10-P questionnaire.

Result: In total, 365 patients were enrolled (mean age 45.5 years; 54.3% male; median duration of epilepsy 10 years). Patients previously used, on average, 2.5 AEDs; 57.1% receiving monotherapy at baseline. Average ZNS maintenance dose was 260 mg/day (25–500 mg/day). Mean seizure frequency fell from 8.2 at baseline to 3.4 in the last 8 weeks of ZNS therapy. The proportions of patients with ≥50% and ≥75% seizure frequency reduction were 78.6% and 52.8%, respectively; 36.0% became seizure-free. QOL improvement was noted in 43% of patients, QOL deterioration in 4%. 12.6% of patients developed AEs, with 6.3% prematurely terminating ZNS, primarily due to CNS and gastrointestinal AEs.

Conclusion: Adjunctive ZNS was effective and well tolerated at moderate doses in patients with partial seizures less refractory than typically included in randomized controlled trials.

Study supported by Eisai GmbH.

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OZONE: A PROSPECTIVE, OBSERVATIONAL, OPEN-LABEL STUDY OF PATIENTS WITH PARTIAL EPILEPSY TREATED WITH ADJUNCTIVE ZONISAMIDE THERAPY IN EVERYDAY CLINICAL PRACTICE IN FRANCE

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Purpose: To evaluate the efficacy and tolerability of zonisamide (ZNS) in current medical practice in patients aged ≥18 years with focal epilepsy treated by neurologists in hospital or private offices. ZNS is known to be an effective adjunctive therapy in patients with partial epilepsy previously receiving monotherapy.

Method: Prospective, observational, open-label study, with 6 months' follow-up of patients already treated with ZNS ≥3 months (dose adjustment was permissible during this period). Principal analysis: patient description, disease history, and frequency and severity of seizures before and after adjunctive ZNS treatment. Secondary analysis: efficacy and tolerability of ZNS in postmonotherapy groups.

Result: One hundred thirty-two neurologists included 476 patients (428 evaluable, of whom 52 discontinued early) presenting with partial seizures onset. Mean age was 42.5 (range 18–88) years. Before adding ZNS, 151 (35.3%) patients received monotherapy. Of the 428 evaluable patients, 42.3% demonstrated ≥50% improvement (responders); 15.4% were seizure-free for ≥3 months. When ZNS was added to monotherapy with another antiepileptic drug (AED), responder and seizure freedom rates were, respectively: 70.0% and 33.3% for levetiracetam (30 evaluable patients); 78.3% and 21.8% for lamotrigine (23 evaluable patients); and 85.0% and 45.0% for valproate (20 evaluable patients). During the dose adjustment period, 24.8% of patients reported ≥1 adverse event(s) vs. 22.2% during the stable dosage period.

Conclusion: ZNS demonstrated favorable efficacy when used adjunctively with all other AEDs in this study, particularly in patients previously treated with levetiracetam or valproate monotherapy. ZNS was well tolerated with all other AEDs.

Supported by Eisai France.

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A 12-MONTH OBSERVATIONAL NORDIC STUDY IN EPILEPSY PATIENTS PRESCRIBED ZONISAMIDE IN EVERYDAY CLINICAL PRACTICE: PRELIMINARY RESULTS FROM ZENIT

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Purpose: ZENIT is evaluating a range of outcomes in epilepsy patients being prescribed zonisamide (ZNS) in everyday clinical practice. ZNS is currently licensed in Europe for adjunctive treatment of focal seizures in adults. Here we report preliminary data from the study.

Method: An observational, multicenter study in a naturalistic setting in epilepsy patients (age ≥18 years) prescribed ZNS in Denmark, Finland, Norway and Sweden. Patients are followed according to clinical practice for approximately 12 months. Primary outcome measure is retention rate at 12 months. Other assessments include efficacy (reduction in seizure frequency), health care resource utilization, health-related quality of life (QOLIE-31), antiepileptic drug (AED) use, and safety (adverse events).

Result: Overall, 152 patients (80 female/72 male) have been enrolled, the majority with focal (77.0%) or idiopathic generalized (13.0%) epilepsy. At baseline, mean age was 43.2 years (SD 13.7), mean duration of epilepsy was 17.6 years (SD 14.6), and median number of seizures in

previous 3 months was 8.0. ZNS was initiated mainly due to lack of efficacy (82.9%) or tolerability problems (40.1%) with current AEDs. Mean number of concomitant AEDs at ZNS initiation was 1.53 (SD 0.75). At last visit, mean ZNS dose was 189.9 mg/day (SD 157.9). To date, 35.5% patients have completed the 12-month study, 43.4% are ongoing and 21.1% have withdrawn. Adverse events have been reported by 48.7% patients; most frequently, headache (6.6%), nausea (6.6%), dizziness (4.6%) and fatigue/tiredness (3.3%).

Conclusion: The study will provide valuable information on ZNS use in a naturalistic setting.

Study supported by Eisai.

p511
AN OPPORTUNITY OF COMBINED INFLUENCE OF DEPAKIN-CHRONOSPHERA WITH ANTIOXIDANT MEXIDOL ON EPILEPTIC SYSTEM IN CLINIC-EXPERIMENTAL STUDY

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Purpose: To evaluate the impact of combined therapy with Depakin Chronosphera and antioxidant mexidol on epileptic system in clinic-experimental study.

Methods: Experimental research was carried out on white rats with epileptogenic cobalt lesions in the left frontal cortex and chronically implanted electrodes in the right frontal cortex, dorsal hippocampus and lateral hypothalamus. It was shown, that the combined therapy by Depakin Chronosphera (in an ineffective at monotherapy dose 20 mg/kg) and antioxidant mexidol (in a dose 50 mg/kg) has revealed significant strengthen action of mexidol on Depakin Chronosphera effects. The clinical study included 16 patients with symptomatic and/or cryptogenic focal epilepsy. All patients were basically treated with Depakin Chronosphera at doses of 900–1200 mg/day. Mexidol was fixed in a dose 5% 4.0 intramuscular 10 days. Space organization of bioelectric activity of brain by alpha and theta-activity was evaluated with index of coherence.

Result: As opposed to effects of separate use of preparations, under influence of their combination significant reduction of epileptic activity not only in hypothalamus, but in right frontal cortex at all stages of development of the epileptic system, with the maximal reduction of number and duration of bursts at a stage of generalization was observed. After the course of combined treatment the reliable decrease of indexes of coherence for all interhemisphere links was revealed, mainly alpha-activity in central-occipital and theta-activity in frontal zone.

Conclusion: Antioxidant mexidol intensifies an action of Depakin Chronosphera in clinic-experimental study.

Poster Session: Alternative therapies I
Tuesday, 30 August 2011

p512
ENCAPSULATED GALANIN RELEASING CELLS SUPPRESS FOCAL EPILEPTIC ACTIVITY IN THE HIPPOCAMPUS

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Purpose: Galanin is a neuropeptide widely expressed throughout the central nervous system and in the hippocampus is found in noradrenergic fibers. Galanin has the ability to decrease glutamate release from excitatory synapses, which results in inhibitory effects on seizure activity. To explore potential for clinical application, we delivered galanin through encapsulated cell biodelivery (ECB) devices in a rat model of epileptogenesis, kindling and in a chronic model of epilepsy with spontaneous seizures post–status epilepticus (SE).

Method: ECB devices filled with galanin producing cells, non–genetically modified control cells or empty devices were implanted bilaterally in the hippocampus. Two different galanin-expressing cell clones were tested, a high-releasing and a low-releasing clone. At the same surgical session a stimulation/registration electrode was implanted in the hippocampus. One week after implantation seizures were induced using the rapid kindling protocol. SE was induced by intrahippocampal injection of kainic acid.

Result: ELISA measurements performed prior to implantation showed a release of galanin around 8 ng/ml/24 h for the low-releasing clone and 12 ng/ml/24 h for the high-releasing clone. Results from the rapid kindling showed decreased focal afterdischarge durations only with the high galanin-releasing clone, while there was no seizure suppressant effect on the low galanin-releasing clone. The high-releasing clone was then further used in a chronic post-SE model of epilepsy. The results of these experiments will be presented at the meeting.

Conclusion: Our study shows that implantation of galanin-releasing ECB devices can influence epileptic seizures and may represent a future potential approach for treatment of epilepsy.

p513
CAREGIVER SEIZURE MANAGEMENT SYSTEM IN CANINE EPILEPSY

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Purpose: A seizure management system was developed for canines with epilepsy which alerts caregivers in the event of prolonged or repetitive life-threatening seizures.

Methods: Four canines with naturally occurring epilepsy were implanted with a seizure management system which is an implantable device that captures and wirelessly transmits intracranial EEG to an external device. The external device contains an embedded seizure prediction and detection algorithm designed to forecast seizure likelihood and remotely alert caregivers when prolonged or repetitive seizures occur. In the event of a prolonged or repetitive seizure, an automated message was sent to a veterinary clinician and a rescue therapy protocol was implemented. Drug concentrations of the rescue therapy and EEG were monitored. The performance of the epilepsy alert system was evaluated over the course of 4 months.

Result: The four canines exhibited electrographically similar onset and progression characteristics of human complex partial seizures. Once taken off antiepileptic drugs, the canines experienced spontaneous unprovoked complex partial seizures that secondarily generalized. Three prolonged or repetitive seizures occurred in two of the canines. On each occasion, alerts were sent to a staff neurologist who confirmed the seizure activity via remote video-monitoring. A rescue medication protocol was then administered and the repetitive seizures were aborted in both animals.

Conclusions: This pilot study demonstrates in canines the feasibility of a seizure management system to notify a remote caregiver of prolonged or repetitive life-threatening seizures, enabling rescue medications to be delivered in a timely manner. This technology could provide alerts to caregivers of people with epilepsy, enabling timely intervention during

prolonged or repetitive seizures, potentially preventing or reducing physical harm or death while improving quality of life.

p514

COMPARISON OF TARGETS FOR NEURAL TRANSPLANTATION IN THE BASAL GANGLIA AND IDENTIFICATION OF SUITABLE CELL SOURCES IN AN ACUTE SEIZURE MODEL

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Purpose: Transplantation of GABA-producing cells into basal ganglia regions is one promising approach to overcome pharmacoresistance in epilepsy. Previous studies on GABA-producing cells grafted into the substantia nigra pars reticulata (SNr) revealed significant but only transient anticonvulsant effects. Our present studies mainly address the questions: (1) Are specific subregions of the SNr or other basal ganglia regions such as the subthalamic nucleus (STN) more suitable for grafting GABA-producing cells? (2) Which cell types will prove advantageous regarding long-term anticonvulsant efficacy after transplantation into basal ganglia regions?

Method: By using microinjection of vigabatrin in the pentylenetetrazole (PTZ) seizure threshold test, we firstly identified promising target regions for inducing robust anticonvulsant effects by increased GABAergic inhibition.

Currently, we are grafting (1) spherical aggregates and (2) mature human model neurons of Ntera-2 cells as well as (3) rat striatal precursor cells from medial and (4) lateral ganglionic eminence.

Result: Microinjection of vigabatrin into subregions of the SNr as well as into the STN clearly proved that local increase of inhibition within these regions is anticonvulsant with an at least similar potency than systemic administration.

Preliminary data did not indicate anticonvulsant effects after grafting of differentiated Ntera-2 cells into the STN. Results for precursor cells of Ntera-2 and striatal cells will be presented at the Meeting.

Conclusion: The SNr and the STN are promising targets for neural transplantation. The lack of anticonvulsant efficacy of mature Ntera-2 neurons supports previous data showing that increased inhibition of the SNr or STN is necessary to inhibit seizures emanating from the limbic system. Differentiated Ntera-2 cells, however, comprise excitatory and inhibitory neural phenotypes.

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p515

OPTOGENETIC INHIBITION OF EPILEPTIFORM ACTIVITY IN ACUTE HIPPOCAMPAL SLICES

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Purpose: The potential of optogenetics for the control of specific subpopulation of neurons has recently become an attractive scientific approach for inhibiting seizures. We have previously shown that eNpHR, a light-driven halorhodopsin chloride pump derived from *Natromonas Pharaonis*, when introduced into principal neurons of organotypic hippocampal slices, is able to effectively suppress stimulation train-induced bursting (STIB) activity upon exposure to orange light. Here we explore whether orange light mediated activation of eNpHR can suppress chemically-induced epileptiform activity generated in acute slices from rodents.

Method: A viral vector encoding the eNpHR gene was injected into the rodent hippocampus. Three to six weeks later, transverse hippocampal slices were prepared and transferred to an electrophysiology setup. Epileptiform activity was induced by application of different proconvulsant drugs and 595 nm wavelength light was delivered to the slices via the microscope lenses.

Result: Here we show that expression of eNpHR can be achieved at high levels in the hippocampus of rodents and epileptiform activity can be consistently induced in acute slices by pro-convulsant drug application. Illumination of the slices with orange light can effectively and repeatedly reduce the interictal spike frequency, and in most cases totally abolish epileptiform activity for prolonged periods.

Conclusion: These data show that optogenetic approaches prove useful for controlling acute epileptiform activity, and open possibilities for developing them into future treatment strategies for epilepsy.

p516

STRENGTH PHYSICAL EXERCISE PROGRAM IN RATS WITH EPILEPSY IS PROTECTIVE AGAINST SEIZURES

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Purpose: The positive effect of aerobic exercise programs on seizure frequency and severity has been demonstrated both in human and animals. However, the impact of strength physical exercise on epilepsy is not well established. To this purpose, the present work was aimed to analyze the effect of strength training exercise in rats with epilepsy using the pilocarpine model.

Method: Animals with epilepsy were continuously monitored during 24 h/day for 60 days after the first spontaneous recurrent seizure. The behavioral observation consisted of two periods of 30 days and animals were divided into two groups: sedentary group (n = 6) and trained group (n = 17). For the trained group, the first period was used to determine the number of seizures before the training program and the second period was utilized to determine the number of seizures during the training program. Training protocol consisted of animals subjected to a ladder climbing during 4 weeks with weights attached to their tails.

Result: The mean frequency of seizures in the control group increased significantly from period 1 to period 2 ($p < 0.05$). However, in the training group, the frequency of seizures did not change significantly in the same behavioral periods, that is, the seizure frequency was not increased in the training group as observed in the control group.

Conclusion: Taken together, our data indicate that strength exercise can exert a beneficial effect on seizure frequency and reinforce the positive actions of exercise on epilepsy.

p517

PILOT-TRIAL: HIGH FREQUENCY, POISSON DISTRIBUTED CORTICAL STIMULATION IN A SCREENING MODEL FOR EPILEPTIC SEIZURES

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Purpose: Neurostimulation is a promising potential treatment for patients with refractory focal epilepsy who are not amenable to resective surgery. We have evaluated the effect of high-frequency cortical stimulation on cortical excitability in the motor cortex model (CSM). In the CSM, a ramp-shaped pulse train with increasing intensity is delivered to the motor cortex. The threshold intensity for eliciting forelimb clonus is

determined through behavioral observation, and used as a measure for cortical excitability.

Method: Three Wistar rats were implanted with epidural stimulation electrodes positioned over the motor cortex (AP −1 mm; ML ±3 mm). All rats underwent 1 h of therapeutic cortical stimulation or control stimulation on alternating days (Poisson pulse, 130 Hz, PW 1 ms). The threshold intensity needed to elicit forelimb clonus was determined before and after stimulation (mean of three measurements, performed at 5 min intervals). The intensity of therapeutic stimulation was individually determined for each rat as 100 μA lower than the baseline threshold intensity. Control stimulation was performed with an intensity of 10 μA.

Result: Control stimulation did not significantly alter the threshold to forelimb clonus (436 ± 61 μA before and 454 ± 90 μA after stimulation). Therapeutic stimulation (mean intensity 293 μA) significantly increased the threshold to forelimb clonus from 393 ± 22 before to 537 ± 57 μA after stimulation ($p < 0.05$).

Conclusion: High-frequency, Poisson-distributed cortical stimulation during 1 h decreases cortical excitability. Further studies are needed to determine whether this type of stimulation can become an effective alternative treatment for patients with focal neocortical epilepsy who are not amenable to surgery.

p518
LOCAL DRUG DELIVERY OF LEVETIRACETAM IN THE RAT MODEL OF ACQUIRED EPILEPSY USING PLGA BIODEGRADABLE POLYMER SHEET IMPLANTATIONS

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Purpose: Polymer based therapies offer many potential advantages in the treatment of epilepsy, primarily allowing the delivery of therapeutic agents directly to the relevant area of the brain. Direct administration in this manner would allow much smaller doses of medication to be used, and potentially avoid the side effects associated with systemic administration, as well as bypassing the obstacles presented by the blood brain barrier. Antiepileptic drugs when incorporated into a polymer matrix will break down and gradually release the therapeutic drug directly to the brain. Here we examined the effect on seizures using biodegradable polymer PLGA loaded with 10% Levetiracetam in the post–kainic status epilepticus rat model.

Methods: PLGA sheets loaded with 10% LEV were bilaterally implanted subdural in post–kainic acid status epilepticus rats. The other groups also implanted were PLGA blank and a sham group. Video EEG recordings were carried out 3 days/week for a 6 week period. At the end of the recording periods the rats undergo a series of standard neurobehavioral tests to assess memory function[1]* and anxiety and mobility levels[2]*([1]* – Morris Water Maze [2]* – Open Field Test).

Result: An effect of the two implanted polymer groups, PLGA (+10% LEV) and PLGA (blank) (n = 5), can clearly be seen within the current results which shows a definite suppression of seizures. The average number of seizures/24 h for PLGA (+10% LEV) is 0.111 ± 0.545 and the control group is 1.513 ± 0.221. This clearly shows the seizure reduction when compared with the nonimplanted controls.

(*p = [(1) p = 0.260) (2) p = 0.136 (1, 2) p = 0.588] using two-way ANOVA repeated measures).

Conclusion: Levetiracetam administered in polymer sheets intracranially exerts a significant anticonvulsant effect in a kainic acid model of focal epilepsy. Polymer-based drug delivery systems potentially offer an effective therapeutic method of anticonvulsant administration, permitting used of smaller doses of medication administered directly to epileptic foci. More sophisticated polymer devices will allow complex release strategies, including use of multiple medications and other biologically active substances.

p519
ELECTROPHYSIOLOGICAL RESPONSES TO VAGUS NERVE STIMULATION IN RATS

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Purpose: Vagus nerve stimulation (VNS) for refractory epilepsy requires optimization of stimulation parameters to improve outcome. Measuring electrophysiological activity from the vagus nerve in response to electrical stimulation may provide an objective tool to evaluate the effects of various stimulation parameters in an experimental setup.

Method: Rats were implanted with a stimulation electrode around the left cervical vagus nerve. Electrophysiological recordings were performed using thin point electrodes placed on the vagus nerve 2 and 4 mm rostrally to the cathode. Reference/ground electrode was placed in the wound. The vagus nerve was stimulated with a biphasic, charge-balanced pulse. Silk wire was strapped along the vagus nerve to cause reversible lesions of the nerve.

Result: VNS induced an electrophysiological response consisting of a fast and a slow component. The threshold intensity was 2490 ± 240 and 2067 ± 247 μA respectively. The components reached their maximum amplitude at 3875 ± 530 and 3000 ± 935 μA. Mean latency, at 2 mm, was 0.4 ± 0.1 and 2.6 ± 0.3 ms. Conduction velocity for the fast component was 25 m/s. The fast component disappeared by afferent lesioning the vagus nerve. The slow component disappeared by efferent lesioning, by lesioning the recurrent laryngeal nerve and by applying Vecuronium to the larynx muscles.

Conclusion: A short, single electrical pulse activates fast conducting afferent fibers. Also efferent fibers of the recurrent laryngeal nerve are activated resulting in contraction of larynx muscles. A far field potential was recorded on the vagus nerve. Our setup can be used to evaluate the effect of stimulation parameters at the cervical vagus nerve in rat epilepsy models.

p520
HIPPOCAMPAL DEEP BRAIN STIMULATION EARLY DURING EPILEPTOGENESIS AFFECTS SPONTANEOUS SEIZURES IN THE KAINIC ACID RAT MODEL

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Purpose: Recent studies have shown that hippocampal deep brain stimulation (DBS) can efficiently suppress spontaneous seizures. Despite

these promising results the precise mechanism of action, the long-term effects and the antiepileptogenic properties of DBS remains undetermined. In this animal experimental study, we evaluated the effect of DBS treatment on the development of spontaneous seizures in the kainic acid rat model.

Method: Rats (n = 14) were implanted with a bipolar DBS electrode in the right hippocampus and a bipolar EEG recording electrode in both hippocampi. After recovery from surgery, all rats were subjected to a status epilepticus (SE), that was elicited through intraperitoneal injections of kainic acid (KA). Immediately following SE, one group (n = 5) was subjected to DBS (Poisson distributed stimulation, 130 Hz, 100 μs pulse width, maximal subthreshold intensity with an absolute maximum of 400 μA) during ≥4 weeks; the other group received sham stimulation. Continuous EEG was recorded throughout the entire experiment, to evaluate the latency to the first seizure after SE, and seizure frequency.

Result: The mean latency for the first seizure to occur after the start of the SE is significantly ($p < 0.05$) longer in the DBS group (13 ± 2 days) compared to the control group (8 ± 5 days). There is no difference in seizure frequency during the treatment period after SE, but when comparing seizure frequency during the last 5 weeks of the experiment, when stimulation is stopped, there is a significant difference ($p < 0.05$) in seizure frequency between the DBS group (2 ± 1 Sz/day) and the control (16 ± 7 Sz/day) group.

Conclusion: These results suggest that early treatment with DBS in the kainic acid model is able to modify the development of spontaneous seizures. Early treatment with DBS delays the occurrence of spontaneous seizures after SE, and significantly fewer seizures occur in the DBS treated rats.

p521
SUBSTANTIATION OF RTMS PARAMETERS TO REDUCTION OF EXPERIMENTAL CONVULSIONS

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Purpose: The aim of our study is to reveal the patterns of rTMS anticonvulsive effects in different experimental convulsions models.

Method: We used the MES test at rats and pentiletetrazol model at mice which underwent of rTMS various parameters of frequency (10.0, 1.0, 0.5, 0.3, 0.1 Hz), intensity (0.5, 0.25 and 0.125 T) and procedures number (1, 3 and 10) by magnetic stimulator Neuro-MS (Neirosoft) in accordance with current ethical standards. Pentiletetrazol was subcutaneous injected in ED_{50} dose.

Result: MHLE after one-time rTMS 1 Hz (0.25 and 0.125 T) and 0.5 Hz 0.5 T was absent at 50% of rats ($p < 0.05$). Paroxysm after 1 Hz 0.25 T stimulation not developed in 20% of rats ($p = 0.047$). General paroxysm duration and clonic MES phase duration shortened after all rTMS regimes ($p < 0.04$). Tonic phase duration shortened after all intensity one-time regimes of 0.5 Hz, 1.0 Hz 0.5 T and 0.3 Hz 0.125 T; after three sessions—after regimes of all frequencies at 0.25 T ($p < 0.05$). Most effective in 10 sessions was 0.5 Hz 0.5 T rTMS. Clonic seizures were not observed at 50% of animals in pentiletetrazol model after one session of 10 Hz 0.5 T and 10 sessions of 1.0 Hz 0.25 T. There was prolonged first myoclonus latency after 0.5 Hz 0.25 T session stimulations: 162.6 ± 18.8 s against control 92.73 ± 12.1 s ($p = 0.027$). Degree of seizures severity significant drop at 1.0 Hz 0.5 T rTMS regime ($p = 0.033$).

Conclusion: Finding indicates of rTMS inhibitory effects in different experimental convulsion models. rTMS can change the structure, duration and severity of experimental convulsions periods which will be use in clinical epileptology hereafter.

Poster Session: Alternative therapies II
Tuesday, 30 August 2011

p522
IMPACTS OF A THERAPEUTIC MODEL OF RECREATION

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Purpose: While EAA has offered camps for over 20 years, the last 3 years have seen a refining of the approach to align with theories of therapeutic recreation. With a high proportion of EAA clients stating they feel ''alone'' and isolated or experience seizure anxiety and overprotection, Adventure Therapy enables EAA to design a therapeutic camp experience to target these specific concerns.

Method: 1. Participants set individual goals.
2. Camps are evaluated on whether the experience has:
a. Reduced feelings of isolation.
b. Increased confidence in managing challenging situations.
c. Increased knowledge of seizures and epilepsy.
d. Facilitated ongoing peer support.
3. A standard evaluation form provides baseline measures.
4. The shift between ratings pre- and postcamp is analyzed.
5. Free text comments are themed.

Result: EAA's research shows the greatest impact is in peer support with a 45% increase in participants' rating they have an increased the circle of peers they would contact for support. Results also show a 28% increase in confidence with managing challenging situations and a 14% reduction in feelings of isolation. Increased knowledge of epilepsy shows a smaller yet positive change.

Free text comments indicate some participants consider Adventure Camp a ''life changing experience.''

Conclusion: The shift towards a therapeutic model of recreation has proven successful in making a positive change in clients' lives on a number of variables including peer support, epilepsy knowledge, confidence and reduced feelings of isolation.

p523
THE KETOGENIC DIET AND EEG-BACKGROUND CHANGES

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Purpose: Early EEG-background changes after introduction of the ketogenic diet could be related to the antiepileptogenic effect of the diet and predict seizure reduction.

Methods: Fourteen patients treated with a medium chain triglyceride diet, with interictal epileptiform activity <10% of the time in the EEG were selected. A 24-h baseline EEG1 and an EEG2 after 6 weeks were performed. From twenty 4-s epochs from each EEG a power distribution was calculated in the frequency range with power above 1 uV^2. Responders were identified by ≥50% seizure reduction in 6 months after EEG2 compared to 2 months before EEG1.

Result: In 9/12 patients median power was higher in EEG 2 compared to EEG1, in three patients lower and in two patients there were no changes. Visual inspection of the epochs and power spectra of the patients with higher power, revealed increase in theta- and/or delta-frequencies. From the 2/14 responders, one had a significantly higher power and one had a significantly lower power in EEG2.

Conclusion: Six weeks after introducing the diet, background changes are seen in most of the patients, most often a power increase in the theta- and/or delta-range. The EEG changes could reflect a different behavior of neurons/neuronal networks. Whether these changes relate to seizure reduction or to the depth of ketosis, has to be examined in a larger patient group, with a larger proportion of responders.

p524
EFFICACY AND ACCEPTABILITY OF A NUTRITIONALLY COMPLETE KETOGENIC FORMULA USED TO ADMINISTER THE CLASSICAL 4:1 KETOGENIC DIET IN CHILDREN WITH REFRACTORY EPILEPSY

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Purpose: To assess the ability of a nutritionally complete ketogenic formula to attain/maintain ketosis and achieve seizure reduction in children with refractory epilepsy.

To assess the tolerability and acceptance of the formula.

Method: Seventeen case studies were collected of children 1–15 years with refractory epilepsy who used a nutritionally complete 4:1 (Fat:CHO + Protein) ketogenic formula (Ketocal 4:1, Nutricia) as a sole source of nutrition for between 8 and 16 weeks. Six children, previously established on a modular ketogenic feed, were changed to the nutritionally complete formula and their aim was to maintain any established ketosis and seizure reduction. Eleven were new to ketogenic therapy and were commenced on the formula with the aim of achieving ketosis and seizure reduction.

Result: Children transferring from a modular feed to the nutritionally complete formula (n = 6) maintained ketosis with no deterioration in seizure control. All 11 children new to ketogenic diet (KD) therapy achieved ketosis with 8 (72%) showing >50% seizure reduction of whom 3 (27%) achieved >90% reduction. Thirteen of 17 children experienced mild side effects (vomiting, constipation); most were preexisting problems easily managed with medication or dietary manipulation. Sixteen of 17 children completed the study and all continued the formula post study.

Conclusion: The product provides a convenient and efficacious way of administering the KD for children requiring a nutritionally complete feed. The seizure reduction seen (72% with >50% reduction) was better than many previous reports, possibly due to the guaranteed delivery of a 4:1 ratio.

Acknowledgment: These case studies were supported by Nutricia.

p525
SAFETY AND EFFICACY OF THE KETOGENIC DIET FOR REFRACTORY INFANTILE SPASMS

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Purpose: To review the safety and efficacy of the ketogenic diet for the treatment of refractory infantile spasms.

Method: Retrospective chart review.

Result: Sixteen patients were identified that had medically refractory West syndrome characterized by clinical infantile spasms, developmental delay and/or regression, and a hypsarrhythmia pattern on electroencephalography. All patients had failed previous trials with at least two antiepileptic medications, the majority of which included vigabatrin and/or adrenocorticotropic hormone. Patients were then treated with a traditional ketogenic diet using an RCF-based formula or Ketocal formula at either a 3:1 or 4:1 ratio of fat to carbohydrate plus protein for total daily calories. The diet was initiated during a 3–5 day hospitalization that did not include fasting. Patients were seen in clinic after 1 month and then followed once every 3 months thereafter. Safety monitoring included blood work for serum electrolytes, glucose, lipids, albumin, and prealbumin levels. The majority of patients developed a metabolic acidosis that was managed with oral sodium bicitrate. There were no serious complications from the diet. Thirteen patients were considered to be responders and had at least a 50% reduction in seizures (81%) and three patients were nonresponders with a <50% reduction in seizures. Ten patients (62%) had a robust response with at least a 75% seizure reduction and three patients became seizure-free (19%).

Conclusion: These findings suggest that the ketogenic diet is at least as safe and effective in treating refractory infantile spasms as antiepileptic drugs.

p526
ANTICONVULSANT AFRICAN PLANTS

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Purpose: *Bridelia micrantha* and *Croton macrostachyus* are used empirically in traditional medicine to treat epilepsy (Arbonnier 2000). That is why we are subjecting them to the evaluation for their anticonvulsant properties.

Methods: In vivo mice models (Maximal electroshock, Strychnine, Pentylenetetrazol, Picrotoxin, Isonicotinic hydrazide-induced convulsions were used to evaluate the anticonvulsant activities of plants. Mice were divided in six groups and received: Group I: distilled water, groups II–V: doses of the plant, group VI: diazepam, 5 mg/kg i.p. (Ngo Bum et al. 2009). Experiments were done in accordance with the National (N°.FWA-IRB00001954). ANOVA followed by Dunnet (HSD) and Fisher's exact test were used for statistical analysis.

Result: *B. micrantha* protected 100%, 80%, 80%, and 80% of mice against PIC, STR, PTZ and MES- induced seizures, respectively. *C. macrostachyus* protected 80%, 80%, 80% and 60% of mice against PIC, STR, PTZ and MES- induced seizures, respectively. *B. micrantha* and *C. macrostachyus* delayed also the onset of seizures in INH test.

Conclusion: The effect of the extracts of *B. micrantha* and *C. macrostachyus* suggests anticonvulsant efficacy against generalized tonic-clonic/partial seizures and generalized clonic seizures in man (Kupferberg and Schmutz 1997).

Acknowledgments: Thanks to the University of Ngaoundere for its support.

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p527
PUSHING THE FRONTIER—EASIER, SAFER AND MORE EFFICACIOUS KETOGENIC DIET

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Purpose: The ketogenic diet (KD) has remained almost unchanged since its introduction. High ratios used (4:1 and 3:1) (Kim et al Epilepsia; 2007; 48 (4): 801–805), consequent high blood lipid levels (Kwiterovich P.O. et al., JAMA; 2003; 290: 912–920,) and its use mainly in children have limited its utility. Other than the use of medium-chain triglycerides in the 1960s, whether a particular fat, like polyunsaturated fat KD (PUFAKD) will improve the efficacy of KD has not been fully investigated. (Fraser D.SD. et al., Neurology 2003; 60: 1026–1029), (Fuehrlein B.S. et al, The Journal of Clinical Endocrinology & Metabolism; 89, (4): 1641–1645). Its possible use in brain tumors is illustrated.

Method: Lower ratios (around 2:1) were used along with mixed oils KD (MOKD). KD was used in all age groups. High PUFAKD was tried to improve efficacy in 15 of those who did not have adequate control with MOKD. One example of its use in a pontine glioma is illustrated.

Result: Lower ratios are as efficacious as higher. Responder rate (>50% seizure control) in both groups was around 80% with 90% control being achieved by 28% in high ratio and 49.3% in low ratio group. Blood lipid profile of all 141 patients remained within normal range. Average values: total cholesterol 195 mg/dl, LDL 168 mg/dl, HDL 38 mg/dl, VLDL 20 mg/dl, triglycerides 111 mg/dl. The responder rate was 81.8% for infants, 80% for children, 100% for adolescents and 42.9% for adults. The KD is effective in all ages but less effective in adults. High PUFA KD was effective in 10 (over 90% reduction) and had <50% reduction in only two of those who do not achieve success with MOKD.

The glioma showed significant regression.

Conclusion: Lower ratios and MOKD make the KD easier and safer. The KD can be used in adults too. High PUFA KD may prove more efficacious. KD may have an important role in brain tumors.

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KETOGENIC DIET BENEFITS TO DRAVET SYNDROME PATIENTS: A PROSPECTIVE PILOT STUDY

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Purpose: We aimed to test prospectively the efficacy of ketogenic diet (KD) in patients with Dravet syndrome (DS) unsatisfactory controlled by AEDs. Despite therapeutic improvements, patients with DS often fail to become seizure-free, particularly in infancy and early childhood. The efficacy of KD in this syndrome was suggested based on retrospective studies in patients who did not receive previously stiripentol.

Method: We included prospectively 15 patients with DS aged >3 years with partial response to AEDs including stiripentol. All patients had a seizure diary and clinical examination with Conners and Achenbach (Child Behavior Checklist) scales before KD, at 1 month following onset and every 3 months thereafter. We considered responders the patients with a ≥75% decrease in seizure frequency on KD compared to baseline. For the used scales, we considered as clinically significant a scale of 70 or above (≥2SD) and as improvement a decrease >10 points (1 DS).

Result: At 1 month, 10 patients (66%) had a decrease of seizure frequency ≥75%. Efficacy was maintained in eight responders at 3 and 6 months and in 6 at 9 months. Five patients (33%) remained on KD over 12 months, and one was seizure-free. Besides efficacy on seizure frequency, KD was beneficial on behavior disturbances including hyperactivity. This effect was reported in all responders and in a few nonresponders.

Conclusion: KD should be proposed in patients with DS. It might have a double effect, on seizures control and on hyperactivity and behavior disturbances.

Poster Session: Neuroimaging I
Tuesday, 30 August 2011

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PRESURGICAL DIAGNOSIS OF THE EPILEPTOGENIC FOCUS USING NEAR-INFRARED SPECTROSCOPY MAPPING

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Purpose: For drug resistant epilepsy, an accurate diagnosis of the epileptogenic focus is inevitable in order to get good outcome in a surgical intervention. The purpose of our study is to investigate the utility of near-infrared spectroscopy (NIRS) ictal recording as a new functional mapping technique in the presurgical diagnosis of the epileptogenic focus.

Method: We used 48-channel NIRS system in a conventional mode. Twenty three patients with drug resistant epilepsy admitted for the presurgical evaluation of epilepsy surgery were enrolled in this study. Ictal recording using NIRS has been applied simultaneously with long term scalp video-EEG monitoring. Interictal IMZ SPECT and FDG-PET were also applied.

Result: Ictal NIRS showed increase of regional blood flow in the focus area at the beginning of seizures. We utilized this phenomenon to identify the focus location. Ictal NIRS diagnosed laterality of the epileptogenic focus correctly in 80% of patients which was superior to IMZ SPECT (diagnostic in 47.8%) and FDG PET (diagnostic in 50%). Ictal NIRS showed also higher specificity than that of IMZ SPECT (80% and 47.8% respectively), and higher sensitivity than that of FDG PET (80% and 50% respectively). These results were much more prominent in patients with neocortical epilepsy, as ictal NIRS diagnosed laterality of the epileptogenic focus correctly in all patients (100%) with a specificity and sensitivity of 100%, while IMZ SPECT was diagnostic in 50% of patients with a specificity of 50%, and FDG PET was diagnostic in 33.3% of patients with a sensitivity of 33.3%. Ictal NIRS has been shown also to be superior to IMZ SPECT and FDG PET in the diagnosis of laterality of the epileptogenic focus in patients with normal MRI results (nonlesional epilepsy), as they were diagnostic in 100%, 44.4% and 40% respectively.

Conclusion: These results augment our previous results that ictal NIRS is a valuable and reliable method to diagnose laterality of the epileptogenic focus especially in patients with neocortical epilepsy and patients with nonlesional epilepsy.

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HIGH-DENSITY ELECTRIC SOURCE IMAGING (ESI) IN FOCAL EPILEPSY: A PROSPECTIVE STUDY OF 150 OPERATED PATIENTS

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Purpose: EEG is mandatory in the diagnosis of the epilepsy syndrome. However, its potential as imaging tool is still under estimated. In the present study, we aim to determine the prerequisites of maximal benefit of electric source imaging (ESI) to localize the irritative zone in patients with focal epilepsy.

Methods: One hundred fifty patients suffering from focal epilepsy and with minimum 1 year postoperative follow-up were studied prospectively and blinded to the underlying diagnosis. We evaluated the influence of two important factors on sensitivity and specificity of ESI: the number of electrodes (low resolution, LR-ESI: <30 versus high resolution, HR-ESI: 128–256 electrodes), and the use of individual MRI (i-MRI) versus template MRI (t-MRI) as the head model.

Findings: ESI had a sensitivity of 85% and a specificity of 87% when HR-ESI with i-MRI was used. Using LR-ESI, sensitivity decreased to 68%, or even 57% when only t-MRI was available. The sensitivity of HR-ESI/i-MRI compared favorably with those of MRI (76%), PET (69%) and ictal/interictal SPECT (64%).

Interpretation: This study on a large patient group shows excellent sensitivity and specificity of ESI if 128 EEG channels or more are used for ESI and if the results are coregistered to the patient's individual MRI. Localization precision is as high as or even higher than established brain imagery techniques. HR-ESI appears to be a valuable additional imaging tool, given that larger electrode arrays are easily and rapidly applied with modern EEG equipment and that structural MRI is nearly always available for these patients.

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MULTIMODALITY APPROACH IN PRESURGICAL EVALUATION OF EPILEPSY

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Purpose: Both electroencephalography-functional magnetic resonance imaging (EEG-fMRI) coregistration and high density EEG (hdEEG) map abnormal brain activation elicited by epileptic processes (Gotman et al., 2004; Michel et al., 2004). Clinical assessment of these techniques is done in patients with focal epilepsy.

Method: The standard EEG (32 electrodes) and the fMRI data were acquired during a scanning session. The hdEEG recording was performed using 256 channels. The analysis of EEG-fMRI data was performed by using both the conventional (General Linear Model, GLM) and a novel method, which integrates in the conventional one two new modules: individual-based hemodynamic response function, and EEG protocol. Source localization of interictal epileptiform discharges (IEDs) using 32 (EEG acquired inside the magnet) and 256 EEG channels was calculated.

Result: Changes in BOLD signal were observed in 22 out of 30 patients in whom IEDs are recorded. In 82%, these are concordant with expected epileptic activity defined by EEG and clinical outcome. The remaining eight patients had no significant BOLD activity because of either technical problems or no interictal epileptiform EEG activity inside the scanner. Three patients with activation were selected to underwent a hdEEG and showed significant source localization correlating with the EEG-fMRI activation.

Conclusion: The combination of multimodality techniques such as EEG-fMRI coregistration and hdEEG is a useful tool of a presurgical workup of epilepsy providing two different methods of localization of the same epileptic foci.

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p532
THE CORRELATION BETWEEN ICTAL SEMIOLOGY AND MEG LOCALIZATION IN FRONTAL LOBE EPILEPSY

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Purpose: Ictal semiology (IS) of seizures is usually used for localization and/or lateralization of the epileptogenic region firstly in clinical practice. Previous studies found there are some correlation between IS and EEG recordings, but as far as we know, few studies investigate the correlation of IS and MEG localization in frontal lobe epilepsy (FLE). This study is aimed to find out whether the localization and/or lateralization derived from IS and MEG is accordant.

Method: Seven patients from Nuremburg-Erlangen University Hospital who underwent resective surgery of FLE with Engel 1a outcome were recruited retrospectively. MEG localization was located into five compartments (separate or combined) in frontal lobe: frontal basal (FB), frontal lateral (FL), frontal polar (FP), frontal mesial (FM), and frontal precentral (FPr) area. Based on previous researches which studied the value of IS in localization and lateralization, we compared the experiential localization and/or lateralization of epileptogenic region deduced from IS to the MEG localization.

Result: IS from seizure history and ictal video-EEG monitoring were collected. From IS, lateralizing is easier obtained then localization because of the variety of signs and fast propagation in FLE. They all had specific localization in MEG findings. Two patients had MEG foci in accordance with IS, other two had MEG localization adjacent to the estimated area locating from IS. The remains had some accordant lateralizing information from IS, no correlation to MEG foci.

Conclusion: There are indeed correlation between IS and MEG localization, but it's not always strong. IS itself is not convincible enough to predict the favorable postoperative outcome. Contrarily, MEG can provide precise localization in FLE, indicate the relation between epileptogenic region and lesion, and also correlate to favorable surgery outcome.

p533
SIGNAL CHANGES IN MRI IN PATIENTS WITH FOCAL STATUS EPILEPTICUS

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Purpose: Transient periictal MRI changes have been described in patients with status epilepticus. But these changes could persist and be related to prolonged neurological impairment. The purpose of our study was to compare two groups of patients with focal status epilepticus (FSE) with and without periictal MRI changes (PMC).

Method: We selected patients with FSE admitted in our hospital from 2005 to 2011. Clinical and demographic data were analyzed. We compared in both groups (with PMC versus without PMC) variables such as age, gender, time from clinical onset and MRI performed, treatment onset time, neurological deficit, FSE duration and recovery time of the neurological deficit.

Result: Among 28 patients that were admitted, 17 had MRI. Twenty-eight percent of them (five patients) had signal changes in MRI (DWI, FLAIR and T_2). There were no statistically significant differences between both groups in any variable except recovery time of the neurological deficit (1.22 ± 2.27 days in the group without PMC and 5.67 ± 2.39 days in the group with PMC, p 0.026) and presence of neurological deficit (40% in the group without PMC and 100% in the group with PMC, p 0.04). Among the five patients with PMC, two had persistent lesions in posterior MRI.

Conclusion: Patients with FSE can have periictal MRI changes. These changes can be related neurological impairment and delayed recovery time. Moreover, these changes could be the manifestation of a permanent lesion. In our study, though we could not conclude that a rapid treatment

onset could prevent these patients from having a lesion, we encourage an aggressive treatment in FSE. Further studies are necessary to detect other factors related to the brain injury.

p534
3-TESLA MRI STUDY IN FOCAL EPILEPSY. A PROSPECTIVE STUDY

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Purpose: We aimed to describe the percentage and topography of lesions seen by using a standardized 3T MR protocol in focal epilepsy.

Methods: Patients. One hundred twenty-one consecutive patients with focal epilepsy who underwent a diagnostic MR scan from January to December 2010. MR epilepsy protocol included amongst other sequences 3D-T1-inversion-recovery, 3D-FLAIR, susceptibility-weighted and arterial spin labeling (ASL).

Result: Demographics: Mean age 40 (±16) [16–84] years old. Male 52%. Pharmacoresistant 54%. MRI was normal in 57%, despite 8% of them had nonspecific lesions related to the epileptogenic area. Temporal lobe (45%) and frontal lobe (35%) were the most frequent epileptogenic localizations.

Temporal lobe epilepsy were: Pharmacoresistant 61%. Lesional MRI 57%. Most common causes: Tumor, malformation of cortical development (MCD) and mesial temporal sclerosis around 13% of patients each.

Frontal lobe epilepsy patients showed: Pharmacoresistant 52%. Lesional MRI 50%. Most common causes were vascular, MCD and post-traumatic around 15% of patients each.

ASL showed focal perfusion abnormalities matching the epileptogenic area in a quarter of patients.

Patients over 65 years old had a significant probability to have a vascular cause (87%) within the lesional epilepsies ($p < 0.05$).

In our study population we didn't observe differences in terms of MRI findings between the pharmacoresistant and medically controlled patients.

Conclusion: Addition of proper sequences in MR protocols for focal epilepsy, may detect lesions in more than half of patients with temporal or frontal lobe epilepsy. Usefulness of MR specific protocols in elders is controversial, since the vast majority have either cryptogenic or vascular etiology.

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IDENTIFICATION OF EPILEPTIC FOCUS WITH MULTICHANNEL NEAR-INFRARED SPECTROSCOPIC TOPOGRAPHY (OPTIC TOPOGRAPHY)

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Purpose: Establishing a noninvasive method to identify the epileptic focus is important for the treatment of patients with epilepsy. Near-infrared spectroscopic topography (NIRS) is a noninvasive method to measure the regional cerebral blood volume (rCBV) dynamics coupled with neuronal activities. Therefore, optical topography (multichannel near-infrared spectroscopy) was applied for detecting rCBV changes in the epileptic focus.

Methods: Optical topography was applied to five female patients with epilepsy; patients ranged in age from 5 months to 52 years of age (mean, 13.8). Two patients underwent surgical procedures. The rCBV dynamics was measured with an ETG 7100 (Hitachi Medico Corporation). Probes were placed over the scalp, including the putative epileptic focus which was estimated according to seizure symptoms, and electroencephalograms (EEGs) were performed. The rCBV dynamics during the seizures were analyzed for any changes in oxidized hemoglobin.

Result: In all cases, rCBV changes were examined in the site where the epileptic focus was estimated to be. In a patient with West syndrome, who was believed to have generalized epilepsy, the rCBV focally increased, and the patient was diagnosed with partial epilepsy. After changes in prescription, the number of patient seizures was markedly reduced. A patient with hemimegalencephaly who underwent a functional hemispherectomy became seizure-free, according to the EEGs and rCBV changes.

Conclusions: In addition to EEG, the evaluation of rCBV dynamics with optical topography is considered to be a useful method for noninvasively identifying the epilepsy focus.

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LOSS OF NETWORK EFFICIENCY ASSOCIATED WITH COGNITIVE DECLINE IN CHRONIC EPILEPSY

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Purpose: The nature of cognitive difficulties in chronic epilepsy ranges from memory deficits to global intellectual decline. With functional MRI, abnormal activation and dysfunctional cerebral networks have been linked to cognitive deficits. Previous investigations have focused on predefined cerebral networks, especially language and default mode networks. With graph theoretical network analysis, the topology of the whole cerebral network can be investigated. To study the relation between possibly altered whole brain topology and intellectual decline in chronic epilepsy, a combined study of neurocognitive assessment, and fMRI with graph theoretical network analysis was performed.

Method: Forty-one adult patients with cryptogenic localization-related epilepsy and 23 healthy controls underwent an intelligence test and fMRI with a silent-word generation paradigm. A set of undirected graphs was constructed by cross-correlating the signal time-series of 893 cortical and subcortical regions. Possible changes in cerebral network efficiency were assessed by performing graph theoretical network analysis.

Result: Healthy subjects displayed efficient small world properties, characterized by high clustering and short path lengths. On the contrary, in patients with epilepsy a disruption of both local segregation (lower clustering) and global integration (higher path length) was found. An association of more pronounced intellectual decline with more disturbed local segregation was observed in the patient group. The effect of antiepileptic drug use on cognitive decline was mediated by decreased clustering.

Conclusion: These findings support the hypothesis that chronic localization-related epilepsy causes cognitive deficits by inducing global cerebral network changes instead of a localized disruption only. Whether this is the result of epilepsy per se or the use of antiepileptic drugs remains to be elucidated. For application in clinical practice, future studies should

address the relevance of altered cerebral network topology in prediction of cognitive deficits and monitoring of therapeutic interventions.

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INCREASED AND DECREASED CENTRAL TYPE BENZODIAZEPINE RECEPTOR BINDINGS ASSOCIATED WITH SEIZURE OUTCOMES IN EPILEPTOGENIC CAVERNOUS ANGIOMA AND FRONTAL CORTICAL DYSPLASIA

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Purpose: Single-photon emission computerized tomography (SPECT) analysis of central type benzodiazepine receptors binding by (123) I-labelled Iomazenil (IMZ) has been applied in some neuropsychiatric disorders. The deficit in central type benzodiazepine receptors indicated that abnormal synchronization was mediated by the lack of inhibitory postsynaptic mechanism. In this study we investigate IMZ SPECT in a small series of patients who harbor supratentorial cavernous angiomas (CA) and frontal cortical dysplasia (CD) presenting with seizures and surgically treated in our institute.

Method: Twenty eight (CA:10, CD:18) patients underwent microsurgical resection of lesion which were pathologically confirmed. We performed lesionectomy, extended lesionectomy, standard temporal lobectomy respectively for CA and frontal corticectomy for CD. The preoperative interictal IMZ SPECT findings in these patients were reviewed retrospectively. The data were statistically analyzed using three-dimensional stereotactic surface projection (3D-SSP).

Result: Consequently, about 80% (CA:8/10, CD:14/18) of patients with intractable epilepsy achieved Engel Class I outcomes. Decreases of IMZ uptake were observed in the lesion (which means epileptogenic area) in about 70% (CA:7/10, CD:14/18) of patients. In addition, increases of IMZ uptake neighboring the lesion were recognized in 75% (7/8) of CA patients and in 50% (7/14) of CD patients achieved Engel Class I outcomes. All cases (6/6) of CA patients and 80% (4/5) of CD patients with both of decreased uptake in the lesion and increased uptake neighboring the lesion achieved Engel Class I outcomes. On the other hand, the contralateral area with increases of IMZ uptake were revealed in 70% (7/10) of CA patients and in about 80% (14/18) of CD patients. Additionally, much more increase of IMZ uptake in the contralateral side than lesion side were recognized in 3/7cases of CA and 4/14cases of CD. But on this point there was no correlation with seizure outcomes.

Conclusion: We hypothesize that the increase in benzodiazepine receptor density surrounding the lesion might be related to the intrinsic antiepileptic mechanisms. Further studies are needed to clarify the possible mechanisms.

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WHITE MATTER NETWORK ABNORMALITIES ARE ASSOCIATED WITH COGNITIVE DECLINE IN CHRONIC EPILEPSY

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Purpose: Patients with chronic epilepsy frequently display cognitive comorbidity. These patients might have widespread network abnormalities outside the epileptic zone, which might affect a variety of cognitive functions as well as global intelligence. We aimed to study the role of white matter connectivity as a neuronal correlate of cognitive decline.

Method: Thirty-nine patients with nonsymptomatic localization-related epilepsy and 23 age-matched healthy controls were included for diffusion MRI at three Tesla and neuropsychological (IQ) assessment. Whole brain white matter networks were constructed from fiber tractography and weighted graph theoretical analysis was performed to determine white matter connectional abnormalities associated with epilepsy and cognitive decline. Fiber tract volume was used to model individual differences in connection efficacy.

Result: Patients with severe cognitive impairment showed lower clustering (a measure of brain network segregation) and higher path length (a measure of brain network integration) compared to the healthy controls and patients with little or no cognitive impairment. Whole brain white matter volume was found to be normal in the patient group. Correlation analyses revealed that IQ and the degree of cognitive impairment were strongly associated with clustering and path lengths.

Conclusion: This study reveals neurobiological evidence for impaired white matter connectivity which is associated with cognitive decline in patients with chronic epilepsy. As whole brain white matter volume was preserved in the patient group, our results suggest an important role for the network topology, in terms of volume contribution of different white matter fiber bundles, in epilepsy and cognitive decline.

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NOVEL MULTIMODAL FUNCTIONAL NEUROIMAGING APPROACH FOR NONINVASIVE PRIMARY SENSORIMOTOR CORTEX MAPPING

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Purpose: In presurgical contexts, noninvasive mapping of the primary sensorimotor hand area ($SM1_{ha}$) usually relies on functional magnetic resonance imaging (fMRI) or magnetoencephalography (MEG). Brain lesions may induce distortion, plasticity and neurophysiological/neurovascular disturbances, weakening the robustness of such unimodal approaches. We therefore introduce a novel multimodal $SM1_{ha}$-mapping approach integrating information from fMRI and multiple MEG paradigms.

Method: Seven $SM1_{ha}$ functional indicators were obtained in ten right-handed healthy subjects (range 19–33 years; five males) and two right-handed patients (34 years male, right central tumor; 64 years female, left central cavernoma) based on classical block-design motor fMRI and four MEG paradigms: electrical median nerve stimulation (MNS), mu-rhythm event-related desynchronization (ERD approximately 10 Hz and ERD approximately 20 Hz), corticomuscular coherence (CMC) and corticokinematic coherence (CKC) with fingers touching each others (CKC-TOUCH) or not (CKC-noTOUCH). Functional indicators coordinates were obtained from equivalent current dipole modeling (MNS, CMC, CKC) or parametric maps local maxima (ERD, fMRI). These coordinates relative to their gravity center were subjected to principal component analysis to produce a centered ellipsoid with axis along principal components.

Result: Functional indicators success rate was n = 12 for MNS, n = 10 for ERD approximately 10 Hz, n = 11 for ERD approximately 20 Hz, n = 8 for CMC, n = 9 for CKC-TOUCH, n = 9 for CKC-noTOUCH, and n = 12 for fMRI. In all participants, the ellipsoid covered the anatomical $SM1_{ha}$.

Conclusion: $SM1_{ha}$-mapping obtained from this multimodal approach colocalized with anatomical $SM1_{ha}$ in all participants. Integrating results from multiple modalities investigating different neurophysiological processes increase the confidence in $SM1_{ha}$-mapping, which is crucial in the management of patients with brain lesions.

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Tuesday, 30 August 2011

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POSITIVE BOLD RESPONSE IN THE BRAIN'S DEFAULT MODE NETWORK ANTICIPATES SPIKE AND WAVE DISCHARGES IN IDIOPATHIC GENERALIZED EPILEPSY

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Purpose: Idiopathic generalized epilepsy (IGE) has been the target of several EEG-fMRI studies, which highlighted the neuronal networks involved in generalized spike and wave discharges (GSWDs) as revealed by BOLD changes. We analyzed the dynamic time course of BOLD changes preceding and following GSWDs in a group of 15 IGE patients. Our aims were to evaluate whether an activation of cortical areas before EEG seizure onset was consistent and demonstrable through a second-level group analysis, and to determine if these BOLD changes involved the brain's default mode network (DMN).

Method: Fifteen IGE patients (nine females, mean age: 27.8 years) were submitted to EEG-fMRI coregistration. EEG-related analyses were run both at single-subject and at group level (random effect). The time course analysis was conducted for 3 s time windows before, during and after GSWDs and they were included until no further BOLD signal changes were observed.

Result: All patients had GSWDs during EEG-fMRI (258 total events, mean duration: 4.1 s). The time course group analysis showed BOLD increments since 15 s before GSWDs onset located in the cortical areas of DMN. At GSWDs onset BOLD increments were located in thalamus, cerebellum and anterior cingulate gyrus, while BOLD decrements were observed in the DMN regions persisting until 9 s after onset.

Conclusion: Hemodynamic changes (BOLD increments) occurred in specific cortical areas, namely the precuneus, posterior cingulate and lateral parietal lobe, several seconds before EEG onset of GSWDs. A dysfunction of these brain regions belonging to the DMN may be crucial in generating GSWDs in IGE patients.

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HEMODYNAMIC CHANGES PRE AND POSTSURGICAL INVESTIGATION IN PATIENTS WITH HEMIMEGALENCEPHALY

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Purpose: The aim of this study was to evaluate the clinical usefulness of near-infrared spectroscopy (NIRS) in determining pre- and postsurgical changes in cerebral blood flow (CBF) and cerebral blood oxygenation (CBO) in patients with hemimegalencephaly. Another aim was to determine whether any correlation exists between CBO patterns on NIRS and seizure outcome postsurgery.

Method: Subjects were seven patients with hemimegalencephaly admitted at some point between January 2008 and March 2011. Hemodynamic patterns of oxy- and deoxy-hemoglobin after photic stimulation during sleep were evaluated before and after hemispherotomy using the ETG 4000 (Hitachi Medical Corp.) and compared with ECD-SPECT findings. Seizure outcome was investigated from medical records. Four of the seven cases were analyzed (three were excluded due to body motion artifacts). Informed consent was obtained from the parents before each NIRS study.

Result: Presurgically, like SPECT, NIRS showed CBF was increased in the affected hemisphere and decreased in the unaffected hemisphere in all patients. Postsurgically, three patients who were seizure-free showed CBF was decreased in the operated hemisphere and increased in the unaffected hemisphere compared with before hemispherotomy. However, one case with recurrent seizure showed no significant CBF increase in the unaffected hemisphere, as seen on SPECT. NIRS additionally revealed interesting hemodynamic patterns; arrhythmic or asynchronous changes in oxy- and deoxy-hemoglobin in the unaffected hemisphere.

Conclusion: NIRS is a useful, noninvasive tool to confirm hemodynamic patterns in patients with diffuse hemispherical cortical dysplasia. It has better temporal resolution than SPECT and can predict postsurgical seizure prognosis.

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REORGANIZATION OF VERBAL AND VISUAL MEMORY FOLLOWING ANTERIOR TEMPORAL LOBE RESECTION: RESULTS OF A LONGITUDINAL fMRI STUDY

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Purpose: Anterior temporal lobe resection (ATLR) controls seizures in 70% of patients with intractable temporal lobe epilepsy (TLE) but may impair memory function, typically verbal memory following left and visual memory following right ATLR.

Functional reorganization can occur within the unaffected ipsilateral and contralateral hemisphere. We investigated the reorganization of memory function in TLE patients before and after left or right ATLR and the efficiency of postoperative memory networks.

Method: We studied 46 patients with unilateral medial TLE due to hippocampal sclerosis (26 left) on a 3T GE-MRI scanner. All subjects had neuropsychological testing and performed an fMRI memory encoding paradigm for words, pictures and faces, testing verbal and visual memory in a single scanning session, preoperatively and again 4 months after left or right ATLR.

Result: Event-related analysis revealed that left TLE patients had greater left posterior activation in the medial temporal lobe (MTL) for encoding words and right TLE patients had greater right posterior MTL activation for encoding faces postoperatively than preoperatively.

Relatively greater pre- than postoperative activation for encoding words in left TLE and for encoding faces in right TLE in the ipsilateral posterior MTL correlated with better verbal or visual memory outcome after ATLR.

Four months after left ATLR greater postoperative than preoperative activation in the ipsilateral posterior MTL correlated with less good verbal memory performance, an effect that was not observed for visual memory after right ATLR.

Conclusion: Our findings provide evidence for preoperative reorganization of hippocampal function within the ipsilateral MTL suggesting that

it is the capacity of the posterior remnant of the ipsilateral hippocampus rather than the functional reserve of the contralateral hippocampus that is important for maintaining verbal and visual memory function, while early postoperative reorganization to ipsilateral posterior MTL structures is inefficient.

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EEG-fMRI BOLD RESPONSES ASSOCIATED WITH INTERICTAL EPILEPTIFORM SPIKES IPSILATERAL AND CONTRALATERAL TO THE SEIZURE ONSET ZONE IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY

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Purpose: Mesial temporal lobe epilepsy (MTLE) has different etiologies and prognosis. Multimodal neuroimaging techniques such as combination of EEG and functional MRI (EEG-fMRI) can improve the understanding of MTLE.

Methods: EEG-fMRI was performed in 12 patients with refractory MTLE; seven lesional (six with hippocampal sclerosis and one with low grade parahippocampal tumor) and five nonlesional. All patients had their seizure onset zone (SOZ) determined by ictal EEG or seizure-freedom after mesial temporal lobe (MTL) resection. fMRI was performed using a 3T MRI (Phillips, The Netherlands), with 6–8 sequences with 6 min of echo-planar images (EPIs) ($3 \times 3 \times 3$ mm^3 voxel size, TE = 30 ms, TR = 2 s, 80×80 matrix). EEG was acquired using BrainAmp amplifier (BrainProducts, Germany) and 64 MRI compatible electrodes Ag/AgCl. Acquisition of concomitant EEG was corrected for gradient and ballistocardiogram artifacts with Vision Analyzer2 software. Images were analyzed with SPM8. Time of interictal EEG activity was used to assess the BOLD positive (activation) and negative (deactivation) responses on MRI (*t*-test, lower limit 20 voxels, $p < 0.01$, $T > 2.1$).

Result: Two patients had no EEG epileptiform activity. Five had bilateral and independent temporal lobe spikes and five had only unilateral spikes (three left). We analyzed 15 different studies. Activations were observed in 14 studies and deactivations in 11. MTL activations were more frequent in lesional (37%) than nonlesional (14%) and MTL deactivation was observed in only one patient (lesional). We then divided the studies in those with epileptiform spikes ipsi (ESip) or contralateral (EScon) to the SOZ. Activations in MTL occurred in 40% and deactivations in 10% of studies with ESip. Conversely, no MTL activations or deactivations were observed in studies with EScon. Lateral temporal activations were also more frequent in ESip (60%) than EScon (20%).

Conclusions: BOLD activations and deactivations in MTL are more common in lesional MTLE. In patients with MTLE and bitemporal EEG spikes, BOLD activation and deactivation in mesial or lateral temporal regions are more commonly observed with spikes ipsilateral to the SOZ.

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DETECTION AND LOCALIZATION OF EPILEPTIFORM ACTIVITY USING COMBINED PARAMETRIC MULTICHANNEL ANALYSIS AND PATTERN RECOGNITION TECHNOLOGIES WITH SLORETA ON EEG fMRI DATA

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Background: EEG and fMRI play a crucial role in the presurgical evaluation of patients with refractory epilepsy, due to their complementary properties. EEG analysis in the fMRI environment still possess a challenge due to noise and the need to relate specific EEG patterns to dynamic BOLD signals.

Purpose: To develop new semiautomatic tools for detection and classification of interictal epileptiform discharges (IED) or rhythmic activity (IERA) for the localization of the epileptic source. Specifically, we aimed to: (1) automated detection of IEDs and IERA, (2) source localization of epileptiform activity, and (3) localization of the hemodynamic response correlated with epileptiform activity.

Methods: A two stage approach to detect epileptiform activity included a multi channel screening stage based on the inverse filter principle, followed by cluster analysis was developed. EEG data from 10 subjects with focal epilepsy was analyzed; source modelling was performed on the detected activity using sLORETA. Localization of the hemodynamic response was achieved using statistical analysis comparing ''high'' and ''low'' occurring blocks from EEG-fMRI data.

Result: The system was able to detect and classify focal epileptiform activity and localize its source in all patients. The hemodynamic response was correlated to the activity in spatially related brain areas. Detected source was compared to clinical diagnosis and imaging and corticography findings.

Conclusions: The proposed semiautomated procedure may lead to improvement of noninvasive presurgical localization of epileptiform activity and its application can assist in identifying other physiological and pathological brain activities.

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CHANGES IN STRUCTURAL AND FUNCTIONAL CONNECTIVITY OF THE HIPPOCAMPUS-EXTRATEMPORAL NETWORKS IN UNILATERAL TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS: A COMBINED STRUCTURAL AND FUNCTIONAL MRI STUDY

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Purpose: We aimed to investigate pathologic changes in structural and functional connectivity between the epileptic hippocampus and extratemporal networks in mesial temporal lobe epilepsy associated with hippocampal sclerosis (HS-MTLE), by using high-resolution structural MRI, diffusion tensor MRI (DTI), and seed-based resting-state functional MRI (Rs-fMRI).

Method: Twenty-two patients with unilateral HS-MTLE (12 left and 10 right HS) and 26 controls were examined on a 3T MRI using the following sequences: (1) 3D volumetric T_1-weighted images, (2) DTI (30 noncollinear directions), and (3) Rs-fMRI (240 EPI). Regionally specific differences in grey matter volume were assessed by VBM. Differences in white matter integrity were examined by tract-based spatial statistics (TBSS) analysis of fractional anisotropy (FA) and mean diffusivity (MD) images. Changes in functional connectivity of the pathologic hippocampus were evaluated by positive correlations between the ipsilateral hippocampus and other regions using Rs-fMRI analysis.

Result: VBM showed that both HS-MTLE patients had significant GM volume reductions in ipsilateral hippocampus, adjacent temporal lobe, insular cortex, and bilateral thalamus and caudate nucleus (cluster-level corrected $p < 0.05$). TBSS analysis showed that both HS-MTLE patients had significant FA decreases and MD increases in ipsilateral temporal white matter, internal and external capsules, corpus callosum, anterior cingulum, and bilateral anterior thalamus and frontal white matter (TFCE-corrected $p < 0.005$). Compared to controls, left HS-MTLE patients showed decreased functional connectivity between the ipsilateral hippocampus and anterior cingulate, posterior cingulate, and left middle temporal gyrus (corrected $p < 0.01$ with Monte Carlo simulation). Compared to controls, right HS-MTLE patients showed decreased functional connectivity between the ipsilateral hippocampus and anterior cingulate, posterior cingulate, and right middle and superior temporal gyrus.

Conclusion: Our results showed that HS-MTLE is associated with widespread pathological changes in structural (grey matter and white matter tract) and functional connectivity between the epileptic hippocampus and extratemporal structures, supporting the hypothesis that regional brain abnormalities in HS-MTLE exist not only in the hippocampus and temporal lobe ipsilateral to the epileptic focus, but also in the extensive extratemporal structures.

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LOCALIZATION OF FOCAL EPILEPTIC ACTIVITY WITH EEG-fMRI INFORMED BY EEG VOLTAGE MAPS

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Purpose: In patients with medically refractory focal epilepsy who are candidates for epilepsy surgery, concordant findings from noninvasive multimodal imaging are needed to localize the epileptic focus and guide intracranial EEG recording and/or resective surgery. Simultaneous EEG-fMRI can map focal hemodynamic (BOLD signal) changes related to interictal epileptiform discharges (IED) detected on the EEG and helps to localize the epileptic focus. However, EEG-fMRI studies are negative in 40–70% of cases due to a lack of IED or absence of significant correlated BOLD changes. Here, we used EEG topographic features of the epileptic activity derived from long term clinical EEG monitoring (LTM) to inform EEG-fMRI analysis.

Methods: After building the voltage map of averaged IED recorded during LTM, we calculated the time course of the correlation of this map with the intra-MR EEG topography. This time course was used as a regressor for fMRI analysis in a General Linear Model. In all cases, results were validated by concordance with the target area defined as seizure onset zone on intracranial recordings and/or resection zone in post-operatively seizure-free patients. Concordance was labelled as good (maximal statistical BOLD change ($p < 0.001$ uncorrected) or any corrected BOLD change (family-wise error correction $p < 0.05$) located <15 mm from the target area) or moderate (nonmaximal uncorrected BOLD change <15 mm from the target area).

Result: In 5/5 patients with IED-related BOLD change on conventional analysis, concordant with the seizure onset zone, the topographic analysis gave similar concordant results. In 14/18 (78%) patients with absent BOLD changes on conventional analysis, the topographic method showed good concordance (N = 10) or moderate concordance (N = 4) with intracranial EEG or resection area in postoperative seizure-free patients. All cases with lateral temporal or extratemporal lobe epilepsy showed concordance.

Conclusion: Pathological EEG topographic features have hemodynamic correlates and our method dramatically increased the yield of EEG-fMRI for estimating the localization of the epileptogenic zone. These findings could have important implications in the presurgical evaluation of patients with epilepsy.

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MR SPECTROSCOPIC IMAGING AND DIFFUSION-WEIGHTED MRI FOR DETECTION OF THALAMUS IN CORIARIA LACTONE (CL)–INDUCED STATUS EPILEPTICUS IN RHESUS MONKEYS

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Purpose: Neurophysiological, biochemical, and anatomical evidence implicates the role of thalamus in epileptic seizures. Until recently, however, longitudinal characterization of in vivo thalamus dynamics have not been reported yet. In this study, we investigated the metabolic and structural integrity of the thalamus to identify changes that evolve following coriaria lactone (CL)–induced status epilepticus.

Method: Five rhesus monkeys underwent whole-brain MR imaging and single-voxel MRS on a SIEMENS Trio Tim 3-T MR with a 12-channel head coil. Spectra were processed using LCModel. Scans were performed before and then 1, 7, 21 and 42 days after onset of status epileptics. Analyses compared five seizure (Sz) and five control (Con) animals.

Result: This longitudinal study demonstrated reduced glutamate/glutamine (Glx) levels in the left thalamus 1 and 42 days following status epilepticus in the Sz group compared with the Con group. *N*-acetylaspartate (NAA) declined 1 day following seizure activity and approached baseline level on 42 days, while myo-inositol (mI) elevated significantly on 42 days in Sz group. Our MRS data showed asymmetrical distribution of metabolite in the right and left thalamus within Sz animals. Meanwhile, the apparent diffusion coefficient (ADC) and fractional anisotropy (FA) in thalamus are normal which reflect microstructure integrity.

Conclusion: Our results emphasize the evolution of thalamus in CL-induced status epilepticus in rhesus monkeys. The various expressions of metabolites may implicate that the left thalamus is more vulnerabal to epileptic strike.

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NEUROPHYSIOLOGICAL CORRELATES OF DISSOCIATION IN PATIENTS WITH PSYCHOGENIC NONEPILEPTIC SEIZURES: A FUNCTIONAL MRI STUDY

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Purpose: To investigate whether patients with psychogenic nonepilepti seizures (PNES) differ from healthy controls in their resting-state functional connectivity characteristics, and whether these connections are associated with the tendency to dissociate.

Method: Eleven PNES patients without psychiatric comorbidity and twelve healthy controls underwent task-related (picture encoding and Stroop color naming paradigms) and resting-state functional MRI at 3.0T (Philips Achieva). Intelligence was tested using the Raven's Matrices test and participants completed questionnaires evaluating their dissociation tendency. The study obtained ethical approval, and all participants gave informed consent. Functional MRI data analysis was performed in SPM8 routines in MatLab. Functional connectivity analysis on resting-state

fMRI was based on seed regions extracted from task-related fMRI activation maps.

Result: The patients displayed significantly lower intellectual performance, and significantly higher dissociation scores. A random-effects analysis did not reveal any significant differences between the picture encoding and Stroop color-naming activation maps between controls and patients with PNES. However, functional connectivity maps from the resting-state fMRI were statistically different. For PNES patients, stronger connectivity values between areas involved in emotion (insula), executive control (inferior frontal gyrus and parietal cortex), and movement (precentral sulcus) were observed, which were also significantly associated with dissociation scores.

Conclusion: The abnormal strong functional connectivity found in patients with PNES hints at an underlying psychoform and somatoform dissociation mechanism where emotion can influence executive control, resulting in altered motor function (e.g. seizure-like episodes).

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THE EFFECT OF TOPIRAMATE ON COGNITIVE ACTIVATION: A CROSS-SECTIONAL fMRI STUDY

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Purpose: Topiramate leads to language impairment in patients with epilepsy and healthy individuals, causing in particular word finding difficulties and memory disturbances. We aimed to investigate the effects of topiramate on cognitive fMRI activations in patients with frontal lobe epilepsy (FLE).

Method: We obtained fMRI data using several memory encoding and verbal fluency paradigms in 23 healthy controls and 39 FLE patients (19 left-sided, 15 right-sided, five nonlateralized). Seven patients were taking topiramate (in polytherapy), with the remaining patients taking other combinations of antiepileptic drugs. Using SPM5, we modeled both rest and active conditions for the different tasks and performed group comparisons between patients taking topiramate (TPM-group), not taking topiramate (non-TPM) and healthy controls.

Result: Neuropsychological evaluation did not reveal any differences in verbal fluency, verbal and spatial learning between groups of patients. During the active condition of the memory encoding and verbal fluency tasks, the TPM-group recruited wider areas of frontal and parietal lobe cortex compared to controls and other patients, whereas during the rest condition, the TPM-group did not show any activation of areas involved in the default-mode-network (DMN).

Conclusion: Our results suggest that topiramate may affect the ability of FLE patients to activate the DMN during rest, or deactivate during cognitive tasks, which in turn might explain the cognitive impairment. fMRI can be used to investigate subtle drug effects on cognitive networks not obvious on neuropsychological evaluation, but prospective, longitudinal studies will be necessary to assess the influence of medication on cognitive function.

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RESTING-STATE fMRI STUDY IN TREATMENT-NAÏVE TEMPORAL LOBE EPILEPSY PATIENTS WITH DEPRESSIVE SYMPTOMS

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Purpose: We aimed to characterize regional brain activation in treatment-naïve temporal lobe epilepsy patients with depressive symptoms, comparing them to epilepsy patients without depressive symptoms and healthy controls.

Method: Twenty-three patients and 17 matched healthy controls were recruited, and the patient group was further divided into two groups: patients with depressive symptoms and patients without symptoms, assessed via a self-rating depression scale. All participants underwent a resting functional magnetic resonance imaging (fMRI) scan using a Trio Tim (3T) magnetic resonance (MR) imaging system. The data was processed and analyzed using REST and SPSS 11.5 software.

Result: The patients with depressive symptoms showed significantly higher activity in the bilateral thalamus, insula, caudate and right anterior cingulate as compared to the other two groups ($p < 0.005$, corrected). The brain network connectivity within the prefrontal-limbic system also was decreased in patients with depressive symptoms ($p < 0.005$, corrected). With respect to the whole patient group, the self-rating depression scale score was correlated with limbic components' amplitude of low-frequency (0.01–0.08 Hz) fluctuations (ALFF) value ($p < 0.05$).

Conclusion: The patients with depressive symptoms have a characteristic alteration pattern and disruption of the brain network at the onset of seizure. The depressive symptoms correlated with regional brain activities when taking the whole patient group into account. The present study offers further insight into the underlying neuropathophysiology of the epilepsy with depressive symptoms.

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IMAGE BIAS CORRECTION PROFOUNDLY INFLUENCES VOXEL-BASED MORPHOMETRY IN MESIAL TEMPORAL LOBE EPILEPSY

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Purpose: Voxel-based morphometry (VBM), an automated method based on full-brain MRI data, has been abundantly used to assess volumetric changes in mesial temporal lobe epilepsy (mTLE). A recent review, however, revealed a strong heterogeneity between studies as to which regions show grey matter alterations (Keller and Roberts, 2008). To assess the impact of image bias correction step we systematically varied the relevant parameters (bias regularization, bias FWHM) in a VBM analysis.

Method: Fourteen patients with unilateral mTLE and hippocampal sclerosis (nine left, five right [flipped]) and 20 healthy controls were scanned using a 3T MRI (Siemens Tim Trio) and T_1-weighted, 3D-MPRAGE images were acquired. Next, images were segmented into tissue classes using the SPM8 with bias regularization (0.001, 0.0001 and 0.00001) and bias FWHM (30, 45, 60 and 75 mm). Grey matter maps were normalized and smoothed (8 mm FWHM). Volumetric differences (patients versus controls) were analyzed in a group comparison, thresholded at $p < 0.001$ (uncorrected) and visualized.

Result: We found a direct and significant influence of image bias correction parameters on the VBM-detected volumetric alterations in mTLE. For the thalamus, that is known to be affected in mTLE, this ranged from nondetection (FWHM 45 mm) to clear bilateral volume loss (FWHM 75 mm > 30 mm). Even the extent and location of volume loss in the ipsilateral hippocampus region was clearly dependent on the choice of bias correction parameters.

Conclusion: Our findings indicate that image bias and the attempt/necessity to correct for it within the unified segmentation model may explain some of the overt heterogeneity of VBM results in mTLE studies. It is likely that these effects are not limited to VBM of mTLE but will be relevant for other conditions.

Reference: 1. Keller, S.S., Roberts, N., 2008. Voxel-based morphometry of temporal lobe epilepsy: an introduction and review of the literature. Epilepsia 49, 741–757.

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FDG-PET AND MEG VERSUS SEEG IN PEDIATRIC EPILEPSY SURGERY CANDIDATES

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Purpose: To assess the concordance of [18F]-fluorodeoxyglucose-positron emission tomography (FDG-PET) and magnetoencephalography (MEG) findings as compared to the epileptogenic zone (EZ) defined with intracerebral stereotactic electroencephalography (SEEG).

Method: Fifteen children who suffered from intractable focal epilepsy benefited from a presurgical evaluation including optimal MRI, FDG-PET, MEG and SEEG. Concordance score (CS) of FDG-PET and MEG findings with respect to SEEG conclusion were calculated as follows: 3 = focal abnormality overlapping the EZ, 2 = focal abnormality located nearly the EZ but not overlapping, 1 = large or multifocal findings ipsilateral to EZ, 0 = not localized.

Result: Mean CS was 2.5 for FDG-PET and 1.5 for MEG (paired sample t-test $p < 0.01$). In the six patients with normal MRI, mean CS was 2.2 for FDG-PET and 1.5 for MEG, while in patients with an abnormal MRI, mean CS was 2.7 and 1.6 for the two investigations, respectively. Seven patients underwent surgery (normal MRI = 4). In the five patients with an Engel Ia outcome, FDG-PET had a CS level 3 in each patient, while MEG had a level 2 in four patients, and three in one patient. The two other patients had an Engel class IV outcome with a CS level of 0 or 1 for both FDG-PET and MEG.

Conclusion: In this limited sample population, FDG-PET appears to provide more reliable information than MEG. When focal, PET and MEG abnormalities usually point to the same region, but rarely overlap. Nevertheless, the presence of such regionally concordant focal abnormalities on both investigations appears to be associated with greater likelihood of postoperative seizure freedom.

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THE ROLE OF VOXEL BASED MORPHOMETRY (VBM) IN THE DETECTION OF CORTICAL DYSPLASIAS WITHIN THE TEMPORAL POLE IN PATIENTS WITH THE INTRACTABLE MESIAL TEMPORAL EPILEPSY

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Purpose: To determine whether VBM might contribute to detect malformation of cortical dysplasias (CD) within the temporal pole in patients with mesial temporal lobe epilepsy and hippocampal sclerosis (MTLE/HS).

Method: Twenty patients with intractable MTLE/HS and 30 sex- and age-matched healthy controls were included in the study. All the patients fulfilled the diagnostic criteria for MTLE/HS and underwent anteromedial temporal resection. VBM without a modulation step was applied to the MRI brain images. Statistical parametric maps were used to compare structural characteristics (GMC – grey matter concentration) in terms of temporal pole between each patient and controls separately. The acquired data were then analyzed by statistical approach to determine congruency of visual inspection of MRI scans versus VBM, and both visual inspection and VBM results compared to histopathological findings of CD.

Result: Histopathological examination revealed a CD within the temporal pole in 12 patients. VBM suspected CD in 14 subjects and visual inspection of MRI scans in 13 subjects. VBM correctly detected presence/absence of CD in 14 patients (Cohen $\kappa = 0.43$). In two cases VBM was false negative and in four patients false positive. The correspondence of visual examination to histological proof was not significant, VBM results provided some trend to significance ($p = 0.055$).

Conclusion: We found no significant superior contribution of VBM in the determination of temporal pole CD compared to visual inspection in our study, but still clear-cut trend was found in VBM results and not seen in visual analysis.

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TAYLOR'S HYPOTHESIS REVISITED: A VBM STUDY OF GENDER AND HEMISPHERIC DIFFERENCES IN TEMPORAL LOBE EPILEPSY

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Purpose: Sexual dimorphism related to phenomenology of seizures has been described in temporal lobe epilepsy with mesial temporal sclerosis (TLE-MTS). Probably differences between sexes are expressed early in life, when differential rates of cerebral maturation occur. According to Taylor's hypothesis, there would be a biological basis for the higher vulnerability of the male brain and of the left hemisphere. Our aims were to perform a reanalysis of Taylor's hypothesis in order to evaluate whether age of first seizure varies as a function of laterality and gender; and to investigate the extension of damage as well as brain abnormalities in men and women using voxel-based morphometry (VBM).

Method: Two hundred fifty-two patients with refractory unilateral TLE-MTS were enrolled. Age of first event varying by gender and laterality was analyzed according to three criteria: (1) age of first seizure before 10 years, (2) age of first seizure throughout life and (3) age of occurrence of initial precipitating injury (IPI). For this analysis log linear model was applied. A sample of 120 patients and 50 controls was investigated with VBM5.

Result: Seizure onset occurred more often in the first 2 years of life considering events before 10 years (61.7%), throughout life (45.6%) and as IPI (71.7%), and affected particularly the left hemisphere. While in females a sharp fall was observed after the second year, in males a milder decay occurred with increasing age. In the first decade, age at seizure onset was associated with gender ($p = 0.037$) and laterality ($p = 0.007$). VBM abnormalities were more widespread in left-TLE; while in women temporal areas were the most involved, in men frontal regions were affected.

Conclusion: This study supports Taylor's hypothesis that gender, laterality and age of occurrence of seizures in early life are important factors determining the nature and severity of brain damage. Men and women show different areas of anatomical involvement. Males present damage in frontal lobes, while females in temporal areas.

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FRONTAL AND THALAMIC DYSFUNCTION IN JUVENILE MYOCLONIC EPILEPSY: A MAGNETIC RESONANCE SPECTROSCOPY AND NEUROPSYCHOLOGICAL STUDY

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Purpose: To investigate neuronal dysfunction in the thalami and frontal lobes of myoclonic epilepsy (JME) by using magnetic resonance spectroscopy (MRS) and neuropsychological tests (NPT).

Method: The study group consisted of 20 JME patients and 16 healthy volunteers with an age range of 16–40. All of the subjects had MRS to measure concentrations of *N*-acetyl aspartate (NAA), NAA/creatine (NAA/Cr), glutamate-glutamine (GLX), GLX/creatine (GLX/Cr), choline (Cho) and Cho/Cr in bilateral prefrontal cortex and thalami. A comprehensive NPT battery including verbal-visual attention, verbal-visual memory, visiospatial functions and executive function tests was applied. Statistical Package for Social Sciences (SPSS) was used for analysis.

Result: MRS results showed significantly lower concentrations of NAA in right frontal and left thalamic regions of JME patients ($p < 0.05$). NAA/Cr ratio was lower in the same regions, but this result was not statistically significant. NPT revealed executive functions were affected in patient group, and some of the differences in these tests were statistically significant ($p < 0.05$). Attention, memory and visio-spatial function tests were not different in both groups. Comparing MRS results with NPT results showed positive correlation between left frontal NAA level and spontaneous recall, right thalamic NAA level and Wisconsin Card Sorting test, right thalamic NAA/Cr level and spontaneous recall, left thalamic NAA level and verbal attention.

Conclusion: MRS showed neuronal dysfunction in both frontal and thalamic regions in JME patients. Concordant to these findings, NPT results showed deficits primarily in executive functions and also in attention and memory.

p556
PSYCHOGENIC NONEPILEPTIC SEIZURES: A CORTICAL THICKNESS AND VBM STUDY

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Purpose: Psychogenic nonepileptic seizures (PNES) are among the most common clinical manifestations of conversion disorder, and consist of paroxysmal behavior that resemble epileptic seizures. Preliminary data from functional neuroimaging studies gave plausible evidences that limbic circuits and sensorimotor cortex might be engaged in conversion disorder. Nonetheless, no advanced MRI studies have been focused on patients with PNES.

Methods: We enrolled 20 consecutive patients in whom the diagnosis of PNES was based on ictal video-EEG of the habitual episodes, and 40 healthy subjects matched for age and gender. All patients underwent a formal neuropsychological investigation and a neuropsychiatric assessment. All of them also underwent two distinct morphological whole-brain magnetic resonance measurements, voxel-based morphometry (VBM) and cortical thickness, in a multimethod approach.

Result: None of the patients had serious medical or neurological illness, substance abuse or psychotic disorder, or were on antipsychotic drugs. VBM and cortical thickness analyses revealed abnormal cortical atrophy in the PNES patients of the motor and premotor regions in the right hemisphere and the cerebellum bilaterally. We also observed a significant association between the increasing of depression scores with the atrophy involving the premotor regions.

Conclusion: The results of this study illustrate that motor and premotor regions in the right hemisphere and the cerebellum bilaterally play an important role in the pathogenesis of PNES and these structures are correlated with depressive symptoms. Our findings suggest a multistep model in the pathogenesis of PNES, in which the phenomenology is driven by psychological factors interacting with specific biological abnormalities.

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DTI VOXEL BASED ANALYSIS IN PATIENTS WITH IDIOPATHIC GENERALIZED EPILEPSY

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Purpose: Diffusion tensor imaging (DTI) is a technique which is able to detect white matter abnormalities. The mechanism of seizures generation behind idiopathic generalized epilepsies (IGE) probably involves the thalamocortical network. The objective of this study was to investigate the white matter integrity in IGE subsyndromes using DTI voxel based analysis.

Method: Forty-three patients and 38 controls (17 women, mean age 33 ± 9) were submitted to 3T MRI. DTI images were acquired using single-shot echoplanar imaging sequence. Obtained images underwent to format conversion, gradient directions and b-values extraction. Next, correction for eddy currents artifacts and extraction of the mean diffusivity (MD) and fractional anisotropy (FA) maps were performed. Using a 12-parameter affine transformation, these maps were spatially normalized to a template. A second registration process using nonlinear transformations was done based on a customized template created from the FA and MD images of all the subjects. Voxel-wise statistical analysis was conducted comparing each EGI subsyndrome FA and MD maps to the control group. The level of significance selected was a $p < 0.05$ corrected for multiple comparisons.

Result: Twenty-eight patients had juvenile myoclonic epilepsy (JME, 21 women, mean age 34 ± 8), seven patients had juvenile absence epilepsy (four women, mean age 33 ± 8) and eight patients had generalized tonic–clonic seizures only (GTCS, four women, mean age 34 ± 8). Statistical analysis revealed: (1) increased FA in the anterior limb of the internal capsule for the JME group ($p = 0.009$, cluster size 9761, $x = 11$, $y = 29$, $z=-29$); (2) increased MD in the midbrain for the GTCS group ($p = 0.002$, cluster size 6218, $x = -1$, $y = -21$, $z = -12$). The other comparisons did not revealed significant findings.

Conclusion: The findings presented in here support that there are distinct networks involved in the mechanisms of each IGE subsyndrome.

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FOCAL STRUCTURAL ABNORMALITIES IN JUVENILE MYOCLONIC EPILEPSY: A VOXEL-BASED DTI STUDY

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Purpose: There are contradictory reports of subtle abnormalities in MRI in juvenile myoclonic epilepsy (JME). We evaluated the structural white-matter changes using advanced MRI sequences in patients with JME and healthy controls.

Method: Nineteen patients of JME (21.7 ± 4.3 years; M:F: 7:12) and eight healthy controls (24.5 ± 2.3 years; M:F:4:4) were studied using

diffusion tensor imaging (DTI) to compare the white-matter changes on a Philips-3T MRI scanner (b-1000; 15 directions). Fractional Anisotropy (FA) maps were extracted using FSL-FDT (FMRIB's – software library and diffusion toolbox) software. Voxel-wise analysis was performed on the FA maps using ANCOVA with age, gender and total intracranial volume as nuissance regressors at significance of $p < 0.05$ (FDR corrected) with threshold masking of 0.2 on white-matter segmented FA maps using SPM 5-version.

Result: The age at onset of JME was 13.1 ± 3.3 years. All patients had myoclonus followed by generalized tonic–clonic seizures −13 and absence seizures −2. EEG showed normal background (all) and epileptiform discharges (spike/polyspike and slow wave) in nine patients. Seizures were controlled in 9/13 patients. Routine MRI (brain) was normal in all. Analysis of DTI revealed that patients with JME had decreased Fractional Anisotropy (FA) values in lentiform nuclei (z-4.143), anterior corpus callosum (z- 3.603) and cerebellum (z- left: 4.2382; right: 4.1744) compared to the controls. Parameters in other regions were not different compared to controls.

Conclusion: This exploratory study using DTI indicated focal abnormalities in lentiform nuclei, anterior corpus callosum and cerebellum in JME, hitherto believed to have normal brain structure. However, it requires further study to determine its role in seizure onset.

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DIVERGENCE OF EXPRESSIVE AND RECEPTIVE LANGUAGE LOCALIZATION WITH MAGNETOENCEPHALOGRAPHY IN PATIENTS WITH MEDICALLY REFRACTORY PARTIAL EPILEPSY

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Purpose: Establishing the role of magnetoencephalography (MEG) in localizing language utilizing multiple tasks tapping both expressive and receptive language tasks. Validation of MEG defined localizations as compared to standard techniques including Angio-WADA and direct cortical stimulations in Patients undergoing resective epilepsy surgery

Method: Thirteen consecutive patients with medically refractory complex partial epilepsy (median age of seizure onset 10 years) considered to be candidates for resective epilepsy surgery underwent an MEG study with a large array biomagnetometer utilizing standard epilepsy and language protocols. Word recognition task (tapping receptive tasks) and Picture naming/Verb generation (tapping productive language) were utilized. Laterality indices (LI) were calculated for left and right hemispheric late fields approximately 150–400 ms. Single equivalent current dipole solutions with appropriate >0.90 goodness of fit were superimposed on the patients own MR images of the brain.

Result: In 4/13 of patients there was a divergence of expressive and receptive language localization with shifting of receptive language to the right and preserved left-sided expressive language localizations. One patient had exclusively right sided language localizations. 5/6 patients had sub-lobar colocalization of the MEG defined language localizations with the subdural electrode defined language sites utilizing direct cortical stimulations. Angio-WADA was supportive of either bilateral or concordant language lateralization in all patients that underwent bilateral injections.

Conclusion: Divergent right-sided receptive language representation is found in patients with medically refractory epilepsy. Multiple language tasks may be of clinical importance. MEG may be a useful tool in noninvasively localizing language. These localizations co-localize with language sites validated utilizing direct cortical stimulations.

Poster Session: Neuroimaging IV
Tuesday, 30 August 2011

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OVERLAY OF INTERICTAL EPILEPTIC NETWORKS AND CORTICAL ABNORMALITIES IN MESIOTEMPORAL LOBE EPILEPSY

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Purpose: In mesiotemporal epilepsy (MTLE) ictal propagation pathways have been assessed by SPECT (1) and involved networks show structural abnormalities (2). Simultaneous EEG/fMRI studies have reported concordance of interictal epileptic networks and ictal electroclinical data. Here, we analyzed the spatial distribution of BOLD correlates of interictal epileptic discharges and cortical abnormalities in MTLE.

Method: We examined 10 MTLE patients with simultaneous EEG/fMRI and voxel based morphometry (VBM). Data of three patients with left seizure onset were flipped. Independent component analysis (ICA) was applied to the EEG data to extract epileptic activity as predictor for the BOLD_fMRI. Individual correlation estimation was made at $p < 0.05$ (FDR). Group analysis was performed on an overlay of the BOLD maps of all patients. VBM analysis based on a 3D_MPR T1 weighted sequence (TR/TI/TE 1950/900/2.6 ms) delineated cortical changes by differences to age and gender matched controls (SPM5). Differences were considered significant at $t = 3.1$, extension threshold 1000 mm^3 (two-sample *t*-test).

Result: EEG-derived BOLD correlates delineated an interictal MTLE network involving beyond the seizure onset zone in the hippocampus, in over 50% of patients the ipsilateral insular/operculum, temporobasal and polar neocortex, regions along the central sulcus and bilaterally in the middle cingulate. Widespread cluster were detected in the posterior temporal/occipital lobe and contralateral insula and central areas. Reduced cortical density was detected in the corresponding brain regions except for the central areas and cingulate.

Conclusion: In MTLE brain areas involved in the interictal epileptic network as assessed by EEG/fMRI overlay largely with brain areas with cortical abnormalities.

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HIGH RESOLUTION MRI TEXTURE ANALYSIS OF HIPPOCAMPAL TISSUE: HISTOPATHOLOGICAL CORRELATIONS IN MESIAL TEMPORAL LOBE EPILEPSY

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Purpose: A computational pipeline combining MRI high resolution acquisitions and image processing, texture analysis and pattern classification algorithms was developed aiming to correlate image features with histological data. This approach was used for image-based identification

of histological features in sclerotic hippocampi from patients affected by mesial temporal lobe epilepsy (MTLE).

Method: Image acquisitions of 12 hippocampi surgically obtained from MTLE patients were performed in a 3.0T scanner. Images were acquired with the specimen immersed in formaline 1%. High-resolution images were acquired using Turbo Spin Echo protocol and voxel dimension of, 80 μm × 80 μm × 1.6 mm. Imaging data processing pipeline consisted of preprocessing (noise filtering, background segmentation, intensity normalization), feature extraction (texture calculation) and analysis (data randomization, data resampling, and classification). Feature extraction was performed for every pixel in the image using a set of 150 texture parameters (cooccurrence matrix, run-length matrix; wavelet, fractal dimension, Markov random field and Gabor filters). The region of interest was limited to the dentate gyrus. Classification procedures, using random forest algorithm, focused: (1) cell loss and dispersion; (2) comparison between specimens from patients with or without antecedent febrile seizures history. Results were attested using a 10-fold cross-validation, kappa statistics and receiver operator characteristic (ROC) curves.

Result: Overall accuracy for correctly classified pixels were: 87% for cell loss, 85% for cell dispersion and 90% for correlation with febrile history.

Conclusion: This computational methodology detects subtle MRI signal differences in the sclerotic hippocampus and has a wide range of applications in image-based diagnosis.

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NONVERBAL MEMORY IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY AND AMYGDALA LESIONS

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Purpose: Complex visuospatial memory fMRI tasks reliably activate posterior mesial temporal lobe (hippocampus-parahippocampus, H-PH) bilaterally in healthy controls. Studies on patients with hippocampal sclerosis and mesial temporal lobe epilepsy (mTLE) suggest lateralization of visuospatial memory fMRI activation to the healthy side. We aimed to assess visuospatial memory in patients with mTLE and amygdala lesions.

Method: Seventeen patients (eight women; median age 35 years, range 28–38) with mTLE due to unilateral probable dysplastic amygdala (pDA; right-sided 4, left-sided 13) were tested with fMRI Roland's Hometown Walking Task: mental navigation and recall of familial visuospatial landmarks. All patients underwent neuropsychological assessment. Median age at seizure onset was 24 years (range 16–31), median epilepsy duration – 6 years (range 4–15). Fourteen patients (82%) had pharmacoresistant seizures; 16 (94%) were right-handed. Amygdala lesion was identified on high resolution MRI (1.5T). None of the patients had hippocampal sclerosis or any other structural cerebral abnormality.

Result: In 15/17 (88%) patients, bilateral symmetrical fMRI activation of H-PH areas was observed. Eleven patients with left-sided pDA had bilateral H-PH activation; one patient had activation of left and another one – of right H-PH areas. All four patients with right-sided pDA had bilateral symmetrical fMRI activation of H-PH. In neuropsychological testing, deficits in visual memory were seen only in 3/17 (18%) patients. All three had left-sided pDA and bilateral fMRI activation of H-PH.

Conclusion: Visuospatial memory is intact in the majority of patients with unilateral pDA and mTLE. Both H-PH are involved in visuospatial memory retrieval.

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IMAGING THE INTERACTION: WORKING MEMORY, EPILEPTIC DISCHARGES AND PERFORMANCE

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Purpose: Generalized and focal epileptic discharges (ED) can impair cognition in up to 50% of patients and may have a complex bidirectional relationship with cognitive tasks. A parametric spatial working-memory (WM) task of n-back type was used to delineate ED-related changes in WM-network during the task performance, using video-EEG-fMRI. We hypothesize that EDs during the task affect WM-network and performance of the task.

Method: We studied eight patients with frequent EDs. fMRI data was acquired on a 3-Tesla MRI-scanner. Video-EEG data was acquired using 64-channel EEG, two video-cameras and MR-compatible system. EDs were labelled using Brain-Analyzer2. After preprocessing fMRI data, a general linear model was built using factorial design in SPM5. SPM{T}-maps were obtained to reveal blood oxygen level dependent (BOLD) changes. Statistical analysis was performed in SPSS for the interaction between ED, WM-task and performance.

Result: One patient with idiopathic generalized epilepsy (IGE) had sufficient EDs during the task to perform fMRI analysis. EDs were more during the task than rest and increased significantly with cognitive activation. EDs were significantly associated with wrong/no response in IGE-patient for 2back phase of WM-task. Task-related positive BOLD changes were seen in fronto-parieto-striato-thalamic WM-network. EDs during rest revealed BOLD changes in precuneus and lateral parietal lobes. EDs during WM-task did not reveal any positive BOLD changes in WM-related network, however negative BOLD changes were observed in precuneus and lateral parietal lobes.

Conclusion: We conclude that the presence of generalized EDs during the task affects WM-related BOLD network in IGE patient. Cognitive activation can increase EDs, which in turn may lead to wrong/no responses during cognitive tasks.

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FACIAL EMOTION PROCESSING IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY AND AMYGDALA LESIONS

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Purpose: Functional MRI (fMRI) demonstrates a major role of amygdala in emotion processing. In patients with mesial temporal lobe epilepsy (mTLE), amygdala is often part of an epileptogenic zone. We aimed to test by fMRI how dysplastic amygdalae are involved in an emotion response.

Method: Seventeen patients (eight women; median age 35 years, range 28–38) with mTLE due to unilateral probable dysplastic amygdala (pDA) were tested with fMRI dynamic fearful faces paradigm: a short movie with alternating images of landscape and faces expressing fear. All patients underwent neuropsychological assessment including Ekman Faces Test for recognition of facial emotion. Median age at seizure onset

was 24 years (range 16–31), median epilepsy duration, 6 years (range 4–15). Fourteen patients (82%) had pharmacoresistant seizures; 16 (94%) were right-handed. Amygdalae lesions were identified on high resolution MRI (1.5T). All patients underwent at least two MRIs with the interval of at least 6 months.

Result: fMRI activation in amygdalae was elicited in 8/17 (47%) patients. In patients with left-sided pDA (n = 13), ipsilateral (n = 3, 23%), contralateral (n = 3, 23%), bilateral activations (n = 1, 8%) and no activation in amygdalae (n = 6, 46%) were observed. Patients with right-sided pDA (n = 4) showed ipsilateral activation (n = 1, 25%) or no activation in amygdalae (n = 3, 75%). General deficits in facial emotion recognition (Ekman Faces Test) was observed in 8/17 (47%) patients; deficits in facial expression of fear were seen in 6/17 (35%) patients. There were no significant associations between absent activation in fMRI and deficits in Ekmas Faces Test.

Conclusion: In patients with unilateral pDA and mTLE, fearful faces fMRI amygdala activation is independent from dysplasia side, has no side preference and frequently shows no activation.

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FRONTAL LOBE ACTIVITY DURING ENCODING IN TEMPORAL LOBE EPILEPSY

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Purpose: The medial temporal lobes have a key role in episodic memory. The contribution of the frontal lobes has only been appreciated recently. Functional MRI (fMRI) studies have demonstrated material specific prefrontal cortex (PFC) activations with verbal and nonverbal memory tasks on the left and right respectively in healthy individuals.

We investigated the involvement of PFC in memory encoding for both verbal and nonverbal episodic memory in temporal lobe epilepsy (TLE) patients using fMRI.

Methods: Twenty-four healthy controls and 34 patients with hippocampal sclerosis (17 right) were scanned on a 3T GE Signa Excite MRI scanner. An fMRI paradigm of encoding faces and words was employed. fMRI analysis was performed with SPM8.

Result: Word encoding: controls activated the left hippocampus (HC) and PFC. Patients with RHS similarly showed a left lateralized PFC activation. No HC activation was seen. Patients with LHS showed additional right PFC activations, greater than in controls or the RHS group ($p < 0.05$).

Face encoding: controls showed bilateral HC activations and right lateralized PFC activation. Patients with LHS activated right HC and right PFC. The RHS group activated left HC and bilateral PFC. Significantly greater left PFC activation was seen in the RHS group than the control and LHS groups ($p < 0.05$).

Conclusion: We showed material specific PFC lateralization for verbal and nonverbal memory encoding to the left and right PFC respectively in healthy controls. Patients with HS ipsilateral to side of material encoding showed additional contralateral PFC activations, implying reorganization of the underlying network to involve contralateral frontal lobes.

p566
INCREASED IN VIVO EXPRESSION OF AN INFLAMMATORY MARKER IN TEMPORAL LOBE EPILEPSY

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Purpose: Animal studies and clinical observations suggest that epilepsy is associated with inflammation. Translocator protein 18 kDa (TSPO), a marker of inflammation, is increased in vitro in surgical samples from patients with temporal lobe epilepsy. TSPO can be measured in the living human brain with positron emission tomography (PET) and the novel radioligand [^{11}C]PBR28.

Method: In this study, we sought to determine if in vivo expression of TSPO is increased ipsilateral to the seizure focus in patients with temporal lobe epilepsy. Sixteen patients with unilateral temporal lobe epilepsy and 30 healthy subjects were studied with [^{11}C]PBR28 PET and magnetic resonance imaging (MRI). Uptake of radioactivity after injection of [^{11}C]PBR28 was measured from regions of interest drawn bilaterally onto MR images. We defined brain uptake as the average of standardized uptake values from 60 to 120 min ($SUV_{60–120}$). SUV was calculated as radioactivity concentration divided by injected dose per body mass.

Result: On paired samples *t*-test, brain uptake was significantly higher ipsilateral to the seizure focus in hippocampus, amygdala, parahippocampal gyrus, choroid plexus, and fusiform gyrus, greater in patients with than without hippocampal sclerosis. Repeated measures ANOVA comparing patients and controls showed statistically significant group × hemisphere interactions in the hippocampus ($F = 11.6$, $p = 0.003$), amygdala ($F = 5.72$, $p = 0.027$), parahippocampal gyrus ($F = 4.98$, $p = 0.037$), and fusiform gyrus ($F = 6.42$, $p = 0.019$). In these regions, asymmetry was significantly larger among patients with temporal lobe epilepsy than among healthy subjects. TSPO uptake was higher in patients than controls both ipsilateral and contralateral to the seizure focus.

Conclusion: We found increased expression of TSPO, as evidenced by increased uptake of radioactivity after injection of [^{11}C]PBR28, suggesting a neuroinflammatory response on the side of the epileptogenic focus, possibly associated with increased density of reactive astrocytes and/or activated microglia. In addition, contralateral uptake appeared higher than controls, suggesting a more diffuse pathophysiologic process. The results of our study support a role for inflammation in TLE.

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ASSOCIATION BETWEEN BASAL GANGLIA AND LARGE SCALE BRAIN NETWORKS IN EPILEPSY

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Purpose: Epileptic activity may affect large scale brain networks. A functional brain connectivity study (FC) using functional magnetic resonance imaging (fMRI) was performed to find default mode network (DMN) and somatomotor resting state network (SMN) differences between patients with epilepsy and healthy controls (HC).

Methods: In ten HC, fourteen patients with extratemporal and ten with temporal epilepsy resting state fMRI data obtained using the 1.5 T Siemens Symphony scanner. For independent component analysis the GIFT program was used. The component representing the DMN was chosen according to a spatial correlation with a mask typical for DMN. In a second test we performed a seed analysis form the left primary somatomotor cortex. The impact of epilepsy on the FC between BG and the SMN was studied. A second-level analysis was calculated to evaluate differences among the groups using SPM software.

Result: In HC, the basal ganglia were functionally negatively correlated with typical DMN regions, such as the posterior medial and prefrontal cortices. This negative correlation as well as the FC between BG and SMN was significantly lower in the two groups of patients.

Conclusions: Unlike in HC, in epileptic patients the basal ganglia are not correlated with a DMN component and the FC of BG with SMN is decreased. The epileptic process reduces the FC between BG and large

scale brain networks. This may be interpreted as a sign of an altered or modified function of the basal ganglia in epilepsy.

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EPILEPSY-INDUCED CHANGES IN EFFECTIVE CONNECTIVITY IN THE NONEPILEPTIC TEMPORAL LOBE OF PATIENTS WITH UNILATERAL MESIOTEMPORAL EPILEPSY

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Purpose: To investigate epilepsy-induced changes in effective connectivity between the amygdalohippocampal complex (AHC) contralateral to the sclerotic hippocampus and the rest of the brain in patients with unilateral mesiotemporal lobe epilepsy (MTLE).

Method: Effective connectivity analyses used a design matrix including separately [^{18}F]-fluorodeoxyglucose positron emission tomography (FDG-PET) data of 33 patients with MTLE associated with unilateral hippocampal sclerosis (HS) (20 females, mean age: 36 years, 19 left HS) and 33 adults controls matched for age and gender. Right-HS patients' FDG-PET data were flipped to obtain a left epileptic focus lateralized group of patients. Seven voxels of interest (VOI) were selected within the cytoarchitectonic probabilistic maps of the right AHC (probability level = 100%, SPM8 Anatomy toolbox v1.7). VOI metabolic activity was used as covariate of interest to search, in patients compared to controls, for epilepsy-induced changes in the contribution of AHC contralateral to HS to the level of metabolic activity in others brain areas using pathophysiological interactions (PPI). Age, gender and duration of epilepsy were used as covariates of no-interest.

Result: PPI analyses identified in patients significant loss in connectivity between AHC contralateral to HS and lateral temporal, orbitofrontal, dorsolateral prefrontal and superior parietal cortices bilaterally, the right hypothalamus and the thalamus, temporal pole, mesial prefrontal and posterior cingulate cortices in the epileptic hemisphere.

Conclusion: This study evidences epilepsy-induced loss in connectivity between AHC contralateral to HS and a set of limbic and fronto-parietal structures. These functional changes probably account for emotional and cognitive changes frequently observed in MTLE patients.

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FINGERPRINTS OF BRAIN ACTIVATION IN EPILEPTIC SYNDROMES AND ENCEPHALOPATHIES

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Purpose and Methods: Simultaneous recording of EEG and blood-oxygenation level-dependent (BOLD) functional MRI (EEG-fMRI) is a modern noninvasive technique that allows evaluation of hemodynamic changes in the brain correlated with interictal epileptiform discharges (IED). Here, we report on a number of EEG-fMRI studies which have focused on characterization of epileptic networks in children with different epileptic syndromes and encephalopathies.

Result: In idiopathic generalized epilepsies, EEG-fMRI has revealed a typical network with a significant activation in the thalamus and deactivation in brain areas of the default mode network (DMN) such as precuneus, medial prefrontal cortex and parietotemporal junction. In epileptic encephalopathies, syndrome-specific networks have been specified: bilateral activation in insula and anterior cingulate gyrus associated with continuous spikes and waves during slow sleep, bilateral activation in putamen und brainstem associated with high-amplitude slow activity in hypsarrhythmia, and bilateral activation in thalamus and brainstem associated with multifocal epileptic activity and runs of polyspikes in patients with Lennox-Gastaut syndrome. It seems likely that cognitive deficits in epilepsy may be attributed to interruption of activity in the DMN through interictal epileptiform discharges.

Conclusion: EEG-fMRI has been shown as a powerful technique which may describe epileptic networks which appear as fingerprints in specific epileptic encephalopathies. Even after 15 years of intensive research, however, methodical work is still necessary to increase the value of the method for clinical praxis.

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EVALUATION OF WHITE MATTER ABNORMALITIES IN PATIENTS WITH FOCAL CORTICAL DYSPLASIA USING QUALITATIVE ANALYSIS OF FRACTIONAL ANISOTROPY MAPS

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Purpose: Drug resistant epilepsy is associated frequently with malformations of cortical development (MCD), the focal cortical dysplasia (FCD) is the most frequent type of MCD. The surgical failure in these patients may be due to the presence of more extensive, non-MRI visible epileptogenic FCD. Histopathological anomalies as well as reduced fractional anisotropy (FA) has been reported in the subcortical white matter underlying FCD lesions and even extending beyond the cortical abnormality seen with conventional MRI in some isolated patients. We investigated a serie of patients with FCD using DTI to explore white matter integrity underlying lesions of FCD in order to depict alterations not evident on conventional MRI. It may allow to establish a more sensitive representation of associated white matter changes.

Method: We scanned 21 healthy subjects and 22 patients with drug resistant epilepsy and FCD using DTI (1.5 Tesla Unit, reading 32 noncollineal gradients directions with final isotropic resolution of 2 mm). A qualitative analysis was performed evaluating FA Maps by two independent examiners with extensive experience in neuroimaging blinded to clinical records. Clear asymmetries between regions were defined when both examiners agreed or by consensus when there was discrepancy. These areas of assymetries were superimposed on the structural MRI to evaluate a relationship between the FCD lesion and the asymmetry determined on the FA maps for each individual patient.

Result: Eleven patients (50%) did not evidenced asymmetries in the FA maps, 11 patients showed asymmetries in the FA maps, in eight of these patients the areas of focal decreased FA were around the FCD detected on T1/Flair MRI. The remaining three patients had widespread area of increased or decreased FA which extended beyond the area of FCD.

Conclusion: The asymmetries described were evident during visual analysis of FA maps, and we believe that this could be an additional clinical tool to evaluate noninvasively patients with FCD in clinical practice.

p571
MAGNETIC RESONANCE IMAGING LOCALIZES THE EPILEPTOGENIC ZONE IN TUBEROUS SCLEROSIS COMPLEX

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Purpose: To identify the epileptogenic zone in TSC (tuberous sclerosis complex) patients using MRI blinded to other diagnostic and surgical data.

Methods: MRI's of 31 children with TSC who underwent resective epilepsy surgery in Miami Children's Hospital between 1994 and 2010 were reevaluated. Resection margins were determined using multimodal data, with primary reliance on electrophysiological findings. MRI findings typical of TSC (tubers, calcifications, etc.) and focal cortical dysplasia (increased cortical thickness, abnormal gyration, gray/white matter blurring, transmantle changes) were identified by two experts blinded to all other data. Localization of the suspected epileptogenic zone based exclusively on MRI findings was compared with the location of the resection cavity on the postoperative MRI and correlated with postsurgical seizure outcome (favorable in 23 and unfavorable in eight subjects).

Results: MRI localization alone correctly identified the resection site in 27 of 31 patients; 21 had favorable postsurgical seizure outcome. The resection site was partially confirmed in one patient (with favorable outcome) and unconfirmed in three subjects (one had a favorable outcome). Epileptogenic regions were characterized by ''FCD-like'' changes outside cortical tubers, especially gray/white matter blurring. Suspicious areas of FCD characterized by T2w hypointense cortical regions were most prominent in infants with unmyelinated white matter.

Conclusions: Thorough MRI evaluation can successfully localize the epileptogenic zone in a significant proportion of TSC patients, particularly infants. Our findings lend support for the hypothesis that dysplastic tissue surrounding tubers rather than the tubers themselves is the primary source of epileptic activity in TSC.

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p572
CORTICAL REPRESENTATION OF HIGH-FREQUENCY OSCILLATIONS IN LANDAU-KLEFFNER SYNDROME REVEALED BY MAGNETIC SOURCE IMAGING

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Purpose: High-frequency oscillations (HFOs, 90–140 Hz) concurrent with spike-wave discharges (SWDs) have been recently described in epileptic encephalopathy with continuous spike-waves during slow sleep (CSWS) using scalp electroencephalography (Kobayashi et al., Epilepsia 2010; 51: 2190–2194). Here, we investigate the neuronal correlate of HFOs in three patients with Landau-Kleffner syndrome (LKS) using magnetic source imaging.

Method: Three children (two boys, aged 4.5–8 years) with LKS underwent whole-head magnetoencephalography (MEG) recordings (band-pass: 0.1–330 Hz, sampling rate: 1 kHz; Vectorview, Elekta) under sedation. For each patient, SWDs typical of CSWS were selected. HFOs were indentified using individuals' SWDs spectrograms averaged with respect to SWDs peak power. SWDs and HFOs cortical sources were identified using dynamic statistical parametric mapping.

Result: SWDs epileptogenic sources were located at the right supratemporal auditory cortex (AC) in two patients and at the left AC in one patient. In all patients, SWDs rapidly (<20 ms) propagated to the opposite AC. Spectrograms identified HFOs during SWDs in the 120–140 Hz range on temporal MEG sensors ipsilateral to epileptogenic sources. HFOs neuronal sources colocalized with SWDs epileptogenic sources and reached maximum power on average 20 ms after SWDs onset. No HFOs were observed in AC contralateral to SWDs epileptogenic sources.

Conclusion: This study confirms the existence of HFOs in CSWS syndromes and demonstrates a common neuronal generator for HFOs and SWDs epileptogenic sources in LKS. This study suggests that HFOs might represent a marker of the epileptogenic source in LKS contributing to the driving hemisphere identification.

p573
MRI IN HYPSARRHYTHMIA

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Purpose: Hypsarrhythmia is a well known EEG finding in patients with infantile spasms and West syndrome and can be seen with multiple etiologies. We wanted to investigate the MRI findings in children with Hypsarrhythmia.

Methods: We selected EEG which have been reported as hypsarrhythmia and looked at their MRI. All patients had 1.5 Tesla MRI scan. We also looked at demographics and the reason for EEG referral.

Result: We found 25 patients (12 female and 13 male) with average age (±SD) of 17 (±11) months. There referral diagnosis at the time of EEG and MRI were infantile spasms- 12, West syndrome- 4, global developmental delay- 3, hypoxic ischemic encephalopathy-2, focal seizures-2, cerebral palsy- 1 and HSV encephalitis- 1. MRI showed diffuse cerebral atrophy in 6, hypomyelination in 5, cortical and subcortical hyperintensities in four patients. Two of each had malformations of cortical development, periventricular leukomalacia, focal lesions (left middle cerebral artery stoke and cystic lesion in right centrum semiovale) and normal scans. One of each had colpocephaly and dandy walker syndrome with cerebral atrophy.

Conclusion: Variety of MRI abnormalities was seen in our cohort of patients with Hypsarrhythmia. Diffuse cerebral atrophy and hypomyelination were most frequent.

p574
IMAGING THE EFFECTS OF AGE OF ONSET AND DURATION OF EPILEPSY IN FRONTAL LOBE EPILEPSY

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Purpose: To investigate the effects of different ages of onset and duration of epilepsy in cognitive networks of patients with frontal lobe epilepsy using fMRI.

Method: We studied 38 patients with frontal lobe epilepsy (FLE) and 25 controls with two working memory and two language fMRI paradigms.

Individual maps for each of the tasks were generated using SPM5 software.

fMRI scans were regressed by duration of epilepsy (mean 22.8 years; range 3–47 years) and age of epilepsy onset (mean 10.6 years, range: 0–31). Age of onset was further dichotomized into onset groups prior to age 10 and later to age 13 to account for frontal lobe maturation.

Result: Longer duration of epilepsy negatively correlated with the activation of working memory and language networks in FLE patients. Age of onset prior to functional maturation was associated with a decreased activity in these networks relative to patients with late onset and to controls.

Conclusion: Our data suggest that onset of epilepsy prior to crucial stages in brain maturation may have a greater effect on cognitive networks than later onset at a time when synapses have been formed or pruned normally.

p575
EVEROLIMUS THERAPY REDUCES THE VOLUME OF TUBERS OF PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX (TSC)

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Purpose: Patients with TSC develop a variety of benign tubers in multiple organ systems. Neurological manifestations include subependymal giant-cell astrocytomas (SEGAs) and subependymal nodules (SEN), epilepsy, and neurocognitive deficits. Tubers that develop in primarily white matter contain giant dysplastic neurons, and adjacent white matter may become hypoplastic as a result. Recently, a phase II study in TSC patients with SEGAs showed that everolimus, a mammalian target of rapamycin (mTOR) inhibitor, significantly reduced SEGA volume. As secondary end points the study assessed the effect of everolimus on reducing white matter tuber volume and ventricular volume.

Method: Twenty-eight TSC patients ≥3 years of age with demonstrated serial SEGA growth received everolimus 3 mg/m^2/day orally (titrated to achieve target trough concentrations of 5–15 ng/ml) as part of a prospective, open-label, single-center phase II study. MRI-based volumetric assessments of tubers and ventricular volume were performed at baseline, 3 and 6 months, and every 6 months thereafter by independent central review. Tubers were outlined, volumes calculated, and outlines confirmed by an independent neuroradiologist.

Result: Median duration of everolimus treatment was 21.5 months (range 4.7–34.4), and resulted in mean reduction in tuber volume of 3.39 cm^3 and mean reductions in left and right ventricular volume of 3.22 and 3.15 cm^3, respectively. No change was evident in SEN volume.

Conclusion: Everolimus reduces the volume of tubers of TSC patients. These changes may lead to an improvement in brain abnormalities, which would correlate with our previously reported reduction in seizures and improved behavior/cognition reported by caregivers.

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p576
HEMICONVULSION-HEMIPLEGIA EPILEPSY (HHE) SYNDROME: LONGITUDINAL MRI FINDINGS IN 13 CHILDREN

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Purpose: Hemiconvulsion-hemiplegia syndrome (HHS) is characterized by the occurrence of prolonged unilateral convulsions during the course of a febrile illness in children <4 years of age, followed by an ipsilateral hemiplegia. Later, focal epilepsy is often observed. HHS constitutes a unique sequence of events but its individualization during acute phase remains a challenge requiring exclusion of infective, vascular, metabolic etiologies. We describe 13 patients who presented with HHS analyzing sequential data from neuroimaging.

Method: We included 13 patients followed with a longitudinal neuroimaging study during early, intermediate and late phase and with an extended etiologic workup.

Result: All patients presented, at a mean age of 23 months (range: 8–60), a febrile hemiclonic status epilepticus leading to persistent hemiplegia in 11 cases. Early MRI showed a global hemispheric cytotoxic oedema in nine patients and a more localized posterior hemispheric involvement in 4. Homolateral, contralateral or bilateral basal ganglia involvement was observed in eight patients. Moreover five patients presented a homolateral or contralateral hippocampal involvement. In intermediate stage, morphological, signal intensity abnormalities and the reduction of ADC were consistent with the reduction of cytotoxic oedema. Late stage MRI was realized in nine patients showing a selective cortical-subcortical atrophy of the affected hemisphere in all, of thalamus in one and of caudate nuclei in two and of hippocampus in 6.

Conclusion: This series underlines the fundamental value of neuroradiological workup in individuating HHS since the early stage. Analyzing the role of hippocampus and basal ganglia involvement we suggest new insights in the possible mechanism of HHS.

p577
CASE REPORT: TWO PATIENTS WITH LATE ONSET AND ATYPICAL STURGE-WEBER SYNDROME

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Purpose: Sturge-Weber syndrome is a rare, congenital phacomatosis commonly revealed by seizures in childhood. It is characterized by a leptomeningeal angiomatosis often associated with facial cutaneous hemangioma and ocular disorders. Imaging usually shows leptomeningeal capillary and venous malformation, cerebral atrophy and calcifications. Seizures control improves the neurological outcome. We report two cases of late onset Sturge-Weber syndrome with isolated leptomeningeal involvement shown on CT-scan and MRI.

Method: Two male patients, a 14-years-old and a 17-years-old, presented several partial seizures secondarily generalized. They both had cerebral CT-scan, MRI and angiography. EEGs and a cognitive assessment were practiced in each case.

Result: In both cases, imaging showed an leptomeningeal angioma. Clinically, no cutaneous or ocular abnomalies and no others typical imaging findings as cortical atrophy, or calcifications in the first case, were found. The cerebral angiography was normal. The evolution was favorable with no seizures under medical treatment: oxcarbamezepine in the first case and levetiracetam in the second. The first patient developed a mild cognitive impairment with amnesia.

Conclusion: We describe two cases of late onset Sturge-Weber syndrome without facial angioma, and, in particular, one case without cortical calcifications. These atypical features have to be known because a medical treatment might control the seizures. Long-term follow-up is necessary in such cases to estimate the neurological outcome.

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DIFFUSION TENSOR MRI OF DAMAGE-INDUCED PLASTICITY DURING EPILEPTOGENESIS IN THE RAT HIPPOCAMPUS

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Purpose: Diffusion tensor imaging (DTI) produces images, which are weighted by the microstructural characteristics of water diffusion in the tissue. Our objective was to investigate whether DTI reveals injury-induced plasticity in the hippocampus after status epilepticus (SE) or traumatic brain injury (TBI).

Methods: SE was induced with pilocarpine and TBI with lateral fluid-percussion brain injury in adult rats. Ex vivo DTI was performed at 6–12 months after SE, or at 7 months after TBI. Maps of fractional anisotropy (FA), axial ($D_{\|}$) and radial ($D_{\wedge}$) diffusivities were obtained. After imaging, brain sections were stained with Timm, Nissl, or gold chloride protocols.

Result: After both injuries, DTI parameters were remarkably changed in selected hippocampal subfields. Changes in FA, $D_{\|}$ and $D_{\wedge}$ were mainly found in the CA3 and dentate gyrus. Changes in orientation of the principal eigenvector were more pronounced in the CA3 and stratum lacunosum-moleculare of CA1. As expected based on histology, DTI changes after SE were more robust and widespread than after TBI. Moreover, in TBI the changes were the most clearly in the distal CA3 where the most severe principal cell degeneration occurs.

Conclusion: DTI parameters of each hippocampal subfield can provide additional information about the dynamics of ongoing plasticity in injured hippocampus. The detection of differences in hippocampal plasticity between SE and TBI creates a scenario for the use of DTI to understand the etiology-specific circuitry reorganization during epileptogenesis.

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p579
RESTING-STATE FUNCTIONAL CONNECTIVITY ANALYSIS OF POSTTRAUMATIC EPILEPSY PATIENTS

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Purpose: Functional connectivity (FC) was used to investigate changes in the default-mode network (DMN) and the Temporal Epileptic Network (TEN) of patients with posttraumatic epilepsy (PTE).

Method: The study comprised 21 healthy volunteers (12 females) with mean ± standard deviation (SD) age of 32.2 ± 12.3 years and range of 20–59 years, and three male patients (age of 50.6 ± 4 years; range of 47–55 years) with PTE history following fronto-orbital/occipital traumatic brain injury (TBI). A BOLD echo-planar sequence was used for resting-state data acquisition in a 1.5T scanner. T_1-weighted volumetric sequence was acquired for anatomy visualization. Preprocessing was carried out using SPM5 and DPARSF1.0 software. Filtering of data was done in the 0.01–0.073 Hz frequency range. Averaged time courses in specified seeding regions-of-interest (ROIs) were taken and FC correlation coefficients were determined for each voxel in a voxel-wise manner using REST1.4 software. ROIs were the posterior cingulate/precuneus (BA23/31), which is a node of the DMN, and the mesial temporal structures (MTS:amygdala, hippocampus and parahippocampal gyrus), which are part of the TEN. Using SPM5 two-sample *t*-tests were done for the comparisons between controls and patients.

Result: In patients, a reduced correlation was observed between MTS and BA11, BA39 and BA40, all Brodmann areas related to DMN. This could be related to reduced DMN integrity and integration with other networks as is observed in patients who suffered TBI. Additionally, increased correlations were observed in patients between BA23/31 and the parahippocampal gyrus, and between MTS and temporal areas and the caudate, which are both part of TEN. This could mean that in PTE patients there is an increased activity of TEN similar to what is observed in mesial temporal lobe epilepsy.

Conclusion: The use of resting-state FC was able to highlight changes to the DMN and the TEN integrity in PTE patients. Currently, additional patients are being recruited to complement the preliminary results.

p580
HIPPOCAMPAL ACTIVATION IN SIMULTANEOUS INTRACRANIAL EEG-fMRI: A CASE REPORT

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Purpose: To report the results of a simultaneous recording of intracranial EEG (icEEG) and fMRI in a patient with drug-resistant epilepsy.

Method: We studied a 31-year-old patient with a right parietooccipital lesion due to perinatal vascular insult and seizures starting with déjà-vu, panic sensations and visual illusions. She underwent presurgical evaluation with icEEG (64 subdural contacts temporoparietooccipital grid, 20 subdural contacts temporal grid and six contact depth temporal electrode) and was scanned with a 1.5T scanner during a simultaneously recording with a 64-channels invasive EEG. 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.

Abstracts

Result: We recorded 2295 interictal spikes during the recording sessions and we visually labelled them into different types according to their localization, distribution, amplitude and morphology. We mapped the hemodynamic correlate of the right hippocampal spikes using a general linear model. We found a strong BOLD increase (FWE correction, $p < 0.05$) in the right hippocampus in close proximity to a depth electrode. The ictal EEG onset was first seen on the right mesio-temporal depth contacts.

Conclusion: We found a region of significant BOLD increase related to spikes recorded using a depth electrode in agreement with other electroclinical findings. This proves that icEEG-fMRI can measure highly significant BOLD changes from deep structures such as the hippocampus in close proximity to recording electrodes. Therefore, it allows the study of the hemodynamic correlates of both highly localized activity and responses over the whole brain, helping us better understand epilepsy and neurovascular coupling.

p581
MANGANESE-ENHANCED MRI EVALUATION OF CORIARIA LACTONE-INDUCED NEURONAL ACTIVATION IN RHESUS HIPPOCAMPUS

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Purpose: To investigate the hippocampal neuronal activation in a Coriaria Lactone–induced rhesus model of acute seizure using manganese-enhanced magnetic resonance imaging (MEMRI) and the effect of VGCCs by diltiazem, an L-type calcium channel blocker, in the hippocampal neuronal activation.

Method: Six rhesus macaques were divided into three groups to receive MnCl2 or Coriaria Lactone and MnCl2 or Coriaria Lactone, MnCl2 and diltiazem treatment. MnCl2 was given systemically during the course of seizure induced by Coriaria Lactone. Four hours after MnCl2 injection, T1-weighted MRI was performed followed by analysis of manganese enhancement.

Result: MEMRI studies revealed signal hyperintensity (100.305 ± 2.564) in the hippocampus after Coriaria Lactone and MnCl2 treatment compared with Mn2+ infusion alone ($p < 0.05$. And the MEMRI signal in the hippocampus (71.342 ± 1.727) can be attenuated by diltiazem, an L-type calcium channel blocker ($p < 0.05$).

Conclusion: It indicated that Coriaria Lactone–induced neuronal activation increased remarkably in hippocampus and the activation of glutamatergic neurons through NMDAR and VGCCs play an important role in the pathogenic mechanisms of seizure induced by Coriaria Lactone. MEMRI can be used to investigate the role of calcium channels in the neurological conditions.

p582
COMBINING EEG AND fMRI IN EPILEPSY

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Purpose: The conventional analysis of electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) data is based on the visual identification of the interictal epileptiform discharges (IEDs) on scalp EEG (Al Asmi et al., 2003), it is not automatic and suffers of some subjectivity in IEDs classification. Here, we *used* an easy-to-use and automatic approach for combined *EEG-fMRI* analysis able to improve IEDs identification based on Independent Component Analysis and wavelet analysis.

Method: Thirty-two channels EEG were recorded in eight patients with partial epilepsy inside a 1.5 T magnetic resonance (MR) scanner using a MR-compatible EEG recording system. EEG signal due to IED is reconstructed and its wavelet power is used as a regressor in General Linear Model (GLM). The method was applied on real data set consisting of eight patients with partial epilepsy.

Result: In all continuous EEG-fMRI recording sessions a good quality EEG was obtained allowing the detection of spontaneous IEDs and the analysis of the related blood oxygen level dependent (BOLD) activation.

Conclusion: The main clinical finding in EEG-fMRI studies of patients with partial epilepsy is that focal interictal slow-wave activity was invariably associated with increased focal BOLD responses in a spatially related brain area. Our study extends current knowledge on epileptic foci localization and confirms previous reports suggesting that BOLD activation associated with slow activity might have a role in localizing the epileptogenic region even in the absence of clear interictal spikes.

Reference:

1. Al Asmi A et al., Epilepsia 2003; 44 (10): 1328–1339.

p583
DIFFUSION TENSOR ANALYSIS OF TEMPORAL AND EXTRATEMPORAL TRACTS AND ITS CORRELATION TO THE CLINICOELECTROPHYSIOLOGIC IMAGING FEATURES IN DRUG RESISTANT TEMPORAL LOBE EPILEPSY

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Purpose: To determine if the abnormal water diffusion properties in major white matter tracts (temporal and extra temporal) determine the various clinical, electrophysiologic and magnetic resonance imaging (MRI) characteristics in patients with drug resistant temporal lobe epilepsy (TLE).

Methods: Diffusion tensor MRI measurements (fractional anisotropy and mean diffusivity) obtained from tractography for bilateral corticospinal tracts, arcuate, uncinate, inferior longitudinal and inferior fronto-occipital fasciculi in 201 patients with TLE selected for anterior temporal lobectomy (ATL) from August 2008 to February 2011 were chosen along with 100 age and sex matched controls. The relationship between the various clinical, electrophysiologic, imaging and seizure outcome parameters to the tensor parameters were analyzed by appropriate statistical tests.

Results: All five tracts in the affected hemisphere (side of resection) showed lower mean anisotropy as compared to the opposite side and controls ($p = 0.01$). The uncinate fasciculus showed maximum changes ($p = 0.005$). More severe diffusion abnormalities correlated with absence of aura, presence of secondary generalized seizures, longer duration of epilepsy prior to surgery and temporal lobar/hemispheric atrophy in MRI (in addition to the resected lesion-mesial temporal sclerosis or other foreign tissue lesions). ($p = 0.01$). No significant difference in seizure outcome was noted in the 91 patients who underwent ATL when correlated with diffusion abnormalities at the end of 1-year follow-up.

Conclusions: Abnormal water diffusion occurs in temporal and extratemporal tracts in TLE, especially in the hemisphere of ictal onset suggesting that TLE is a progressive disease. Many of the clinicoelectrophysiologic imaging changes not typical of TLE can be attributed to these functional diffusion changes.

p584
REORGANIZATION OF CEREBRAL NETWORKS FOR FEAR FACES MEMORY IN CHILDREN WITH TEMPORAL LOBE EPILEPSY: PRELIMINARY fMRI FINDINGS

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Purpose: Memory for fear faces is known to involve temporofrontal areas, especially right amygdala. Nevertheless, impact of temporal lobe epilepsy (TLE) on this cerebral network during development remains unresolved. We investigated cerebral activity associated with successful encoding of fear faces using fMRI in two children with right TLE (RTLE) and right temporal lobe resection (RTLR) compared with normal controls (NC).

Method: Twelve NC (11–16 years, mean = 13; 4 ± 2) and two patients participated. IC (girl, 12 year) has active RTLE since age 8. ML (girl, 11; 6 year) is a seizure-free girl since RTLR at 9; 11 year. Participants had to recognize fear and neutral faces they previously encoded during scan. Whole brain ($p < 0.01$, 10 voxels) and ROI analysis (medial temporal and frontal regions, $p < 0.05$) were performed on the contrast: correctly encoded fear faces less than correctly encoded neutral faces (paired *t*-test).

Result: NC recognized more fear faces (0.56 ± 0.13) than neutral faces (0.49 ± 0.14; $t(11) = 2.46$, $\eta^2 = 0.35$, $p < 0.05$) whereas ML (0.47 vs. 0.56) and IC (0.19 vs. 0.46) did not. NC engaged a bilateral frontotemporothalamic network, also observed in patients. As expected, NC but not patients recruited right amygdala. In contrast, patients but not NC activated dorsolateral prefrontal cortex (DLPFC). Finally, ML engaged left amygdala and hippocampus.

Conclusion: Despite the existence of compensatory networks involving left temporal lobe and DLPFC, fear does not enhance memory for faces in these patients, thus suggesting a crucial role of right amygdala for emotional memory modulation during youth.

This study was approved by the ethic committee of CPP Ile de France VI.

p585
FUNCTIONAL CONNECTIVITY AND EPILEPSY: A NONLINEAR RESTING STATE fMRI INVESTIGATION OF TEMPORAL LOBE, FRONTAL LOBE AND IDIOPATHIC GENERALIZED EPILEPSY

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Purpose: Connectivity in epilepsy can be affected by alterations of sources/targets of projections or by plasticity mediated changes related to seizures over the course of the illness. Here we put forward the use of fMRI ''resting-state'' (fMRI-RS) methodology to characterize functional connectivity patterns in epilepsy patients and adress its specificity in different conditions. Furthmore we assessed the possibility to use a wide fMRI-RS normative database for single patient management.

Method: Epilepsy patients accessing the Department of Neurology of the University of Siena – TLE (n = 23 left, 18 right, seven bilateral), FLE (n = 19), EGI (n = 6) – and 150 controls underwent no-task, seizure-free fMRI (1.5 T Philips Intera, 178 scans, TR = 2.5). After preprocessing and spurious variance removal, time series were extracted from anatomically defined ROI. Normalized pairwise connectivity matrices entered specific statistics aimed to address: (1) Group related differences including the focus and at distance; (2) Lateralization; (3) Sensibility of different connectivity measures; (4) The possibility of connectivity-based diagnosis/localization by pulling single cases and comparing connectivities against normative data.

Result: We observed (1) differences inside networks both including the putative focus and at distance; (2) on the bigger patient sample, TLE, hippocampus-to-all-brain connectivity differentiates right versus left TLE; (3) Nonlinear associations—mutual information (<0.1 Hz)—appears to be more sensitive than linear approaches to group differences, and (4) in mapping deviations of single subjects.

Conclusion: We provide evidence supporting the use of connectivity oriented analysis to uncover local and diaschis/compensatory changes useful for epilepsy research and management.

p586
CLINICAL LANGUAGE fMRI WITH REAL-TIME MONITORING IN TEMPORAL LOBE EPILEPSY: VALIDATION OF ONLINE PROCESSING METHODS

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Purpose: The increasing demand for clinical fMRI data has resulted in a need to translate research methods to clinical use. Referrals for language lateralization prior to epilepsy surgery are becoming more common, but time constraints make this unachievable in many busy neuroimaging departments. This study compared two image processing systems, the current gold standard, SPM8 (Wellcome Trust), and BrainWave (GE) to establish whether real time fMRI with online processing could replace conventional offline SPM processing for the purposes of establishing expressive language dominance prior to surgery.

Methods: We analyzed language fMRI results of 30 patients (17 female, 24 right handed, median age 30.5 years (range 18–59) with temporal lobe epilepsy. All patients were referred for presurgical fMRI evaluation of language dominance and underwent our standard verbal fluency paradigm. The SPM and BrainWave images were anonymized and assessed independently by two raters. An overall assessment of language dominance was made. A quantitative assessment of lateralization indices (LI) was performed for comparison with the visual radiological assessment.

Result: Concordance between visual assessment of SPM and Brainwave was 92.8%. There were discrepancies in two cases, both with bilateral asymmetric activations. Lateralization indices correlated closely with visual assessments of lateralization, concordance 85.7%.

Conclusion: BrainWave shows good concordance with the current gold standard SPM, providing a real-time, fast and accurate display of language representation, easily applied in a clinical setting. It can reliably identify typical left language dominance and highlight atypical cases that may require offline postprocessing for full clinical evaluation.

p587
DIFFERENT FUNCTIONAL CONNECTIVITY OF THALAMOHIPPOCAMPUS CIRCUITY IN TEMPORAL LOBE EPILEPSY WITH AND WITHOUT HIPPOCAMAL SCLEROSIS: A RESTING-STATE fMRI STUDY

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Purpose: The thalamus is known to have an anatomical connection to the medial temporal area and to play a role in seizure modulation. The seizure related neuro-network may be different between temporal lobe

epilepsy with hippocampal sclerosis (TLE + HS) and without HS (TLE-HS). Our study is aimed to evaluate differences of functional connectivity in Thalamo-hippocampus circuity between TLE + HS and TLE-HS with resting-state functional MRI (rfMRI).

Method: Twelve patients with TLE + HS and 10 patients with TLE-HS were included in this study. Hippocampal sclerosis were verified by two experienced radiologists. Resting-state fMRI data were acquired on a 3.0T GE MR scanner. Thalamus and hippocampus were drawn manually by the radiologists. Data analysis was performed on Matlab 7.0 and SPM8.

Result: Compared with TLE-HS, the functional connectivity in thalamo-hippocampus circuity in patients with TLE + HS is higher ($p < 0.05$). In addition, greater decreased connectivity relationship between ipsilateral hippocampus and default mode network was observed in TLE + HS patients.

Conclusion: Altered pattern was firstly explored between TLE + HS and TLE-HS patients. Resting-state functional MRI could be a sensitive method for further investigation of the underlying mechanism.

Poster Session: Epilepsy surgery I
Wednesday, 31 August 2011

p588
SURGICAL AND DEVELOPMENTAL OUTCOME AFTER CALLOSOTOMY FOR WEST SYNDROME WITHOUT MRI LESION

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Purpose: We analyzed surgical results, changes of psychomotor developments and prognostic factors of corpus callosotomy (CC) in 51 patients under 5 years old with West syndrome for their intractable epilepsy.

Method: Mean age at the seizure onset was 5 months. Severe developmental delay before the onset of epilepsy was observed in 27. Before CC, video-EEG monitoring, MRI and interictal SPECT were performed. Patient with resectable lesion on MRI was excluded. Mean age at CC was 24 months. For a psychological test, KIDS was used before CC and at each follow-up point. Surgical outcome was categorized as free (F, seizure-free), excellent (E, >80% reduction), good (G, >50%) and poor (P, no significant change).

Result: Epileptic spasm was recorded in all patients. Thirty-four had only epileptic spasm. Seventeen had multiple types of seizure. Preoperative DQ and DA is mean 18.5 and 3.9 months. Surgical outcome was F in 17 (33.3%), E in 8 (15.7%), G in 16 (31.4%) and P in 10 patients (19.6%). 80.4% showed significant improvements after CC. Epileptic spasm abolished after CC in 23 (45.0%). Preoperative prognostic factors were analyzed between F + E group and G + P group. Higher preoperative DA ($p = 0.04$) and normal developments before the onset of epilepsy ($p = 0.001$) are significant predictive factors for seizure control. In F + E group.

Conclusion: CC was important on patients with West syndrome. For postoperative improvements of psychomotor function, an early surgery is recommended before severe psychomotor delay develops.

p589
PEDIATRIC EPILEPSY SURGERY IN RUSSIA: A 5-YEAR EXPERIENCE FROM A SINGLE INSTITUTION

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Purpose: To specify the current level of epilepsy surgery in Russia

Method: One hundred twenty-one children with refractory epilepsy underwent surgery since January, 2006. In 69 cases seizures originated in consequence to various brain malformations (CD, heterotopias etc). The rest of patients had developmental tumors, cavernous malformations and gliosis. In 60 cases the lesions and/or the seizure focus were limited to the temporal lobe; remaining patients had extratemporal epilepsy. Presurgical workup included video-EEG, MRI and neuropsychological testing. Ictal SPECT, high-resolution MRI, interictal PET, MEG, and intracarotid propofol injections were also used in some complex cases. Eleven patients needed second surgery; in other six cases an invasive EEG precluded major procedure. Surgical options employed were: lesionectomy and excision of adjacent epileptogenic brain tissue guided by intraop corticography (69 patients); lobar and multilobar resections (31 cases); microsurgical disconnection (21 patients, in 18 of them – hemispherectomy).

Result: The seizures stopped or ceased after the operation in majority of patients. There were few complications: hemorrhage (2) and permanent neurological deficit (5). One hemimegalic infant has died at the 5th day postoperatively after failed attempt to perform functional hemispherectomy. Follow-up is known for 79 patients and ranges from 2 months to 4.5 years (median, 16 months). An Engel Class I of outcome was achieved in 68 patients (86%). Less favorable results (Class III and IV) were noted in three patients (4%). Six patients persisted with rare disabling seizures (Class II outcome, 8%).

Conclusion: Promising early results show the availability of almost every kind of modern options to assess and to treat surgically epilepsy patients in Burdenko Neurosurgical Institute. Unusually large proportion of postop seizure-free patients might be explained by both the lack of MR-negative cases and a rather short follow-up.

p590
SEIZURE AND DEVELOPMENTAL OUTCOMES OF EPILEPSY SURGERY IN CHILDREN WITH EPILEPTIC ENCEPHALOPATHY

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Purpose: To assess the developmental and seizure outcomes of epilepsy surgery (ES) in pediatric patients with various intractable epileptic encephalopathies (EE).

Method: Ninety-nine children (67 boys, 32 girls) with intractable EE were treated with ES such as resective surgery (RS), hemispherotomy, and corpus callosotomy (CC) at Severance Children's Hospital from 2003 to 2009. The study included 76 children of Lennox-Gastaut syndrome (LGS), 19 children of West syndrome, three infants of early infantile epileptic encephalopathy (EIEE), and one patient of Rasmussen encephalitis. They were serially assessed the Intelligence Quotient (IQ) and Mental and Psychomotor Developmental Indices (MDI, PDI) by the age-appropriate Korean-Wechsler Intelligence Scales or Bayley Scales before and at 6-month intervals after ES during mean 2.6-year follow-up.

Result: Of 99 patients with EE, RS was performed in 42 patients (42.4%), CC in 41 (41.4%), and hemispherotomy in 16 (16.2%). Engel's class I outcomes were achieved in 10 patients of 16 (62.5%) who had hemispherotomy, in 25 of 42 (59.5%) who had RS, and in 11 of 41 (26.8%) who had CC. IQ and MDI/PDI before and after the surgery were measured in 19 and 14 patients, respectively. Mean IQ of 19 children before and at the last follow-up after ES were 39.74 ± 10.26 and 34.88 ± 6.88, respectively. Mean MDI/PDI of 14 patients before and at the last follow-up were 55.12 ± 12.13/60.69 ± 20.39 and 52.33 ± 5.77/69.67 ± 34.93, respectively. The level of IQ and MDI/PDI were stable without significant decline after ES. Especially, PDI had a tendency of improvement during long-term follow-up after ES. Malformations of cortical development including microdysgenesis and cortical dysplasia were the most common pathology seen in children undergoing RS or hemi-

spherotomy, as follows: in 26 of 39 patients (66.7%) with LGS, in 11 of 15 (73.3%) with West syndrome, and in two of three (66.7%) with EIEE.

Conclusion: ES in children remained the level of intelligence and development without significant decline. We propose considering early surgery in children with catastrophic EE.

p591
LIFE AFTER HEMISPHERECTOMY IN CHILDHOOD

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Purpose: To highlight environmental factors in very long-term outcome of hemispherectomy, we selected two cases, a boy and a girl who underwent hemispherectomy for intractable seizures due to Rasmussen encephalitis. Both had been developing well until the onset of seizures and both had deteriorated cognitively thereafter. The model of the International Classification of Human Functioning (ICF, WHO, 2001) guided the interpretation of (hetero) anamnestic, cognitive, behavioral data and quality of life.

Method: Eleven years after the hemispherectomy, at the age of 23 years, patients and parents were interviewed, and patients underwent assessment of cognitive skills (wide-range test battery) and behavioral screening (Strength and Difficulties Questionnaire). Patients and parents rated health-related quality of life (EuroQuol EQ-5D).

Result: On the ICF-level of *functions*, (1) seizures had ceased after hemispherectomy and (2) cognitive impairments remained. Yet, on the level of *activities* and *participation* the two children are completely different. Both adolescents reported some difficulties in daily activities. With respect to *environment*, the parents of case 1 have an overly caring, sheltering attitude, not allowing autonomy. He lives with his parents, is depending, poor in initiative, developing neither social nor sport activities. The parents of Case 2 promoted autonomy. She leads a harmonious, responsive and rewarding life. She has an independent attitude, several social and sport activities and she lives semiindependently.

Conclusion: How the child/adolescent fares in everyday life depends not only on the remaining impairments. Parenting attitude can have stimulating but also inhibiting effect on the way of life of their child.

p592
EPILEPSY SURGERY IN CHILDREN WITH ELECTRICAL STATUS EPILEPTICUS DURING SLEEP

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Purpose: To describe the electroclinical presentation and postsurgical outcome of three children with symptomatic electrical status epilepticus during sleep (ESES) with particular attention to neuropsychological aspects.

Method: All children had ESES preoperatively. Two (P1 and P2) had perinatal left hemispheric destructive lesions and underwent functional hemispherectomy at 6.9 and 6.8 years of age. The other (P3) had a left frontal cortical dysplasia, undergoing lesionectomy at 9.9 years of age. Serial pre- and postsurgical video-EEG recordings and neuropsychological evaluations were analyzed.

Result: Postoperative resolution of ESES was consistently demonstrated in all cases. P1 had daily asymmetric tonic seizures, and ESES since 1 year before surgery; he remains seizure-free at 18 months postsurgery and significant cognitive improvement has been documented (developmental quotient [DQ] increase from 31 to 61) with disappearance of conduct regulation troubles, although cognitive executive functions disturbances continue. P2 had only sporadic seizures, but was experiencing progressive cognitive deterioration and behavioral disturbances since ESES onset 10 months before surgery; at 3 months postsurgery, cognitive deterioration has ceased (DQ 51 → 53) with disappearance of inhibitory control and emotional regulation disturbances, although severe sustained attention disturbances persist. P3 had intractable epilepsy with repetitive nonconvulsive status epilepticus, right motor seizures, and intermittent ESES since 18 months before surgery; he remains seizure-free at 18 months postsurgery with a slight progressive Full Intelligence Quotient decline (87 → 85 → 77) and persisting remarkable deterioration of cognitive executive functions.

Conclusion: In addition to seizure control, resolution of ESES and cognitive improvement can be obtained after resective surgery in some symptomatic cases.

p593
RESULTS OF SURGERY FOR TEMPORAL LOBE EPILEPSY IN CHILDREN

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Purpose: To retrospectively evaluate results of surgical treatment in a consecutive series of children with drug-resistant temporal lobe epilepsy (TLE).

Method: Between 2001 and 2010, 68 children (aged ≤15 years) received surgery for TLE. All patients underwent accurate anamnestic definition of ictal clinical semiology, interictal EEG and tailored high-resolution MRI. Ictal video-EEG recording was available in 41 cases. Stereo-EEG was required in 3. Seizure outcome (Engel's score, minimal follow-up 12 months) was analyzed as a function of several presurgical, surgical and postsurgical variables.

Result: All patients presented ictal clinical semiology indicative of temporal lobe seizures. In all cases, EEG provided lateralizing information; in 45 cases interictal or ictal modifications were restricted to the temporal lobe. In all cases MRI showed anatomical abnormalities in the temporal lobe (focal in 44 cases, double pathology in 13, isolated MTS in 8 and additional extratemporal extension in 3). Surgery consisted of anterior temporal lobectomy in 64 cases and neocortical lesionectomy in 4. Fifty-eight patients (83%) were in Engel's class I at last follow-up.

Statistical analysis showed a significantly increased risk of seizure recurrence for: presence of sensory-motor deficit or of mental retardation, additional extratemporal lesion at MRI, history of generalized seizures or of status epilepticus, negative histology, immediate postoperative seizures and ipsilateral epileptiform activity at postoperative EEG.

Conclusion: Surgery for childhood TLE is an effective treatment with excellent results on seizures. Presurgical evaluation does not necessarily require expensive and time-consuming investigations when semiologic, electrical and neuroimaging data are carefully collected and integrated.

p594
GLIONEURONAL TUMORS: CLINICAL AND COGNITIVE OUTCOME IN A CHILD AND ADOLESCENT POPULATION

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Purpose: Glioneuronal tumors are a recognized cause of focal epilepsies in children and young adults. Conflicting data about the clinical and neurocognitive outcome after surgery have been reported. The present study was aimed to evaluate the effects of glioneuronal tumors surgery on

cognitive outcome and seizure evolution in a child and adolescent population.

Methods: Clinical reports of 21 patients who underwent surgery for removal of glioneuronal tumors were retrospectively reviewed. Mean age at surgery was 10.3 years (range: 2–17). Tumor location was temporal in 16 cases, and extratemporal in five cases. Preoperatively, mean duration of epilepsy was 40 months (range: 1–180). Complete lesionectomy was achieved in all the five children with extratemporal lesions and in ten children with temporal lesion. Mean follow-up was 5 years (range 6 months–10 years). Seizure outcome was assessed at the 2-years follow-up using the Engel classification system.

Result: Eighty-eight percent of patients enter Engel class I (seizure-free) at 2 years. Antiepileptic medications were stopped in eight children and reduced in the remaining patients. Preoperatively, neuropsychological assessment showed a normal cognitive and behavioral profile in patients younger than 8 years, while cognitive dysfunctions and emotional disturbances were reported in the older. After surgery, no cognitive deterioration was seen in all patients; however, a slight worsening of psychiatric symptoms was reported in patients older than 8 years at surgery.

Conclusion: Surgery determined seizure freedom in the majority of cases, regardless of age, epilepsy duration at surgery and lesion location. Early age at time of surgery preserved cognitive and affective development.

p595
IMPACT OF SURGERY ON QUALITY OF LIFE AND CLINICAL IMPROVEMENT: RESULTS IN THE FIRST EIGHT SURGICAL CASES FOR DRUG RESISTANT EPILEPSY IN PEDIATRIC PATIENTS IN EL SALVADOR

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Purpose: The study reports the clinical outcome and the impact on patient and family quality of life (QOL) after surgery for drug resistant epilepsy (DRE).

Method: Eight patients between the ages of 3 and 18 years were studied. Questionnaires to evaluate seizure severity (HASS), side effects of antiepileptic drugs (HASES), quality of life of the pediatric patient with epilepsy (QOLCE) and quality of life of family group (IPES) were used. Such tools previously validated in Holland (Carpay H el al., Epilepsy Research 1996; 24: 173–181), Australia-USA (Sabaz M et al., Epilepsy & Behavior 2003; 4: 680–691) and Canada respectively were filled out by the patient's parents prior to surgical procedure and after 6 months of follow-up. Clinical improvement was assessed according to seizure outcome (Engel Classification).

Result: Seven out of eight patients (87.5%) showed a favorable impact on their QOL and that of their families after surgery. The same amount of patients showed clinical improvement (Engel Class I) evidenced by reduction in quantity and severity of the seizures. A significant reduction on the intake of antiepileptic drugs (AED) and their side effects is also reported, as well as a decrease in comorbidities.

Conclusion: By combining different validated tools that measure improvement on QOL, reduction of seizures and their severity and reduction of AED administered and their side effects, it is possible to obtain a comprehensive assessment on the effectiveness of surgery for DRE. Long-term follow-up is necessary to establish sustainability of results over time.

p596
EVOLUTION OF FUNCTIONAL HEMISPHERCTOMY

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Functional hemispherectomy for intractable hemispheric epilepsy has evolved over the last 60 years, from anatomical hemispherectomy to functional, which itself has been further modified to focus on less brain resection and more disconnection.

In order to achieve maximum benefit of the procedure, we modified it further to include the insular cortex, by recording directly from the surface and the depth of its cortex using electrocorticography, specially in cases where the possibility of being involved is significant, for example Corical dysplasia, and hemimegalencephaly.

We present the results of our series; 52 patients underwent functional hemispherectomy. (19 cases) Rasmussen encephalitis, (12 cases) hemimegalencephaly, (six cases) cortical dysphasia, (six cases) stroke, (nine cases) structural lesions.

Conclusion: Recording from insular cortex has proved in some cases it's involvement in the epileptogenic activity of the hemisphere

p597
EVALUATION OF EFFICACY AND SAFETY OF CALLOSOTOMY IN CHILDREN WITH REFRACTORY SEIZURES

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Purpose: This study was conducted to evaluate the efficacy and safety of callosotomy (conventional technique and radiosurgery) on children with refractory seizures.

Method: Candidate patients underwent callosotomy by one of two Methods:

Radiosurgery or conventional approach. Seizure response and procedure complications in the next year were evaluated.

Result: Eight patients (six male, mean age 6.3 years) were included, they were randomized to radiosurgery or conventional surgery. Six of them had Lennox-Gastaut syndrome criteria. Time of surgery was 4.4 years (mean) from the diagnosis of epilepsy. All the patients had ≥80% decrease in seizure frequency for atonic seizures, without significative difference in both groups. Only one patient (radiosurgery group) was on Engel classification 1 after 1 year of the procedure. Serious adverse events did occur, one patient in the radiosurgery group died after 3 months of procedure because of unknown cause (withdrawal of follow up). Fifty percent of the patients (n = 2) on the conventional group present immediate complications after the procedure (bleeding and temporary mutism in one patient and neuroinfection in the other) without complications along the follow up. Two of the patients in the radiosurgery group presented complications in the follow up period, one with persistent mutism at last follow-up and one of them with hemiparesis secondary to hemispheric infarctation at month 6th. The whole patients continued the pharmacological treatment before the surgery, those on the radiosurgery group received a short course of steroid. There was no relation between the kind of antiepileptic drug used and the changes in seizure frequency.

Conclusion: Callosotomy produces higly favorable outcomes for atonic seizures, but it continued to be a procedure with different complications in our serie, including immediate complications for conventional callosotomy and late complications for radiosurgery callosotomy.

p598
SUCCESSFUL ANATOMICAL HEMISPHERECTOMY IN A 3.4 KG INFANT WITH INTRACTABLE EPILEPSY AND HEMIMEGALENCEPHALY

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Purpose: We report a 3.4 kg male infant with sporadic hemimegalencephaly who successfully underwent an anatomic left hemispherectomy at 6 weeks of age for refractory status epilepticus. Hemimegalencephaly is a rare malformation of cortical development consisting of abnormal proliferation of neuronal and glial cells which leads to hypertrophy of the affected cerebral hemisphere. Infants with hemimegalencephaly present with refractory epilepsy and have poor developmental outcomes.

Method: (Case report).

Result: A full-term male infant developed focal seizures in the first week of life. A MRI of the brain showed diffuse dysplasia of the left cerebral hemisphere consistent with hemimegalencephaly. He was commenced on phenobarbitone and later vigabatrin but remained refractory. He was transferred to our pediatric intensive care unit (PICU) and commenced on a midazolam infusion along with phenobarbitone, levetiracetam, phenytoin and vigabatrin. Despite maximal therapy he continued to be in refractory status epilepticus over 11 days.

His EEG showed almost continous spike and sharp wave discharges intermixed with periods of background suppression on the left. Intermittent right frontal sharp waves and spikes were seen but not independently. A PET study showed a generalized increase of 18F-Flurodeoxyglucose uptake in the left cerebral hemisphere particularly in the left frontal lobe and subcortical nuclei.

He underwent an anatomical hemispherectomy with careful intraoperative hemostasis and fluid balance management with preoperative hydration and intraoperative fluid replacement with using crystalloids, packed red blood cells and fresh frozen plasma blood products. The estimated blood loss was 300 ml.

He was discharged from PICU on day 5 and 3 weeks later discharged home. At 7 month follow up, he remains seizure-free off antiepileptic medication, has a mild hemiparesis and is meeting social and language developmental milestones.

Conclusion: A good outcome, without complications, can be obtained in very small infants undergoing hemispherectomy with careful preoperative and intraoperative fluid replacement. To our knowledge this is the smallest infant to have undergone successful anatomical hemispherectomy.

Poster Session: Epilepsy surgery II
Wednesday, 31 August 2011

p599
COST SAVINGS AFTER SUCCESSFUL EPILEPSY SURGERY ARE SIGNIFICANT BUT ONLY APPARENT AFTER 3 YEARS

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Purpose: Economic austerity demands both clinical and economic justification of expensive therapeutic intervention such as epilepsy surgery. Few such economic evaluations have been performed and evidence regarding long-term cost-effectiveness is lacking to inform those who prioritise health care funding. We considered how good surgical outcome reduced health care resource use over 5 years compared with the patients who relapsed post-op.

Method: Retrospective analysis of 115 consecutive surgical cases (2003–2005). Demographic, clinical and resource use data considered over 5 year post-op period with unit costs determined from secondary care NHS perspective (which represents majority of NHS cost in refractory epilepsy). Good surgical outcome defined as 1–2 vs. poor outcome 3+. Characteristics of patients lost to follow up considered. Sensitivity analysis performed.

Result: Five year follow-up data analyzed for 78 cases (male = 34). No difference in economic costs observed between good and poor outcome groups during year 1 and 2 (£1267 vs. £1859, $p > 0.05$; and £804 vs. £1185, $p > 0.05$). Beyond 3 years, economic costs were significantly different and absolute savings were >60%. By 5th year post-op average costs were £406 vs. £1721 ($p < 0.001$). These findings were robust to sensitivity analysis of unit costs and clinical missing data.

Conclusion: Our data support the view that epilepsy surgery is unlikely to produce early (year 1/2) savings in secondary care costs incurred by people with epilepsy, and highlight the need for those funding health care to consider a long-term economic perspective (>3 years) when considering this patient group. Our data also indicate thresholds to guide those making preoperative estimates of surgical cost-effectiveness according to ex ante probability of good outcome.

p600
SEIZURE OUTCOME IN PATIENTS WITH EPILEPTOGENIC LESIONS 2 YEARS AFTER EPILEPSY SURGERY IN SWEDEN

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Purpose: Seizure outcome after epilepsy surgery is to an important extent related to underlying etiology. In this study of all patients who underwent epilepsy surgery with a lesional etiology in Sweden 1990–2004, the aim was to investigate seizure outcome and prognostic factors.

Method: All patients operated during the time period with a histopathological diagnosis of a lesion and a 2-year follow-up were identified in the population based Swedish National Epilepsy Surgery Register. Epileptogenic lesions were defined as: gangliogliomas (GGL), dysembryoblastic neuroepithelial tumors (DNET), cavernous hemangiomas (CAV) and lowgrade astrocytomas (AST). Univariate and multivariate analyses were performed to determine the independent contribution of the following variables to seizure outcome: age at surgery; epilepsy duration; preoperative seizure frequency; localization of the resection and histopathology.

Result: Of 156 patients (103 adults and 53 children) 71% had temporal, 16% frontal and 13% parietal and occipital lobe resections. Mean presurgical epilepsy duration was 13 years in adults and 5 years in children. Main histopathological diagnosis was GGL or DNET in 67 patients, CAH in 42 and AST in 47. Seventy-seven percent of patients were seizure-free 2 years after surgery. Multivariate analysis revealed that lower age at surgery and diagnosis other than AST were independently associated with seizure freedom. There was no decrease in the duration of epilepsy until surgery when comparing three 5-year periods (1990–1994, 1995–1999 and 2000–2004) in spite of improved neuroimaging.

Conclusion: In this population based series 77% of 156 patients with epileptogenic lesions were seizure-free 2 years after surgery. Many of them had a long epilepsy history. Seizure outcome can be improved if epilepsy surgery is considered earlier in patients with epileptogenic lesions.

p601
IS EPILEPSY SURGERY POSSIBLE IN COUNTRIES WITH LIMITED RESOURCES?

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Purpose: For a number of reasons, surgery for epilepsy is either highly under utilized or overly delayed, in countries with limited resources. Experience from India suggests that epilepsy surgery is not only possible in a country with limited resources, but can also be undertaken in a cost-effective way (Malla et al., Epilepsia (Supp1. 4):S3 l–S34, 2000). This

experience can be utilized by other countries with similar socioeconomic background to develop epilepsy surgery programmes.

Method: Based upon predominantly, a standardized noninvasive presurgical evaluation protocol, the author has performed over five hundred epilepsy surgery procedures during the past 15 years. These procedures mostly involved anteromesial temporal resections for mesial temporal sclerosis with the rest being temporal and extra temporal resections for lesions including focal cortical dysplasia and various other pathologies.

Result: Even in a country with limited resources, people with drug resistant focal epilepsy with a surgically remediable lesional epilepsy syndromes achieved surgical outcome at par with the established centers in the industrialized countries. The incidence of surgical complications is low and within acceptable limits as per the published literature.

Conclusion: It is crucial to identify the ideal surgical candidates who can benefit with various types of resective or disconnective procedures. It is necessary for young neurosurgeons to understand the intricacies of epilepsy surgery procedures and be aware of potential pitfalls, in order to maximize surgical outcome and reduce neurological complications. During this presentation, the author will discuss strategies for developing epilepsy surgery programme in countries with limited resources.

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THE USE OF ANTIEPILEPTIC DRUGS 10 YEARS AFTER RESECTIVE EPILEPSY SURGERY: A POPULATION-BASED, PROSPECTIVE, LONGITUDINAL STUDY

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Purpose: Reports on long-term antiepileptic drug (AED) use following epilepsy surgery are scarce. The aim of this study was to look at medication status related to seizure outcome 10 years after resective epilepsy surgery.

Method: The Swedish National Epilepsy Surgery Register encompasses data on all epilepsy surgery procedures in Sweden since 1995. Data is collected before and at surgery, and then after 2, 5 and 10 years. In this study, we analyzed the AED use preoperatively and 2 and 10 years after surgery for all patients who underwent resective epilepsy surgery in Sweden 1995–1997, N = 188.

Result: Of the 188 resections performed, 133 were temporal lobe resections and 55 extratemporal resections. After 10 years, 16 patients had been reoperated, 12 had died, and 14 were missing from follow-up (7%). Ten years after surgery, 87 patients were seizure-free (with or without aura, 60% of those followed), compared to 89 after 2 years. Of the seizure-free patients, 53% were off AEDs completely after 10 years, compared to 21% after 2 years.

Conclusion: In this prospective, population-based study, more than half of the patients who were seizure-free at long-term had stopped AED medication completely 10 years after surgery which is a substantially higher proportion than reported in most earlier studies. Whether the reason is greater trust in seizure freedom with time or active advice from treating physicians could not be addressed in this register study.

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SOCIOECONOMIC STATUS AND HIPPOCAMPAL SCLEROSIS IN MEDICALLY INTRACTABLE EPILEPSY

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Purpose: Low socioeconomic status has been previously associated with poorer outcomes following epilepsy surgery in patients with medically intractable epilepsy. We hypothesized that these patients might have different preoperative clinical characteristics to their more affluent peers. The purpose of this study was to examine the relationship between the extent of pathology in patients with hippocampal sclerosis and measures of socioeconomic status in presurgical patients with medically intractable epilepsy.

Method: The socioeconomic status of 285 patients with medically intractable temporal lobe epilepsy and hippocampal sclerosis (HS) was calculated using the UK Index of Multiple Deprivation (IMD) associated with their postcode. Hippocampal volumes were quantified using three tesla MRI. Ninety-three had right hippocampal sclerosis (RHS), 130 had left hippocampal sclerosis (LHS) and 62 had bilateral hippocampal sclerosis (BHS).

Result: The extent of ipsilateral hippocampal volume loss was significantly correlated with the measures of socioeconomic status in the patients with unilateral hippocampal sclerosis ($r = 0.15$, $p = 0.01$). This relationship was also present in the patients with bilateral hippocampal sclerosis where both hippocampal volumes were significantly correlated with the IMD.

Conclusion: Hippocampal pathology in patients with low socioecominic status is less extensive than that observed in their more affluent patients. Although this may initially appear counterintuitive, it is a robust finding. We propose a model of ''reduced resiliance'' to explain these results whereby a lesser degree of pathology is associated with medically intractability in the context of an impoverished socioeconomic environment.

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BEYOND THE LEARNING CURVE IN EPILEPSY SURGERY: THE INSTITUTIONAL AND INDIVIDUAL PERSPECTIVE

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Purpose: Skilled activity gets further refined with repeated performance. The concept of a learning curve raises ethical questions and surgical training related dilemmas. Objective parameters to evaluate it are not clearly defined and maybe implicit to a particular procedure. We aim to evaluate the learning curve for a common standard epilepsy surgical procedure (anterior temporal lobectomy and amygdalohippocampectomy (ATL AH) for mesial temporal sclerosis) from an individual and institutional perspective.

Method: Single center retrospective analysis of consecutive patients (aged 12–60) who underwent ATL AH over a period of 14 years (1995–2009). The procedure was performed by five different surgeons (A–E) and their individual experience was subdivided into ''early''(case1–25), ''mid''(26–50) and ''late''(50+). The overall institutional experience was also subdivided into early (1–200), mid (201–400) and late (400+). Learning curve in each subset of experience was evaluated with respect to the operative time, minor/major surgical adverse events and seizure outcome (1 year).

Results: A total of 674 patients included in the study were operated by five different surgeons (194, 64, 60, 257, 99). Mean age of the patients was 28 years (SD 17.3) The mean operative time comparison among the early, mid and late experience was found to be significant only among surgeons A and F (using ANOVA test, sig.<0.05). No significant difference in the experience subsets were noted in the incidence of major adverse events for all surgeons. Minor adverse events were significantly lesser with increasing experience in all surgeons. Seizure outcome was not significantly different at 1 year across the surgeons learning curve. The institutional experience showed a significant reduction in the minor

adverse event rates and operative time across the subsets of surgical experience.

Conclusion: Individual variations exist in the epilepsy surgery learning curve implying that the number of cases to attain an asymptote level for proficiency in the procedure may be difficult to define. Collective surgical experience over time makes the institutional learning curve less steep than the individual one. The study sets a background for a prospective evaluation of the learning curve with subsets of the ''whole'' surgical task including other epilepsy surgical procedures, thus having surgical training and seizure outcome implications.

p605
DISCONTINUATION OF ANTIEPILEPTIC DRUGS FOLLOWING SUCCESSFUL EPILEPSY SURGERY: A SURVEY OF CANADIAN EPILEPTOLOGISTS

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Purpose: To identify the perceived practice among Canadian epileptologists regarding discontinuation of antiepileptic drugs (AEDs) following successful resective surgery for temporal and extratemporal surgery.

Method: We performed a survey of pediatric and adult epileptologists in Canada, using a 77-item questionnaire to explore attitudes, timing, rate of withdrawal, and factors contributing to the decision to withdraw AEDs after successful epilepsy surgery. Surveys were mailed with a postage-paid return envelope. Two subsequent surveys were mailed to non-respondents at 1-month intervals. All procedures received institutional review board approval.

Result: Surveys were sent to 80 epileptologist in all the Canadian provinces. At the time of this report, completed surveys from 57 (71%) of potentially eligible respondents have been received, representing all epilepsy centers across Canada. The minimum seizure-free period after epilepsy surgery before considering discontinuation of AEDs, varied substantially among responders, ie. ≥6 months in 9%, 6–11 months in 23%, ≥1 year in 49%, ≥2 years in 11%, and >2 years in 6%. EEG was required prior to deciding to discontinue AEDs by 72% of participants, MRI was required by 49%, and serum AED levels by 46%. Forty-five percent of participants considered the opinion of the patients very important in their decision to reduce or stop AEDs. Focal pathology and anterior temporal resection increased the likelihood of AED discontinuation, and persistent auras decreased it. Other results will be presented.

Conclusion: Little information is available to guide decisions to discontinue AEDs in postsurgical seizure-free patients. Canadian epileptologists indicated that and EEG, and often an MRI and AED levels are performed before stopping AEDs. Generally, a good candidate for stopping AEDs has focal pathology, is completely seizure-free, has anterior temporal lobe resection, complete resection of seizure focus, and has no remaining epileptiform discharges in the EEG. The data pertain to self-reported practice styles, and actual practice may differ.

p606
STRESS IN PARENTS OF CHILDREN WITH EPILEPSY BEFORE AND AFTER EPILEPSY SURGERY

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Purpose: To know whether epilepsy surgery changes inordinate stress in parents of children with medically intractable epilepsy. The data are from an ongoing country-wide 2-year follow-up study of social cognition in children before and after epilepsy surgery.

Method: The Dutch adaptation of the Parenting Stress Index (Brock et al., 1992) allows tracing the source of stress by distinct parent- and child domains. The parent domain consists of seven sub-scales (Competence, Role restriction, Attachment to Child, Depression, Health, Social Isolation and Spouse) and six child related domains (Adaptability, Mood, Distractibility/Hyperactivity, Demandingness, Reinforces Parent and Acceptability). Parents (two fathers, nine mothers) of 11 children filled out this questionnaire before and 2 years after epilepsy surgery of their child of whom 10 were seizure-free after surgery.

Result: Before epilepsy surgery, parents reported more than average stress in parent domains Role Restriction (feeling dominated by the needs of the child) and Spouse (deficient emotional and factual support) and child domains Distractibility/Hyperactivity, Demandingness (demanding more attention and time) and Acceptability (accepting disappointing intellectual, emotional and physical features). Two years after epilepsy surgery, all group scores normalized. Remarkably, the parents of the child with ongoing seizures reported less stress in all sub-scales 2 years after surgery.

Conclusion: Pharmacologically intractable epilepsy of children causes inordinate parenting stress, which has a high chance of normalizing after epilepsy surgery.

p607
NATURAL COURSE OF MEDICALLY REFRACTORY EPILEPSIES: A RETROSPECTIVE STUDY IN PATIENTS WITH EPILEPSY SURGERY

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Introduction: Epilepsy surgery renders up to 80% of patients with medically refractory partial epilepsies seizure-free. However, epilepsy surgery is frequently delayed due to various reasons. Thus, it is possible to observe a natural course of epilepsy in these patients. We aimed to study the influence of epileptogenic zone and epilepsy clinical features on the course of seizure disorder.

Methods: We retrospectively analyzed the data of 200 patients with medically refractory partial epilepsies who were included in the ''Epilepsy Surgery Program Innsbruck'' between 09.03.1998 and 24.06.2009. Clinical features, course of epilepsy and time to intractability were examined according to three acknowledged definitions.

Result: We included 174 patients (88 men; mean age 44.2 ± 12.7 years) with temporal lobe epilepsies [TLE] (148/174, 85.1%) and extratemporal lobe epilepsies [ETE]; (26/174, 14.9%) in the study. Epilepsy was symptomatic in 152/174, 87.4% (hippocampal sclerosis 87/174, 50.0%, cortical dysplasia 38/174, 21.8%, others 27/174, 15.6%) and cryptogenic in 22/174 (12.6%). We found three courses of disease: primary pharmacoresistent (88/174; 50.6%), secondary pharmacoresistent (61/174; 35.1%) and relapsing-remitting (25/174; 14.4%). The results comparing the time of intractability did not significantly differ between TLE and ETE according to the three definitions. Epileptiform discharges ($p = 0.002$) and ictal pattern ($p = 0.015$) occurred more frequently in TLE compared to ETE. Patients who had undergone surgery during the second observation period (17 February 2005–24 June 2009) were significantly younger (mean 35.8 vs. 39.8 years) and were operated-on earlier (mean 19.3 vs. 26.2 years) compared to those who underwent surgery during the first observation period (09 March 1998–17 February 2005).

Abstracts

Conclusion: The localization of epileptogenic zone seems to influence clinical features of epilepsy. In the natural course of epilepsy, only half of patients have primary pharmacoresistent epilepsies. This may contribute to delayed epilepsy surgery. However, our results reflect, that since 2005 (second observation period), there is a tendency for pharmacoresistent patients to undergo surgery at an earlier stage during the course of their disease.

p608
IMPLICATIONS OF SURGERY FOR REFRACTORY EPILEPSY IN CLINICAL AND PSYCHIATRIC OUTCOMES

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Purpose: Clinical and psychiatric outcomes in patients with refractory temporal lobe epilepsy and mesial temporal sclerosis (TLE-MTS) submitted to surgical treatment may follow opposite trajectories. In order to highlight this discordance, two cases are reported.

Methods: Revision of patients' medical files. Psychiatric evaluations were performed by the same psychiatrist through DSM-IV criteria.

Result: The cases of a 44 year-old right-handed woman (Patient 1) and a 23 year-old right-handed man (Patient 2) are reported. Both presented left TLE-MTS and impairments on neuropsychological assessment. Patient 1's VEEG showed theta wave bursts and sharp wave discharges predominating in left temporal region, whereas Patient 2 showed bursts of slow waves predominating in left anterior temporal region. Patient 1 had no psychiatric disorders (PD) in presurgical evaluation, and patient 2 had an interictal psychosis. Both patients underwent left corticoamygdalohippocampectomy. Patient 1 became seizure-free (Engel IA) without any abnormalities on postsurgical EEG, but developed a de novo psychosis. Patient 2 presented no electrographic or clinical improvement (Engel IV), but evoluted with a complete remission of psychotic symptoms.

Conclusion: Clinical and psychiatric outcomes in patients with refractory TLE-MTS submitted to corticoamygdalohippocampectomy may follow different trajectories. In this report, although presurgical clinical data and surgical intervention were similar, patients presented opposite clinical and psychiatric outcomes. Once there is a scarce in literature data which allows us to determine precipitant factors that accurately predict postsurgical psychiatric outcome, possible explanations, including forced normalization, were revised.

p609
TO ASSESS THE CHILDREN OPERATED FOR DRUG RESISTANT EPILEPSY FROM A LARGE TERTIARY CARE CENTER IN INDIA

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Purpose: Retrospective, QOL (quality of life): prospective. Preoperative assessment included interictal EEG, MRI (as per epilepsy protocol), video EEG. Ictal SPECT (with subtraction) and PET was performed when required. QOL scores assessed using the HASS or SSQ for Seizure Severity, Quality of Life in Childhood Epilepsy (QOLCE) for quality of life, Child Behavior Check List (CBCL) for behavior.

Method: One hundred twenty-nine operated from January 2000 to June 2010 by the senior author (corresponding). One hundred and eighteen patients with least 1 year follow up included in study. Mean age at surgery 9.8 (±4.3) years. In addition, 40 patients underwent quality of life assessment prospectively both pre- and postsurgery.

Result: Mean duration of epilepsy 5.3 (±3.3) years. Class I outcome (Engel's) was seen in 79.5% patients, Class II in 8.6% patients, Class III in 10.7% patients and Class IV in one patient. As per surgical procedures, Class I outcome in 76%, 87% and 72% in patients who underwent temporal resection, hemispherotomy and extratemporal resection, respectively. QOL scores correlated with duration of seizures, epileptic encephalopathy and out come of surgery, but not with side of surgery, age and sex.

Conclusion: This study, the largest reported from India, has demonstrated satisfactory results for epilepsy surgery in children.

p610
MULTIMODALITY INVESTIGATION TECHNIQUES IN PEDIATRIC EPILEPSY SURGERY: A CASE REVIEW

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Purpose: Children with drug resistant focal epilepsy may benefit from respective surgery; the challenge often remains in defining the area to be resected. We report a case where multimodality imaging led to significant benefit.

Method: A 9-year-old girl underwent full presurgical evaluation for drug resistant focal seizures involving left-hand sensation, with and without progression to stiffening of ipsilateral side.

Result: Presurgical scalp ictal EEG documented seizures localized to the right centroparietal region. An initial normal 1.5T MRI and good seizure control led to an original decision not to proceed with surgery. Decision reconsidered following increased seizure frequency and concerns with academic progress. Repeat neuroimaging included 1.5T MRI, language/motor fMRI, PET and ictal/interictal SPECT, all found to be either noncontributory or nonconcordant. 3T MRI showed a possible ill-defined focal area of abnormality on the right lateral to motor cortex. Invasive monitoring was performed to further localize seizures and map eloquent cortex. Initial placement of subdural grids/strips poorly localized seizures. Decision for extended invasive monitoring, including elastography at surgery and multiple depth electrodes. Elastography showed a well circumscribed lesion posterior to sensory cortex not seen with any of the presurgical multimodality imaging techniques. Seizures again poorly localized and maximal discharges found over the motor area with sensory auras with occasional secondary tonic seizures. Lesion found with elastography resected encompassing sensory hand area. Postoperatively (at 12 m), seizures significantly reduced in frequency and severity, but remain similar in semiology.

Conclusion: New imaging techniques such as cerebral-elastography may be useful in the presurgical workup for focal epilepsy when high-resolution neuroimaging is unremarkable.

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ANTIEPILEPTIC DRUG REDUCTION AND SEIZURE RECURRENCE AFTER EPILEPSY SURGERY

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Purpose: To compare the long term seizure freedom rates of patients initially free of seizures after resective epilepsy surgery according to whether antiepileptic drugs (AEDs) remained unchanged after surgery or whether medication was tapered. We also examined individuals' reasons for choosing to continue or stop AEDs.

Method: Three hundred and thirty people who underwent resective epilepsy surgery between 1991 and 2005 completed a questionnaire about their seizure history postsurgery. These data were collated with clinical information from hospital and primary care records.

Results: Two hundred and fifteen questionnaire responders were seizure-free, or had simple partial seizures only for the first 2 years of follow up. About three quarters remained seizure-free. Seventeen percent made no significant changes to their medication, whilst the others reduced to monotherapy or stopped AEDs. Univariate analysis found that those who decreased their AEDs to monotherapy or stopped AEDs were less likely to have seizure recurrence than those who remained on more than one AED. Risk of recurrence appeared to be affected by the year of surgery, the number of AEDs tried prior to surgery and side of surgery. Multivariate analysis suggested that only year of surgery and preoperative AEDs remained significant. Principal reasons for continuing AEDs related to fear of further seizures, whilst those electing to stop most frequently cited adverse effects as their reason for discontinuing AEDs.

Conclusion: In this observational study of individuals who had been seizure-free for two years after resective epilepsy surgery, AED withdrawal was not associated with increased rates of seizure recurrence.

Poster session: Epilepsy surgery III
Wednesday, 31 August 2011

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IS AMYGDALOHIPPOCAMPECTOMY AS EFFECTIVE AS STANDARDIZED TEMPORAL LOBECTOMY IN "PURE" MESIAL TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS?

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Purpose: Surgical treatment of pharmacoresistant temporal lobe epilepsy with hippocampal sclerosis (TLE with HS) is the recommended strategy today. However, over years there has been a controversial discussion whether selective amygdalohippocampectomy (sAHE) or anterior temporal lobectomy (ATL) is the superior approach. We addressed this question by a retrospective investigation. The postoperative outcome of two cohorts of patients with "pure" mesial TLE with HS was compared.

Methods: Three hundred thirty-six patients with mesial TLE with HS were selected. Each had undergone epilepsy surgery between 2000 and 2009; 161 taken from the Kork Epilepsy Centre and 175 from the University Hospital of Strasbourg, France. Patients were selected using strong criteria. Finally, 93 patients could be analyzed who had undergone either sAHE (46 patients) in Germany or ATL (47 patients) in France. All patients were contacted to estimate surgical outcome using Engel Classification and quality of life scale.

Results: In the 46 patients who underwent sAHE, 76% continued to be seizure-free. They all had a better quality of life. Of the 47 patients who received ATL, 87% continued to be seizure-free, and again all reported that quality of life had improved. No statistical differences could be demonstrated.

Conclusion: This preliminary retrospective study suggests that there is no apparent difference in terms of outcome for epilepsy patients with unilateral hippocampal sclerosis who undergo sAHE or ATL.

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WHAT HAPPENS AFTER SEIZURE RECURRENCE ON ANTIEPILEPTIC DRUG WITHDRAWAL FOLLOWING SUCCESSFUL ANTERIOR TEMPORAL LOBECTOMY?

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Aim: To assess long term seizure outcome and antiepileptic drug (AED) status in patients who had seizure recurrence on AED withdrawal following anterior temporal lobectomy (ATL).

Methods: Three hundred ten consecutive patients who underwent ATL for drug resistant mesial temporal lobe epilepsy associated with hippocampal sclerosis (MTLE-HS) were followed up prospectively. In seizure-free patients, we started AED tapering at 3 months in patients on duotherapy/polytherapy and at 1 year after ATL for those on monotherapy. Out of 258 patients in whom AED withdrawal was attempted, 64 (24.8%) had seizure recurrence. These patients were prospectively followed for subsequent seizure outcome. AED tapering was again attempted in patients who were seizure-free for two years.

Results: The mean age at time of surgery was 30.34 ± 10.64 years and mean preoperative epilepsy duration was 17.6 ± 8.9 years. The median duration of the follow-up following surgery was 9 (range, 2–15) years and following first seizure recurrence was 5 (range, 1–14) years. Thirty-eight patients had recurrence on AED tapering while 26 had recurrence after complete AED withdrawal. During terminal 1-year of follow-up, 57 (89%) patients were completely seizure-free. AED could be subsequently stopped in 08 (14%) patients. Doses and number of AEDs could be reduced in another 49 (86%) patients as compared to their AED status at time of first seizure recurrence.

Conclusion: The long-term seizure outcome is favorable in patients who had seizure recurrence on AED withdrawal following ATL for MTLE-HS. AED can be subsequently reduced in majority and even stopped in few patients.

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AMYGDALOHIPPOCAMPECTOMY: SURGICAL TECHNIQUE AND RESULTS

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Purpose: Since 2007 we performed selective amygdalohippocampectomy, with hippocampal disconnection instead of removal, for treatment of refractory temporomesial epilepsy due to nontumoral lesions. The surgical technique and results are presented (with video-illustration of the technique).

Method: Observational study of 21 patients (14 females) aged 20–58 years (mean: 41 year) operated with this technique: selective ablation of lateral amygdala plus perihippocampal disconnection (2/3 anterior on dominant hemisphere), including the parahippocampal gyrus; left side on 11 cases, right on 10. In 20 patients the follow-up time was 12–40 months (average: 28 months).

Results: Operative time was reduced with this technique in 30 min (15%) in average and no risk due to intrasubarachnoida vascular dissection was present. The histopathology diagnosis was: mesial temporal sclerosis with amygdala gliosis in 20 patients (in one patient material was not enough).

Surgical outcome (>1 year follow-up): good/very good in 19 patients (95%), with Engel Class I-A in 15 (75%) and II-A in 4 (20%); bad in one patient (5%) in Class IV (patient with extratemporal focus appeared later).

Surgical morbidity: one patient with hemiparesis (hypertensive hemorrage 12 h after surgery), two with memory worsening, three with quadrantanopia; three cases of late psychiatric depression.

Conclusion: Advantages: Amygdalohippocampotomy is safer and as effective as amygdalohippocampectomy, and a time saving procedure.

Disadvantages: Some epileptiform EEG activity may be seen after surgery.

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IMPACT OF PRESURGICAL PSYCHIATRIC DISORDERS ON THE POSTSURGICAL CLINICAL OUTCOME IN PATIENTS WITH REFRACTORY TEMPORAL LOBE EPILEPSY AND MESIAL TEMPORAL SCLEROSIS SUBMITTED TO SURGICAL TREATMENT

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Purpose: To verify the impact of presurgical psychiatric disorders (PD) on the postsurgical clinical prognosis with respect to seizures in patients with refractory temporal lobe epilepsy and mesial temporal sclerosis (TLE-MTS) who underwent surgical treatment (corticoamygdalohyppocampectomy).

Method: The medical files of 115 patients were reviewed. Inclusion criteria were the presence of electroclinical diagnosis of TLE based on ILAE classification and having been treated for at least 6 months with stable doses of AED. All patients had clear MRI findings consistent with unilateral MTS. Interictal and ictal EEG data were analyzed. Presurgical psychiatric evaluation was performed through DSM-IV criteria. Seizure outcome was determined according to Engel's classification, in the last available follow-up consultation. Engel 1A was defined as favorable outcome.

Results: Data from 115 TLE-MTS (65 females; 56.5%) were analyzed. MTS occurred more frequently on left side (75 patients; 65.2%). PD, particularly mood, anxiety and psychotic disorders were diagnosed in 52 patients (45.2%) in presurgical evaluation. Of these, 108 (93.9%) had a recent Engel classification. Forty-five (41.6%) had favorable seizure outcome, which was associated to the absence of a presurgical PD ($p = 0.03$).

Conclusion: In accordance with the literature, we observed an association between favorable clinical postsurgical prognosis and absence of PD. Such negative consequence on postsurgical outcome requires a careful presurgical psychiatric evaluation in order to determine the impact of presurgical PD on the postsurgical prognosis in patients with refractory TLE-MTS.

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SURGICAL TREATMENT FOR DRUG-RESISTANT TEMPORAL LOBE EPILEPSY IN NEUROPHYSIOLOGIC PECULIARITIES ASPECT OF EARLY AND LATE EPILEPTOGENESIS

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Purpose: Development of surgical treatment strategy in drug-resistant temporal epilepsy basing on neurophysiologic indicators of epileptogenesis.

Method: Results of electroclinical examination (monitoring EEG, ECoG, ESCG, SEEG) and surgical treatment were studied in 300 resistant temporal epilepsy patients aged 20–49.

Results: A program applying neurophysiologic and visualizing (MRI, SPECT) technologies to study dynamics of epileptogenesis in the process of epileptic syndrome forming has been elaborated. Based on focal EEG-SEEG trait-markers peculiarities of initial (preclinical), temporal (early) and extratemporal (later) epileptogenesis were depicted clinical-neurophysiologic forms of focal and multifocal temporal epilepsy on different stages of the disease depending on pathways of epileptization. It was shown that temporal epileptogenesis is characterized by peculiar localization and extent of the epileptic focus. In our series, ECoG-ESCG studies revealed a vast epileptic area, comprising combined neocortical and limbic (hyppocampus, amygdala) damage in the majority of the patients (79%), this optimizes technology of open surgical treatment (anterior temporal lobectomy). According to EEG-SEEG data limbical-brain-stem pathways of epileptogenesis were followed-up: hippocampus and amygdala via thalamic nuclei are involved in cyclic Papez and Livingston-Escobar systems, forming multifocal forms, which is of importance in neuromodulating interventions.

Conclusion: Revealed neurophysiologic peculiarities of early and later epileptogenesis found help determining strategy of differentiated surgical treatment of resistant temporal epilepsy. For monotemporal forms anterior temporal lobectomy under ECoG-ESCG-control is optimal (78–80% positive effect), in cases requiring additional use of multiple subpial transection in eloquent cortex. Neuromodulating stereotaxic operations used in multifocal forms of temporal epilepsy (bitemporal, temporofrontal, temporoparietal).

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TEMPORAL LOBE EPILEPSY SURGERY OUTCOME PREDICTORS

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Purpose: Temporal lobe epilepsy (TLE) although the commonest focal epilepsy but has capricious radiological and pathological findings that may be considered as predictors for satisfactory surgical outcome.

Method: Two hundred ninety-five consecutive patients with TLE were treated surgically between the period from 1998 and 2009 were analyzed. All patients had complete preoperative assessment including; video EEG, MRI, PET and neuropsychological testing in addition to intracranial EEG recording, WADA test, and cortical mapping in certain group of patients. Surgical outcome was correlated with radiological and pathological diagnosis. The radiological feature was divided into two subgroups; mesiotemporal sclerosis (MTS) group and nonlesional group. The pathology diagnosis was also divided into two groups; MTS group and other pathology group.

Results: One hundred eleven (85.4%) patients had Engel class I outcome out of 130 patients of the radiologically diagnosed MTS group with a mean follow-up of 1 year. Fourteen out of 22 patients in the nonlesional group had Engel class I outcome (63.6%). Seventy-seven patients out of 88 with histopathology diagnosis of MTS had Engel class I outcome (87.5%). One hundred one patients out of 128 of other pathologies had Engel class I outcome (78.9%).

Conclusion: Outcomes following temporal lobe surgery can be predicted by MRI findings and histopathology diagnosis.

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CORRELATION OF INTERICTAL SPIKES, ICTAL ONSET PATTERN, PROPAGATION TIME AND POSTOPERATIVE DISCHARGES WITH OUTCOME IN PERSONS UNDERGOING EPILEPSY SURGERY

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Purpose: Several factors have been identified for prognosticating a patients outcome after epilepsy surgery. Our aim was to identify prognostic factors in our population as it will help in better management of persons with drug refractory epilepsy (DRE).

Method: We analyzed prospectively 574 patients who had been operated in unit one neurology with a diagnosis of surgically remediable DRE from 1997 to 2010. Fifty-five patients had only 1 year follow up the rest had more that 1 year of follow-up. Preoperative seizure frequency, duration of epilepsy, interictal EEG, scalp Video EEG, MRI, SPECT and PET, postoperative sequential EEGs, and location of ictal onset zone was recorded.

Results: In this study 278 patients were of mesial temporal sclerosis (MTS) and rest had other etiologies for intractable epilepsy. In univariate analysis, there was significant correlation of surgical outcome with preoperative seizure frequency, clinical localization of seizures, presence of secondary generalized tonic–clonic seizures (SGTCS), post operative interictal epileptiform discharges (IEDs), propagation time of the ictal rhythm and postoperative[i1] IEDs. After regression analysis, laterality of the spikes in the preictal EEG and slow propagation time of ictal rhythm were found to be the most significant predictor for the surgical outcome. Persistence of spikes 12 months or beyond was associated with a worse outcome.

Conclusion: We could fairly predict the outcome by seeing the IEDs and ictal rhythm propagation. IEDs are the most important predictors of the surgical outcome: unilateral and less frequent spikes in the interictal EEG signifies good outcome. Slow propagation time (>1 s) also predicts a good surgical outcome.

p619
HYPERMOTOR SEIZURES IN TEMPORAL LOBE EPILEPSY PATIENTS

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Purpose: Hypermotor seizures are typically associated with frontal lobe epilepsy, however this seizure type has been observed also in some of temporal lobe epilepsy (TLE) patients. Clinical significance of the finding in this patient group has not been established. The aim of the study was to identify clinical characteristics of TLE patients who present with hypermotor seizures.

Method: From series of 161 adult refractory TLE patients who underwent temporal lobe resection in the period 1999–2009 all patients with hypermotor seizures recorded in preoperative video-EEG monitoring were selected. Demographic, electroclinical and imaging data, histopathological finding and seizure outcome were analyzed.

Results: In series of 161 patients hypermotor seizures were observed in ten patients (6.2%). In this group males prevailed (7/3), mean age of epilepsy onset was 9.7 years and electroclinically all patients suffered from right-sided TLE. Oral automatisms preceded or followed hypermotor seizure in half of the cases. A lesion in temporal pole and/or amygdala was revealed by MRI in half of the patients, hippocampal sclerosis in two. In four patients invasive study was necessary. Anteromedial temporal lobe resection was performed in seven patients, temporal pole and amygdala resection in two and one patient underwent modified temporal lobe resection. Histopathology revealed focal cortical dysplasia in all cases – in 70% as isolated finding, in 30% associated with hippocampal sclerosis or ganglioglioma. One year after surgery 70% of patients were seizure-free, one patient had rare seizures, one patient was improved and one was unchanged.

Conclusion: Hypermotor seizures were associated with developmental lesion in the right temporal lobe in all patients. Seizure outcome in this group is comparable to other TLE patients, however invasive evaluation is more frequently needed. Typical temporal lobe semiology (aura or oral automatisms) preceding or following hypermotor part of the seizure and/or temporal lobe MRI lesion can indicate correct localization of epileptogenic zone.

p620
SEIZURE OUTCOME AND PATHOLOGICAL CORRELATION IN DRUG-RESISTANT TEMPORAL LOBE EPILEPSY SURGICALLY TREATED

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Purpose: To evaluate seizure outcome in relation to pathological findings in drug-resistant temporal lobe epilepsy (TLE) surgically treated.

Method: One hundred patients (53 females) who underwent anterior temporal lobectomy for drug-resistant anteromesial TLE (right TLE in 51, left in 49) with a postsurgery follow-up of at least 1 year (range 1–10 years) were evaluated. Noninvasive presurgical neurophysiological evaluation, 3Tesla MRI and histopathological examination were performed in all patients.

Results: Mean age at epilepsy onset was 13.8 years (range 6 months–33 years), mean age at surgery was 34.8 years (range 3–60 years), mean duration of epilepsy was 20.1 years (range 6 months–44 years). Seizure outcome in relation to histopathology was: in low-grade tumors (24 cases) 93% of cases were Engel Class I (85% Class Ia); in mesial temporal sclerosis (MTS) (14 cases), 75% of cases were Engel Class I (66.6% Class Ia); in MTS associated with cortical dysplasia (41 cases), 77% of cases were Engel Class I (56.6% (Class Ia), in cortical dysplasia (18 cases), 62% were Engel Class I 50% Class Ia), in vascular malformations (3 cases), two were in Class I and one in Class II. Outcome was not significantly related to sex, side of epileptic focus, age at epilepsy onset, age at surgery, duration of epilepsy.

Conclusion: Seizure outcome after temporal lobectomy for drug-resistant anteromesial TLE vary according to the underlying pathology. The best results were obtained in TLE associated with low-grade tumors, suggesting that this condition should be considered for a surgical evaluation early after epilepsy onset.

p621
SUCCESSFUL TEMPOROMEDIAL RESECTION WITHOUT REMOVING THE HOMOLATERAL LESION IN PATIENTS WITH DOUBLE PATHOLOGY: ILLUSTRATIVE CASE REPORTS

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Purpose: We present two patients with temporal lobe epilepsy and double pathology, who underwent successful epilepsy surgery removing the ictal onset zone in the affected temporomedial region but not the possibly primary lesion itself.

Case 1: Fifty-one-year-old male with a left frontal porencephalic cyst and homolateral hippocampal sclerosis detected by MR scans. The patient suffered from frequent complex partial (automotor type) and less frequent GTC seizures. In 1988 the left frontal lesion was operated

without any effect on seizure frequency and semiology. MRI, neuropsychological assessment, invasive (with frontal and temporal subdural strip electrodes) video-EEG monitoring, electrostimulation on strip electrodes was performed. The seizure onset was recorded in the left temporomedial region with fast propagation to the other side and to the homolateral frontal region. Left temporopolar and medial resection was performed. Histology showed classical hippocampal sclerosis.

Case 2: Eighteen-year-old female patient with right sided occipitotemporobasal leasion (porencephalic cyst in the territory of posterior cerebral artery) and increased T_2 and FLAIR signal intensity in the homolateral hippocampus. The patient had 3–4 automotor complex partial seizures per week. MRI, fMR, neuropsychological testing, invasive video-EEG monitoring and cortical EEG mapping were performed with subdural strip electrodes. The ictal EEG showed clear right hippocampal seizure onset. We performed selective right temporomedial resection. Lesionectomy as a second step was planned. The hippocampal principal cell loss was mild and patchy.

Both patients have been seizure-free (Engel Class IA) for more then two years. The postoperative sleep EEG did not show epileptiform abnormalities in either of the patients. These cases offer further experience of surgical treatment in cases of epilepsy with double pathology, with temporomedial and homolateral nontemporal lesion.

p622
POSTTRAUMATIC PHARMACORESISTANT TEMPORAL LOBE EPILEPSY ASSOCIATED WITH CORTICAL DYSPLASIA AND DENTATE GYRUS NEUROSPHERES PROLIFERATION: CASE REPORT

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Posttraumatic epilepsy (PTE) is a recurrent seizure disorder secondary to brain injury following head trauma. The mechanism by which trauma to the brain tissue leads to recurrent seizures is unknown. Neuronal migration alterations as cortical dysplasia are an heterogeneous group of disorders of nervous system development commonly causing epileptic seizures.

Recent findings demonstrating neurogenesis in the adult human brain suggest that neuronal migration disorders leading to epilepsy may occur also during postnatal adult life (acquired cortical dysplasia).

We report a case of a 42-year-old woman who suffered a severe brain trauma with right temporal lobe contusion when she was 18. At 35 years of age, she developed pharmacoresistant temporal lobe epilepsy. MRI showed right posttraumatic temporal lobe malacia and gliosis; long-term video EEG monitoring concluded for a. right antero-mesial temporal lobe seizure onset. Tailored anteromesial temporal lobe resection was performed. Histological examination revealed cortical lamination abnormalities (architectural cortical dysplasia) adjacent to posttraumatic gliotic tissue (FCD Type IIId according to recent Classification of ILAE Commission, Blumcke et al, Epilepsia 2011). The in vitro neurosphere assay showed an high level of dentate gyrus proliferation of neural stem cells (NSCs).

These results may suggest that also in humans trauma can stimulate abnormal reparative neurogenesis, as described in animal models of head trauma, eventually resulting in ‘‘acquired’’ epileptogenic cortical dysplasia.

Therefore, the cortical dysplasia should be considered not always a stable fixed lesion developed during the embrional life, but, it may also occur as an acquired and progressive lesion.

p623
RADIO-ANATOMICAL LOCALIZATION OF THE FORAMEN OVALE ELECTRODE IN CHILDREN WITH TEMPORAL LOBE EPILEPSY

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Purpose: Foramen ovale (FO) electrodes are frequently used in the presurgical assessment of temporal lobe epilepsy. One of the supposed limitations of this semiinvasive technique is its limited localizing accuracy with regard to the temporomesial structures, as compared with depth electrode recording.

Method: Among 110 children and adolescents who underwent FO electrode recording at our institution from 1997 through 2006, we recently performed high resolution MRI in 8 consecutive patients in order to define more accurately the anatomic location of the electrode contacts (each electrode had 5 or 10 contacts).

Results: Localization for each electrode contact was performed using 2D and 3D reconstructions and could be quantitatively related to the parahippocampal gyrus (PHG), the hippocampus and the amygdala. In all patients, the FO electrode was located in the subdural space, with all contacts immediately adjacent to the PHG, with low variability between the patients.

Conclusion: This radio-anatomical study demonstrates the reproducible positioning of the foramen ovale electrode contacts which were adjacent to the PHG cortex in all children. The recorded signal can therefore be reliably related to the temporomesial region.

p624
CHOICE OF ADEQUATE SURGICAL STRATEGY IN TREATMENT OF TEMPORAL LOBE EPILEPSY

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Purpose: Surgery for temporal lobe epilepsy (TLE) is well-established procedure with good results. The aim of report is to demonstrate the results of different surgical approaches for TLE.

Method: Forty-five pts with TLE (25 adult and 20 children) underwent surgical treatment. Patients were divided on two groups: group I included 21 pts who applied epilepsy surgery functional approach which involves the removal of disturbed brain tissue epileptogenic zone, all of them underwent anterior temporal lobectomy (ATLE) in different variations; group II included 24 pts with TLE who underwent only lesionectomy.

Results: Mean age of patients in both groups was almost the same, but durations of epilepsy in group I was 13 years while in group II – 6.5 years. Psychical disturbances dominated in group I and observed in 13 pts in this group (62%), in group II only 2 pts (8%) had psychical abnormalities. In postoperative follow-up (for both groups—mean 4.5 years) in group I 17 pts became seizure-free or have rare seizures (scale Engel I) and in two cases seizure frequency reduced significantly (scale Engel II), in remain 2 cases seizure frequency reduced slightly. Totally, good result achieved in 19 pts (90.5%). In group II 3 pts became seizure-free or have rare seizures (scale Engel 1), in six cases seizure frequency reduced significantly (scale Engel II). Good result achieved in 9 cases (37.5%). In 8 cases seizure frequency reduced slightly and in nine cases seizure frequency did not change. So insufficient result in group II observed in 15 pts (62.5%).

Conclusion: For refractory TLE detailed presurgical evaluations are mandatory to identify the concordance of the lesions and brain electrical activity discharges. Anterior temporal lobectomy in different variations leads to a good control for seizures in patients with TLE.

p625
TEMPOROMANDIBULAR JOINT DISORDERS IN SURGICAL MTLE PATIENTS: A PROSPECTIVE EVALUATION BETWEEN PRE- AND POSTOPERATIVE STATUS

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Purpose: To perform a prospective evaluation of pain and temporomandibular disorders (TMD) before and after craniotomy for refractory MTLE. Despite good seizure control, some patients develop postoperatory TMD which have been under evaluated.

Method: We investigated 24 patients (mean age 37.3 ± 10 years; 17 women) who underwent surgery for refractory mesial temporal lobe epilepsy (MTLE). All patients were evaluated pre and postoperatively for both presence of temporomandibular disorders signs (assessed by clinical examination, according to the Research Diagnostic Criteria for Temporomandibular Disorders) and maximum mouth opening (MMO, in millimeters). We calculated the ratio between post and preoperatory MMO. We performed paired and unpaired *t*-test and Fisher's exact test for statistical analyses.

Results: Paired comparison revealed reduced MMO after surgery ($p < 0.0001$); fifteen subjects had increased incidence of pain of the temporomandibular joint (TMJ) after surgery ($p < 0.03$). Patients with postoperatory pain on TMJ presented reduction in MMO (ratio 0.67 ± 0.18), compared to patients without (ratio 0.89 ± 0.07) ($p = 0.002$), as well as those with postoperatory TMJ articular disk displacement (ratio 0.7 ± 0.2) compared to those without (ratio 0.86 ± 0.08) ($p = 0.036$). Those with preoperatory disk displacement presented a tendency of reduction in MMO after surgery (0.66 ± 0.23), compared to patients without disk displacement (ratio 0.81 ± 0.13), ($p = 0.059$).

Conclusion: Craniotomy for refractory MTLE appears to be associated with an increased risk of subsequent TMD in subjects with a predisposition to TMJ disk displacement. Our study confirmed the need for preoperatory dental examination to assess joint health and a subsequent postoperative follow-up to minimize trauma of TMJ.

Poster session: Epilepsy surgery IV
Wednesday, 31 August 2011

p626
OUTCOME FOLLOWING RESECTIVE SURGERY AND ITS DETERMINANTS IN DRUG RESISTANT POSTERIOR CORTEX EPILEPSY (PCE)

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Introduction: In comparison to temporal or frontal resective epilepsy surgeries, the predictors of outcome following surgery in patients with drug resistant posterior cortex epilepsy (PCE) are sparse.

Objective: We evaluated the various factors predicting seizure outcome after epilepsy surgery in lesional PCE.

Methods: Seventy-nine consecutive patients (55-males, 24-females) with PCE who underwent resective surgery between January 2001 and December 2008 were studied. Their electroclinical, neuroimaging, interictal and ictal electroencephalographic (EEG) data, type of surgery, histopathology, postoperative EEG and long-term seizure outcome were analyzed in detail. The outcome was dichotomized as favorable if patient is seizure-free (with or without antiepileptic medications) or unfavorable if any type of seizures occurred after surgery. Appropriate statistical methods were employed to assess the predictors of seizure outcome.

Results: At a mean follow-up of 4.4 years (range 2–9 years), 54 patients (68.3%) had a favorable outcome. Factors predicting good outcome were shorter duration of epilepsy prior to surgery, completeness of the resection as defined by the operating surgeon's inspection or postoperative imaging and/or spikes in intraoperative electrocorticography and absence of spikes in any of the postoperative EEGs. Factors predicting poor outcome were presence of auditory aura/generalized tonic–clonic seizures, spikes in EEG at 3 months, 1 year and/or at the last follow-up. Neuroimaging, preoperative EEG, ictal onset patterns and histopathology did not influence the surgical outcome.

Conclusions: Our study depicts the various factors predicting outcome in a large cohort of patients with PCE and confirms the effectiveness of resective surgery in PCE in long-term.

p627
INDIVIDUALLY TAILORED EPILEPSY SURGERY IN STRICTLY EXTRATEMPORAL LOCALIZATION: OUTCOME PREDICTORS IN A POPULATION OF 37 CASES WITH EPILEPSY ONSET UNDER 12 YEARS

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Purpose: Surgery for refractory extratemporal lobe epilepsy (ETLE) in childhood occurs more frequently than TLE, however, there have been relatively few studies characterizing the features and exploring the prognostic factors of postoperative outcome of ETLE surgery within a pediatric population, an essential element for counseling families for epilepsy surgery.

Method: We performed a retrospective study of 37 patients, followed by a single national tertiary care centre, with epilepsy onset before 12 years of age who, consecutively, underwent individually tailored strictly ETLE surgery for resistant seizures, mostly in pediatric age: 21 with frontal, seven parietal, five occipital, four with multilobar (without involvement of temporal structures) localization.

Results: Cryptogenic cases represented the 24%, 59% of patients underwent SEEG and, at histopathological analysis, focal cortical dysplasia (FCD) represented the 46%. Complete seizure freedom was achieved for 72% of patients. Seizure-free subjects represented the 62.5% of the cryptogenic population and the 62% of subjects who beneficed of SEEG.

Shorter duration of epilepsy, total exeresis of the epileptogenic zone (EZ), absence of acute postoperative seizures, a more severe FCD subtype, and on presurgical scalp EEG: absence of interictal slowing, ictal pattern of rapid band activity, as well as tendency of ictal and interictal discharges to remain localized, represented significant predictive factors of good outcome. Absence of generalized tonic–clonic seizures, a neuroradiologically identifiable lesion, anterior localization of the EZ and no invasive presurgical evaluation represented marginally significant predictors of favorable outcome.

Conclusion: We conclude that surgical outcome of ETLE in carefully selected pediatric population can be excellent.

Abstracts

p628
MEDICALLY INTRACTABLE PARIETAL LOBE EPILEPSY: EXPERIENCE FROM A LARGE COMPREHENSIVE CANADIAN EPILEPSY PROGRAM

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Purpose: There is scarce information on surgical treatment of patients with medically intractable epilepsy of parietal lobe origin. We present our experience.

Method: The Epilepsy Surgery Database for the University of Western Ontario-Epilepsy Program was interrogated for all parietal lobectomies. Consecutive cases, since the inception of the Epilepsy Program in 1977 until December of 2005, were included. The origin of seizures was determined by interictal and ictal findings on the EEG. If seizure origin was unclear, intracranial EEG was performed with the use of subdurally placed electrodes. All patients underwent MRI of the brain as well as neuropsychological evaluation. Resective surgery was performed in those cases in which there was concordant information from different modalities, including intracranial electrodes. Patients were followed after surgery for up to 3 years.

Results: A total of 1066 epilepsy surgeries were performed. We identified 43 cases diagnosed with parietal lobe epilepsy (15 females). The average age at seizure onset was 12.6 (range: 2 weeks to 51 years), the mean age at surgery was 23.4 years. Thirty-nine cases were diagnosed with extraparietal lobe epilepsy as well (likely regional epilepsy involving the parietal lobe). Ten cases were nonlesional. Of the lesional cases, 11 had low-grade tumors (including DNETs), five had malformations of cortical development, and 16 other lesions. Twenty-three cases required implantation of intracranial electrodes for further delineation of the epileptogenic focus. Nine cases underwent resections in the parietal lobe exclusively, 11 more than one lobe (including the parietal one), four underwent hemispherectomies, 11 resections outside the parietal lobe, three callosotomies, two multiple subpial transections, and six did not undergo surgery. Twelve (28%) became seizure-free after surgery (Engel's I) at the 3 year follow-up.

Conclusion: Our experience indicates that localization of the epileptogenic zone is a difficult task in this particular group of patients since involvement of other areas outside the parietal lobe is common. A great number required evaluation with intracranial electrodes and seizure freedom occurred in a minority.

p629
REOPERATION FOR FAILED EPILEPSY SURGERY

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Purpose: To evaluate the surgical outcome in patients undergoing reoperation for intractable partial epilepsy.

Method: We performed a retrospective analysis of 281 patiens who were operated at our department from 1994 to 2009. Thirty-five were reoperated because of failure of the first operation. Nine patients underwent nonresective procedures – vagus nerve stimulation. We analyzed seizure outcome data (Engel scale) in 35 patients with resective operation who were followed a minimum of 2 years after their last operation.

Results: The mean age at the first surgery was 30.8 (range 16–51 years). The interval between the first and second operation was 4.9 years (range 1–30 years). Longer intervals we found in patients who underwent the first operation at another institution (eight patients). The most frequently performed procedures were extended lesionectomy, temporal lobe resections after failed radiosurgery and resections following VNS implantation. Ten patients underwent three or more operations. We determined seizure outcome after resective reoperation. We did not include nine patients in whom resective surgery could not be planned and vagus nerve stimulator was implanted. Twenty-five patiens (69%) were Engel I, two patiens (6%) Engel II, four patients (11%) Engel III and five patiens (14%) Engel IV.

Conclusion: Reoperation may be an appropriate alternative form of treatment for selected patients with intractable partial epilepsy who fail to respond to initial surgery.

p630
SURGICAL TREATMENT OF THE PATIENTS WITH RASMUSSEN'S ENCEPHALITIS – 20 CASES

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Purpose: To describe the clinical, electrophysiologic, neuroradiologic and histologic findings of patients with Rasmussen encephalitis (RE) and to evaluate the outcome of their surgical treatment.

Method: Twenty RE patients were confirmed by presurgical evaluation including semiology, magnetic resonance imaging (MRI), interictal/ictal scalp video-electroencephalography (VEEG), intracranial recording and biopsy. Presurgical evaluation modalities and surgical treatment were analyzed retrospectively.

Results: Eleven functional hemispherectomy (FH), five anatomical hemispherectomy (AH), five hemispherotomy, three tailed resection, one multilobar resection and one bipolar electro-coagulation on functional cortexes (BEFC) procedures were undertaken, of which 14 were right-sided and six were left-sided. Three patients underwent two surgical procedures, two patients underwent three surgical procedures. According to Engel's criteria, six patients (80%) achieved an Engel Class I status, and one patient (5%) had an Engel Class II outcome, one patient (5%) had a significant decrease in seizure frequency (Engel Class ?) and two patients (10%) had no change in seizure frequency (Engel Class III). One patient showed contralateral seizure after AH and be diagnosed as bilateral RE. All of the patients excepting one bilateral RE had increases in cognitive abilities, behavior, and quality of life after the surgery. After the surgery, most of the patients could walk independently, but the fine movement of the hands was lost. The main early complications were fever (35%) after hemispheric surgeries. Postoperative hydrocephalus was observed one and a half years after AH in one patient and no death in of this series.

Conclusion: Hemispherectomy and hemispherotomy were confirmed as both beneficial procedures in controlling seizures and improving quality of the life in cases with RE.

p631
SURGICAL OUTCOME AND PROGNOSTIC FACTORS OF FRONTAL LOBE EPILEPSY SURGERY

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Background: Frontal lobe epilepsy (FLE) surgery is the second most common surgery carried out to treat refractory epilepsy. The present challenge is to identify factors that predict the outcome in seizure control after frontal lobe epilepsy surgery. We review frontal epilepsy surgery results over the last 10 years and discuss the related factors that influenced the outcome.

Methods: We retrospectively studied the operative outcome in 63 consecutive adult and pediatric patients who underwent resective surgery for intractable frontal epilepsy between 2000 and 2010. Clinical history,

results of imaging, invasive EEG recording, pathology and surgical outcome were reviewed in detail.

Results: The age of patients was between (6–51 years). The onset of seizures was from 4 days to 30 years. Thirty-three patients out of 64 required an invasive EEG recording. The handedness was left in 7 of 64 patients. The MRI brain finding were normal in 12 patients, tumor (18), focal cortical dysplasia (15), atrophy (10), cyst (5) and 1 AVM. The histopathology were 24 patients with focal cortical dysplasia, oligdendroglioma (8), DNET (8), Astrocytoma (3), glioneural tumor (2), gliosis (9), normal (1) and 1 none specific. The seizure-free outcome was observed in 28 patients out of 63 (44%), and the excellent outcome was 17%.

Conclusion: Our experience match the international frontal lobe epilepsy results, and indicates the importance of appropriate selection of potential surgical candidates.

p632
PARIETAL LOBE EPILEPSY: GREAT IMITATOR AMONG FOCAL EPILEPSIES

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Purpose: Parietal lobe widespread network projections can produce false localization/misinterpretation of scalp EEG and clinical semiology in patients with parietal lobe epilepsies (PLE). Our aim was to test the reliability of electroclinical features in PLE as compared to frontal (FLE) and temporal (TLE) lobe epilepsies.

Method: We included 50 consecutive patients with pharmacoresistant focal epilepsy who were rendered seizure-free for ≥12 months following resections limited to either the frontal (n = 17), temporal (n = 17) or parietal (n = 16) lobes. Interictal EEG (iiEEG), single representative ictal EEG (iEEG) and seizure video were extracted from long-term scalp video-EEG monitoring. Two blinded raters (R1, R2) independently reviewed the EEG. Seizure videos were then presented and raters formulated electroclinical impression (ECI) to either PLE/TLE/FLE/nonspecified.

Results: Groups did not differ significantly in demographics, absence of iiEEG, epilepsy onset or presence/absence of MRI abnormalities. Interobserver agreement (IOA) was substantial/outstanding across different aspects of the iiEEG. iiEEG in PLE patients showed greatest scatter outside the lobe of origin as compared to other groups. PLE group had higher number of iiEEG populations than FLE (p = 0.032). iEEG IOA was moderate/substantial. Localized iEEG was different in all groups: TLE (70.6%), FLE (50%) and PLE (37.5%) (p = 0.024). ECI IOA was poor. In patients whereby raters confidently categorized ECI to one epilepsy type, PLE was often misidentified: correct/specified R1 – (FLE 8/8, TLE 12/14, PLE 4/8; p = 0.034) R2 – (FLE 14/14, TLE 13/13, PLE 6/10; p = 0.002).

Conclusion: Electroclinical features are likely to be falsely localizing and/or mislateralizing in PLE compared to FLE and TLE patients.

p633
OUTCOME OF EXTRATEMPORAL EPILEPSY SURGERY AND HEMISPHERECTOMY AFTER EVALUATION WITH A NONINVASIVE PROTOCOL

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Purpose: To assess the outcome of surgery in patients with medically refractory extratemporal epilepsy (ETLE) and hemisperectomy patients evaluated with a noninvasive protocol and to determine the predictors of outcome following surgery.

Method: Retrospective analysis of presurgical (ictal EEG, MRI, fMRI, SPECT, FDG PET, neuropsychology and pathology) data was performed in 48 patients who underwent surgery for ETLE and 12 patients following hemispherectomy and who had at least 1 year post surgery follow up. WADA, invasive monitoring was not done. Outcome was assessed according to Engel's outcome classification. Stepwise multiple logistic regression analysis was employed in data analysis.

Results: Mean follow up was 32 (12–68) months. Thirty-six (60%) were males. Intraoperative electrocorticography was used in 42 and cortical stimulation in 23. Frontal resections were the commonest (28), followed parietal resections. The pathology showed cortical dysplasia in 21, gliosis in 8 and low grade tumoral lesions in 10. Transient postsurgery complications occurred in 3. At last follow up seizure-free outcome was noted in 37 (77%) with ETLE and 9 (75%) after functional hemispherectomy. After stepwise multiple logistic regression analysis, the variables found to be significant ($p \leq 05$) and predicting favorable outcome were normal IQ and absence of acute postoperative seizures.

Conclusion: Favorable outcome after epilepsy surgery can be obtained in patients with extratemporal epilepsies after evaluation with a noninvasive protocol if presurgical evaluation is carefully planned.

p634
PREDICTORS OF SEIZURE OUTCOME FOLLOWING RESECTIVE SURGERY FOR DRUG RESISTANT EPILEPSY ASSOCIATED WITH FOCAL GLIOSIS

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Aim: To study long-term postoperative seizure outcome and its predictors following resective surgery for drug resistant epilepsy caused by focal gliotic lesions (DRE-FGL).

Methods: Sixty-five consecutive patients (out of 137 extratemporal focal resection) who underwent resective surgery from 2001 to 2009 for DRE-FGL (identified by MRI) and completed minimum 01 year of postoperative follow-up formed the study cohort. All underwent long-term ictal recordings and high resolution MRI while functional imaging and intracranial monitoring were undertaken in selected patients with nonlocalizing or discordant data. Completeness of resection was defined by preoperative findings, >75% reduction of spikes on postoperative acute electrocorticography and postoperative MRI. Freedom from seizures and aura during the entire follow-up period was defined as favorable outcome.

Results: The mean age of the cohort was 19.83 ± 7.88 years and mean preoperative epilepsy duration was 12.7 years. Thirty-four (53%) had unilobar (14 occipital, 10 frontal, five parietal, and four temporal), 19 (29%) had bilobar and 12 (18%) had multilobar involvement. Invasive monitoring was required in 21 (32%) patients. At median follow-up period of 03 (range, 1–9) years, 41 (63%) patients had favorable outcome. Presence of well-defined aura (65.9% vs. 30.4%, p = 0.009) and complete resection (69.2% vs. 30.8%, p = 0.02) were significantly associated with favorable outcome. Patients with multilobar gliosis had a trend towards poor outcome (15% vs. 61%). Other pre- or postoperative variables failed to predict seizure outcome.

Conclusion: More than 60% patients become seizure-free following resective surgery for focal gliotic lesions. Presence of aura indicating a well-defined ictal onset and completeness of resection predict favorable outcome.

p635
POSTOPERATIVE LONG-TERM OUTCOME IN 203 PATIENTS WITH FOCAL CORTICAL DYSPLASIA

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Purpose: Focal cortical dysplasia (FCD) is a common cause of pharmacoresistant epilepsy. Thus, these patients are candidates for epilepsy surgery. In this study we analyzed the long-term outcome of patients with FCD after epilepsy surgery.

Method: Inclusion criteria for this study were a follow-up period available for at least 12 months and histologically confirmed FCD. The outcome was classified according to Engel.

Results: A total of 203 patients fulfilled inclusion criteria. The follow-up period ranged from 12 to 132 months, mean 51 months. One hundred and forteen patients underwent temporal lobe surgery, 63 unilobar extratemporal (mainly frontal) surgery, and 26 had a multilobar resection. One year postoperatively 66% of patients were Engel class I (57% Ia), 16% Engel class II, 8% Engel class III, and 11% Engel class IV. The respective data five years postoperatively were 68% (56%), 9%, 16%, 7% and eight years postoperatively 73% (45%), 7%, 10% and 10%. In 67% of patients the postoperative outcome remained stable after the first postoperative year. In 22% of patients seizure outcome declined during the follow-up. In 11% of patients, improvement of seizure outcome was seen during the follow-up. In 12 patients (6%) a second operation was performed. In five of them, a second operation led to considerable seizure improvement, however, in seven a second operation did not contribute to seizure reduction. A trend to unfavorable postoperative outcome was seen in MRI negative patients with extratemporal FCD. Incomplete resection of MRI-visible FCD was a negative predictor in both temporal and extratemporal FCD. In only 17% of patients medication was stopped, 41% of patients remained on a monotherapy and 42% of patients were treated by two or more antiepileptic drugs.

Conclusion: Postoperative long-term seizure outcome was favorable in FCD-patients and remained stable in two thirds of patients after the first postoperative year. Although about 50% of patients were Engel Ia, in only few patients (17%) antiepileptic medication was stopped.

p636
TREATMENT WITH EVEROLIMUS REDUCES SEIZURE ACTIVITY AND ALTERS WHITE MATTER MICROARCHITECTURE IN PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX (TSC)

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Purpose: TSC is a genetic disorder characterized by formation of benign tumors in multiple organs, including the brain. Epilepsy is present in 70–80% of TSC patients. Neurosurgical resection, the current standard treatment for intractable epilepsy, is effective in 35–45% of patients. A prospective open-label, phase II trial (NCT00411619) of everolimus, a selective mTOR inhibitor, in TSC patients with subependymal giant cell astrocytoma (SEGA) included secondary end points assessing the effect of everolimus on seizure frequency and white matter microarchitecture.

Method: Twenty-eight patients (aged ≥3 years) with TSC diagnosis and documented SEGA growth received oral everolimus 3 mg/m^2/day (titrated to achieve target trough concentration of 5–15 ng/ml). Seizure activity was reported by patients at each visit and in caregiver diaries, and 24-h video-electroencephalography (EEG) was performed at baseline and 6 months. Diffusion tensor imaging (DTI) was used to assess change in brain white matter microarchitecture.

Results: Twenty-six patients had assessable epilepsy data (caregiver observations); at baseline 27% had daily seizures, compared with 8% and 4% after 6 and 12 months of everolimus therapy, respectively. Mean number of electrographic seizures (EEG available for 16 patients) was 2.75 seizures/24-h at month 6 versus 6.30 seizures/24-h at baseline ($p = 0.022$). In MRI scans taken 12 to 18 months from baseline, DTI revealed increased fractional anisotropy and decreased radial and mean diffusivity in otherwise normal-looking white matter, indicating improved white matter integrity.

Conclusion: Everolimus therapy significantly reduced seizure activity in patients with TSC, and DTI findings are consistent with improvement in the integrity of normal-appearing white matter.

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SUPPLEMENTARY MOTOR AREA SURGICAL SERIES OF PATIENTS PRESENTING WITH LESIONAL/NONLESIONAL INTRACTABLE EPILEPSY

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Purpose: To describe our supplementary motor area surgical series of patients presenting with lesional/nonlesional intractable epilepsy.

Method: We retrospectively reviewed our series of 52 patients who underwent complete lesion/epileptogenic zone resection in the SMA cortex, operated at the National Institute of Neurology and Neurosurgery and the ABC Medical Center, in Mexico City, from January 1999 to December 2010. Inclusion criteria were: patients presenting with diagnosis of intractable SMA epilepsy. Presurgical evaluation was carried out utilizing a modified international protocol that included among others: complete medical history, MRI, fMRI, surface EEG, Video-EEG, neuropsychological testing and psychiatric evaluation, in some particular cases SPECT and PET-CT; phase II evaluation was performed in 20% of cases, usually utilizing two grids of 24 contacts each, placed in the interhemispheric fissure. Different etiologies: low grade tumors, vascular malformations, cortical dysplasia and others.

Results: Mean age was 37, 77% were men and 33% women, mean seizure frequency per month before surgery 22 events. Etiology: 63.4% (33) patients with tumors, 25% (13) cortical dysplasia, 9.6% (5) with vascular malformations and 1.9% (1) with granuloma. Surgical outcome: 31 patients 60%, Engel I. Engel II 31%. Engel III 9%.

Conclusion: Principal etiology was tumoral, SMA intractable epilepsy demonstrates significant beneficial results with functional neurosurgery and epilepsy surgical techniques. We propose SMA epilepsy surgery cases to be considered apart from general frontal lobe epilepsy surgery series. Even more, different compartments of frontal epilepsy should be consider.

Poster session: Epilepsy surgery V
Wednesday, 31 August 2011

p638
INTRAOPERATIVE ULTRASOUND ELASTOGRAPHY IS SUPERIOR TO MRI AT IDENTIFYING EPILEPTOGENIC AREAS

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Purpose: Focal cortical dysplasias (FCD) and dysembryoplastic neuroepithelial tumors (DNT) are often difficult to visualize on MRI. Intraoperatively these lesions often look very similar to normal brain. However, these lesions are often stiffer than normal brain; a property exploited by the surgeon to determine extent of resection. Ultrasound elastography (UE) is an objective method for identifying stiff regions within an ultrasound plane. It was hypothesized that UE used intraoperatively would be superior to MRI at identifying these lesions.

Method: Five patients were recruited into the study. Four patients underwent invasive electrode recording. One patient had no lesion demonstrable on MRI. UE was performed following dural opening and prior to resection. Comparison of UE with the surgical findings and MRI findings was performed.

Results: There were two cases of FCD and two DNT and one case there histology was inconclusive. In all cases there was concordance between UE findings and surgical findings in terms of stiffness compared to brain. In the four cases where a lesion was demonstrable on MRI, the location of the lesion on UE was in concordance with the MRI findings. Furthermore the lesion brain interface was far better defined on UE compared to MRI. It was possible to define the lesion shape as a wedge originating from the deep white matter in the periventricular area using UE.

Conclusion: Our results suggest that UE is superior to MRI at identification of epileptogenic lesions and would be a useful adjunct when resecting these lesions.

p639
CAN WADA TEST PREDICT VERBAL MEMORY OUTCOME AFTER ANTERIOR TEMPORAL LOBECTOMY IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY?

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Purpose: Verbal memory (VM) exacerbation is a major concern after anterior temporal lobectomy (ATL) of memory-dominant hemisphere in patients with mesial temporal lobe epilepsy (MTLE). We elucidated the reliability of the Wada test for predicting the VM outcome after ATL.

Methods: Thirty-five patients (age range: 13–58, mean: 39.0 years) who were subjected to the Wada test for lateralizing verbal-memory dominancy (VMD) were divided into two groups based on the Wechsler Memory Scale-revised (WMS-R) VM scores: >90 (A) and <90 (B). Lateralized VMD was defined as follows: word recognition scores of >6 and <3 (total: 9 tasks; three before and six after propofol injection) for lateralizing unilateral and contralateral hemispheres, with scores of >4 and <2 (total: six tasks after propofol injection) for the similar lateralizing procedures, respectively.

Results: In A and B, the Wada test predicted lateralized VMD in four of 16 (25%) and in one of 19 (5.3%) patients, respectively. Among 17 ATL-treated patients, 4 (3 in A) had lateralized VMD: two of these four patients suffered exacerbated VM (>10; lower than preoperative scores) after memory-dominant ATL, while the remaining two had preserved memory after memory-nondominant ATL. Of the remaining 13 patients, VM in 2 (A) of six language-dominant ATL and in 3 (two in A) of seven language-nondominant ATL cases exacerbated after surgery.

Conclusions: Patients with preoperative well-preserved VM may show memory disturbance even after language-nondominant ATL. The Wada test may be useful for predicting VM outcome in lateralized VMD patients.

p640
TASK SPECIFIC STEREO-EEG CHANGES DURING PRESURGICAL NEUROPSYCHOLOGICAL EVALUATION OF PATIENTS WITH FOCAL PHARMACORESISTANT EPILEPSY

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Purpose: In epilepsy surgery candidates, intracranial recordings may be required for definition of the epileptogenic zone (EZ). In ~30% of cases postsurgical outcome is not ideal with respect to seizure suppression and cognitive performance. The identification of task-related anatomical areas during neuropsychological test performed in recording session and the comparison of these areas with the location of the EZ should help to predict and improve postsurgical outcome.

Method: A new method for computerized stereo-EEG analysis signal with Elpho-SEEG? software, was developed to compare traces during neuropsychological tests and quiet wake. Fluency tasks (phonemic and semantic) and classification tasks were analyzed on 10 adults and four children with focal drug-resistant epilepsy explored in one or both frontal lobes.

Results: Different frequencies and the relative power evaluated by Fourier transformation and further integral algorithms were simultaneously analyzed in all recording leads. Direct comparison of difference in the power of frequencies (0.1–250 Hz) during quiet wake and tasks was performed. The anatomical position and Brodmann area of each electrode contact was identified. A reproducible task-dependent stereo-EEG pattern and specific anatomical areas were found. Correlation between task-activated areas and the position of the EZ was utilized to retrospectively compare the output of the model with the postsurgical outcome.

Conclusion: Frequencies modification during specific task was constantly observed by quantitative software analysis. Anatomic position of reproducible activity patterns can be reconstructed and identified. Comparison between EZ and task-activated areas can be utilized to improve post surgical outcome. Supported by Pierfranco e Luisa Mariani Foundation grant (R08-71).

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SURFACE BASED INDIVIDUAL ASYMMETRY WITH STATISTICAL PARAMETER MAPPING (SPM) ANALYSIS TO 18-F-FDG PET METABOLIC ABNORMALITIES IN EPILEPSY SURGERY PATIENTS

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Purpose: We have retrospectively analyzed the concordance of surgical site to cortical hypometabolic lesion in patients' seizure outcomes using surface-based individual asymmetry with statistical parameter mapping (SPM) of MRI and PET images.

Method: Ten patients (mean age at surgery: 10.28 years) with refractory epilepsy were included in this study. Their clinical data, results of presurgical evaluation, and subdural EEG monitoring were evaluated. 18-F-FDG PET and MRI images were coregistered for image preprocessing.

Results: The hypometabolic lesions were matched with surgical sites of all patients. Among Engel Class III patients, three of them did not have resections that covered all of the hypometabolic area due to inadequate grid covering or the significance of the area. In the other Engel Class III patient, the result of subdural EEG monitoring showed no signs of seizure-onset or irritative area. On the other hand, on Engel Class I patients, only one showed hypometabolic area that included, but were not limited, to the resection area. Other five patients had no asymmetric lesion outside the surgical sites.

Conclusion: We observed a relatively high overlap rate between the hypometabolic area and surgical sites of the patients with successful seizure-free outcomes using surface-based individual asymmetry with SPM. In contrast, a relatively low overlap rate was seen in those of seizure recurring patients. The main caveat of this study is the limited sample size, and further study with a larger pool of patients is called for.

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MULTIPLE SUBPIAL TRANSECTION FOR EPILEPTOGENIC FOCI ASSOCIATED WITH LANGUAGE AREA DETECTED BY ELECTRICAL CORTICAL STIMULATION

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Purpose: To assess the efficacy and safety of combination of multiple subpial transection (MST) and resection in patients with refractory epilepsy involving the language area (LA).

Methods: MST and resective surgery were performed in three patients with epileptogenic foci in one or more lobes including the LAs. Epileptogenic foci were detected by intracranial subdural recording, and the LAs were detected by electrical cortical stimulation mapping.

Results: Patient 1 underwent MST in Broca's LA and frontal lobectomy. Patient 2 underwent MST in multiple lobes including Broca's and Wernicke's LAs and partial resection in the temporal lobe. A 2-stage procedure was performed for the third patient. Initially, we performed right anterior temporal lobe resection guided by intraoperative electrocorticography for temporal lobe epilepsy. Subdural grids were implanted after 3 years. A combination of MST in multiple lobes including Broca's and Wernicke's LAs and partial resection in the frontal lobe was performed. Follow-up period was 143, 37, and 44 months. According to Engel's classification, two patients had a class three outcome and one patient had a class one outcome. In patient 1, language function deteriorated immediately after surgery and almost no spontaneous speech was heard for a month after surgery. Speech functions of patients two and three were partially impaired after surgery. Their language functions improved and recovered gradually within 6 months as shown by the results of Standard Language Testing for Aphasia in Japanese.

Conclusion: If epileptogenic foci extend to the LAs, and if 2 lobes are involved, a combination of MST and resective surgery can be useful to improve seizure outcome and language function after surgery.

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MATERIAL-SPECIFIC MEMORY OUTCOMES AFTER SURGERY FOR INTRACTABLE TEMPORAL LOBE EPILEPSY

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Purpose: Minimizing postoperative memory deficits is of key concern when offering surgery to individuals with mesial temporal lobe epilepsy (TLE). The model of material specificity is arguably the most widespread and influential conceptualization of memory impairment that is encountered in TLE patients. Current literature suggests much uncertainty regarding the material-specific amnesia hypothesis, which may arise in part from heterogeneity methods of memory assessment, as well as heterogeneity of patients studied. In this study, we report on a sample of patients with TLE offered surgery on the basis of volumetric MRI identified hippocampal sclerosis.

Method: The present study included auditory and visual Wechsler Memory Scale (WMS-III) index data collected from 90 patients (46 left TLE, 44 right TLE) who had undergone unilateral anterior temporal lobectomy (ATL), and had completed pre- and postoperative neuropsychological assessment between 1997 and 2010.

Results: There were no statistically significant presurgical differences in verbal or visual memory indices between LTLE versus RTLE patient groups (all p's >0.1). LTLE patients showed no change in their verbal memory abilities and significant improvement in visual memory abilities. In contrast, RTLE patients demonstrated the reverse pattern. These effects were highlighted in the significant interaction between memory type (verbal vs. visual), assessment time (pre- vs. postoperative) and side of seizure focus (LTLE vs. RTLE) $F_{1,88} = 12.29$, $p < 0.01$.

Conclusion: Results of this study show that, when selected for surgery on the basis of hippocampal volumetric imaging, mean verbal and visual memory performance does not significantly deteriorate after ATL, evidenced by a large and homogenous sample of patients with TLE. In addition, both patient groups showed modest improvements in contralateral memory function. Findings demonstrate further evidence for the functional adequacy hypothesis and the value of volumetric MRI for determining seizure foci lateralization and structural markers of hippocampal integrity.

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POSTOPERATIVE NEUROPSYCHOLOGICAL EVALUATION IN PATIENTS WITH TEMPORAL LOBE EPILEPSY IN ARGENTINA

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Purpose: The aim of the present study was to evaluate postoperative neuropsychological evaluation, and to compare with findings obtained before surgery.

Method: Thirty-five patients with refractory temporal lobe epilepsy and an anterior temporal lobectomy were selected. Neuropsychological evaluation was performed before surgery, 6 months and a year afterwards. Neuropsychological protocol evaluate Attention, Verbal Memory, Visual Memory, Executive Function, Language, Intelligence Quotient and Handedness.

Results: There was a significant improvement ($p = 0.030$) in the group with visual memory deficit after surgery, no changes were observed across patients with verbal memory deficit. On language assessment after surgery, no changes were observed. On executive function evaluation with the Wisconsin Card Sorting Test, 6 months after surgery, significant improvement was observed ($p = 0.035$).

Conclusion: Postoperative prognosis of cognitive impairments depends on the patient's prior condition. Patients with deficits after surgery showed no alterations in their overall quality of life, and patients who did not display a cognitive deficit preoperative, remained stable.

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PROVOCATIVE MEMORY TEST FOR AMYGDALO-HIPPOCAMPECTOMY USING DEPTH ELECTRODES IMPLANTED IN THE ENTORHINAL AREA

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Purpose: Amygdalohippocampectomy (AHP) has been widely applied for intractable temporal lobe epilepsy (TLE). However, its indication for the dominant hemisphere is limited because of the fear of postoperative memory disturbance. To prevent this disabling and unpredictable complication, we have assessed the memory function around the hippocampus before resection using electrical stimulation through depth electrodes. Here, we describe its efficacy based on our preliminary experience.

Methods: Verbal and visual memory functions were evaluated by provocative test on nine adults with intractable TLE in dominant hemisphere. Recall (immediate, delayed) and recognition during verbal and visual tasks were assessed under electrical stimulation through the depth electrodes inserted to the entorhinal area with stereotaxic technique. Among these patients, five underwent AHP and their postoperative memory function was compared to those of the preoperative period.

Results: During the provocation test, delayed recall with verbal tasks was affected in 7, and recognition disturbance was observed in six of the nine patients. Among the five patients who underwent AHP, postoperative memory impairment developed in two patients in whom both delayed recall and recognition disturbances were provoked, while memory function was intact in two without stimulation-induced memory disturbance and in one who showed delayed recall disturbance only. AHP was considered not applicable to the remaining four patients according to the result of provocation test.

Conclusion: Provocative test using depth electrodes implanted in the entorhinal area might be a promising technique to prevent the memory disturbance following AHP of dominant hemisphere, although the use of this technique warrants further evaluation.

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VERBAL MEMORY DECLINE RELATED TO TEMPORAL LOBE RESECTION FOR EPILEPSY IS LESS FREQUENT 10 THAN 2 YEARS POSTOPERATIVELY

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Purpose: There is an extensive variation in verbal memory outcome after temporal lobe resection (TLR) for epilepsy. The aims of this study were to investigate individual short- and long-term verbal memory changes and to explore risk factors for decline after TLR.

Method: Fifty-one patients who had undergone TLR (23 in the language-dominant temporal lobe, DTL; 28 in the nondominant temporal lobe, NDTL) were tested preoperatively, 2 and 10 years postoperatively. Twenty-three healthy controls were assessed at corresponding intervals. Learning/immediate recall and delayed recall of word list and word pairs were studied. Changes were defined using cutoff scores of reliable change indices (RCI) of the controls.

Results: Fewer patients had decline at 10-year (8–16%) than at 2-year follow-up (24–27%). For the DTL patients, this was most marked in delayed recall (13–17% vs. 35–44%). More NDTL patients had improved at 10 than at 2 years (18–30% vs. 4–22%), especially in learning/immediate recall (19–25% vs. 4–11%). Six potential prediction variables were selected: age, verbal memory and verbal IQ at baseline and seizure outcome, laterality and presence of cortical dysgenesis. A DTL resection predicted decline both 2 and 10 years postoperatively. Also, intact baseline verbal memory predicted decline in delayed recall at short-term, but not at long-term.

Conclusion: The only risk factor for verbal memory decline both short- and long-term after TLR was DTL resection. While most patients were stable in verbal memory 2 to 10 years after surgery, more patients had a partial recovery than a lasting decline. This is valuable knowledge in presurgical counselling.

Poster session: Epilepsy surgery VI
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RELIABILITY OF EQUIVALENT CURRENT DIPOLE CLUSTER ON MAGNETOENCEPHALOGRAPHY: PRESURGICAL EVALUATION FOR INTRACTABLE EPILEPSY

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Purpose: Magnetoencephalography (MEG) localizes an epileptic focus as an equivalent current dipole (ECD) cluster; however, MEG results may differ on sequential examinations in the same patient. Therefore, we examined the reliability of multiple MEG results in presurgical evaluation for intractable epilepsy.

Method: All 27 patients (12 mesial temporal lobe epilepsy (MTLE) and 15 neocortical epilepsy (NCE) cases) underwent MRI, prolonged scalp-video EEG (SVEEG), multiple MEG, and intracranial video-EEG (n = 12). Persurgical MEG was performed twice (n = 22), three (n = 4), and four (n = 1), accordingly. Based on MEG results, patients were classified into 4 groups; non-ECD cluster on repeat MEGs (A), presence of a secondary cluster without any in first MEG attempt (B), clusters with same distributions on repeat MEGs (C), and clusters with different distributions on each MEG (D).

Results: Incidence in A, B, C, D for MTLE and NEC were 5, 5, 1, 1 and 6, 1, 4, 4 cases, respectively. The localizations of ECD cluster in groups B and C indicated concordance with SVEEG (100%) and IVEEG (100%) in MTLE, and scored 60% and 100% in NCE patients, respectively. Among patients with tapering medications, ECDs were successfully clustered in MTLE (4/5) and NEC (1/4) patients. One patient (group D) manifested an ECD cluster each in bilateral hemispheres and another opposite the MRI lesion. IVEEG results may reflect potential epileptic foci according to previous seizure semiology.

Conclusion: Tapering medications facilitated ECD cluster formation on repeat MEGs. Inconsistent MEG results may reflect potential epileptic foci or sleep-deprived accentuated spikes.

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INTEGRATING MAGNETIC-SOURCE AND FUNCTIONAL IMAGING FOR NEURONAVIGATION OF ELECTRODE IMPLANTATION AND RESECTION OF FOCAL CORTICAL DYSPLASIA IN PATIENTS WITH INTRACTABLE EPILEPSY

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Introduction: Focal cortical dysplasias (FCDs) are intrinsically epileptogenic lesions. Surgical removal is frequently the best treatment option for intractable epilepsy. However, FCDs may be functional and are often extended to subcortical areas. Magnetoencephalography (MEG) localizes an epileptic zone as an equivalent current dipole (ECD) cluster, while MR-tractography facilitates identification of white matter fibers. This study elucidated the efficacy of neuronavigation-guided our novel method combining subdural grid and depth-electrode implantation for seizure and functional monitoring and subsequent resection of FCDs.

Methods: Presurgical evaluations were conducted on three patients with FCD-related intractable epilepsy. An epileptic focus located in the area adjacent to the eloquent cortex (with extensions to the subcortical areas) was portrayed in each patient. Neuronavigation with ECD cluster/MR-tractography integration was used for monitoring the subdural grid and additional depth-electrode implantation. Depth-electrodes (3–4) per patient were inserted near the FCD margin to establish the deepest possible ECD cluster site for monitoring seizure and function.

Results: FCDs were located at the right frontal (Patient 1), parietal (Patient 2), and perisylvian (Patient 3) regions. Patients 2 and 3 manifested ictal onset zones synchronously in the superficial and deep-sited FCD lesions. Functional mapping using depth-electrodes identified somatosensory (hand) fibers (Patient 2) and optic radiation (Patient 3), and allowed us to spare these functional structures on subsequent resection. Patients 1 and 2 had excellent seizure outcome (Engel class I) and Patient #3 achieved >90% seizure reduction (Engel class II).

Conclusion: Multimodal integrative neuronavigation may facilitate electrode implantation and preservation of functional brain sites in resection of deeply sited FCDs.

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INTRACRANIAL EEG SIGNAL PROCESSING: A PILOT STUDY

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Purpose: To enhance the value of the intracranial EEG in patients with MRI-negative epilepsy by means of elaboration of a diagnostic protocol for mathematically analyzing the EEG signal.

Method: We report a ten-year-old girl with nonlesional focal epilepsy who underwent two-stage resective epilepsy surgery. Seizure semiology and scalp EEG findings were suggestive of the right supplementary motor area (SSMA) involvement. FDG-PET showed a small region of hypometabolism in the right dorsal-mesial frontal cortex. To delineate precisely the seizure onset zone and its relationship to the primary motor area (PMA), two subdural grids were implanted on the right mesial and lateral frontocentral cortex. The single channel technique based on the instantaneous frequency estimation procedures and the multichannel algorithms based on directed transfer function estimation were used for mathematically analyzing the EEG signal.

Results: Visual analysis of the intracranial EEG revealed two regions of active spiking that were also early involved in seizure onsets: First localized in the SSMA and second in the PMA area. Digital signal processing clearly proved the SSMA seizure onset zone and a fast spread of the epileptiform activity to the PMA. After SSMA resection, the patient is seizure-free.

Conclusion: Comparing with conventional methods of intracranial EEG evaluation, an automatic signal processing of the intracranial EEG represents a more precise and unbiased identification of the epileptogenic zone. It could help us to understand spatial and temporal characteristics of the epileptiform activity and significantly improve seizure outcome in complicated patients with normal MRI findings.

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RECONSTRUCTING THE OPTIC TRACT PRIOR TO AN ANTERIOR TEMPORAL LOBE RESECTION USING fMRI-seeded DTI tractography

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Purpose: Anterior temporal lobe resection (ATLR) is a frequent form of surgery in case of refractory temporal lobe epilepsy (TLE). A visual field deficit (VFD) as complication of an ATLR is due to disruption of the anterior part of the optic tract, the Meyer's loop (Yogarajah et al., Brain 2009). To reduce postoperative morbidity a method to predict the risk of a VFD was developed, using combined functional (f)MRI and diffusion based tractography (DTI).

Method: A feasibility study was performed in patients with a known VFD (n = 3) and in patients who were candidates for an ATLR. For the surgical candidates (n = 7) the experiment was performed twice, before and after resection, with 4 of these patients currently awaiting surgery. The experimental session consisted of checkerboard stimulation that allows to locate selectively the primary visual cortex at fMRI, used together with the lateral geniculate nucleus (LGN) as seed point in a probabilistic tractography algorithm (Sherbondy et. al., Journal of Vision 2008).

Results: Both the fMRI and DTI results were in line with the retinotopic projection, with the lower quadrant stimulus projecting via the posterior bundle to the upper lip and the upper quadrant projecting via the Meyer's loop to the lower lip of the calcarine sulcus. The results showed disruption of the Meyer's loop and a reduction in BOLD response in the pathologic compared to the nonpathologic hemisphere, which was in accordance with the perimetry test results, the golden standard to assess visual field loss. Reconstruction of the optic tract in the presence of brain malformations was, however, quite challenging, especially, if the LGN as second seed region was hard to define.

Conclusion: The use of fMRI to create seed points for the reconstruction of the optic tract using DTI incorporates both structural and functional information into the process that matched the clinical test results. The applicability of these methods requires, however, further developments mainly regarding accurate reconstruction and matching of pre- and post-operative images.

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DISAPPEARANCE OF EPILEPTIC DISCHARGES AND SEIZURES WITH CRYOPROBE IN RAT BRAINS

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Purpose: In order to verify the effectiveness of cryosurgery as a treatment of an epileptogenic lesion, a new type of cryoprobe has been developed by our group and tested against penicillin-induced epileptic activities in rats.

Methods: Wistar rats weighting 400 ± 34 g were anesthetized with Isoflurane (1–2%) via a nosepiece. The right parietal area of the skull was exposed and a craniotomy was performed with a dental drill. The craniotomy area was located between 4 mm rostral and 3 mm caudal from the coronal suture and between 1 mm and 6 mm lateral from the sagittal suture. An injection cannula was inserted for injection of an epileptogenic substance. The injection point was located the right primary somatosensory and motor cortex with a depth of 2 mm. In order to induce stable epileptic activities, Penicillin G, which is a potent epileptogenic substance, was used. The penicillin (400 IU/μl) was injected at a speed of 0.2 μl per minute by the injection-cannula for 5 min. After epileptic discharge and seizure were stably-induced, the cannula was removed, and the cryoprobe was inserted at the same depth as the tip of the cannula. R-410a was used as a refrigerant. The body temperatures of rats were kept constant at a temperature of 37 ± 0.5°C. Freezing-period was set as 20 min.

Results: At the beginning of freezing, epileptic seizures were drastically disappeared. Meanwhile, epileptic discharges were gradually suppressed during freezing-period and were finally disappeared. After freezing-period, tiny epileptic discharges were temporary relapsed depending on rats. However, these activities were vanished in dozens of minutes. And, histological evaluation indicated that the cryoprobe could make an ice-ball which the diameter was about 3.5 mm. In most parts of the ice-ball area, cell necrosis caused by the cryoprobe.

Conclusion: These experimental results suggest that cryosurgery must be useful as one of the surgical treatments of epilepsy.

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FOCUS DETECTION IN INTRACTABLE NEOCORTICAL EPILEPSY USING MAGNETOENCEPHALOGRAPHY

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Purpose: To identify a useful analytical method for detecting epileptic foci in intractable neocortical epilepsy using magnetoencephalography (MEG).

Method: In three patients (Cases 1–3) with an epileptic focus detected by a cluster of equivalent current dipoles (ECDs), morphological characteristics of 171 spike sources were investigated. In another three patients (Cases 4–6) in whom no epileptic focus was detected by ECDs, ictal MEG data were estimated using gradient magnetic field topography (GMFT).

Results: In Cases 1–3, mean time from beginning to the top of spike sources and mean amplitude of spike sources were 21.0 ± 7.4 ms and 449 ± 160 fT/cm when indicating a focus and 28.9 ± 10.7 ms and 783 ± 307 fT/cm when not indicating a focus, respectively. Epileptic spike sources showed significantly short duration ($p < 0.0001$) and low amplitude ($p < 0.0001$). GMFT of ictal MEG showed onset from the left frontal pole before propagation to the other side in Case 4, onset from the left temporal lobe before propagation to the ipsilateral occipital and frontal lobes in Case 5, and onset from the right temporal lobe before propagation to the ipsilateral frontal and occipital lobes in Case 6. In all six patients, seizures were eliminated after focus resection.

Conclusion: ECD analysis should be preferred to identify spike sources with low power and short duration as an epileptic focus. GMFT analysis of ictal MEG can visualize the temporal course and spatial resolution of epileptic propagation. Complementary use of ECD and GMFT analyses of high-resolution MEG enables detection of the epileptic focus.

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MINIMALLY INVASIVE ECOG RECORDING USING THE NOVEL SUBDURAL ELECTRODES MANIPULATED BY A SHAPE MEMORY ALLOY GUIDEWIRE

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Purpose: Due to the electrical characteristics and to the physical layout of the subdural strip/grid electrodes, the spatial resolution of ECoG recording is worse than few millimeters, and the recoding area is limited by the surgical area of craniotomy. In order to improve the resolution and to reduce invasiveness, we propose the novel subdural microelectrodes guided by a 0.3 mm-diameter shape memory alloy (SMA) guidewire.

Method: The platinum electrodes were mounted on the SMA guidewire whose shape were memorized in advance. Since the SMA guidewire is thin and flexible enough in the room/body temperature, the microelectrodes is able to be slipped into the subdural space without injury. After insertion, the electric current is applied and the SMA guidewire is heated by Joule heat. Then the microelectrodes are deployed to the desired positions. Here, the main part of the SMA guidewire was programmed to recover a hexagonal shape, and the microelectrode was mounted on the each vertex of the hexagon.

Results: In a rhesus monkey under general anesthesia, the microelectrodes were slipped into the subdural cavity around the primary somatosensory cortex through a 7 mm-diameter hole made on the skull, and were deployed by the DC current. The somatosensory evoked potential was successfully measured with electrical stimulation on the contralateral upper limb.

Conclusion: The SEP of a rhesus monkey was measured by the proposed minimally-invasive ECoG recording method. The results suggest that the proposed method would improve the ECoG recording for the focus detection of intractable epilepsy.

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APPLICATION OF INTRAOPERATIVE CT ANGIOGRAPHY FOR IMPLANTATION OF SEEG ELECTRODES IN INTRACTABLE PARTIAL EPILEPSY PATIENTS

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Purpose: Investigation of the utility of intraoperative computed tomography (CT) angiography avoiding intracranial hemorrhage during stereotactic electroencephalography (SEEG) electrode implantation. Invasive presurgical evaluation using SEEG is an indispensible diagnostic tool for localizing the epileptic zone in patients with medically refractory partial epilepsy. Despite technical and imaging advances in guiding the electrode placement, vascular injury is still one of the most serious complication of this diagnostic procedure.

Method: Trajectory data from 12 patients who underwent SEEG electrode implantation were studied in details. This part included analysis of implantation of 146 SEEG electrodes which were guided by intraoperative CT angiography in addition to the standard planning (of electrode placement) based on the preoperative contrast-enhanced magnetic resonance imaging (MRI).

To double check this approach, the safety of the procedure was approved by the retrospective analysis of the postinterventional CT of 87 patients who received 1300 electrodes.

Results: There was no complication related to the CT angiography itself. While the trajectories were safe according to the planning based on the preoperative MRI in most cases, in 10 of the 146 implantations a severe vascular complication has verifiable been adverted by intraoperative CT angiography. The safety of this current approach was confirmed by the retrospective analysis (for 87 patients) with the postinterventional CT which revealed a symptomatic hematoma for one single electrode (out of 1300 implanted).

Conclusion: This study shows that intraoperative CT angiography in addition to the preoperative MRI as the current gold standard is useful to guide SEEG electrode implantation. Combination of both imaging modalities essentially minimizes the risk of serious hemorrhagic complication and should be superior to any single imaging modality.

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SYNCHROTRON-GENERATED INTERLACED MICROBEAMS AS AN ANTIEPILEPTIC THERAPY: PROOF OF CONCEPT IN A RODENT GENETIC MODEL

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Purpose: In recent years, modern radiosurgical devices using collimated gamma-rays have shown their efficacy in the treatment of drug-resistant epilepsies. However, the use of these high-energy photons is often limited by the beam's lateral penumbra, which prevents the deposition of curative doses in the target without damaging the surrounding tissue. Here, we present Interlaced Microbeam Radiation Therapy (IntMRT), a novel irradiation method taking advantage of the brightness and low divergence of the synchrotron's low-energy x-ray microbeams. As a proof of concept, we tested the long-term consequences of a homogeneous 200Gy dose in the somatosensory cortex of the GAERS rat (a genetic model of absence epilepsy), a region known to initiate spike-wave discharges.

Method: Fifty micrometer-wide and 200 μm-spaced microbeams were interlaced within the target through several ports of irradiation, between which the animal was rotated using a kappa-type goniometer. Spike-wave discharges were monitored using chronically implanted electrodes, or intracellular recordings of irradiated neurons. Behavioral side effects were evaluated by open-field and Rotarod.

Results: Two months after irradiation, seizure duration was decreased by 60% in animals irradiated within the somatosensory cortex, while no behavioral impairments were observed. In vivo intracellular recordings revealed that irradiated neurons remained viable but hyperpolarized and silent, unable to oscillate in synchrony with their neighbors during seizures. Moreover, they maintained their ability to produce physiological responses when depolarized.

Conclusion: Our results confirm that synchrotron-IntMRT allows the precise deposition of high radiation doses in delimited brain structures. They suggest that IntMRT prevents irradiated structures from generating seizures, while preserving their physiological function.

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IDENTIFYING SEIZURE ONSET ZONE AND EPILEPTIC NETWORKS WITH THE DYNAMIC IMAGING OF COHERENT SOURCES

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Purpose: In the presurgical evaluation of children with refractory focal epilepsy the main difficulty is to locate the exact point of seizure onset. The aim of this study was to characterize the areas of seizure onset as well as the epileptic network involved in seizure propagation using *Dynamic imaging of coherent sources (DICS)* of ictal EEGs.

Method: DICS is an inverse solution in the frequency domain which describes neuronal networks and coherence of oscillatory brain activity by applying a spatial filter (Gross et al. PNAS 2001; 98:694–699). In 15 children with refractory focal epilepsy, typical seizures were selected from the EEGs recorded during the presurgical evaluation. For every seizure, two data sets of 10 s duration were extracted: one EEG segment contained the seizure onset and the other segment included the middle part of the seizure. For both segments, the frequency range was defined and analyzed with DICS. The brain area with the strongest power in the corresponding frequency range was defined as a reference region and its coherence with the entire brain was computed using DICS. The result of the reference region was compared with the electroclinical localization of seizure onset as well as with the postoperative resection site to determine concordance.

Results: For the beginning of the seizure, a good concordance between results of the DICS localization and postoperative outcome was achieved in all 15 patients. The analysis of seizure propagation revealed an epileptic network which resembled reverberation of epileptic activity between different brain areas.

Conclusion: DICS may be a useful tool to define the seizure onset zone and study epileptic networks.

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NAVIGATION GUIDED LESS INVASIVE SELECTIVE AMYGDALOHIPPOCAMPECTOMY VIA INFERIOR TEMPORAL GYRUS

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Purpose: Selective amygdalohippocampectomy (SAHT) has been reported to achieve better outcome to control the temporal lobe epilepsy than treatment with medication. Since now several procedures have been reported for AHT. We have developed less invasive procedure for SAHT approaching from the inferior temporal gyrus using neuronavigation system.

Method: Eighteen patients with the temporal lobe epilepsy (left: 14 cases, right: four cases) have undergone this surgical procedure for SAMH. Surgical procedure was; (1) front-temporal craniotpmy, (2) electrocorticography (ECoG) study, (3) Nelaton catheter insertion from anterior part of inferior temporal gyrus to the temporal horn as an anchor using MRI guided navigation system, (4) cortical incision along the tube with a width of 1.5–2.0 cm, (5) en bloc resection of 2.0–3.0 cm of hippocampus, amygdala, uncus and parahippocampal gyrus.

Results: The postoperative outcomes of 17 of all 18 cases were seizure-free categorized in Engel class I. One patient noted deteriorations of verbal memory. Four cases represented subclinical homonemous subquadrantic anopsia.

Conclusion: Trans inferior temporal gyrus approach with neuronavigation sytem for SAHT is simple and less invasive procedure and it could achieve excellent outcome for the patients with MTLE.

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UTILITY OF FDG-PET COREGISTRATION WITH 3 TESLA MRI IN PRESURGICAL EVALUATION OF CHILDREN WITH FOCAL CORTICAL DYSPLASIA

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Purpose: To analyze the utility of FDG-PET coregistration, with 3 Tesla MRI (PET/MRI) to define the epileptogenic zone in children with refractory epilepsy associated with focal cortical dysplasia (FCD).

Method: Forty pediatric patients studied by means of video-EEG monitoring and PET-MRI, diagnosed as having an epileptogenic FCD. Nineteen (47%) of them had previous "nonlesional" 1,5T MRI scans. Epilepsy surgery was performed in 25 patients, 13 after invasive EEG evaluation with subdural (13) and depth electrodes (5).

Results: Scalp video-EEG monitoring showed useful localizing information in 97% cases, including focal interictal and ictal EEG patterns, as well as semiological signs. Focal findings were identified also in several patients who had evolved into epileptic encephalopathies. 3T MRI showed findings suggesting FCD in 38 (95%), corresponding to subtle changes on gyral anatomy and/or signal intensity in nine of them (24%), and concordant with electroclinical findings in all except two cases. PET/MRI detected metabolic changes in 39 (98%) (hypometabolism in 90%, hypermetabolism in 8%), superimposed to MRI abnormal cortex in most of them. The most common location of FCD was the frontal lobe (53%). After surgery, seizure outcome was better in cases with small (<3 cm) PET/MRI findings (9/11, 81% Engel class I) than in those with more extensive abnormalities (6/14, 43% Engel class I). Most cases (73%) with <3 cm PET/MRI changes corresponded to Type II FCD, including five children who showed typical EEG epileptiform discharges in intracranial recordings.

Conclusion: FDG-PET coregistration with 3 Tesla MRI improves identification of the epileptogenic zone in children with refractory epilepsy associated with focal cortical dysplasia.

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SIMULTANEOUS DENSE ARRAY EEG AND INTRACRANIAL ECOG: INTERICTAL SPIKE DETECTION AND LOCALIZATION IN TEMPORAL LOBE EPILEPSY

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Purpose: To evaluate the clinical utility of dense array electroencephalography (dEEG) for the detection yield and source localization of interictal spikes in temporal lobe epilepsy.

Methods: We simultaneously recorded 256-channel dEEG and electrocorticography (ECoG) in patients with medically refractory temporal lobe epilepsy. ECoG were recorded with subdural electrodes implanted over the lateral and mesial temporal lobe. We calculated the dEEG spike detection rate for mesial temporal spikes which were confirmed by ECoG and the maximal spike amplitude. We applied source estimation to dEEG and compare the localization.

Results: DEEG clearly detected 42% of mesial temporal spikes and 86% of lateral temporal spikes with the 256 channel of whole-head topoplot. The maximal ECoG amplitude of dEEG detectable spikes was 1045 μV, but that of dEEG undetectable spike was 742 μV ($p < 0.05$). All spikes detected in dEEG were localized to the temporal lobe. Eighty-five percent of dEEG detectable mesial spikes were well localized in mesial temporal lobe, close to the position confirmed by subdural electrodes.

Conclusion: Two hundred fifty-six-channel dEEG used in conjunction with electrical source analysis may provide more precise information for the localization of interictal epileptiform discharges than conventional EEG and MEG in patients with deep spike foci. It may also be clinically useful in the presurgical workup for epilepsy as it shows excellent accuracy of source estimation noninvasively.

Poster session: Epilepsy surgery VII
Wednesday, 31 August 2011

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INTRAOPERATIVE NEUROPHYSIOLOGICAL RESPONSES IN EPILEPTIC PATIENTS SUBMITTED TO HIPPOCAMPAL AND THALAMIC DEEP BRAIN STIMULATION

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Purpose: We report on our intraoperative macrostimulation findings during thalamic and hippocampal DBS implantation.

Method: Eighteen patients were studied. Six patients with temporal lobe epilepsy were submitted to hippocampal DBS (Hip-DBS); six patients with focal epilepsy were submitted to anterior thalamic nucleus DBS (AN-DBS) and six patients with generalized epilepsy were submitted to centro-median thalamic nucleus DBS (CM-DBS). Age ranged from 9 to 40 years (11 males). All patients were submitted to bilateral quadripolar DBS electrode implantation in a single procedure and intraoperative scalp EEG monitoring. Final standard stimulation parameters were 6 or 130 Hz, 4 V, 300 μs.

Results: Bilateral recruiting response (RR) was obtained after unilateral stimulation in all patients submitted to AN and CM-DBS using LF stimulation. RR was widespread but prevailed over the frontotemporal region bilaterally. HF stimulation led to background slowing and a DC shift. RR obtained after LF Hip-DBS was restricted to the stimulated temporal lobe. HF stimulation yielded no visually recognizable EEG modification. In five of the six patients submitted to Hip-DBS, an increase in interictal spiking was noted unilaterally immediately after electrode insertion. Hippocampal HF was effective in abolishing interictal spiking in four of the six patients studied.

Conclusion: Thalamic-DBS (Th-DBS) RR was always bilateral after unilateral stimulation. Contrary to Th-DBS, Hip-DBS gave rise to localized RR over the ipsolateral temporal neocortex. Increased spiking was seen over temporal neocortex during hippocampal electrode insertion. The relationship between these intraoperative findings and seizure outcome is not yet clear and should be further evaluated.

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MICROLESIONAL EFFECT AFTER DBS ELECTRODE INSERTION IN PATIENTS WITH REFRACTORY EPILEPSY: "HONEYMOON" PERIOD

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Abstracts

Introduction: A microlesional effect of variable duration has been noted after DBS lead insertion in patients with Parkinson's disease and other movement disorders. Little is known about this type of event in patients with epilepsy submitted to DBS.

Methods: Eighteen patients with refractory epilepsy were studied. Six had generalized epilepsy and were submitted to thalamic centro-median DBS (CM-DBS); seven had extratemporal epilepsy or failed temporal lobe resection and were submitted to thalamic anterior nucleus DBS (AN-DBS) and five had temporal lobe epilepsy and were submitted to hippocampal DBS (Hip-DBS). AN- and CM-DBS patients had daily seizures. Mean seizure frequency in the Hip-DBS group was 1.5/week. Patients were considered to have had seizure frequency reduction when there was at least 50% reduction in seizure counts.

Results: There was no seizure frequency worsening after DBS. One patient in the AN-DBS group showed seizure frequency decrease which lasted for 1 week. That happened in five patients in the CM-DBS group; this effect lasted 28 days (mean). In the Hip-DBS group, four patients had decreased seizure frequency immediately after DBS, which lasted 26 days (mean).

Discussion: Our findings suggest that the distinct targets used in our patient population differed in relation to the occurrence and duration of post-DBS microlesional effects. This ''honeymoon'' effect was mostly noted in patients with CM- or Hip-DBS and lasted for approximately a month, and was basically absent in AN-DBS patients. These findings have practical implications regarding patient care and in the future development of clinical protocols as well.

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HABITUAL SEIZURES INDUCED BY DBS IN A PATIENT WITH REFRACTORY EPILEPSY: CASE REPORT

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Purpose: DBS has been used to treat refractory epilepsy over the last years. Both deep and cortical targets have been tried. The hippocampus is a highly epileptogenic structure, and its resection leads to seizure freedom in a high percentage of patients with mesial temporal sclerosis. The effects of hippocampal stimulation on seizures are not yet fully understood. We report a patient in whom DBS was able to systematically reproduce his habitual seizures.

Method: S., a 38-year-old male, had epilepsy since the age of 12 years. He had daily complex partial seizures. Interictal and ictal EEG suggested a left temporal lobe seizure onset. MRI disclosed right hemisphere atrophy and a normal left hippocampus. He was submitted to bilateral hippocampal electrode implantation; the generator was inserted during the same procedure.

Results: He got 70% reduction in seizure frequency after the onset of left hippocampal stimulation (2.0 V, 130 Hz, 300 μs). Any attempt to increase stimulation over 3.0 V led to his typical complex partial seizure.

Conclusion: This is, as far as we know, the first report of such a patient in the literature. This patient might prove to represent a relevant subject for the definition of the adequate parameters for DBS in patients with temporal lobe epilepsy.

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VAGAL NERVE STIMULATION FOR DRUG-RESISTANT EPILEPSY: THE DIFFICULT TASK TO ASSESS THE RESULTS

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Purpose: To assess the response to vagal nerve stimulation (VNS) in drug-resistant epilepsy.

Method: Seventy patients suffering drug resistant epilepsy have been submitted to VNS (1995–2010) in UCSC. The etiology of epilepsy was criptogenetic in 34 patients (48.6%), symptomatic in 36 (51.4%). The diagnosis was: Lennox- Gastaux in three patients, severe multifocal epilepsy in five patients, epilepsy with partial seizures in the remnant 62. The mean age of implantation was 30.8 years (6–65); 12 patients were in pediatric age (6–17 years), 58 were adults; history of epilepsy ranged from 3 to 59 years (mean 22.3). The outcome was determined comparing the frequency of seizures after stimulation (3, 6, 12, 18 months and from 2 to 10 years) with the baseline considered as the number of seizures/month in the last 3 months before the implantation of VNS. Minimum follow-up accepted was 1 year.

Results: Of the 70 patients submitted to VNS, five patients were followed elsewhere after the device's implantation, four patients had a follow up lower then 1 year, five patients didn't report correctly the data. The evaluation, according to the indicated methodology, concerns 56 VNS patients monitored in UCSC: a reduction of the seizures number occurred in 45% of patients. According with the literature data, after 3 years of follow up 23% only among our patients should be considered as ''Responder'' (≥50% seizure frequency reduction). Interestingly 42% among our patient required to continue the stimulation when the generator expired. The decision to proceed with VNS was based on the reduction of the:

1. Total number of seizures;
2. Number of generalized seizures;
3. Postictal period.

Conclusion: We confirm the efficacy and the duration in time of results obtained with VNS. The seizure number reduction, the lower violence and duration of the seizures and of the postictal episodes determinate patients' satisfaction and thus pulse generator's change.

The not fulfilled ''wonder expectation'' can bring to treatment drop out, even with good results.

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RIGHT-SIDED VNS THERAPY: SIMPLE AND EFFECTIVE OPTION

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Purpose: Despite some evidence in the literature that right-sided vagus nerve stimulation (R-VNS) is effective and safe, this option is still not used routinely in epilepsy centres as an option. We present a case of a young man treated with R-VNS.

Method: We treated one patient, with refractory epilepsy, previously implanted with a L-VNS. After many years with a good response to left vagus nerve stimulation, the patient experienced a sudden worsening of seizure intensity and severity. Impedance was high suggesting malfunctioning of the electrodes. X-ray couldn't identify any break of the electrode. During the surgery we concluded that he had a break proximally, 1 cm from the nerve contacts. We decided to remove this cable and to do a complete cardiological test with ECG and Holter and to exclude left vocal cord paresis previous to decide to implant a R-VNS. After these tests, we implanted a R-VNS connected to left subclavicular implanted generator.

Results: After implantation on the right vagus nerve, the patient experienced hoarseness not related to stimulation during approximately 3 weeks. After 2 months of therapy, seizure intensity and severity are both reduced with no cardiac or respiratory side effects.

Conclusion: This technic is both safe and effective and is much better than trying to reimplant again an electrode in a previously scared left

vagus nerve. We believe that, regarding the existing literature and this single case, R-VNS is a valid option and should be more widely used.

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EXTRAVENTRICULAR APPROACH TO THE ANTERIOR NUCLEUS OF THALAMUS FOR EPILEPSY TREATMENT

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Purpose: The stimulation of the anterior nucleus of thalamus (ANT) for the treatment of refractory epilepsy became a significant alternative after the SANTE study. We present our experience of the first two patients submitted to this technique. We give special emphasis on technical details concerning the different approach routes—transventricular versus extraventricular—to ANT.

Method: The complete data of the first two cases of ANT stimulation are analyzed, from the inclusion criteria to the trajectory planning and electrode implantation. Final coordinates are retrieved from postoperative CT merged in our navigation system (CT-MR initial imaging fusion) in order to refer these values to AC-PC line.

Results: No major difficulties were found during planning. On both cases we decided to go outside the ventricle to avoid huge thalamo-striatal veins; on the first case there were also very narrow frontal horns. No surgical complications were seen in these two cases. The follow-up is still too short to draw conclusions regarding efficacy of the treatment.

Conclusion: The treatment of refractory epilepsy with stimulation of ANT needs to be further discussed between European Epilepsy Surgery Groups in order to reach an agreement about the indications and standardization of the procedure. In this regard the extraventricular approach to ANT seems to be a safe alternative. A new multicentre study to clarify some questions not answered in previous studies should be addressed.

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VAGUS NERVE STIMULATION FOR EPILEPSY: QUALITY OF LIFE AND PATIENTS' SATISFACTION

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Purpose: Vagus nerve stimulation (VNS) therapy reduces seizures in certain patients with pharmacoresistant epilepsy who are not candidate for resective surgery. Despite the extensive research in this field there is a variability in the impact of VNS on quality of life (QOL) and patients' satisfaction rate.

Method: A group of 24 consecutive patients who underwent VNS therapy for epilepsy managment at our institution were analyzed. The patients were divided into two groups; responders and nonresponders. The response to VNS was defined as >50% reduction of seizure frequency. QOL was measured using QOLEI-31 inventory for the adult group and patients' satisfaction was rated based on a scale from 0 to 10. These were correlated with the epileptic syndromes, radiological and neuropsychology findings in addition to procedure related complications.

Results: Twenty adults and four pediatrics with a mean follow-up of 16 months after VNS implantation were identified. Of those, 33% (n = 8) were considered responders (>50% seizure frequency reduction). Only one patient from the adult group reached Engel class-II. Sixteen percent (n = 4) had a satisfaction of >50% and 20% (n = 5) had more than 50% improvement in quality of life score. Radiological and neuropsychological abnormalities did not correlate with seizure frequency reduction or QOL scores. The main factor that impact QOL is the significant seizure frequency reduction (>70%). In this group most of the patient with Lennox Gastaut syndrome responded to VNS therapy. Complications includes hoaresness in two patients and intermittent shortness of breath in one. None of these side effects impact QOL or patients 'satisfaction.

Conclusion: Significant seizure frequency reduction (>70%) was the main factor that impact quality of life and patients' satisfaction. However, this result need to be varified in a study with large number of patients.

p667
DEEP BRAIN STIMULATION OF THE ANTERIOR NUCLEUS OF THE THALAMUS FOR REFRACTIVE EPILEPSY: EXPERIENCIE IN THE FIRST TWO PATIENTS

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Purpose: Given the large proportion of patients who fail medical therapy and are not candidates for resective surgical treatment, the encouraging results of the SANTE trial are leading to the worldwide implementation of DBS for epilepsy targeting the anterior thalamic nucleus (ANT).

Method: We report our results in the first two patients suffering from farmacoresistant epilepsy who were not suitable candidates for resective surgery and underwent anterior thalamic nucleus-deep brain stimulation (ANT-DBS) for the treatment of their epilepsy.

Results: Patient 1: A 25-year-old female with temporal focal epilepsy due to cardioembolic stroke, had a mean of 10 partial complex seizures/day and one atonic seizure/day. Bilateral 3387 electrods were implanted in ANT by a transventricular approach. ANT-DBS was started after 1 month. After 9 months of follow-up, she had almost complete remission of complex partial seizures (1/month), and her atonic seizures were reduced to one per week, only after a 6-month period. Patient 2: a 53 years-old male presenting initially with eating seizures and predominantly nocturnal epilepsy, which after a severe head injury evolved to a multifocal epilepsy. The seizure followed a pattern of 2–3 cluster per month (3–4 seizures per cluster), including frequente drop attacks. In this patient, because of abnormal large thalamic veins, we performed an alternative procedure to the transventricular approach to NAT with 3389 electrods. In a 3 months-follow-up, the seizure cluster frequency was reduced to 1 per month and the patient is seizure-free from Feb 19, 2011.

Conclusion: Despite our short sample and follow-up, there seems to exist a few evidence showing that ANT DBS is a promising therapy for severe refactory epilepsy patients, and the benefit may be seen after a relatively long period after the start of the stimulation.

p668
COMBINED APPLICATION OF ELECTROCORTICOGRAM AND ELECTRICAL CORTICAL STIMULATION IN PARIETAL EPILEPSY SURGERY

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p669
EPILEPSY SURGERY IN CHILDREN WITH TUBEROUS SCLEROSIS, EPILEPTIC SPASMS AND MULTIPLE SEIZURE FOCI

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Purpose: To determine the influence of early seizure onset, epileptic spasms (ES) and multifocal seizures on outcome of epilepsy surgery in tuberous sclerosis (TS).

Method: Review of clinical, video-EEG monitoring (VEM), operative and outcome data in 45 consecutive children with TS who underwent epilepsy surgery at our centre.

Results: The 45 children were 0.3–18 years old (median 3.2, 62% ≤3 years) at the time of first surgery. Age at seizure onset was ≤2 years in 31 children with ES, and 0–7 years in 14 children without ES. VEM revealed a single seizure focus in 16 children, multiple seizure foci in 24, and no focus in 5. Intracranial EEG monitoring was performed in 18 children (bilateral in 14, performed two or more times in 4), most of whom were younger than 5 years and had ES and multiple seizure foci. Tuberectomies (1–10 per surgery) were undertaken once in 26 children, twice in 11 and three or more times in 8. At follow-up (median 2.4 years), 21 children (47%) are seizure-free and 21 had a significant seizure reduction or remission of seizure types. Seizure freedom was greater in children with a single seizure focus ($p = 0.006$), though 9/24 with multiple seizure foci are seizure-free. Age at seizure onset, ES and intracranial EEG monitoring did not predict outcome.

Conclusion: Epilepsy surgery yields favorable results in young children with TS and ES. In children with multiple seizure foci, multiple procedures may be required and seizure improvements are more modest.

Poster session: Pediatric epileptology X
Wednesday, 31 August 2011

p670
EFFICACY AND SAFETY OF ADD-ON LACOSAMIDE IN CHILDREN WITH REFRACTORY EPILEPSY

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Purpose: To evaluate the efficacy and safety of lacosamide (LCM) as add-on therapy in children with refractory epilepsy.

Method: This was a retrospective review of 50 consecutive pediatric patients under 18 years of age with refractory epilepsy who were exposed to LCM for at least 6 months. All patients were analyzed for changes in seizure frequency per month, seizure freedom and adverse events (AEs). We also evaluated retention rate of LCM and potential synergistic antiepileptic effect of LCM coadministration with other antiepileptic drugs (AEDs).

Results: Thirty-nine patients had focal epilepsies, four patients had generalized epilepsies and seven had epileptic encephalopathies. Twenty-six of the 50 patients (52%) showed a seizure reduction of ≥ 50%, and seven patients (14%) became seizure-free for at least 2 months. The mean maintenance dose of LCM was 6.75 mg/kg/day, and mean follow-up duration was 12.5 months. Thirty-three patients (66%) reported AEs. The most common AE was dizziness (58%). Treatment was discontinued in 10 patients (20%) because of AEs. Improvement in attention and reactivity was observed in 50% of patients. LCM had a retention rate of 60% at 6 months and 48% at 12 months.

Conclusion: LCM adjunctive therapy is effective and safe for childhood intractable epilepsy and has a good retention rate. LCM neurotoxicity was more frequently associated with concomitant use of sodium channel-blocking AEDs and improved with a stepwise progressive reduction of those AEDs. Otherwise, the association of lacosamide and levetiracetam had a positive synergistic antiepileptic effect and an excellent tolerability.

p671
ANTIEPILEPTIC TREATMENT OF SYMPTOMATIC FOCAL FORMS OF EPILEPSY IN CHILDREN WITH CONGENITAL CEREBRAL MALFORMATIONS

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Purpose: To make the analysis of the efficiency of using antiepileptic drugs of different generations under treatment of symptomatic focal forms of epilepsy in children with different congenital cerebral malformations.

Method: Fifty-seven children aged from 1 month to 17 years old and divided into two groups according to using antiepileptic drugs were included into current analysis. Researchers have used following drugs during treatment: sodium valproate, lamotrigine. All drugs were used in therapeutics doses in monotherapy or in combined therapy with other antiepileptic medication.

Results: Good result (seizure freedom and reduction of seizure frequency by 50% or more) was achieved in 35% patients used sodium valproate, and in 65% patients used lamotrigine. In six patients detected seizure aggravation (in four patients, used sodium valproate and two patients, used lamotrigine).

Conclusion: This study has shown that lamotrigine is more effective in treatment focal forms of epilepsy in children, than sodium valproate. Moreover, seizure aggravation was less peculiar to lamotrigine. Anyway, we need to take into account quantity of members that have taken part in this study and this fact calls forth for making more extensive studies with greater number of patients involved into study for validation of results. Such studies are in progress.

p672
CLINICAL AND ELECTROENCEPHALOGRAPHIC CHARACTERISTICS OF PATIENTS WITH PANAYIOTOPOULOS SYNDROME

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Purpose: Evaluation clinical and EEG characteristics of children with diagnosis of Panayiotopoulos syndrome.

Method: We retrospectively analyzed 27 children with diagnosis of Panayiotopoulos syndrome. Criteria for diagnosis were clinical (ictal autonomic symptoms, normal development, normal neurological state, normal brain imaging) and electrophysiological (focal epileptiform patterns on EEG).

Results: Onset of seizures occurred between 18 month and 11 years. Number of seizures before treatment was: 1 in 7 (26%) patients, 2–5 in 13 (48%), more that 10 seizures in 4 (15%) and status epilepticus in 3 (11%) patients. Increasing number of attacks is proportional to the impairment of consciousness.

Six month after introducing treatment seizures were appeared in 12 (44%) patients. During the first seizure ictal vomiting was present in 21

(78%) and nausea in 6 (22%) patients. Headache was reported in seven patients, pallor in 7, sweating in one and hypotonia in four patients (alone or in combinations). Impairment of consciousness was reported in 21 (78%) patients in at least one seizure, eye deviation in 17 (63%), hemiconvulsion in 3 (11%) and generalized convulsions in 9 (33%) patients. Initial EEG was with focal epileptic patterns in all patients, with F-C localization in 7 (26%), occipital localization in 12 (44%) and multifocal in 8 (30%) patients. After 6 month follow-up EEG was still with epileptiform patterns in 20 (74%) patients. Shifting of spikes in different recording occurred in 12 (44%) patients.

Conclusion: Panayiotopoulos syndrome occurred with various clinical and electrophysiological manifestations. Therefore establishing a diagnosis in time could be a challenge.

p673
PARENTAL CONCERNS ABOUT USING BUCCAL MIDAZOLAM FOR PROLONGED SEIZURES

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Purpose: Several recent articles have observed that buccal midazolam is faster, more effective, and preferred over rectal diazepam for the treatment of prolonged seizures. However, the use of the medication remains minimal.

Method: An informal survey was conducted at a large children's hospital tertiary care clinic to investigate the level of parental comfort with giving either of these medications.

Results: Approximately ten families were interviewed. For families already using rectal diazepam, the most common fears of using buccal midazolam were of placing fingers in the mouth of a patient who is having a seizure in order to administer the medication. There were also concerns of knowing whether or not the patient received the medication due to excessive. For families who had not used either medication, the preference seemed to be for buccal midazolam. For all families interviewed, availability of buccal midazolam was a concern.

Conclusion: Both medications are safe and effective. There are concerns about the administration of buccal midazolam by parents and caregivers. Education on safe administration of the medication is warranted.

p674
CAN CARBAMAZEPINE INDUCE HYPONATREMIA IN EPILEPTIC CHILDREN?

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Purpose: Carbamazepine (CBZ) can induce hyponatremia, but there are few studies of the prevalence of this effect in epileptic children during treatment with CBZ monotherapy. The aim of this study was to investigate the relationships between CBZ dosage, serum concentrations, age, and serum sodium levels.

Method: Sixteen patients (nine males and seven females, 7 months to 14 years of age) newly diagnosed or previously diagnosed with epilepsy were included in the study after informed parental consent was obtained. Serum sodium and concentration of CBZ were measured using commercially available kits at all scheduled visits. Serum sodium levels were categorized as follows; <135 mM, hyponatremia; 135–145 mM, normonatremia; >145 mM, hypernatremia.

Results: All patients showed normonatremia at the administration of CBZ. Treatment with CBZ monotherapy resulted in a statistically, but not clinically, significant decrease in serum sodium levels and serum osmolality below the reference range. During treatment with CBZ, we found hyponatremia without clinical symptoms in seven children (44%). The categorization of patients into two different age ranges, under 7 years and 7–14 years, disclosed that serum sodium levels were statistically significant lower in elder patients ($p = 0.01$). None was occurred clinically relevant hyponatremia. Decreases in serum sodium levels were related to increasing age and female gender, but not to CBZ dose or blood concentrations.

Conclusion: Hyponatremia during treatment with CBZ monotherapy may occur in children and it is probably common finding.

p675
DYNAMIC MODEL CHANGES OF THREE TIMES INTERICTCAL SPECT OF EPILEPSY PATIENTS WITH LONG-TERM CONTROL WITH AEDS AND ITS CLINICAL SIGNIFICANCE (63 CASES)

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Objective: To discuss the dynamic mode changes and its significance of abnormal perfusion foci in brain of epilepsy patients with long-term control with antiepileptic drugs (AEDs).

Methods: The research test the results of three times interictcal SPECT and long-term V-EEG of epilepsy patients.

Results: The total number of diagnosed epilepsy patients is 63 cases with male 44 and female 19 and with average 42 months controlled. The mean age is 15.3 years old, mean course is 1.3 years with etiology 57.1%. The seizure type are GTCS 32 cases, focal seizure29 cases and the other in 2 cases. First SPECT abnormality 84.1% and long – term V-EEG anomalies 93.7%, epileptic discharge 93.3% and CT/MRI abnormal 26.9%. Three times changes of abnormal perfusion focal are 45 cases (71.4%). Three kinds of dynamic mode changes cover 20 subtypes and comprehensive four types, there are three times consistent type, intermediate change type, last changes type and intermediate last changes type. Normal SPECT increase 26.9% after treatment, total focal numbers reduce 38 (42.7%), normally EEG increase 36 cases (57.1% $p < 0.05$) and epileptic discharge reduce 67.3%.

Conclusion: It was found in longitudinal study that epileptic patients with brain abnormalities perfusion focal under long-term control still at low perfusion focal – high perfusion focal – normal different patterns or repeated the dynamic changing mode (20 subtypes mode and four comprehensive types) and it related with epilepsy neural network and part of abnormal perfusion focal can be repaired. The change of dynamic model to the clinical significance of epilepsy course should be paid much attention.

p676
OUTCOME PREDICTORS IN CHILDREN WITH DIFFERENT TYPES OF EPILEPSIA PARTIALIS CONTINUA: THE BELGRADE COHORT STUDY

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Abstracts

Purpose: Evaluation of outcome predictors in children with different types of epilepsia partialis continua (EPC).

Method: Investigation included 51 children with EPC, aged 2 months to 18 years, treated in two Belgrade tertiary clinical centers, for 16-years period. All patients were divided into two groups regarding the etiology: EPC type 1 and EPC type 2 or Rasmussen encephalitis. Predictive value of selected demographic, clinical and neurophysiologic factors and treatment on prognosis in children with EPC were analyzed. Severity of illness, neurological and intellectual status was classified as: severe, moderate or mild disturbance. The outcome was divided in three categories: unchanged neurological status, neurological consequences and lethal outcome. Statistical analysis included: *t*-test, χ^2 test, Kaplan–Meyer curves, long-rank test and Cox regression proportional hazard models.

Results: The most important predictors for neurological consequences were background EEG abnormalities (HR = 0.4, 95% CI 0.2–0.8, p = 0.006) and periodic EEG patterns (HR = 0.4, 95% CI 0.2–1.1, p = 0.08). Predictors for lethal outcome were: onset of EPC in terminal phase of disease (HR = 12.9, 95% CI 2.2–76.2, p = 0.005) and applying of artificial ventilation (HR = 0.1, 95% CI 0.1–0.5, p = 0.010). Kaplan–Mayer curves showed that 5-year survival probability was 86.0 ± 5.5%, with no significant difference between EPC type 1 and 2 (long-rank test 1.345; p = 0.246).

Conclusion: In children with EPC, the most important predictors for lethal outcome were EPC onset in terminal phase of disease and applying of intensive therapy, while EEG abnormalities were the main predictors for neurological consequences.

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STEROID PULSE THERAPY AS AN EFFECTIVE TREATMENT FOR REFRACTORY EPILEPSY IN CHILDREN WITH GLUTAMATE RECEPTOR (GLUR) ANTIBODIES

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Purpose: To determine the efficacy of steroid pulse therapy (SPT) for children with refractory epilepsy and GluR antibodies.

Method: Patients: five children (aged 2–13) with refractory epilepsy. Their clinical features include West syndrome, Lennox-Gastaut syndrome, FLE, undefined focal epilepsy and acute encephalitis with refractory, repetitive partial seizures (AERRPS). We evaluated patients' clinical features and EEG findings, determined whether they had GLuR antibodies, and administered STP to them one to four time, with follow-up periods from 6 to 24 months.

Result: All six patients showed autoantibodies against GluR and tested positive to IgG-ϵ 2 in CSF. After 3 weeks of treatment, two cases were seizure-free and their EEG paroxysms had improved. One of the two (a case of FLE) remained seizure-free for two years and thereafter decreased her medications. The other (Lennox-Gastaut syndrome), worsened after 6 months. In the remaining, three cases, seizure frequencies of seizure and paroxysmal EEG discharges were reduced and the patients' quality of life improved. There were no major side effects in any of the five cases.

Conclusion: GluR antibodies are a contributing factor to refractory epilepsy. Steroid pulse therapy can be effective epilepsy treatment for children with GluR antibodies.

p678

EFFICACY OF CORTICOSTEROIDS IN THE MANAGEMENT OF REFRACTORY NONCONVULSIVE STATUS EPILEPTICUS (NCSE) IN CHILDREN

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Objective: NCSE is an epileptic state with nonconvulsive clinical symptoms associated with ongoing ictal activity on EEG. This is frequently more refractory to conventional drugs than convulsive status epilepticus. Objectives were to assess the clinical responder rate, remission of electrical status, quality of life and behavior improvement with the trial of corticosteroids.

Method: Single armed drug trial with add on corticosteroid therapy was performed over a period of 24-weeks. Intravenous Methyl-prednisolone (30 mg/kg/day) was administered for 5-days followed by oral Prednisolone (2 mg/kg/day) for 9-days. Subsequently Steroids were tapered over a period of 6-weeks. Pulses of prednisolone were commenced (twice a week) to complete the 24-weeks. Patients were monitored closely.

Results: Fourteen children aged 2.5–16.3 (mean-6.8) years; fulfilled the inclusion criteria. Variation in conscious level (9/14), fluctuating behavior (5/14), motor automatisms/subtle motor phenomena (4/14), poor balance/falls (4/14) and drooling of saliva (3/14) were the commonest clinical manifestations. Three dropped out before day-14 due to severe hospital acquired infection, uncontrollable hypertension and parental concerns. The rest complied with subsided symptoms by day-14.

Entire sample had continuous generalized ictal EEG discharges (mean frequency-3.3 Hz). Ten had electrical remission by day-14. One did not respond. One relapsed at 24-weeks.

In the responders changes observed in the height velocity, blood pressure and the serum biochemistry were unremarkable. The BMI was increased at 12-weeks ($p < 0.05$).

Quality of life (PedsQL) and Childhood Behavior scores improved ($p < 0.05$) in the sample at 24-weeks.

Conclusion: Majority achieved a sustained electrical remission, significantly improved quality of life/behavior scores with minimal adverse effects by the corticosteroid regimen trialed.

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INSULIN-DEPENDENT DIABETES MELLITUS AND EPILEPSY: A STUDY OF THREE CASES

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Purpose: Insulin-dependent diabetes mellitus and epilepsy rarely coincide, especially in childhood. The purpose of this study was to present three such cases.

Method and Results: The children were diagnosed with diabetes mellitus around six years ago and immediately started on the insulin therapy. The first one, a 12-year-old girl, developed complex partial seizures three years ago. The second, a 17-year-old girl, had tonic–clonic seizures up to five years ago. The third, a 16-year-old boy, had absence seizures during two years up to six years ago. The children were treated with valproid acid in dosage 25–35 mg/kg/day for three years, resulting in total absence of the seizures. A 17-year-old girl is now 1 year without the antiepileptic treatment. Laboratory examinations showed good glycemic control and almost stable glycated hemoglobin levels before and during the antiepileptic treatment.

Conclusion: The children with type 1 diabetes mellitus suffering also from epilepsy are treated with valproic acid with a good result.

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TWO OPEN-LABEL, SINGLE-ARM, MULTICENTER, SAFETY, TOLERABILITY AND PHARMACOKINETIC STUDIES OF INTRAVENOUS LEVETIRACETAM IN CHILDREN (>1 MONTH TO 16 YEARS OLD) WITH EPILEPSY

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Purpose: Two studies evaluated safety, tolerability, and pharmacokinetics of intravenous (IV) levetiracetam (LEV), as adjunctive or monotherapy treatment in children with epilepsy: 1 month to <4 years, N01275 [NCT00505934]; ≥4 to 16 years, N01274 [NCT00535392]).

Method: Patients were hospitalized for reasons requiring short-duration LEV IV. Patients received repeated administrations of LEV IV 15 min infusion every 12 h for ≤4 days. LEV IV dosing for patients already taking oral LEV: equivalent (mg-for-mg) to label-recommended age-dependent oral doses. For LEV naive patients: 14–20 mg/kg/day. Safety and tolerability measures: TEAE reporting, laboratory tests and neurological examinations. Samples for pharmacokinetic analysis were taken 4 times/infusion day.

Results: Nineteen (N01275) and 33 (N01274) patients were recruited. All patients received ≥1 LEV infusion. In study N01275, 12/19 (63.2%) patients experienced treatment-emergent adverse events (TEAEs). Most frequent TEAEs were pyrexia (three patients), bradycardia, pneumonia, metabolic acidosis and hypotension (two patients each): three deaths occurred (pneumonia, abdominal sepsis, bradycardia, and metabolic acidosis; respiratory failure; cardiac arrest and metabolic acidosis: all considered unrelated to study medication). In study N01274, 21/33 (63.6%) patients experienced TEAEs. Most frequent TEAEs were convulsion (four patients), vomiting, nausea, dry mouth, pyrexia and hypotension (three patients each). No trend in TEAEs by age group, dose category, or previous LEV use was identified. Laboratory analyses, vital sign/ECG measurements and LEV plasma concentrations were within expected ranges for both studies.

Conclusion: LEV IV was well tolerated in children with epilepsy (1 month–16 years) as a short-term replacement where oral treatment was not feasible.

UCB-Sponsored.

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ADJUNCTIVE THERAPY OF RUFINAMIDE IN LENNOX-GASTAUT SYNDROME

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Background: Lennox-Gastaut syndrome (LGS) is a catastrophic pediatric epilepsy syndrome characterized by multiple types of seizures and characteristic electroencephalographic (EEG) features. Even with multiple antiepileptic drugs, most of the patients remain in disabling seizures and progressive psychomotor retardation.

Method: We conducted retrospective analysis of the efficacy and safety of rufinamide add-on treatment in children and adolescents with LGS intractable to one or more antiepileptic drugs (3.3 ± 1.1) in Severance Children's Hospital. Eligible patients between 1.8 and 20.5 years of age had multiple types of seizure with a minimum of four seizures in a month during baseline period and slow spike and waves on EEG. Rufinamide was titrated over 1–2 weeks, followed by maintenance for another 12 weeks. Seizure reduction rate and adverse events were evaluated after 12 weeks of the treatment.

Result: Among 118 patients enrolled in the study, 105 patients (89.0%) maintained rufinamide for 12 weeks. Maintenance dose was 31.7 ± 8.7 mg/kg/day. Out of 105 patients, 39 patients (37.1%) experienced seizure reduction more than 50% in frequency. Median percentage reduction in main seizure frequency was 32.5%, and the highest reduction was observed in tonic seizure type at 39.6%. Eight (7.6%) achieved seizure freedom; 19 (18.1%) had 75–100% reduction in seizure frequency; 12 (11.4%) had 50–75% reduction, and 9 (8.6%) had less than 50% reduction. Seventeen patients (14.4%) reported adverse events (14.4%) that most commonly included rash (five patients, 4.3%) and somnolence (four patients, 3.4%). No severe adverse events were reported.

Conclusion: Rufinamide adjunctive therapy was effective and well-tolerated in LGS.

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INTELLIGENCE AND VERBAL LEARNING AFTER HEMISPHERIC DISCONNECTION IN CHILDREN WITH EPILEPSY

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Purpose: Neuropsychological study in children undergoing by vertical parasagittal hemispherotomy (VPH) for hemispheric epilepsy, in order to determine parameters influencing long-term outcome in the amazing situation of "*growing with a single hemisphere (SH).*"

Method: Thirty children (15 girls, 19 left VPH) with a mean age of 13.5 years (SD = 3.2 years) at evaluation. Mean age at seizure onset was 3. Six years (SD = 2.8 years) and mean age at surgery was 7.8 years (SD = 3.8 years). Etiology were early (N = 19) or late hemispheric lesion (Rasmussen encephalitis, N = 11). Cognitive assessment included verbal and performance intellectual quotient (VIQ-PIQ), language and reading abilities, as well as short term memory and verbal learning. Statistical analysis focused on the following factors: side of VPH, age of seizure onset, etiology, preoperative delay and postoperative follow-up.

Results: IQ was heterogeneous: normal (N = 2), moderate mental retardation (N = 14) or dissociation between VIQ and PIQ (N = 14). On the opposite, verbal learning scores exhibited normal score in 25 patients. Statistical analysis pointed out relationship between side of surgery and VIQ, language and reading capacity, short-term memory: children with left SH obtained higher scores. Moreover, we found statistical relationship between age of onset of epilepsy and postoperative follow-up on verbal abilities: these capacities were better with late seizure onset and improved during the postoperative course.

Conclusion: These results are in favor of an early left hemispheric dominance for language and the existence of late cognitive plasticity of the SH with preserved verbal learning abilities in most of our patients.

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FUNCTIONAL CONNECTIVITY IN CHILDREN WITH FOCAL EPILEPSY

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Abstracts

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Purpose: Network analysis can provide valuable information into the complex arrangement of functional connectivity of the brain. Recent studies revealed disrupted network configurations in patients with epilepsy. In this study, we analyzed whether functional connectivity is altered in children recently diagnosed with focal epilepsy.

Method: We included children diagnosed with focal epilepsy at the outpatient department of pediatric neurology University Medical Centre Utrecht (The Netherlands) in the period 2006–2010. Children in whom the diagnosis epilepsy was excluded were used as controls. Both patients and controls were excluded if they had a history of neurological or psychiatric disease, suffered febrile seizures, showed developmental delay or were using antiepileptic drugs. Extensive medical history, routine EEG, and MRI was available for each child. Functional connectivity was analyzed in artefact free epochs of routine EEG recordings. Network analyses were carried out using Brainwave-software. Synchronization likelihood was computed to analyze global connectivity. Centrality measures were used to investigate local connectivity.

Results: Thirty-five children with focal epilepsy were included (11 girls, mean age 10.3 years (±3.1 years). The control group of 35 children was individually matched on age and sex. In both groups there was a significant increase of functional connectivity with age ($p < 0.05$). Although we did not find clear differences between groups on global connectivity, local connectivity tended to distinguish children with focal epilepsy from controls.

Conclusion: Alternations in connectivity may influence optimal network configurations in patients and potentially interfere with normal brain development leading to chronic epilepsy or cognitive and behavioral dysfunction.

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DISCONNECTION AS AN ALTERNATIVE TO PARTIAL OR COMPLETE LOBECTOMIES

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Purpose: Historically in cases of neocortical epilepsy, when a focus is identified, a focal resection is done. If a substantial portion of a hemisphere is involved, the procedure previously done, anatomical hemispherectomy, has been replaced by hemispheric disconnection techniques. It was decided to explore whether disconnections of focal neocortical regions were as effective as complete or partial lobectomies

Method: All cases that underwent phase 2/3 epilepsy surgery (January 2010 to present) were reviewed. Of 25 cases completed, six cases had partial disconnections. All had neuropsychology, MRI, VEEGs, fMRI, PET and/or SPECT imaging. During the phase 2 evaluations in all cases of frontal disconnections, cortical stimulation for language or motor mapping was completed.

Results: The regions identified as the itcal focus were disconnected but not removed. Frontal lobe disconnections were done in four cases, and two patients had posterior disconnections. There was no acute surgical morbidity in five of six cases and there was rapid recovery and discharge in all. Four cases are seizure-free. In one case of recurrence the patient initially presented as status epilepticus and resection was done to abort status. There was approximately 75% seizure reduction. In the other case of seizure recurrence the patient had frequent daily seizures and significant bilateral cortical pathology. Post parietal-occipital disconnection he has had approximately one brief seizure per week.

Conclusion: Disconnections may be an option when there is a large itcal cortical focus. It can potentially minimize surgical pathology, surgical duration, and often expedite time to recovery.

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INTERICTAL ELECTROCLINICAL PATTERNS IN CORTICAL DYSPLASIA: STUDY OF SIX CASES WITH SCHIZENCEPHALY

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Purpose: Define a characteristic interictal electroclinical pattern in electroencephalography (EEG) in patients with schizencephaly.

Method: Realize an EEG of an hour of length to six patients with the diagnostic of schizencephaly confirmed by neuroimages in control at the Hospital of Antofagasta, Chile.

Results: The average age of the patients was 10 years, 8 months (between 3 years, 8 months and 18 years, 7 months). Five patients presented unilateral schizencephaly (three left side of closed-lip, one right side of closed-lip, one right side of open-lip), one patient with bilateral schizencephaly (of closed-lip). One patient with unilateral schizencephaly presents alterations associated (bilateral polymicrogyria). All presented motor impairment, three patients presented cognitive impairment. All developed epileptic seizures. The average age of the seizures beginning was 7 years, 1 months (between 1 year, 1 month (patient with bilateral schizencephaly) and 18 years, 7 months). The EEG was abnormal in all cases. The most frequent alterations were focal interictal epileptiform activity (6/6), focal decrease of the voltage (2/6), fast rhythms (2/6) and absence of physiological elements of the sleep (2/6). Fast rhythms and absence of physiological elements of sleep was present in the cases with bilateral impairment (bilateral polymicrogyria and bilateral schizencephaly).

Conclusion: It exists an interictal electroclinical pattern in schizencephaly characterized by the presence of focal alterations (interictal epileptiform activity and decrease of the voltage) related to the place of the cleft, and the presence of fast rhythms and absence of physiological elements of sleep in the cases of bilateral impairment.

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INTERNALIZING DISORDERS AND PSYCHOSOCIAL FUNCTIONING IN THE CONTEXT OF SUCCESSFUL EPILEPSY SURGERY IN CHILDREN: IMPLICATIONS FOR A COMPREHENSIVE APPROACH AND A GLOBAL PERSPECTIVE OF TREATMENT

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Purpose: There is growing evidence that successful epilepsy surgery improves behavioral comordities and quality of life in children. Our aim was to conduct a literature search to identify: pre and postoperative prevalence of emotional disorders, predictors of psychosocial outcome.

Method: From the 107 articles meeting the inclusion criteria: pediatric epilepsy, psychopathology, psychosocial outcome, and reviewed in full text, we included studies that:

1. Provided with pre and postsurgery data on quality of life dimensions and on internalizing disorders,
2. Used a systematic method for psychosocial assessment,
3. Used DSM or ICD criteria for diagnosis.

Ten articles met the eligibility criteria.

Results: Prevalence of emotional disorders in the context of resective epilepsy surgery ranged from 8% to 44% and, despite successful surgery, rates remained elevated over time. De novo postoperative depression rate was 12.5–18%.

Among children who achieved seizure freedom, 71–79% reported a positive psychosocial outcome, while 15–28.5% reported ''no change''.

Beyond seizure outcome, factors of good psychosocial outcome were improvement in self-perceived competencies and in social functioning, implying increase in independence, self-esteem and social acceptance. Factors of absence of benefits in functioning domains were social isolation and epilepsy stigma perception and, in a less degree, academic underachievement.

Conclusion: Despite limitations of studies (comedication and developmental changes not taken into account, two studies with epileptic controls), emotional disorders are overrepresented, though underdiagnosed and undertreated, and persist even in seizure-free children. Educational intervention to reduce epilepsy stigma and support of adjustment to the new seizure-free condition could have an impact on the incidence of de novo depression.

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COGNITIVE OUTCOME OF TEMPORAL LOBE RESECTION IN CHILDHOOD WITH TEMPORAL LOBE EPILEPSY

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Purpose: Surgical intervention for intractable temporal lobe epilepsy (TLE) in pediatric population has become an increasingly available option. Seventy to 80% of pediatric patients who underwent TLE surgery are seizure-free after operation. The outcome of cognitive function is as important as seizure-free rate in TLE surgery. The outcome studies concerning cognitive changes after surgery in children with TLE are rare. Therefore, the aim of this study is to evaluate the surgical and neuropsychological outcomes after surgery in children with TLE.

Methods: We retrospectively reviewed the medical records of 18 patients who underwent TLE surgery from 1997 to 2008 under the age of 18 years. The preoperative and postoperative neuropsychological tests were done in all patients.

Results: The mean age of seizure onset was 98.3 months, and the mean interval from seizure onset to surgery was 62.8 months. The mean age at surgery was 161.1 months. Eight patients underwent left temporal resection. The mean follow-up duration after operation was 40.8 months. Evaluating their surgical outcomes, 16 patients (89%) belonged to Engel class I, and the other two patients belonged to class III and IV respectively. There was no significant difference in verbal IQ, verbal memory, visual memory and frontal function test after the surgery. However, the performance IQ ($p = 0.001$) and full scale IQ ($p = 0.002$) was significantly improved after the surgery.

Conclusion: Most of the children with TLE were seizure-free after surgery without significant deterioration of memory, frontal function and verbal IQ. In addition, there is significant improvement of performance IQ and full scale IQ.

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LONG-TERM EVALUATION OF EFFICACY OF VAGUS NERVE STIMULATION (VNS) AND ON-DEMAND MAGNET USE IN CHILDREN AND ADOLESCENTS WITH EPILEPSY

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Purpose: To evaluate long term efficacy of VNS treatment and on-demand magnet use in children and adolescents under 18 years with drug-resistant epilepsy.

Method: Fifty-seven children and adolescents (32 M, 25 F; 59.6% ≤12 years) were prospectively evaluated. Mean age at implantation: 11.4 ± 3.85 years; mean duration of epilepsy: 9.2 ± 4.14 years. Seizure reduction was evaluated after 6, 12, 24, 36 and 48 months of VNS therapy. Magnet effect was evaluated within the first week after implantation (''early magnet effect'' – EME) and after 6, 12, 24, 36 and 48 months (''stable magnet effect'' – SME).

Results: There was a significant mean seizure reduction of 48.2%, 52.4%, 55.6%, 55.8% and 57.7% at 6, 12, 24, 36 and 48 months. The responders rate at 6 month was 46.4% and at 48 month – 55.4%. At 36 and 48 month 14.3% of patients were seizure-free. EME: cessation of seizures, 16.1%; partial effect, 73.2%; no effect: 10.7%. SME: cessation of seizures, 8.9%, at 6 months and 5.6% at 48 month; partial effect, 69.6%, and 55.6%; no effect, 21.4%, and 38.9%, respectively. A subanalysis of children ≤12 years showed similar results in comparison with the whole group. Intermittent ''hoarseness of voice'', cough'' and local pain and paresthesias'' were present in 24.56%, 17.54% and 15.79% of patients respectively.

Conclusion: VNS is an effective treatment for children and adolescents with drug resistant epilepsy of all ages with stable effect over time. Magnet stimulation was useful (cessation of seizures or partial effect) in approximately 2/3 of the patients.

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TEMPORAL EPILEPSY PRESENTING AS PANIC ATTACKS: A SUCCESSFUL EPILEPSY CASE

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Purpose: Isolated panic attacks are rare manifestations of mesial temporal lobe epilepsy, (reviewed in Sazgor et al, 2003[1]). Ictal panic has been most often associated with right temporal lobe epilepsy, although a smaller subset of patients displays left side epilepsy (Guimond et al, 2008[2]).

Case report: Nuno, age 8 years, male; family history positive for epilepsy. He had a normal development up to age 2 years. At the age of 2 years he began mainly nocturnal, but also some diurnal, paroxystic episodes of panic, motor agitation, with preserved consciousness. With the onset of these paroxystic episodes, behavior began to deteriorate, with hyperactivity and impulsivity. The interictal EEG revealed rare left temporal lobe interictal spikes, and the long-term video-EEG recording showed left anterior temporal rhythmic spike activity at seizure onset. Epilepsy remained highly resistant to several associations of antiepileptic drugs, with up to fifty seizures per day. The MRI showed hippocampus asymmetry, suggesting left hippocampus lesion, concordant with the neurophysiologic studies. He was submitted to left amigdala-hipocampectomy and temporal pole removal in 2008, with rapid control of all seizures. The behavior problems improved partially. He is now seizure-free for 3 years.

Conclusion: Panic is an unusual presentation of epilepsy, and there is often a delay in the diagnosis. Temporal epilepsy should be excluded in children with new-onset panic symptoms, and surgery should be rapidly considered in refractory cases. [1]Epileptic Disord 2003; 5: 93–100; [2]Epileptic Disord 2008; 10 (2): 101–12.

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EPILEPSY AND MALFORMATIONS OF CORTICAL DEVELOPMENT

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Introduction: Malformations of cortical development (MCD) are increasingly recognized as an important cause of epilepsy, motor dysfunction and developmental delay. Up to 25% of children with severe

epilepsy have a cortical malformation. MCD encompass a wide spectrum with underlying genetic etiologies and clinical manifestations.

Purpose: We analyze the clinical and neuroimaging features of 43 patients diagnosed with malformations of cortical development. Patients were evaluated from the clinical, electroencephalographic (EEG) and neuroradiological point of view. Their ages at the time of the first presentation ranged from 4 weeks to 14 years.

Results: Twenty-six patients were diagnosed as lissencephaly, 12 patients as polymicrogyria – schizencephaly complex, heterotopias were seen in three patients and focal cortical dysplasia in two patients. Thirty-four patients (80%) experienced epileptic seizures with onset during first year of life. Eighten patients (53%) had epileptic seizures resistant to conventional treatment. Clinically, 28 patients (65%) had various types of motor deficits, 22 patients (51%) had microcephaly, and nine children (21%) had facial dysmorphism. Mental retardation was observed in 36 cases (83.7%) and was severe in 27 cases.

Conclusions: The MCD lesions may be highly epileptogenic and a frequent cause of intractability. This malformations should be investigated to establish the etiology of early-onset childhood epilepsy and it should be considered in children with developmental delay with or without microcephaly and facial dysmorphism.

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OCCULT CEREBRAL VASCULAR MALFORMATIONS—CAUSES OF EPILEPSY BEFORE AND AFTER SURGERY

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Introduction: In our practice, occult cerebral vascular malformations can be a source of epileptic seizures. There are insufficient published prospective, population-based studies concerning detection of any type of OCVMs: cavernous malformations, venous malformations, capillary telengectasia and arteriovenous malformations (AVM).

Aim of the work: We are trying to assess the necessity of using MRI as a decisive tool in reaching the diagnosis of an OCVM, as underlying background for symptomatic epilepsy.

Methods: Every patient diagnosed with epilepsy underwent brain MRI and if a lesion compatible with an OCVM was described, then angiography, CT or biopsy were further performed.

Results: MRI was performed in 45 cases of newly diagnosed epilepsy. In nine cases we have found lesions concordant with an OCVM. Two of the patients underwent surgery and one of them is seizure-free after 2 years.

The other seven cases had also been evaluated in the Neurosurgery Department, and surgery have been delayed until drug treatment would become inefficient or neurological impairment further appeared. Surgical risks of consecutive neurological impairment and lesion hemorrhage were also considered. All patients were treated with AED before and after surgery and remained on medication although free of seizures for 2 years.

Conclusions: MRI is a sensitive and specific tool for the diagnosis and morphological characterization of the OCVMs. We suggest that MRI should routinely be performed in all patients presenting with epileptic seizures.

p692
ENGEL CLASS OUTCOME IN CHILDREN AFTER IMPLANTATION OF THE VAGUS NERVE STIMULATOR: AN INTERNATIONAL EXPERIENCE

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Purpose: To describe Engel Class outcomes reported by a group of international centers after vagus nerve stimulator (VNS) implantation in children with epilepsy.

Method: Twenty-one member centers were surveyed by the ILAE subcommittee on epilepsy surgery. Outcomes of all patients undergoing initial VNS implantation in 2004 with follow-up of 1 year or more are described by Engel Class.

Results: One hundred ninety-seven patients (mean age 10.1 ± 0.3, range 1.7–18.5 years) were reported from North America (82%), Asia (11%), Europe (6%), and South America (1%). By Engel Class, 10% were free of disabling seizures (Class I), 8% had rare disabling seizures (Class II), 33% had worthwhile improvement (Class III), and 49% did not have worthwhile improvement (Class IV). Small differences were seen among subgroups in terms of percentage achieving at least ''worthwhile outcome'' (Engel Classes I, II, or III): 55% with age <10 years compared to 49% with age <10 years ($p = 0.42$), 53% in nonlesional cases versus 51% versus in lesional cases ($p = 0.77$), and 43% in LGS patients versus 50% in non-LGS patients ($p = 0.43$), none nearing statistical significance. Of 197 patients, 8 (4%) became seizure-free and in 9 (4.5%) seizures worsened.

Conclusion: Ten percent of patients achieved an Engel Class I outcome. In half of VNS-implanted patients the procedure was not felt to have been worthwhile from the perspective of one or more years of follow-up. While there was a range of degrees of improvement, the magnitude of any placebo effect could not be assessed. We were not able to identify patient subgroups with preferentially improved outcomes.

Poster session: Pediatric epileptology XII
Wednesday, 31 August 2011

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NEUROIMAGING FINDINGS AND OUTCOME OF EPILEPSY IN CHILDREN WITH TUBEROUS SCLEROSIS

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Purpose: The incidence and outcome of epilepsy in tuberous sclerosis (TS) patients are not thoroughly investigated previously. The aim of this study is to evaluate the clinical features and prognosis of epileptic seizures in children with TS.

Methods: Thirty-five patients who were diagnosed as TS at the department of pediatrics, CNUH, between January 2000 and December 2010 were reviewed. The charts and neuorimaging studies of 29 patients who had been followed up over at least 2 years were analyzed focusing on the onset of seizure, the efficacy of treatment and EEG findings. Brain imaging studies were reanalyzed on the number and distribution of cortical tubers and subependymal nodules.

Results: Mean follow up periods of 29 patients (16 males, 13 females) was 8.3 (2–14) years. Twenty-six presented with seizure and 15 (57%) was diagnosed as infantile spasm. Nine (34%) of them became seizure-free during the follow-up period. Mean duration before seizure remission was 5.1 years (1 month–11 years) and mean period of seizure-free state was 11.4 years (1 month–12 year 7 months). Mean number of cortical tubers was 2.0 (0–16) and subependymal nodules 6.2 (0–14). Initial EEG showed no epileptiform discharges in 5 (55%) of them. Seizures were uncontrolled in 17 (58%) patients even with multiple drugs and 10 (58%) of them showed initial seizures before 1 year of age. In this group, mean number of cortical tuber was 6.1 (0–20) and subependymal nodule 6 (1–11). Fifteen (88%) of them showed epileptic discharges on their first

EEGs. Three patients did not show any seizure during the periods and all visited hospital because of skin lesions whose mean age at diagnosis was 9.6 years (5–14). Mean number of cortical tuber was 1.3 (0–2) and subependymal nodule was 4.3 (0–9).

Conclusion: Nearly 60% of TS children with epilepsy revealed intractability, and the majority of them showed epileptic discharges in their first EEGs. The number of cortical tubers and subependymal nodules on neuroimaging studies might be correlated with the outcome of epilepsy in TS.

p694
PROFILE OF SEIZURE PRECIPITANTS IN CHILDREN WITH EPILEPSY: EXPERIENCE FROM A DEVELOPING COUNTRY

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Purpose: Literature on seizure precipitants in childhood epilepsy is sparse particularly from the developing world. This study investigated the profile of seizure precipitants in children with epilepsy.

Method: Study participants included 233 children, 6–16 years with active epilepsy attending the Pediatric Neurology Outpatient Clinic. Details regarding precipitants were obtained by interviewing children and parents using a questionnaire which enlisted them. Parents were asked to maintain seizure diaries for a period of 3 months in which precipitants were noted if seizures recurred and thereafter they were analyzed.

Results: The mean age was 8.81 ± 2.72 years and 65.2% were males. The mean age of onset of epilepsy was 5.33 ± 3.27 years and the mean duration was 41.12 ± 34.81 months. Seizure precipitants were noted by 67% and one third of them stated more than one precipitants. Seizure inducing factors were more frequent than triggering factors (75% vs. 25%). The most common inducing factors were sleep, fever/minor illness; stress and triggering factors were television, noncompliance and noise. Among the precipitants 65% were potentially preventable. There were no differences in prevalence of seizure precipitants according to age, sex or type of epilepsy. While younger children commonly reported fever as a common precipitant older girls cited stress. Sleep was frequently mentioned by children with partial seizures. Of those who had seizure recurrence 70% noted precipitants of which 37% were new precipitants.

Conclusion: Significant number of children with epilepsy reported precipitants and majority were potentially preventable. Thus prompt recognition and avoidance of these factors may have practical implication in their management.

p695
NOCTURNAL HYPERMOTOR SEIZURES IN CHILDREN WITH MUCOPOLYSACCHARIDOSIS: IS NOCTURNAL FRONTAL EPILEPSY?

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Purpose: We report three children, two boys and one female, with mucopolysaccharide disorders (two Hunter's syndrome and one Sanfilippo's Syndrome) that went to our observation because of their severe sleep disorder and complex behavior characterized by aggressive and hyperkinetic manifestations. Parents described frequent nocturnal arousal with settling difficulties, night wandering and hypermotor phenomena mimicking frontal seizures. No seizures during the day were reported. The goal of our study was to describe the electrophysiological findings of nocturnal phenomena and their correlation with daily behavior in order to choose the best treatment.

Method: Nocturnal video-EEG monitoring, minimum for two nights, was performed evaluating single phenomena in terms of duration, clinical expression and electrical findings.

Results: All children during sleep showed long sequences of frontal sharp-waves and/or spikes. In addition, in all children were recorded very frequent arousal and/or hypermotor manifestations with fear and chaotic motor movements related to frontal theta rhythmic activity. In two of them the association with CBZ and CLB obtained the best control of hypermotor seizures and their daily behavior.

Conclusion: Children with mucopolysaccharidosis often present behavior and sleep disorders. We think that is mandatory to rule out any epileptic nature of these disorders. In our three cases we recorded arousal but even clear hypermotor seizures that require a specific therapeutic approach. Moreover, polysomnography in larger group of mucopolysaccharidosis could help clinicians to clarify the relation between these seizures and nocturnal frontal epilepy.

p696
CLINICAL FEATURES AND OUTCOME OF EPILEPSY IN PATIENTS WITH HEMIPARETIC CEREBRAL PALSY

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Purpose: The aim of this study was to identify the clinical characteristics, neuroimaging findings and outcome of epilepsy in our patients with hemiplegic cerebral palsy (CP).

Method: Retrospective study included 24 children, adolescents and young adults with hemiparetic CP and epilepsy (14 male, 10 female) aged from 5 to 26 years (mean 13), followed at least 3 yaers. A detailed history and examination, cognitive testing, EEG recordings and brain MRI were performed in all patients.

Results: Tventy-one percent of our patients were born preterm. Mental retardation has been found in 58%. Seizure onset during the first four years of life was noted in 71%. Focal seizures with or without secondary generalization were the most common seizure types (83%). Infantile spasms were observed in one child. Two patients had startle epilepsy. Initial EEG showed generalized epileptiform discharges in three patients, focal/multifocal epileptiform discharges in 10, both focal and generalized activity in seven and nonspecific abnormalities in four patients. Complete seizure control (seizure-free period of at least one year) was achieved in 75%. Carbamazepine has been the most frequently used antiepileptic drug. Valproate or lamotrigine were the most frequent next choice if initial therapy failed. Periventricular leukomalacia (33%), unilateral cortical/subcortical atrophy (29%) and porencephaly (25%) were the most common MRI findings.

Conclusion: Partial seizures with or without secondary generalization were the most common seizure types. Complete seizure control was achieved in the majority of our patients.

p697
PATTERN SENSITIVITY IN PATIENTS AFFECTED BY DRAVET SYNDROME: USE OF BLUE LENS

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Photo- and pattern-sensitivity represent a serious problem for children affected by Dravet syndrome (DS) because of their presence in the daily activity and low control by antiepileptic drugs (AEDs).

We report the data of two children affected by DS with pattern sensitivity.

Case 1: A 33-month-old boy, healthy until 8 months, when the first generalized convulsion occurred, later on followed by several seizure types

including two convulsive status epilepticus, generalized prolonged clonic seizures and focal seizures triggered by fever. At age 11 months, atypical absences with myoclonic jerks appeared during fixation of patterns consisting of white and dark vertical stripes or multiple dark circles. Stiripentol associated with valproate and clonazepam controlled febrile seizures but not the pattern-induced seizures. During pattern fixation, EEG showed diffuse 3 Hz irregular spike-waves associated with atypical absences with or without myoclonic jerks. Pattern sensitivity disappeared when the child wore specific blue sunglasses.

Case 2: A 16-year-old girl presented the first clonic unilateral convulsion at age 8 months, later on followed by other similar seizures triggered by fever and atypical absences with myoclonic jerks. At age 8 years, pattern sensitivity appeared, fixation of vertical stripes triggering myoclonic twitching involving mostly head, eyelids and arms, not improved by AEDs. EEG showed generalized 3 Hz irregular spikes during pattern fixation and photic stimulation, clinically associated with myoclonic jerks, which reduced when the girl wore blue sunglasses.

In conclusion, blue lens can help children affected by DS with pattern-sensitivity, improving their quality of life.

p698
RECURRENCE OF CHILDHOOD ABSENCE EPILEPSY AS PYKNOLEPSY IN ADOLESCENCE

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A developmentally normal adolescent boy with a history of childhood absence epilepsy (CAE) presented with recurrence of pyknolepsy after a 7-year remission. The characteristics of his EEG showed the same 3-Hz generalized spike-wave discharge as his previous EEG in childhood. To our knowledge, this is the first case report describing recurrence of CAE as pyknolepsy in an adolescent.

p699
FOCAL SEIZURE SEMIOLOGY IN THE FIRST THREE YEARS OF LIFE

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Purpose: The aim of this study is to analyze the early (first 10 s) and late seizure semiology of focal epilepsy in the first three years of life.

Method: We reviewed 157 video-EEG seizures from 22 patients aged 1–36 months (mean 12 months). We analyzed the early and late semiology and correlated it with the hypothetic epileptogenic zone (HEZ).

Results: The most frequent manifestations were: behavioral arrest: 42 (27%) seizures, six patients; ocular manifestations: 37 (23%) seizures, 6 p.; and postural change, 39 (24%) seizures, 8 p. The most frequent late manifestation was focal tonic activity, in 31 (20%) seizures, 8 p. Ten patients (45%) had a frontal HEZ (85 seizures, 55%). The most frequent early seizure semiology was behavioral arrest in 35 seizures.(41%) and the most frequent late manifestation were motor automatism, 15 seizures (10%). Six patients (27%) had a temporal HEZ (35 seizures, 22%). The most frequent early semiology was automatism in 17 seizures (48%), p = 0.001; and autonomic manifestations in 16 (45%) seizures, p = 0.001. Sixteen seizures (45%) had secondary generalization, p = 0.0002. Six patients (23%) had an occipital HEZ (37 seizures, 23%). The most frequent early semiology was ocular manifestations, (17 seizures, 45%), p = 0.0002, and focal tonic seizure as a late manifestation in 15 (40%).

Conclusion: Seizure semiology is different during the first three years of life is different from other pediatric cohorts and adults. Frontal epilepsy is predominat in this group.

We observed a statistically significant correlation in seizure semiology of temporal and occipital HEZ.

p700
COMPUTERIZED VIDEO ANALYSIS AND QUANTIFICATION OF LIMB MOVEMENTS IN AUTOMATION OF SEIZURE DETECTION IN CHILDREN

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Purpose: Many efforts have been made to automate seizure recognition. Most have focused on automated analysis and detection of EEG patterns. Systems based on accelerometers or markers have been utilized for physical seizure analysis in adult patients. However, these solutions are unsuitable for a pediatric population. Our objective is to develop a nonintrusive video-based prototype for seizure detection.

Method: Our prototype only requires a patient to wear a pajama with specific colors, without attaching any sensor or marker. Video of patient activities in a clinical epilepsy monitoring unit (EMU) are captured using a camera mounted on the ceiling. Epochs of activities are excerpted and subjected to automated video analysis following simple manual initialization. The position and angle of patient's limbs are automatically extracted and displacement, velocity and frequency of limb movements estimated. Distinct characteristics between seizure and nonseizure activities are quantified.

Results: Fifteen seizures in five subjects were analyzed. Through computerized analysis of the recorded video data, we observe sustained displacement from baseline and presence of strong oscillation during focal motor seizures, which are not present during interictal activity. Statistical analysis shows a significant difference between ictal and interictal activity.

Conclusion: Our video-based prototype is able to automatically delineate limbs, quantify their movements, and extract distinct characteristics between ictal and interictal body movements for seizure detection. This noninvasive modality is more feasible for pediatric patients and promising for home monitoring applications.

p701
PROGNOSTIC VALUE OF COMBINED USE OF ELECTROENCEPHALOGRAM AND NEUROIMAGING IN INFATS WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY

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Purpose: In infats with hypoxic-ischemic encephalopathy (HIE), prediction of the prognosis is based on clinical, neuroimaging and neurophysiological parameters.

Method: Electroencephalogram (EEG), cranial ultrasound, MRI and follow-up findings of 53 infants with HIE were studied to assess their contribution in predicting outcome.

Results: The neurological outcome at the age of seven years was normal in 84% of infants, moderately abnormal (i.e. mild hypotonia, hypertonia and/or asymmetry) in 9% and severely abnormal in 7% (CP). Grade I HIE was present in 70% of infants, grade II in 15%

and grade III in 15%. EEGs recorded during the follow up were normal in 65%, moderately abnormal (intermediate pattern) in 23% and severely abnormal (abnormal background and presence of epileptiform discharge) in 12%. Neuroimaging findings were normal in 70%, moderately abnormal (mild and localized basal ganglia and thalamic and white matter lesions) in 10% and severely abnormal (diffuse and severe basal ganglia and thalamic and white matter lesions with cortical involvement) in 20%. All infants with grade III HIE had severely abnormal neuroimaging findings associated with abnormal EEG background pattern. Diffuse white matter lesions were highly predictive of adverse outcome (6/8 infants). Normal to mildy abnormal neuroimaging findings were associated with variable EEG findings.

Conclusion: Early EEG and neuroimaging findings are highly predictive of outcome in infants with HIE.

p702
THE DIAGNOSTIC VALUE OF SYNCHRONOUS TILT-TABLE TEST AND VIDEO-EEG MONITORING IN SUDDEN LOSS OF CONSCIOUSNESS AND TONUS

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Purpose: Syncope and seizure share similar clinical features which may cause diagnostic challenge especially during childhood and adolescence. The differentiation is essential as they have distinct therapeutic approaches. The study is designed to make an understanding for the diagnostic value of synchronous TILT-Table Test and video-EEG monitorization for cases whose diagnosis couldn't be clarified by standart diagnostic methods. The predictive value of a questionnaire formed to reveal the nature of the event is also evaluated.

Method: Nineteen cases who describe transient loss of tonus and conciousness with normal basal cardiac and neurologic examinations were included. Synchronous TILT-Table Test and video-EEG monitoring was performed. The questionnaire was filled by the witnesses.

Results: Nine of the cases experienced the paroxysmal event during the study. Three of them had pure vasodepressor type syncope while five of the cases had cardio-inhibitory type vasovagal syncope. The one, who was receiving antiepileptic treatment for three years had prolonged cardiac aystole and required cardiac pacing. The ninth case, who had alteration in conciousness and posture without any change either in ECG or EEG was diagnosed as psychogenic nonepileptic seizure. The most complicating finding was the limb jerks which was actually a sign for reflex anoxic seizures but making the physician closer to epileptic seizure activity. The reliability of the questionnaire was found 50%.

Conclusion: Synchronous TILT-Table Test and video-EEG monitoring provide important additional information for the differential diagnosis in patients having sudden loss of consciousness and tonus.

p703
DETECTION SYSTEMS AND ALGORITHMS FOR MOTOR SEIZURES IN PEDIATRIC PATIENTS WITH EPILEPSY

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Purpose: Since a significant number of epileptic seizures contains a motor component, many detection systems are based on movement analysis, using video, Doppler radar, microelectromechanical and/or ECG detection.

Our study focuses on the diagnostic use of three-axial accelerometers (ACM), which measure acceleration in three orthogonal directions.

Method: We obtained 665 nocturnal seizures in 78 datasets of 29 pediatric patients: 254 spasms (17 patients), 10 series of spasms (six patients), 186 myoclonic (18 patients), five series of myoclonic (three patients), 26 clonic (seven patients), 110 tonic (11 patients), three versive (one patient), 12 tonic–clonic (four patients) and 59 hypermotor seizures (seven patients).

Our datasets contain synchronized EEG, upper arms EMG, wrists/ankles ACM, audio, video and ECG data: as such, these can be used for future testing of any detection system based on those features and detection algorithms aiming to identify any of the above seizures.

In view of the possibly serious medical consequences, we focus on development of algorithms for detecting hypermotor and (tonic–) clonic seizures.

Results: For four patients with hypermotor seizures, we obtained 98–100% sensitivity and a Positive Predictive Value (PPV) of 66%. For three patients, performance was lower but for two of them, only limited data (2–3 seizures per patient) were available. The algorithm for detecting (tonic–) clonic seizures is under development.

Conclusion: We obtained promising results for detecting hypermotor seizures, however no parameter setting was found so that sensitivity and PPV were 100% for all patients. Our future work will include optimization of the algorithms for detecting nocturnal hypermotor and (tonic–) clonic seizures in children.

p704
THE USEFULNESS OF EEG IN PATIENT WITH UNPROVOKED SEIZURES

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Purpose: The EEG is known for useful diagnostic tool in patient with unprovoked seizure or seizure like activity. So we studied the usefulness of EEG in patient with new onset seizures.

Method: The study population included 237 (117 males and 120 females) patients who had seizure and were performed EEG before treatments at SanggyePaik Hospital. We evaluated seizure onset age, EEG performed age, the gap between the first or last seizure and EEG date, seizure type, EEG characteristics, MRI abnormality and perinatal history.

Results: Seizure onset age was 91.5 ± 50.3 month (1–203 month) and EEG performed age was 95.5 ± 51.5 month (1–203 month). Abnormal EEG (group A) showed in 88.2% patients (209/237) and normal EEG (group B) in 11.8% (28/237). According to seizure semiology, results were as follows; (1) generalized tonic–clonic seizure was 59.9% (142/237, A:120/142 vs. B: 22/142): (2) partial seizure was 24.1% (57/237, A:5/57 vs. B:52/57): (3) partial seizure with secondary generalization was 9.2% (22/237, A:22/22 vs. B: 0/22): (4) others was 6.8% (16/237, A:15/16 vs. B:1/16). Of all, idiopathic etiology was 49.8% (118/237, A: 114/118 vs. B: 4/118), cryptogenic etiology 40.5% (96/237, A:75/96 vs. B: 21/96), symptomatic etiology 9.7% (23/237, A:20/23 vs. B:3/23). When compared with group A and group B, there was no difference in the gaps between the first or last seizure and EEG date, seizure onset age.

Conclusion: The EEG is useful diagnostic tool in patient with unprovoked seizure and in classifying seizure or epilepsy.

p705
ICTAL APNEA IN INFANCY

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Purpose: To create an awareness of apnea as a manifestation of seizures.

Method: Review of EEG data over four years in a regional pediatric neurology center.

Results: Three patients with video EEG evidence of apnea as a seizure manifestation were identified.

The first patient presented at 4 months of age with seizures. EEG showed hypsarrythmia and he was treated with ACTH for infantile spasms. He represented 3 months later with apneic spells. During these he became cyanosed and apneic with markedly reduced oxygen saturations. He required resuscitation with bag and mask on a number of occasions. Ictal EEG was difficult to lateralize with bisynchronous discharges in both temporal regions. His seizures responded to treatment with Gabapentin.

The second patient presented at 4 months of age with cyanotic episodes. During these he became centrally cyanosed, then apneic, with a marked drop in pulse oximetry readings. He was also noted on a number of occsasions, to have subtle seizure activity such as eyelid flickering, slight lip smacking and slight limb jerking. Interictal EEG was normal. Ictal EEG confirmed that the apneic episodes were associated with right temporal lobe activity, confirming focal epilepsy of right temporal lobe origin. Seizures responded to treatment with topiramate.

The third patient presented with multifocal epilepsy at 4 weeks of age. Multiple seizure types were observed. However, some seizures which were captured on telemetry manifested purely as apnea with associated desaturations. These had a focal origin from either left or right frontotemporal regions. He has required multiple admissions to PICU and to date his epilepsy is proving intractable.

Conclusion: This case series highlights the presentation of apnea as a manifestation of seizures. This can be life-threatening and families should be trained in basic life support techniques.

Epilepsy should be considered as a differential diagnosis in any infant presenting with apnea.

We also discuss the mechanism of this presentation in infants.

Poster session: Pediatric epileptology XIII
Wednesday, 31 August 2011

p706
DRAVET SYNDROME IN SWEDEN: A SURVEY OF AN EPILEPTIC SYNDROME

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Purpose: Dravet syndrome (DS) is a severe epileptic encephalopathy with seizure onset in the first year of life. Prolonged hemiclonic or generalized seizures associated with fever are typical and later on atypical absences, myoclonia, learning disability and autism develop. Seventy-five percent of patients have amutation in the *SCN1A* gene, which codes for a neuronal sodium channel. This severe myoclonic epilepsy was first described in 1978, and, since then, more than 500 cases have been described. The purpose of the study was to collect and summarize data regarding all Swedish children diagnosed with DS.

Method: A letter was sent to all neuropediatricians in Sweden, asking if they have patients with the electroclincial profile of DS. If they had such patients, they were asked to complete a questionnaire about family history of febrile seizures and epilepsy, genotype, seizure types, seizure frequency, age at seizure onset, age at diagnosis, level of mental capacity, other features, medications, habilitation and financial support.

Results: Out of 28 patients (aged 2–20) identified 23 had the *SCN1A*-mutation, 25 had mental retardation, 15 had autism, 20 had crutched gait and/or ataxia, 22 had had status epilepticus, 22 had myoclonia, 21 had focal seizures, seven were seizure-free. Median age at seizure onset was 4 m, and at diagnosis 4 year.

Conclusion: Other studies have shown an incidence of DS of around 1/30000, which would approximate the number of cases in Sweden to 53. However, in our study we found only 28 cases of diagnosed DS, indicating that the condition is underdiagnosed in Sweden.

p707
INFANTILE SPASMS (IS) IN PATIENT WITH DOWN SYNDROME (DS): VARIABLE SHORT-TERM RESPONSE TO THE TREATMENT

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Purpose: The purpose of this study was to examine short-term response to treatment of IS in DS.

Method and Results: We examined retrospectively 10 patients with DS and IS. None had pathological perinatal history. Nine had free trisomy 21 and one had chromosomal mosaicism. All the patients lost developmental milestones several days before the first spasm, onset between 2 and 7 months of age and showed symmetrical spasms. The interictal EEG showed typical hypsarrhythmia. The first MRI did not show abnormalities. The treatment was early onset in eight patients. Two patients had the first spasm after a vaccine. One of them received initially VGB and the other one received pyridoxine (B6), though the spasms disappeared with B6 in the first case and with VGB in the second patient. In a third patient the spasms disappeared with ACTH, after receiving B6 and VGB. The spasms were controlled in a fourth patient with VPA after receiving B6-VGB-ACTH. Five patients received sequentially VGB – B6 – ACTH – VPA, three of them responded with TPM, the other one with ZNS and the fifth patient with CLB. The tenth patient didn't respond to drugs.

Conclusion: In our series the response to treatment was variable and very different from what usually is observed in idiopathic IS or other series of patients with DS. When they responded to usual drugs, it was immediate, if not we considered to change quickly the treatment. The behavioral changes and higher prevalence of IS in DS should alert pediatricians to prevent late diagnosis and treatment.

p708
A NOVEL MUTATION IN THE *ATP7A* GENE IN A KOREAN PATIENT WITH MENKES DISEASE

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Menkes disease is an infantile-onset X-linked recessive neurodegenerative disorder caused by diverse mutations in a copper-transport gene, *ATP7A*. Affected patients are characterized by progressive hypotonia, seizures, failure to thrive and death in early childhood. Here, we report a case of Menkes disease presented by intractable seizures and infantile spasms. A 3-month-old male infant had visited our pediatric clinic for lethargy, floppy muscle tone, poor oral intake and partial seizures. His hair was kinky, brown colored and fragile. Partial seizures became more frequent, generalized and intractable to antiepileptic medications. An EEG showed frequent posteriorly dominant generalized spikes that were consistent with a generalized seizure and evolved to hypsarryhthmia on

the following record. Biochemical markers showed low serum copper (9.0 μg/dl, reference range: 70–130 μg/dl) and ceruloplasmin (5.6 mg/dl, reference range: 16–31.5 mg/dl) levels. From a genetic analysis, a c.2743C>T (p.Gln915X) mutation was detected. The mutation was a novel one that has not been previously reported as a cause of Menkes disease.

p709
DOOSE SYNDROME – NATURAL HISTORY OF A GROUP OF PATIENTS

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Purpose: To present a group of patients with Doose syndrome (DS), to document their clinical and neurophysiological characteristics, and long term outcome.

Method: From the neurophysiology database we identified twelve patients fulfilling the modified ILAE criteria for DS. A retrospective analysis of clinical files and EEG recordings was done.

Results: Ten patients were male. Mean follow-up time was 7.62 ± 4.13 years. Mean age at DS onset was 2.97 ± 0.76 years. Ten patients had generalized tonic–clonic seizures and one a focal seizure, previous to DS onset. Mean age at treatment was 2.92 ± 0.73 years. Eleven patients were seizure-free 5.90 ± 4.08 months after treatment onset. At first clinical remission all were treated with valproate + lamotrigine, additionally five with ethosuximide, one with levetiracetam. In five EEG normalized 4.67 ± 4.00 years after clinical remission, the remaining maintaining interictal paroxysmal activity. In three patients with a follow-up greater than 10 years, after an initial EEG normalization/improvement, paroxysmal activity with photosensitivity appeared. Two of these had myoclonic seizures appearance at the same time (8.91 and 9.33 years after the first clinical remission). Five patients have normal cognition, the remaining present slight to severe intellectual disability.

Conclusion: Doose syndrome is considered a severe epileptic encephalopathy, but outcome may range from seizure freedom to intractability. The majority of our patients achieved seizures remission. Nonetheless, in a few patients different types of seizures occurred later with different paroxysmal activity, suggesting an evolution to another epileptic syndrome.

p710
CLINICAL VARIABILITY IN THE EXPRESSION OF *SCN1A* GENE

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Purpose: Generalized epilepsy with febrile seizures plus is considered to be a genetically heterogeneous and mutation-related to sodium channels and GABA syndrome. We discuss whether the observed phenotypic expression is due to mutations in other genes different from those found so far, or to the variable expression of the *SCN1A* gene. We report two patients with mutations of the *SCN1A* gene and different clinical and neurophysiological manifestations.

Method: Patient 1: 4- year-old girl, debuting at 7 months of age with hemigeneralized seizures as recurrent status epilepticus, related to intercurrent febrile and afebrile infectious processes, which are not controlled despite of different therapeutic options used. All intercritical electroencephalogram and neuroimaging studies were normal. Neurocognitive development of the girl is normal. The genetic study has showed a mutation in the *SCN1A gene (C1662 + 1 G>C), not described so far. Patient 2: 3-year-old boy, from 4 months of age has presented several episodes of status epilepticus with generalized tonic–clonic and myoclonic seizures, refractory to antiepileptic drugs, ketogenic diet, immunoglobulins and steroids. The neurophysiological studies showed paroxysmal focal and generalized alterations with spike and polyspike-wave discharges, at baseline and after intermittent light stimulation. Brain imaging studies performed have been normal. The child has a moderate neurocognitive developmental delay. The genetic study showed a mutation in the SCN1A* gene (c.4298delG, p.G1433DfsX4) described in patients with Dravet syndrome.

Conclusion: It is possible that molecular alterations observed in these patients may be an epiphenomenon, but could support the view of the variable phenotypic expression of mutations in *SCN1A* gene.

p711
MALIGNANT MIGRATING PARTIAL SEIZURES IN INFANCY (MMPSI): A FOLLOW-UP STUDY

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Purpose: Epilepsy with malignant migrating partial seizures in infancy (MMPSI) is a rare epileptic syndrome first described in 1995 in 14 patients, characterized by an age of onset of seizures before 6 months, multifocal seizures involving both hemispheres independently brain without an identifiable cause and associated with a poor outcome. The aim of our study was to refine clinical and electroencephalographic phenotyping and consider reflection etiological syndrome.

Method: Eighteen patients were included in this national retrospective multicenter study. MMPSI was recurrent in two sibs with unreleated parents and five children had a family history of epilepsy or seizures. This syndrome has homogeneous electroclinical presentation with three stages: Early onset (first weeks) with partial motor seizures showing an increasing frequency. Around the age of 3 months, seizures become highly pharmacoresistant and present specific aspect on critical EEG with multifocal discharges and migrant seizures from one focus to another and from one hemisphere to another. Concomitantly, all patients presented slowing of psychomotor development. By the end of the second year, epilepsy was less active and mental and motor delay were evident.

Conclusion: MMPSI is a electroclinical syndrome recognized by the classification on the International League Against Epilepsy of unknown etiology. The clinical course is severe and conventional antiepileptic drugs are ineffective. The existence of two familial cases emphasizes the genetic origin of this syndrome. Further genetic studies are needed to confirm this hypothesis.

p712
LENNOX-GASTAUT SYNDROME, A VARIANT IN CLINICAL AND ELECTROGRAPHICAL FEATURES AMONG SAUDI POPULATION

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Purpose: To evaluate basic clinical data, EEG features of 15 patients at centre for the patients with Lennox-Gastaut syndrome.

Method: Retrospective study was done among 15 patients at King Fahad Medical city in Riyadh, A referal hospital for neuroscience. Looking at their clinical presentation, EEG features, respond to various treatment & prognosis.

Results: Eighty-six percent were typical presentation of the disease. Fifty-two percent had a bad prognostic EEG, yet the done very well clinically their respons to treatment was variable to diffrent antiepileptic treatment (see the result section).

Conclusion: Our local population are similar in the basic clinical features to other studies, but the EEG features were not consisting with the prognosis or the response to treatment.

p713
BENIGN FAMILIAR NEONATAL SEIZURES: A THREE GENERATIONS FAMILY

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The Benign Familiar Neonatal Seizures (BFNS) is a rare epileptic syndrome presenting in the neonatal period by partial or generalized seizures (often tonic). Seizures start in the first days of life and disappear spontaneously. The pathogenesis is based on mutation of the KCNQ1-KCNQ5 subunits with autosomal dominant inheritance. The treatment with AEDs is not necessary in mild forms, in severe cases the phenobarbital or valproate (phenytion) is recommended, with planned withdrawal after 3–6 months.

We diagnosed two siblings (boys), whose mother and grandmother had suffered neonatal seizures temporarily treated by AEDs, with complete remission in infancy. Both the siblings suffered by numerous tonic seizures with marked apnea started in the 3rd resp 5th day of life. The secundarity (like MRI lesions of the brain, metabolic disturbances) was excluded. The course of the seizures was the reason for setting them into AEDs. The phenobarbital was not effective in either of the cases. The breakthrough was phenytoin in the older brother and valproate in the younger one. They are seizure-free, now. The treatment was finished at the age of 1 year in the older and still continues in the younger one.

Conclusion: The BFNC should be considered in cases of neonatal seizures with the aim of a proper setting of the intensity of antiepileptic therapy. We observed a family with five cases of BFNC in three generations with relatively severe, but time limited tonic and apneic neonatal seizures. There are about 350 cases reported in the medical literature (Plouin P. et al. In: Roger J. et al, Epileptic Syndromes in Infancy, Childhood and Adolescence. John Libbey Eurotext, 2005;3–15).

p714
OPTIMIZED INDIVIDUAL AED PROTOCOLS IN PATIENTS WITH DRAVET SYNDROME USING ELECTRONIC DOCUMENTATION WITH EPIVISTA®

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Purpose: Can we improve seizure control in patients with Dravet syndrome using electronic documentation and include the orphan drug Stiripentol (STI) to optimize the individual treatment protocols in patients with Dravet syndrome?

Method: Twelve patients with the Dravet syndrome aged 3–25 (median 14.5) years have been continuously seen in our epilepsy centre since 7–2008. A pathogenic SCN1A mutation had been found in 10 of these patients. Electronic treatment documentation with EpiVista® was used in all patients to optimize the individual AED combinations.

Results: Our patients received 2–4 AEDs in combination. The following drugs (median dose in mg/kg) were used after AED optimization: VPA (n = 12; 22.5 mg/kg), TPM (n = 10; 2 mg/kg), STI (n = 7; 25 mg/kg) and CLB (n = 6; 0.15 mg/kg), FBM (n = 1; 38 mg/kg). Two patients became free of seizures (>6 months) and another seven patients had seizure reduction >90% compared to baseline. Three patients remained unchanged.

Conclusion: Seizure control was markedly improved in 9/12 patients with Dravet-syndrome using STI in the combination with VPA and CLB, when using electronic treatment documentation to optimize AED treatment. 2/12 patients with Dravet syndrome became free of seizures.

p715
PERIORAL MYOCLONIA WITH ABSENCE STATUS: A RARE SYNDROME

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Purpose: Perioral myoclonia with absences is rare syndrome of Idiopathic Generalized epilepsy defined by typical absence seizures and localized rhythmic myoclonus of perioral facial muscles. Age of onset ranges 2–13 years (median 10 years), with normal intelligence. Absence status epilepticus is very common (57%) and frequently ends with generalized seizure. Generalized tonic–clonic seizures (GTCS) occur in all but usually infrequent. We describe a child with perioral myoclonia and absence status, partially refractory to treatment, misdiagnosed as epilepsia partialis continua.

Method and results: 7-year-old boy, with normal birth and developmental history was admitted with history of two episodes of GTCS following short febrile episode. Few days later he developed involuntary, rhythmic, bilateral twitching of the lips and lower face, occurring continuously and he also became inattentive and hyperactive. There was no history of abnormal movements elsewhere, no motor, sensory or cranial nerve deficits. Neurological examination was normal except perioral, continuous, arrhythmic, myoclonic movements. MRI Brain with contrast, CSF studies were normal. EEG revealed continuous generalized 3 Hz spike and wave discharges, rhythmic, variable amplitude, with occasional polyspikes. He was started on valproate but developed drug rash, zonisamide was added instead and facial movements subsided over the next few weeks. Serial EEGs done over next 8 -9 months revealed normalization of background with 3hz spike and wave pattern persisting, of shorter duration, occurring every 10–12 s. His behavior improved, with no recurrence of GTCS and is in follow up.

Conclusion: This rare seizure type is usually underdiagnosed and can be misdiagnosed as focal epilepsy, so needs accurate recognition.

p716
MALIGNANT MIGRATING PARTIAL SEIZURES IN INFANCY OR COPPOLA–DULAC SYNDROME

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Purpose: Malignant migrating partial seizures in infancy (MMPSI) are rare epilepsy syndrome with debut at the first 6 months of life and characterized by multiple continuous electroencephalographic and electroclinical focal ictal patterns involved different independent areas of both hemispheres with severe arrest of psychomotor development. Publication of the first case was done by G. Coppola et al. (1995) and the most cases (n = 20) were observed and described by O. Dulac (2005).

Method: At the period of 2006–2011 in Child Neurology Department of Russian Children Clinical Hospital were newly revealed and investigated 19 infants (10 boys, nine girls) with MMPSI. For all the children were provided dynamic video-EEG monitoring, MRI and genetic tests.

Results: Among population of infants with MMPSI (n = 19) were revealed and distinguish the four subtypes of this syndrome: (1) ''classic'' form with pharmacoresistant migrated status epilepticus (SE) of migrating multifocal seizures, and with absolutely poor prognosis (n = 7); (2) Severe pharmacoresistant mixed form (MMPSI + EME) with combination of electroclinical characteristics of MMPSI with migrating multifocal SE and also of early myoclonic encephalopathy (EME) with chaotic ''erratic'' myoclonus and ''suppression-burst'' pattern with diffuse polyspike-waves on the EEG (n = 5); (3) ''mild'' variant with evolution from monofocal epilepsy into multifocal with MISF pattern on EEG (PE-MISF syndrome) and then to MMPSI with SE episodes. Due to combined AEDs therapy seizures could decreased, and this variant had better prognosis for life and psychomotor development (n = 5); (4) ''subtle'' form with only poor visually identified minimal motor and inhibitory seizures, subclinical migrating

multifocal SE pattern on EEG, multiple partial awakenings during sleep due to ictal patterns, severe delay of psychomotor development (n = 2).

Conclusion: Malignant migrating partial seizures in infancy is new form of epileptic encephalopathy and a special form of status epileptic in infancy. Is proposed the definition of this syndrome as: ''malignant epilepsy of infancy with migrating multifocal seizures'' or ''Coppola–Dulac syndrome''. This type of epileptic encephalopathy could be divided on subtypes with specifications in clinical course, EEG-features and prognosis.

p717
SEVERE MYOCLONIC EPILEPSY IN INFANCY: FIRST FUNCTIONAL MRI RESULTS

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Purpose: The aim of this study was to describe neuronal networks in patients suffering from Severe Myoclonic Epilepsy in Infancy (SMEI, Dravet-syndrome). SMEI is characterized by typical seizures which occur in the first year of life, often triggered by hyperthermia. After the onset of seizures, psychomotor retardation is a common feature of this syndrome.

Method: Eight patients (mean age 13.5 ± 8.6) with diagnosis of SMEI and with a mutation in the SCN1A-gene and eight patients with rolandic epilepsy for the control group (mean age 8.7 ± 2.3) underwent 20 min EEG-fMRI measurement in resting state condition (EEG: 32 electrodes, 10–20 system. Scanner: 3T Philips Achieva, TR = 2250 ms). Interictal epileptiform potentials (IED) were marked visually by two experienced neurophysiologists. fMRI was corrected for movement and smoothed as well as normalized to MNI brain using SPM5 software. For the single subject and the group analysis the IEDs were treated as event of interest for the SMEI-patients. Additionally for both groups the functional connectivity within areas of the default-mode network, thalamus and brainstem was measured.

Results: The group analysis does not reveal a common activation pattern in the SMEI-group. However, in the single subject analysis significant ($p < 0.001$) activations were found in cortical areas in all patients (medial prefrontal cortex, cingulate cortex, occipital cortex, temporal lobe, primary motor cortex, inferior parietal cortex). Subcortical activations in the thalami and caudate nucleus were found in three patients. Compared to the control group, the SMEI patients showed stronger functional correlations within areas of the default-mode network.

Conclusion: In the most SMEI patients, the IED related symmetrical activations were found in brain areas which are part of the default-mode network (DMN). The younger the patient, the more often regions of the DMN were involved. It could be hypothesized that the disturbed activation and abnormal connectivity in the DMN may explain cognitive deficits and frequent mental retardation in SMEI patients.

p718
THE LONG-TERM EVOLUTION AND OUTCOME OF LANDAU-KLEFFNER SYNDROME IN CHILDREN IN A TERTIARY REFERRAL EPILEPSY CENTER

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Purpose: To determine the long-term relationship between electroencephalographic characteristics and the characteristics of speech, language, cognitive en motor characteristics in children with Landau-Kleffner syndrome (LKS) referred to a tertiary referral epilepsy center.

Method: We retrospectively looked for eight children with LKS. They underwent regularly long-term EEG/video registration including full night of natural sleep as well as several speech-language examinations (comprehension, production, word finding) and psychological examinations (intelligence, memory, speed, behavior) were performed.

Results: Over years all children had a regression or stagnation in their development of speech and language. The later the onset of the LKS the better the outcome however it was never certain that the premorbid level was regained. The auditory capacities remained limited, except for those with a later onset LKS. It seems that the antiepileptic drugs ethosuximide, sulthiam and corticosteroids were most successful. The cognitive deficits were not as significant as those of speech and language. Nevertheless we regularly saw a pattern of decline and partial recovery of intelligence, memory and speed and also of motor impairment, especially dyspraxia, simultaneously with the evolution of speech and language.

Conclusions: As described in the literature younger children suffering from LKS have a worse outcome than elder children. Despite a good response of the EEG on AED therapy the recuperation of speech and language is disappointing: especially the expressive vocabulary improves but comprehension remains a problem.

Poster session: Pediatric epileptology XIV
Wednesday, 31 August 2011

p719
IMPACT OF INFANTILE SPASMS ON COGNITION: A MULTICENTER RANDOMIZED CONTROLLED TRIAL OF FLUNARIZINE AS ADD-ON THERAPY

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Purpose: Although diagnosis and treatment of infantile spasms (IS) have improved, only 10% of patients achieve normal cognitive development. We studied cognitive outcome in a multicenter, randomized, placebo-controlled trial using flunarizine as neuroprotective add-on therapy. Vigabatrin was the first line anticonvulsant, ACTH the second and topiramate the third when both failed. We also evaluated the impact of cryptogenic versus symptomatic etiology, treatment lag and response to vigabatrin or ACTH on outcome.

Methods: Patients presenting with IS and hypsarrhytmia were randomized to receive flunarizine 10 mg/day or placebo for 6 months. Vineland interviews with parents and objective cognitive assessment using the Bayley Scales of Infant Development were conducted at diagnosis and 24-months follow-up.

Results: Of 101 children diagnosed, 69 were enrolled. Neuropsychological testing and Vineland interviews were available at baseline and 24-months for 45 children. Regression was observed after 2 weeks of spasms in all but three. At 24 months, 10 children had a mental DQ above 80 (22%) and an additional six (13%) obtained scores between 70 and 80. Children with cryptogenic spasms showed greatest improvement ($p = 0.008$). Although no significant differences between flunarizine and placebo treatment were observed in the global cohort, the flunarizine-treated subgroup scored higher on the Vineland ($p = 0.03$) than the placebo-treated subgroup and tended to perform better on the Bayley ($p = 0.07$).

Conclusion: IS lead to a loss of developmental skills after 2 weeks. Etiology is the major determinant of cognitive outcome, favoring crypto-

genic patients. Flunarizine has the potential to further improve cognitive outcome in cryptogenic IS.

p720
LEVETIRACETAM MONOTHERAPY IN CHILDREN AND ADOLESCENCE WITH EPILEPSY IN KOREA

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Purpose: Levetiracetam had been used in adjuvant Therapy. Levetiracetam is also used in monotherapy in other countries, so we also studied the effect and efficacy of Levetiracetam monotherapy in Korea.

Method: We retrospectively studied the types of epilepsy, EEG, doses of drug. We studied 101 epilepsy children treated by Levitiracetam monotherapy who visited our hospital since August 2007 to July 2009.

Results: The Age is from 1 month to 20 years. The mean age of taking Levetiacetam initially is 11 ± 4 years (from 3 years to 21 years). The types of epilepsy showed partial seizures in 57.4% and generalized 42.6%. The mean dose started initially is 6 ± 4 mg/kg/day (from 2 to 30 mg/kg/day). The mean final dose is 30 ± 8 mg/kg/day (from 6 to 60 mg/kg/day). The mean duration of therapy is 21 ± 11 months, and the duration of therapy ranged from 1 to 38 months. 85.1% of patients became seizure-free, 88.1% decreased at least 50% seizure reduction during 12 months. The side effects showed behavioral change (8), asthenia (2), cognitive change (1), rash (2), headache (5), inadequate seizure control (2), and increased seizure (5). Levetiracetam was discontinued because of inadequate seizure control (2), increased seizure (5) and side effects (2).

Conclusion: We studied efficacy and tolerability of monotherapy of Levetiracetam. Levetiracetam is effective and tolerable in the monotherapy of epilepsy in Children and adolescence in Korea.

p721
DISSOCIATIVE DISORDER SECONDARY TO ABSENCE SEIZURES IN A CHILD RESOLVED THROUGH ASSOCIATION WITH VALPROIC ACID AND ETHOSUXIMIDE

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Purpose: Series from patients referred to neurology clinics have found that 5% to 20% of patients referred for epilepsy have psychogenic nonepileptic seizures (PNES). The interval from first event to PNES diagnosis averages more than 8 years. We present a case report of a child with absence epilepsy not controlled by medication who has, at a distance of approximately 1 year after the onset of epilepsy, prolonged dissociative episodes secondary to the absence seizures.

Method: A 7-years-old girl with classical absence epilepsy, not responding to valproic acid (VPA) presents a lot of seizures during a day, frequent interictal paroxysmal EEG abnormalities, especially during the sleep, and 2 months before admission there was the appearance of prolonged dissociative state secondary to seizures. During video-EEG-monitoring we detected no paroxysmal activity correlate to dissociative episodes. Psychological and cognitive assessments detect a behavioral emotional functioning characterized by communication, social and daily skills in line with expectations than chronological age. We added the ethosuximide to VPA.

Results: We observed soon a reduction in intensity and duration of dissociative episodes and absence seizures, until clearance and marked EEG improvement with the achievement of the therapeutic dose of the drug.

Conclusion: Uncontrolled absence seizures and frequent interictal paroxysmal EEG abnormalities induce a dissociative disorder similar to PNES in a child whom disappear after control of seizures with AED. Adequate recognition and treatment of this condition will prevent possible structure of persistent mood or personality disorders, or other type of psychopathology, in patients with benign epilepsy.

p722
SINGLE ORAL DOSE OF LEVETIRACETAM AS A FAST, EFFECTIVE AND SAFE TREATMENT FOR PHOTOSENSITIVE EPILEPSY IN CHILDREN

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Purpose: To evaluate effectiveness, safety and practical use of single oral dose of levetiracetam as a first, rapid, and safe option in the treatment of photoparoxistic epilepsies in children during their diagnostic EEG.

Method: We recluted 15 children, between 5 and 17 years old, six boys and nine girls, at the moment of the procedure in their diagnostic study EEG, during June 2010 until February 2011, that showed evident abnormal photoparoxysmal EEG response at Intermittent Photic Stimulation (IPS). During the same procedure, they were loaded with single dose of levetiracetam (30 mg/kg/PO). The IPS response was evaluated after the loading, every 15 min during 1 h. Thirty minutes.

Results: Eleven children (73%) showed total normalization of the EEG during IPS, 3 (20%) improved partially and 1 (7%) showed no changes. The total normalization was progressive, presenting complete response from 45 to 60 min after loading in 10 of them, and only one showed total response after 75 min. Transitory somnolence was the only side effect. All children with 100% positive response went out of the laboratory under levetiracetam treatment and have stayed asymptomatic in their evolution (4–9 months).

Conclusion: Single oral loading doses with levetiracetam during the EEG procedure is an excellent possibility of evaluating and initiating immediately, safely and effectively treatment during the first EEG study in photosensitive epilepsies in children, making a fast and positive therapeutic solution to their epilepsy, decreasing the parents anxiety and giving them a great satisfaction.

p723
THE ELECTROCLINICAL FEATURES AND TREATMENT OF MYOCLONIC-ATONIC EPILEPSY

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Purpose: To analyze the electroclinical features and treatment of myoclonic-atonic epilepsy (MAE).

Method: Video electroencephalography (EEG) monitoring was performed in all patients, and some of them were examined simultaneously with electromyography (EMG). The seizure semiology, electrophysiology features were analyzed. The treatment and its effects were followed up in all patients.

Results: In 47 MAE children, 25 of them had a history of febrile seizures (FS), 20 patients had a family history of FS or epilepsy. All patients had a normal development before the illness. The age of seizure onset was between 1 year and 5 months to 5 years and 3 months. The first afebrile seizure was generalized tonic–clonic seizure (GTCS) in 41 cases (87.2%). All patients had multiple seizure types, including GTCS (97.9%), myoclonic-atonic seizures (72.3%), myoclonic seizures (100%), atonic seizures (68.1%), atypical absences (76.6%) and tonic seizures (6.4%). All patients had a history of ''drop attack''. EEG backgrounds were slow or showed parietal θ rhythm during the frequent

seizure period. Interictal EEG showed 1–4 Hz generalized spike wave, or polyspike wave discharges in all patients. Seizures were controlled by antiepileptic drugs (AEDs) in 41 patients (87.2%). Valproate was used in 37 cases. Lamotrigine was used in 26 cases. Seizures were controlled in two patients by ACTH. Mental retardation was observed in 10 patients (21.3%) after the illness.

Conclusion: The clinical features of MAE include normal development before the illness, the onset seizure type is often GTCS, all patients have multiple generalized seizure types. EEG showed generalized discharges, the backgrounds were slow or showed parietal θ rhythm during the frequent seizure period. Early diagnosis and rational choice of AEDs are benefit to obtain a better prognosis.

p724

EPILEPTIC ENCEPHALOPATHY WITHOUT SUPPRESSION BURST WITH A DELETION OF MUNC18 GENE: A LONG TERM RESPONSE OF INFANTILE SPASMS TO ZONISAMIDE

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Purpose: MUNC 18 is a new gene identified in patients with epileptic encephalopathy (EE) with suppression bursts (SB). The relation of EE with Suppression bursts and infantile spasms (IS) is well reported. We question this relation and the role of MUNC18 in infantile spasms without preceding EE with suppression bursts.

Method: We report the history, clinical and EEG presentation and follow up of a patient girl who presented a deletion in 9q33.3–9q34.1 region including the encoding gene for Munc 18.

Results: The patient was born prematurely at 27 weeks. She was admitted to neonatal intensive care unit for 2 weeks for assisted ventilation than to neonatal board for one additional month without episodes of acute distress. She had psychomotor delay with dysmorphic features since the first examination. She had normal EEGs and brain ultrasounds controlled till the age of 2 months. She presented epileptic spasms at 4 months of chronological age. The EEG showed atypical hypsarythmia without suppression burst. She was treated with vigabatrin, corticosteroids, topiramate, levetiracetam, ketogenic diet without efficacy. MRI showed a thin corpus callosum with cortical atrophy. She is spasms free with zonisamide with a follow up of 9 months.

Conclusion: This report emphasizes the possible role of Munc 18 in IS without preceding SB. To our knowledge, it is the first case with a deletion in Munc 18 gene associated with epileptic encephalopathy without suppression burst.

p725

ELETTROCLINICAL PATTERN IN CHILDREN AFFECTED BY CARDIOFACIOCUTANEOS SYNDROME WITH GERMLINE MUTATION IN BRAF

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Purpose: Literature data shows that 50% of patients affected by cardiofaciocutaneous syndrome (CFCS) and mutation in BRAF present not otherwise characterized seizures. The aim of our study is to describe the electroclinical features of 10 patients affected by CFCS with BRAF mutation.

Method: Ten patients were included (eight females and two males, mean age 8 years). We performed clinical examination, neurocognitive assessment, seizure semiology analysis, awake and sleep video-EEG, ictal video-EEG (three patients), neuroimaging.

Results: Our patients had a typical phenotype with congenital heart defects, particular facial appearance, failure-to-thrive and cutaneous abnormalities.

As for the neurological profile, they had moderate to severe mental retardation; brain MRI showed small posterior fossa (two patients), severe cortical atrophy (four patients), temporal poles hypoplasia (one patient); hippocampal sclerosis (one patient). Among the 10 children only five presented epileptic seizures. Two of them had occasional apparently generalized seizures and three had a drug-resistant epilepsy. Early seizure onset was observed in all of them, with partial seizures in two, and infantile spasms in one. After three years, seizures reappeared with febrile or afebrile tonic–clonic status epileptic, myoclonic jerks, asymmetrical spasms. The EEG pattern is characterized by multifocal abnormalities prominent in the parietotemporal regions. Despite many polytherapy, seizure control was not obtained and two of them had developmental regression.

Conclusion: Despite in literature data seizures were reported in 50% of CFC with BRAF mutation, electroclinical pattern was not well characterized.

We observed similar pattern in three patients with multidrug resistant epilepsy. The possible correlation between genotype and electroclinical phenotype will be discuss.

p726

TREATMENT AND PROGNOSIS OF THE MOST SEVERE EARLY INFANTILE EPILEPTIC ENCEPHALOPATHIES: CAN THE PATIENTS BE PREVENTED FROM BEING BEDRIDDEN?

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Purpose: Ohtahara syndrome (OS), early myoclonic encephalopathy (EME) and migrating partial seizures in infancy (MPSI) are the most severe early infantile epileptic encephalopathies (SEIEE). Seizures (Sz) are intractable and daily, and the patients inevitably become bedridden and speak no words. Treatment for SEIEE and whether these severe conditions could be prevented were studied.

Method: Twenty-eight cases of OS including 15 with hemimegalencephaly (HMG), one with lissencepahly, and 12 without cortical dysplasia, nine cases of EME including 1 with multilobar dysplasia, and 9 cases of MPSI were followed-up for 1 and 26 years and finally evaluated at 1.3 and 26 years. Sz freedom (SF) at the last evaluation (SF-le), epochs with ≥1 year SF during the follow-up period (SF-epoch), motor development (M5: run, M4: walk unaidedly, M3: walk with support, M2: sit, M1: bedridden), and intellectual development (I4: make conversation, I3: speak phrases, I2: speak words, I1: speak no words) were evaluated.

Results: Forteen cases with HMG underwent hemispherotomy and two cases without cortical dysplasia had callosotomy in early infancy, and 10 cases with hemispherotomy and one case with callosotomy, along with high-dose phenobarbital (H-PB) ± KBr ± other antiepileptic drugs (AEDs), resulted in SF-le, 13 cases had SF-epoch, nine cases had M5-M2, and 8 cases had I4-I2. Among 12 nonsurgical cases of OS, 9

showed SF-le on H-PB and/or ZNS ± KBr ± other AEDs, nine cases had SF-epoch, four cases had M3-M2, and two cases had I3-I2. In EME, one case with multilobar transection and one case on H-PB and KBr obtained SF-le, three cases had SF-epoch, and only one case with multilobar transection obtained M2 and I2. In MPSI, three cases achieved SF-le, seven cases had SF-epoch, two cases had M4-M2, and one case on H-PB + KBr ± other AEDs achieved I3.

Conclusion: Early surgery and H-PB + KBr ± other AEDs were effective for SEIEE and prevented 37% of the patients with SEIEE to be the severest condition.

p727

TREATMENT OF CHILDREN WITH RESISTANT EPILEPSY

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p728

ANTIEPILEPTIC TREATMENT OF SYMPTOMATIC FOCAL FORMS OF EPILEPSY IN CHILDREN WITH SCHIZENCEPHALY

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p729

ANTICONVULSIVE TREATMENT PECULARITIES IN PATIENTS WITH ANGELMAN'S SYNDROME

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p730

IN UTERO KNOCKDOWN OF THE EPILEPSY/SPEECH RELATED PROTEIN SRPX2 CAUSES ALTERED DEVELOPMENT OF THE RAT BRAIN CORTEX

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Early developmental alterations of the human brain cortex are increasingly recognized as a major determinant of common pathologies such as autism, dyslexia, epilepsy, or language disorders. Mutations in sushi-repeat containing protein SRPX2 cause disorders of the eloquent cortex that manifest as rolandic seizures with verbal dyspraxia (p.N327S) or with perisylvian polymicrogyria (p.Y72S). (Roll et al. 2006). Together with its cell surface receptor uPAR (plasminogen activator receptor) and with its transcriptional regulator FOXP2 (forkhead-box transcription factor), SRPX2 forms a molecular network variably implicated in the aforementioned disorders (Royer-Zemmour et al., 2008; Roll et al. 2010). In the present study the possible role of SRPX2 in the development of the brain cortex was questioned. In utero RNA silencing of Srpx2 led to cell-autonomous delayed radial neuronal migration that was rescued by concomitant expression of wild-type rat and human SRPX2 proteins. In contrast, the two mutant SRPX2 proteins failed to rescue the migratory phenotype and evidence for loss-of-function and for dominant-negative mechanisms, respectively, was obtained. A defect in neuronal migration was also shown by time-lapse ex vivo analyzes (videomicroscopy). Post-natal analyzes are currently being done to study the long-term epileptogenic consequences. How SRPX2 is involved in cell migration is also being investigated at the molecular level. Altogether, our data demonstrate a role for Srpx2 in the development of the brain cortex and support a developmental basis for the various SRPX2-related epileptic disorders of the speech cortex in human.

p731

DIFFERENT PATHOPHYSIOLOGY OF FOCAL CORTICAL DYSPLASIA IIA AND IIB: SPECIFIC NEOCORTICAL-LAYER MARKER EXPRESSION

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Purpose: Transmantle dysplasia (TD) is a rare focal cortical dysplasia (FCD), a regional neuronal migration disorder. The pathological feature of TD is the same as that of FCD IIA and IIB.

Method: To investigate the primary pathomechanism of FCD, we studied expression patterns of layer-specific markers, TBR1, CTIP2, SATB2, FOXP1, FOXP2 and CUTL1, in 5 FCD IIA and 3 FCD IIB surgical specimens. In addition, we performed double-staining with Nestin, PROX1, MAP2/2B, GFAP, Iba-1 and CD68.

Results: Layer-specific marker cells continuously distributed from deep white matter to cortical surface. Some specific markers showed unique expression patterns and could be classified into FCD IIA and IIB. TBR1+, SATB2+ and FOXP1+ cells were diffusely observed in the cortex and/or white matter. TBR1+ and FOXP1+ cells of FCD IIB distributed significantly in the cortical molecular, and upper layers and deep white matter, compared with FCD IIA. It is suggested that the malformation and pathological onset of FCD IIB are more severe and earlier than those of FCD IIA, and that FCD IIB shows a definite premature formation of these connections. All layer-specific marker cells had MAP2/2B, but no microglia markers, Iba-1 and CD68. FOXP1+, FOXP2+ and CUTL1+ cells contained within a premature neuron marker, Nestin/PROX1. However, TBR1+, CTIP2+ and SATB2+ cells had only a mature neuron marker, MAP2/2B. It is suggested that putative upper-layer marker cells can maintain neuronal prematurity.

Conclusion: Abnormal expression of various layer-specific markers in FCD II is evidence of premature neuronal differentiation and cortical malformation.

p732
CYTOARCHITECTURAL ABNORMALITIES OF THE DENTATE GYRUS IN REFRACTORY MEDIAL TEMPORAL LOBE EPILEPSY

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Purpose: To describe specific dentate gyrus alterations in patients with mesial temporal lobe epilepsy subjected to surgery.

Method: Twenty sclerotic hippocampi obtained during epilepsy surgery were carefully oriented, trimmed and sectioned. Sixty-micron coronal slices through the entire extension of the hippocampus were stained with Nissl. Semiquantitative assessment was made focusing on dentate gyrus abnormalities, particularly cytoarchitectural disorganization (dispersion and bilamination). Granular cell dispersion (GCD) was graded from zero (no abnormality) to 3 (very intense abnormality). Bilamination of granular cell layer was described as present or absent. The estimate of cell density for neurons and glial cells was obtained in granular cell layer and the hilus of the dentate gyrus using the software Stereo Investigator (MBF Bioscience, USA).

Results: GCD was characterized by a thicker cell layer with a lower cell density, when compared to normal areas. Sixty percent of cases showed GCD, in which 30% was severe. GCB was characterized by a focal or complete duplication of the granular cell layer in which an additional band of granular cells can be observed above the ordinary granular layer, with a thin strip of white matter in between. GCB was observed in 15% of cases. Dentate gyrus abnormalities were absent in 20% of cases. Estimated neuronal cell density was 589.02 ± 310.03 cells/mm^3 in the granular cell layer and 65.13 ± 24.75 cells/mm^3 in the hilus. Estimated glial cell density was 842.50 ± 260.48 cells/mm^3 in the granular cell layer and 1003.25 ± 340.86 cells/mm^3 in the hilus.

Conclusion: Cytoarchitectural abnormalities of the dentate gyrus have distinctive characteristics in sclerotic hippocampi from patients with temporal lobe epilepsy.

p733
MORPHOMETRIC PARAMETERS AND CLINICAL DATA IN TEMPORAL LOBE EPILEPSY ASSOCIATED WITH HIPPOCAMPAL SCLEROSIS: A COMPARATIVE STUDY

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Purpose: This study aimed to compare morphometric parameters and clinical data in patients with temporal lobe epilepsy associated with hippocampal sclerosis.

Method: Ten human hippocampi from surgical resection were entirely histologically processed for Nissl staining. One out of five sections of each hippocampus was scanned and morphometric evaluation was performed using ImageJ software (NIH, Bethesda, MD, U.S.A.). Thickness of the granular cell layer of the dentate gyrus was evaluated with linear measurements (maximum, minimum and mean values). Volume estimates were obtained using the Cavalieri method. Pearson's correlation test and two-tailed unpaired *t*-test were performed to compare clinical data (age at epilepsy onset, epilepsy duration and occurrence of initial febrile precipitant insult) to morphometric parameters using GraphPad InStat (GraphPad Software, San Diego CA, U.S.A.).

Results: Linear (maximum, minimum and mean values) and volumetric measurements of the granular cell layer showed no association with the patient's age at epilepsy onset ($p = 0.49$, $p = 0.62$, $p = 0.48$, $p = 0.58$ respectively), epilepsy duration ($p = 0.65$, $p = 0.3$, $p = 0.36$, $p = 0.99$ respectively) as well as when patients with or without initial febrile precipitant insult were compared ($p = 0.63$; $p = 1.0$, $p = 0.68$, $p = 0.65$ respectively).

Conclusion: There was no significant relation between clinical data and morphometric parameters analyzed.

p734
NEUROPATHOLOGIC STUDY OF RESECTED BRAIN TISSUE FROM PATIENTS WITH INFANTILE SPASMS WHO RECEIVED CORPUS CALLOSOTOMY AND SUBSEQUENT SURGERY

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Purpose: The neuropathology of children with West syndrome (WS) has not been well evaluated except autopsy materials. To investigate neuropathology of the cerebral cortex or subcortical structures in WS, we observed the cortical tissue resected from infants and children underwent callosotomy and subsequent surgery.

Method: Among of 149 children who received a callosotomy for refractoy epilepsy patients with nonfocal onset seizures, resective/disconnective surgery was subsequently performed in 19 patients based on the findings of residual partial seizures and unilateral epileptiform discharges on electroencephalography (EEG) after callosotomy. Seven of 19 children demonstrated epileptic spasm and diagnosed as WS. Four of them showed no lesion on MRI and unilateral frontal interictal epileptiform discharges (IIDs), and received resective surgery of ipsilateral frontal lobe.

Results: We examined the neuropathology of resected frontal lobe in four children. Two of four were 1 year old, and others were 3 years old. All cases except one showed the focal cortical dysplasia (FCD) with abnormal cortical lamination and gliosis. Two of three FCD cases showed dysmorphic neurons without balloon cells (FCD type IIa), and the other showed both dysmorphic neurons and balloon cells (FCD type IIb). The remaining one demonstrated normal cortical lamination and gliosis in white matter.

Conclusion: Three of four children who resected frontal lobe after callosotomy with MRI-negative WS revealed the focal cortical dysplasia (two in type IIa and one in type IIb). These characteristic findings may lead to the pathophysiology of WS.

p735
IS HEMIMEGALENCEPHALY A FETAL TAUOPATHY?

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Background and Purpose: Up-regulation of abnormally phosphorylated tau protein is a feature of many adult neurodegenerative diseases, but is not reported in fetuses or infants. Abnormal tau during development potentially can interfere with growth, differentiation and migration of neuroblasts and glioblasts by microtubular disruption, resulting in dysgenesis and hamartoma. Several reports have identified enhanced mTOR cascade signaling in hemimagalencephaly (HME).

Methods: We examined surgical resections for epilepsy of brains of three infants with HME. One case died postoperatively of complications and autopsy was performed promptly, providing opportunity to examine other brain structures. Multiple immunocytochemical cell markers, mildly phosphorylated tau antibody and α-B-crystallin were examined, as well as ultrastructural examination. The mTOR pathway also was studied.

Results: Overexpression of tau protein was demonstrated in the hippocampus and neocortex. Antibodies against α-synuclein, ubiquitin and TDP45 were nonreactive, but α-B-crystallin was positive. Many dysmorphic cells showed mixed neuronal/glial lineage and expression of nestin and vimentin. Resident stem cells in the dentate gyrus were proliferated. EM exhibited lipidoic degeneration of many hippocampal neurons. The contralateral hemisphere, by contrast, did not show tau overexpression, except in rare, scattered dysmorphic neurons, and none in subcortical structures. Robust immunolabeling for the phosphorylated isoform of S6 protein, a marker of activated mTOR signalling, was identified in the dysmorphic cells.

Conclusions: Abnormal tau expression may be a factor in the pathogenesis of HME by disrupting microtubule assembly through the mTOR pathway during cellular growth and differentiation. It represents a fetal tauopathy.

p736
NEUROFIBRILLARY TANGLE PATHOLOGY AND BRAAK STAGING IN CHRONIC EPILEPSY: A POST-MORTEM STUDY

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Purpose: The long-term pathological effects of chronic epilepsy on normal brain aging are unknown. Previous clinical and epidemiological studies show progressive cognitive decline in subsets of patients and an increased prevalence of Alzheimer's disease (AD) in epilepsy.

Method: In a postmortem series of 138 patients with long-term, mainly drug-resistant epilepsy, we carried out Braak staging for AD neurofibrillary pathology using AT8 immunohistochemistry. The stages were compared to clinicopathological factors, including seizure history, cognitive decline and presence of old traumatic brain injury (TBI).

Results: Overall, 31% of cases were Braak stage 0, 36% stage I/II, 31% stage III/IV and 2% stage V/VI. The mean age at death was 56.5 years and correlated with Braak stage ($p < 0.001$). Analysis of Braak stages within age groups showed a significant increase in mid Braak stages (III/IV), in middle ages (40–65) compared to data from an aging nonepilepsy series ($p < 0.01$). There was no clear relationship between seizure type, frequency, age of onset and duration of epilepsy with Braak stage although higher stages were noted with focal than with generalized epilepsy syndromes ($p < 0.01$). In 30% of patients, there was pathological evidence of traumatic brain injury which was associated with higher Braak stages ($p < 0.001$). Cerebrovascular disease present in 40.3% and cortical malformations in 11.3% were not significantly associated with Braak stage. Astrocytic-AT8 correlated with the presence of both traumatic brain injury ($p < 0.01$) and high Braak stage ($p < 0.001$). Hippocampal sclerosis, identified in 40% (bilateral in 48%), was not associated with higher Braak stages. In over half of patients with cognitive decline, the Braak stage was low indicating causes other than Alzheimer's disease pathology.

Conclusion: There is evidence of accelerated brain aging in severe chronic epilepsy although progression to high Braak stages was infrequent. Traumatic brain injury but not seizures were associated with AT8 accumulation in this series. It is likely that Alzheimer's disease pathology is not the single explanation for cognitive decline associated with epilepsy.

p737
MITOCHONDRIAL ULTRASTRUCTURAL ALTERATIONS OF ENDOTHELIUM IN INFANTILE MITOCHONDRIAL CYTOPATHIES: MUSCLE BIOPSY AND IMPLICATIONS FOR EPILEPSY

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Background and Purpose: Electron microscopy (EM) is the most reliable method of diagnosing mitochondrial disorders in striated muscle biopsies in infancy; histochemistry and biochemistry are not always diagnostic at early ages. Ultrastructural alterations are seen not only in mitochondria of myofibers, but also in capillary endothelium and reflect generalized vascular changes in other tissues including brain.

Methods: Quadriceps femoris muscle biopsies of three infants and two toddlers, ages 23 days to 3.5 years, were performed for clinical, MRI and metabolic serum markers suggestive of systemic mitochondrial disease. Pathological studies included histochemistry, EM and biochemical assay of respiratory chain enzymes.

Results: Diagnosis of mitochodrial disease was confirmed in all. EM demonstrated frequent severe ultrastructural alterations of mitochondria in capillary endothelial cells more than in myofibers. Changes included stacking or whorling of cristae and paracrystallin structures, including mitochondria within long, looped villi extending into the lumen.

Conclusions: Mitochondrial ultrastructural alterations in young infants and toddlers with mitochondrial cytopathies are more frequent in the endothelium than in myofibers in muscle biopsies. This distribution may explain the frequent lack of prominent histochemical changes and biochemical abnormalities in homogenates of muscle biopsies of young patients. Endothelial involvement in the brain may contribute to epilepsy and neuronal death by not only by ischemia but by impaired transport of molecules to the brain and toxic metabolites from the brain.

Poster session: Neuropsychology/ psychiatry III
Wednesday, 31 August 2011

p738
COGNITIVE AND AFFECTIVE FUNCTIONS IN ADJUNCTIVE THERAPY WITH LACOSAMIDE

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Purpose: Lacosamide (LCM) is one of the newer antiepileptic drugs used in the treatment for partial-onset seizures. We examined the impact of LCM as adjunctive therapy on cognition and affect.

Method: Thirty epilepsy patients with refractory partial-onset seizures were investigated. In addition to their preexisting, stable antiepileptic medication, LCM was titrated in a dosage of 200–400 mg/day. Variables of cognition and mood were assessed before and 3 months after titration. A computerized neuropsychological test (CCTE) covered the cognitive domains of attention, cognitive speed, working memory, verbal and figural memory. Emotional variables of depression, anxiety, irritability, sleep quality, positive feeling and subjective performance were recorded by visual scales.

Results: No significant changes of the patients' cognitive profile related to LCM add-on were detected. Comparing data before and after titration,

median to high correlations were proven for all subtests ($p < 0.05$), which indicates a stable performance. In some tasks a slight but not significant improvement was shown, which might be interpreted as practice effect. Concerning emotional variables, subjects rated themselves being less irritable and in a better mood after titration of LCM ($p < 0.05$).

Conclusion: Results show that LCM as adjunctive therapy does not induce significant changes in the cognitive profile. Subjective improvement of irritability and positive feeling may be related to better seizure control after change of medication. It indicates that, concerning cognitive and mood side effects, LCM is a well-tolerated antiepileptic drug and is unlikely to impair those functions.

p739
A CRITICAL REVIEW OF CLINICAL TRIALS INVESTIGATING THE EFFECTS OF ANTIEPILEPTIC DRUGS ON COGNITION IN EPILEPTIC CHILDREN

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Purpose: Epilepsy can be associated with cognitive impairment, this meaning that especially in children learning abilities can be affected, leading to long-term effects on academic achievements as well as on social interactions and quality of life. A review of clinical trials evaluating the effects on cognition of antiepileptic drugs (AEDs) in epileptic children is presented.

Method: A search on PubMed database was conducted of articles related to clinical trials assessing cognitive effects of AEDs in epileptic children below 18 years of age, using different combinations of search terms.

Results: The search conducted with ''antiepileptic AND children AND cognitive'' as search terms yielded a total of 93 articles. Among these, 24 articles could be selected that reported clinical trials in which the effects of AEDs on cognitive function of epileptic children were evaluated by employing specific instruments, with 12 having been published in the last 5 years. Clinical trials largely differed in several respects: selection criteria, sample size, cognitive domains evaluated, measurement instruments, type of epilepsy, control arm. The assessment of the effects of AEDs on selected aspects of cognitive function was reported as the primary study end point in only a few trials all of which explored relatively short term treatment durations.

Conclusion: To date, the role of different AEDs in affecting cognitive abilities of children with epilepsy has been investigated in a limited number of clinical trials. These studies are characterized by the lack of standardized methods of measurement and by substantial differences in study designs. Although there is a growing interest for the potential effects on cognition of AEDs, methodological flaws mean that study results are not always reliable and difficult to extrapolate to a more general patient population. The importance of the choice of adequate neuropsychological tests is discussed, also with respect to their cultural adaptation and validation for multicenter and multinational clinical trials.

p740
WORKING MEMORY BINDING IN EPILEPSY PATIENTS WHO UNDERWENT UNILATERAL MEDIAL TEMPORAL LOBECTOMY

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Purpose: Long-term memory deficits are well established in epilepsy patients who have undergone medial temporal lobectomy, but whether working-memory functions are affected is less clear. Recent studies indicate hippocampal involvement during active maintenance of associated information over brief delays. Moreover, several studies found hippocampal involvement during maintenance of single items over delay periods of 6 s and longer. The present study examined working-memory binding functions in patients who have undergone unilateral medial temporal lobectomy as treatment for their intractable temporal lobe epilepsy.

Method: A group of 43 patients who underwent medial temporal lobectomy (23 patients with left medial temporal lobectomy and 20 patients with right medial temporal lobectomy) and 20 healthy controls were examined with a Delayed-Match-to-Sample task. During this task participants had to maintain either single or associated items over short and long delay periods.

Results: Whereas standard working memory tests in neuropsychological assessment generally show no impairments, results on the DMS task indicate significant poorer performance of the patient groups compared to the healthy controls (MTL < controls, $p < 0.02$). Specifically, patients performed significantly worse than healthy controls on interitem binding ($p < 0.03$) and extrinsic intraitem binding ($p = 0.06$). Moreover, patients performed significantly worse than healthy controls on maintaining single items over 6 s delay periods ($p < 0.001$).

Conclusion: In conclusion, the present study shows selective impairment of working memory functions in patients who underwent medial temporal lobectomy. Our results support the proposal that the medial temporal lobe, including the hippocampus, is not purely involved in long-term episodic memory formation, but also in working memory binding functions.

p741
LONGITUDINAL STUDY OF POSTOPERATIVE CHANGES IN EMOTIONAL RECOGNITION AND SOCIAL COGNITION IN TEMPORAL LOBE EPILEPSY PATIENTS

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Purpose: The abilities to identify facial expression and to infer emotional experiences may be impaired in patients with temporal lobe epilepsy (TLE). The aim of our prospective study was to compare the ability to detect facial emotion and social faux-pas in TLE patients pre- and postoperatively.

Method: We included 15 refractory TLE patients indicated for epilepsy surgery; ten left-sided (preoperatively 34 years, FSIQ 90, VIQ 92, PIQ 90, postoperatively 35 years, FSIQ 93, VIQ 93, PIQ 94), five right-sided (preoperatively 37 years, FSIQ 108, VIQ 110, PIQ 104, postoperatively 38 years, FSIQ 104, VIQ 103, PIQ 106). Besides routine neuropsychological testing, an experimental protocol focused on social cognition and emotion recognition was performed before and 1 year after surgery in all patients. Faux-pas test based on identification of a clear social faux-pas in three short stories was used to test social cognition. To assess for emotion recognition an adapted version of Ekman and Friesen emotion recognition test containing 25 facial expressions was used. The cut off scores for both tests were set in the group of healthy controls.

Results: There was no significant difference in emotion recognition and faux-pas detection before and after epilepsy surgery in our group of TLE patients in general. Two patients have deteriorated to pathological values and two other have normalized in emotion recognition test. One patient deteriorated in faux-pas test. A correlation between emotion recognition and faux-pas identification was detected.

Conclusion: Epilepsy surgery does not seem to cause significant deterioration in emotion recognition or faux-pas detection in general. However, improvement or worsening can be observed in individual TLE patients. No specific group in risk can be identified based on our data. Further studies with larger series are needed.

Abstracts

p742
A MULTICENTER COMPARATIVE TRIAL OF ZONISAMIDE AND TOPIRAMATE AS MONOTHERAPY IN EPILEPSY PATIENTS: SAFETY FOR COGNITIVE FUNCTION

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Purpose: Topiramate (TPM) and zonisamide (ZNS) have a structure of sulfa moiety, an action of carbonic anhydrase inhibition and a unique side effect of stone formation in common. We compaired the cognitive effects of TPM and ZNS as monotherapy.

Method: From September 2005 to December 2006, thirty subjects (>13 years old) with either newly diagnosed epilepsy or epilepsy that has not been treated with antiepileptic medications for more than 4 months completed open-label, randomized multicenter study incorporating 24 weeks treatment periods of TPM and ZNS titrated to a target dosage of 100 mg/day and 200 mg/day, respectively. Evaluation of 16 objective neuropsychological measures yielding 26 variables of cognitive function occurred at two times; pretreatment baseline and after 24 weeks treatment. Groups did not differ with respect to epilepsy relevant variables and neuropsychological variables at baseline.

Results: Mean scores of some neuropsychological measures declined after 24 weeks treatment from baseline pretreatment. ZNS group (70 subjects) showed significant differences in the performance of forward digit span ($p < 0.05$), backward digit span ($p < 0.01$), semantic and phonemic word fluency ($p < 0.05$). TPM groups (63 subjects) showed significant differences in the performance of prose memory ($p < 0.05$), backward digit span ($p < 0.05$), semantic ($p < 0.05$), and phonemic word fluency ($p < 0.001$). There are no significant differences between TPM and ZNS group on these cognitive effects.

Conclusion: This study demonstrates the comparable effects of TPM and ZNS on cognitive function. TPM and ZNS appears to be associated with negative cognitive side effects. But, there are no significant differences between TPM and ZNS on these cognitive effects.

p743
MEMORY FOR MORPHED FACES AFTER TEMPORAL LOBECTOMY IN CHILDREN

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Purpose: In adults, right temporal lobectomy usually causes changes in nonverbal memory equal to or greater than those caused by left temporal lobectomy. It is not clear whether this is the result of hemispheric asymmetries in processing of nonverbal material. We investigated changes in memory for morphed faces—a particular type of nonverbal material—after temporal lobectomy in children.

Method: Prospective, longitudinal, controlled follow-up of consecutively included children (0–18 years) receiving left or right temporal resection. Patients (right temporal lobectomy: n = 6, left temporal lobectomy: n = 7) were assessed shortly before surgery and 6 and 12 months thereafter. For each patient, two age- and gender-matched healthy controls were assessed at equal intervals (right controls: n = 12, left controls: n = 13). We presented a photograph of a face, followed by a photograph that was a morph of the same face and another face. By varying the degree of morphing over pairs of faces we determined the smallest degree of morphing that was detected by the child.

Results: Patients performed worse than controls ($p = 0.019$). There was no significant difference for side of surgery or for assessment ($p > 0.1$). None of the interactions were significant. The considerable deterioration after left temporal lobectomy was not statistically significant, likely due to insufficient power of the study.

Conclusion: If corroborated in a larger group, deterioration of memory for morphed faces after left temporal lobectomy would support the notion of local processing in the left hemisphere.

p744
QUALITY OF LIFE OUTCOME ACROSS YEARS AFTER ANTERIOR TEMPORAL LOBECTOMY FOR DRUG-RESISTANT TEMPORAL LOBE EPILEPSY

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Purpose: Although over two-thirds of patients with drug-resistant temporal lobe epilepsy (TLE) become seizure-free following anterior temporal lobectomy (ATL), there is scarcity of data on the long-term quality of life (QOL) outcome following ATL and the various factors influencing it. We extensively evaluated the impact of ATL and various other clinical, demographic and social factors on the QOL of patients who have undergone ATL across years in the long-term.

Methods: Between March 1995-March 2009, 583 patients who underwent ATL (273 right, 310 left) with mean follow-up of 5.29 ± 3.05 years (range-1–13 years) were studied. The mean age at onset of epilepsy was 10.7 ± 7 years and duration of epilepsy was 18.45 ± 9.1 years. Mean education of the group was 10.8 ± 3.5 years. QOL was assessed using QOLIE-31 administered before ATL and yearly thereafter till last follow-up. The various factors affecting QOL was assessed by Pearson correlation coefficient, unpaired *t*-test and linear regression method.

Results: The mean baseline QOL score pre-ATL was 49.32 ± 11.45. Overtime following ATL, there was a steady improvement in QOL score which peaked at 1 year after which it remained stable ($p \leq 0.001$). A positive correlation between QOL and years of education ($p \leq 0.001$) and IQ ($p = 0.01$) was noted. Patients who had secondary generalized seizures, psychiatric comorbidity and who never had seizure freedom for at least 2 years following ATL had poor QOL.

Conclusions: In patients with drug resistant TLE, ATL results in steady improvement in QOL over time. Complete seizure freedom and higher educational status were the most important determinants of QOL outcome following ATL.

p745
EFFECTS OF ESLICARBAZEPINE ON COGNITION IN PATIENTS WITH FOCAL EPILEPSY

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Background: Eslicarbazepine acetate (ESL) is a novel antiepileptic drug for the treatment of focal epilepsies. In healthy volunteers ESL seems to have no relevant effects on cognition. To date there has been little research on the cognitive effects of ESL in epilepsy patients. We investigated the effects of ESL on various areas of cognitive functioning in patients with focal epilepsy, switched from oxcarbazepine (OXC), mostly.

Methods: Twelve adult patients with uncontrolled structural epilepsy (nine male, three female, age 38 ± 10 years.) were assessed regarding the effects of ESL on cognition (attention, cognitive speed, long and short term memory, word fluency). The assessments took place before ESL therapy (T1) and after a stable dosage had been established based on individual response (T2) (ESL dosage 2083 ± 828 mg). Prior to ESL treatment, patients had been treated with oxcarbazepine (N = 10, six retard,

four immediate release, dosage 2031 ± 529 mg) or carbamazepine (CBZ, N = 1), which were discontinued. One patient was drug-naïve prior to ESL treatment. For statistical analysis regarding changes in cognitive performance between T1 and T2 the Wilcoxon test was conducted.

Results: There were no significant changes over time in any of the cognitive parameters. 16.7% of patients were seizure-free at T2.

Discussion: The results show no changes after the substitution of OXC or CBZ for ESL. We found no decline in cognitive functioning even in the high dosage applied. These findings should be replicated in a larger sample of patients with structural epilepsy.

p746
EXPLORING COGNITIVE FUNCTIONS DURING INSULAR STIMULATION BY MEANS OF INTRACEREBRAL ELECTRODES IN PATIENTS WITH DRUG-RESISTANT EPILEPSY

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Purpose: Seizures arising from the insula may induce linguistic deficits. Neuroimaging studies in normals have demonstrated the insular involvement in tasks of verbal fluency. Invasive recordings (stereo-EEG), to define the epileptogenic zone, offer the unique opportunity to directly explore the cognitive performance of patients while stimulated. We implemented a short neuropsychological assessment to study more systematically the role of the insula in verbal production. We investigated five patients candidate to surgery who had implanted electrodes for epileptological reasons also into the insular cortex.

Method: Patients were administered with a Phonemic Fluency test. Time of testing: baseline condition (T0), during stimulation per choc (Intensity: 5 mA; duration of a stimulation: 30 s) (T1). Side of SEEG: two right, three left (one of these left-handed). Data analyses: Repeated measures *t*-test ($p < 0.05$), comparing T0 with T1 performances for each stimulated contact (in total: thirteen contacts).

Results: At T1 we registered a significant improvement in Phonemic Fluency ($p = 0.011$) in all patients.

Conclusion: Although our results are very preliminary we found quite surprising such a diffuse significant improvement, independently on the side of stimulation. This result seems to be quite contradictory compared with the linguistic production impairments described during insular seizures. As SEEG ensures on the anatomical precision of the electrical stimulation, we think that further research is needed to better understand the possible role of the insular cortex in linguistic production and cognitive functions.

p747
IMPACT ON AUTOBIOGRAPHICAL MEMORY OF UNILATERAL TEMPORAL RESECTION FOR CONTROL OF INTRACTABLE EPILEPSY

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Purpose: To investigate the very long term effects of temporal resection (TR), mainly but not only on autobiographical memory and expand our previous results (Voltzenlogel et al., Epilepsia 2007; 48, 605–608) on different cognitive outcome following TR lateralization.

Method: Eighteen patients, nine with right TR (RTR) and nine with left TR (LTR), completed an autobiographical memory test, preoperatively, and 12 months and 5-year postoperatively. They had to retrieve past personal memories, from different life periods, using cue words. Memories referring to a single event specific in time and place, detailed or richly detailed were scored 4 or 5 points respectively; generic memories, detailed or richly detailed were scored 2 or 3 respectively; semantic facts were scored 1; no response were scored 0.

Results: RTR patients recalled significantly more autobiographical memories for three time periods after surgery than before TR. Importantly, performance on postoperative autobiographical memories at 5-year after surgery, was normalized for RTR patients.

RTR patients recalled significantly less specific events (scored 4 or 5 points) preoperatively than controls, but there was no significant difference 5 years after surgery.

No changes were observed in the LTR group, their performance remained impaired after surgical treatment with significantly more 0 and 1 responses, together with significantly less 4–5 points responses, compared to controls.

Conclusion: We highlighted positive effects of RTR on autobiographical memory and suggest that, in the absence of recurrent seizures, the relative integrity of the left hemisphere together with residual right hemisphere structures sustain postoperative autobiographical memory.

p748
MEMORY PERFORMANCE AFTER AMYGDALOHIPPOCAMPAL DEEP BRAIN STIMULATION IN PATIENTS WITH MEDICALLY REFRACTORY TEMPORAL LOBE EPILEPSY

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Purpose: To investigate the effects of amygdalohippocampal deep brain stimulation (AH-DBS) on memory functioning in patients with medically refractory temporal lobe epilepsy who are not suitable candidates for resective epilepsy surgery.

Methods: The population consisted of 10 patients (seven men) with medically refractory temporal lobe epilepsy, treated with ipsilateral (n = 8) or bilateral (n = 2) AH-DBS (mean age: 31 years 9 months). We performed verbal and visual memory tests both before and 6 months after initiation of the AH-DBS.

Results: Group analyses revealed significant amelioration for the immediate and delayed recall of the Rey-Osterrieth Complex Figure Test ($p < 0.05$) but this possibly reflects a retest effect. No significant changes on learning, recalling or recognizing learned verbal or visual material on group level were found. Individual Reliable Change Indices showed significant amelioration of verbal memory in one patient who received left AH-DBS, no other effects were noted.

Conclusion: AH-DBS seems a valuable treatment alternative for patients with refractory epilepsy that holds only limited consequences for memory functioning. While studies examining patients with epilepsy before and after surgery often show a higher risk for verbal memory deficits after surgery in the left hemisphere, this does not seem to be the case for AH-DBS.

p749
NEUROPSYCHOLOGICAL STUDY IN CHILDREN WITH SYMPTOMATIC PARIETOOCCIPITAL EPILEPSY TREATED BY SURGERY

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Purpose: Thirteen children affected by lesional POE (parietooccipital lobe epilepsy) who underwent a surgical treatment of lesion excision, were enrolled, in order to evaluate the epileptic and neuropsychological outcome.

Methods: All the participants, before surgery and at outcome, underwent clinical examination, neurological and developmental assessments, video-EEG, neuroimaging. Neuropsychological assessments consisted of global cognitive scales and specific function tests, (Memory, Visuoperceptual and Visuospatial abilities, executive functions and language).

Results: Mean age at seizure onset was 8.6 years; mean age at surgery 9.9 years. The etiology consisted of: brain tumors (11 cases) and two cortical displasias. Surgery consisted of a lesionectomy in all cases (total resection in 11 cases, subtotal in 2).

Mean postsurgical follow-up: 5.5 years. Epileptic outcome was Engel class IA in 11 patients. In the other two cases, with subtotal resection, Engel class II-III were observed.

Visual field deficit was observed in three case before surgery; it persisted unchanged afterwards.

Presurgically, we found a normal IQ in 11 cases and a mild mental delay in two cases, with definite differences between verbal and nonverbal quotient (mean values: 110.9 vs. 93). After surgery TIQ and VIQ remained substantially unchanged, while, in four cases, PIQ improved significantly.

Among the assessed specific abilities, defects in visual attention, visuoperceptual, visuomotor praxias and visual working memory were observed in almost half of patients before surgery, with only partial improvement afterwards.

Conclusion: Our data revealed that performance abilities are more compromised than verbal ones, with significant improvement after surgery. The most compromised domain involved the "processing" of visual informations.

p750
DOSE-DEPENDENT GABAPENTIN-INDUCED SEXUAL DYSFUNCTION

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Purpose: Sexual dysfunction, characterized by decreased libido, ejaculatory inhibition/failure, anorgasmia, and erectile dysfunction/impotence, is a key adverse effect leading to medication noncompliance. Gabapentin is an antiepileptic drug approved by the FDA for the treatment of postherpetic neuralgia and adjunctive treatment of partial seizures with/without secondary generalization. It is frequently used off-label in psychiatry and pain management. This case addresses gabapentin-induced sexual dysfunction when used off-label to treat anxiety.

Method: Case analysis with literature review.

Results: Thirty-four-year-old male presented with major depression, social anxiety, and anxiety disorder nos on duloxetine 60 mg bid and bupropion 300 mg qam. Gabapentin was initiated for social anxiety. With gabapentin 100 mg qhs, no sexual side effects were noted. After 3 weeks on gabapentin 200 mg qhs, he required prolonged foreplay to attain an erection with ejaculatory delay. As depressive/anxiety features persisted, bupropion was increased to 400 mg total daily dose and gabapentin to 300 mg qhs with continued duloxetine. Subsequently, he noted progressive sexual dysfunction: (1) within 1 week, decreased libido; (2) within 2 weeks, partial erection with anorgasmia; (3) at 4 weeks, no libido, anejaculation, anorgasmia, and impotence. He independently titrated himself off gabapentin by 100 mg/week. One week after discontinuation of gabapentin, he reported normal libido, erectile function, orgasm, and ejaculation. On duloxetine and higher dose bupropion, he denied any further depressive/anxiety features.

Conclusion: Low dose gabapentin may result in marked sexual dysfunction. Sexual dysfunction from gabapentin may be dose-dependent. Patients often do not volunteer sexual adverse effects and require targeted questions. Psychiatrists, neurologists, and pain management physicians need to be cognizant of this adverse effect.

Poster session: Neuropsychology/psychiatry IV
Wednesday, 31 August 2011

p751
NEUROPSYCHOLOGICAL ASSESSMENT IN CHILDREN WITH ROLANDIC EPILEPSY

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Purpose: Although there is a good prognosis concerning seizures and normal intellectual and neurologic development, recent studies have shown some specific neuropsychological dysfunctions in children with benign childhood epilepsy with centrotemporal spikes (BCECTS) or rolandic epilepsy (RE). The aim of this study was to identify and describe possible neuropsychological deficits in children with RE.

Methods: Twenty-five children with clinicoeletroencephalographic diagnosis of RE, QI >80, aged 6 to 15 years and 11 months, underwent a comprehensive neuropsychological assessment: intellectual level, attention, memory (verbal and visual), praxis, language (naming, comprehension and expression) and executive functions. The battery included: WISC III to assess intellectual level, Trail Making Test A/B (TMT), Boston Naming Test (BNT), FAS, WRAML (Wide Rangement Assessment of Memory Learning (WRAML) and Wisconsin Card Sorting Test (WCST). The results were compared with the results of 28 normal children (same age and school level) utilizing the Mann–Whitney test.

Results: There was a statistically significant difference between the two groups, with worse performance in the RE group: WCST (number of errors and completed categories), TMT B (most children with RE scored below the lower mean) and memory for learning at WRAML (seven children with RE scored below the lower mean).

Conclusion: Children with RE, despite normal intellectual level, can show deficits in executive functions, attention and memory for learning. This must be considered in the assessment and management of those children in order to avoid further learning impairment and jeopardize their quality of life.

p752
ATTENTION DIFFICULTIES IN CHILDREN WITH ABSENCE EPILEPSY REFERRED TO A TERTIARY CLINIC

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Purpose: The aim of the present study has been to investigate possible undetected attention difficulties in children with absence epilepsy. In the tertiary clinic we saw several patients with benign absence epilepsy who had academic and social difficulties. After thorough neuropsychological evaluation many of them had attentional difficulties compatible with ADHD.

Method: The study group consisted of 30 patients with absence epilepsy. Patients with any other kind of seizures were excluded from the study, as were patients with psychiatric disorders other than ADHD and patients that had undergone epileptic surgery. Criteria for attention difficulties were identified according to DSM-IV-TR standards. The facts that indicated possible attentional difficulties in the patient were accumulated from notes by former and present doctors, psychologists, physiotherapists, nurses and teachers.

Results: Based on the medical records 22 of the patients with absence epilepsy appeared to have attentional difficulties, this is a total of 73% (N = 30). Of this group 59% (n = 13) are female and 41% (n = 9) are male. In six cases the patients' apparent attentional difficulties have not been investigated and no measures have been taken, 83% (n = 6) of these patients are female.

Conclusion: The results indicate that when treating children with classical absence epilepsy it is important to be aware of possible attentional difficulties in the child.

The study that has been carried out underlines an important point. Despite the fact that absence epilepsy is considered easily treated, it can have implications such as attentional difficulties that should be given pedagogical consideration.

p753
COGNITIVE AND ADAPTIVE FINDINGS IN PEDIATRIC EPILEPSY

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Purpose: Pediatric epilepsy is associated with impairment in cognitive skills, behavior and adaptive development. These problems are probably due to ongoing seizures, genetics, brain abnormalities, antiepileptic drugs treatment, and to psychological issues.

To assess psychomotor development, adaptive functioning and behavior, and to provide a more comprehensive profile comparing differences between children with idiopathic, symptomatic, and cryptogenic epilepsies.

Method: We evaluated 82 children (40 females, 42 males) aged between 8 months to 17 years. Twenty patients were affected by idiopathic, 28 by symptomatic, and 34 by cryptogenic epilepsies. Patients were evaluated with cognitive and psychomotor development (DQ), adaptive functioning, and behavioral tests. Epilepsies were drug resistant in 44 patients (53.7%).

Results: The DQ score was higher in the idiopathic epilepsy group (mean 91.6) in comparison with symptomatic and cryptogenic epilepsies groups (mean 73.3 and 73.0, respectively, $p < 0.05$). In symptomatic and cryptogenic epilepsies groups the lowest quartile was <60. Children with drug resistant epilepsies performed significantly worse than responders (mean 71.3 ± 20.9 vs. 85.2 ± 20.4 $p < 0.01$). All groups had low results in adaptive functioning.

Conclusion: These findings suggest that a proper classification of epilepsies since the onset, together with their etiologies is an important issue for prognosis purposes regarding the patients' neuropsychological outcome.

p754
EPILEPTIFORM ACTIVITY, RELATED TO AUTISTIC DISORDERS

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Purpose: To study EEG features in childhood autism and their contribution to mechanisms of disorder.

Method: In 14 children of 3–10 years old with childhood autism and ÅÀ, having no seizures, distribution of ÅÀ was studied, using computerized EEG methods.

Results: Frontal ÅÀ was found in 6 (43%) patients: 5 – left, bilateral in 1. In two patients there were centrotemporal spikes, prevailing in one left, in other – right. Two patients had temporal ÅÀ with sours in mesial temporal area left in one and right in the other. In three patients ÅÀ was presented by occipital spikes right posterior (O4-T4-P4). In nine patients bilaterally synchronous discharges were present prevailing frontally in six and in two presented with typical absence pattern. Treatment with valproic acid (in 11) and levetiracetam (in 2) suppressed ÅÀ in EEG and improved clinical condition in 10 of 13 followed up patients.

Conclusion: Localization and distribution of ÅÀ in our patients correspond to structures in model of ''social brain.'' It includes planning and executive frontal systems, right posterior visuospatial structures, emotional and motivational limbic temporal mechanisms and their connections. Disintegrating epileptic discharges in any part of the system may result in autistic disconnection disorder. Clinical improvement, related to suppression of EA, supports the concept.

p755
THE PENELOPE SYNDROME[1]: MEMORY CONSOLIDATION IN CHILDREN WITH SLEEP-INDUCED EPILEPTIFORM ACTIVITY (ESES)

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Purpose: To study the effects of ESES on memory consolidation during sleep.

Method: Nineteen children with ESES underwent 24 h EEG-recordings, and during this completed one verbal and two nonverbal learning/acquisition tasks in the late afternoon (a list of 10 words and series of 16 faces and five abstract designs, respectively). Recall/recognition was assessed the next morning and percent forgotten was calculated. Spike indexes expressed as percentage of time within consecutive 10 min. epochs where spike-activity with a frequency >1/3 Hz was forthcoming were calculated for the time while the child was awake (SI-Aw), while in slow wave sleep (SI-Sws), and while in REM-sleep (SI-REM) [(2)].

Results: Mean SI-Aw, SI-Sws and SI-REM were 6% (range 0.2–62), 56% (range 23–88) and 21% (range 5–62), respectively. There were significant negative correlations particularly between SI-REM, SI-Aw and measures of acquisition on the verbal and one of the nonverbal memory tasks (design recognition). There were no effects of epileptiform activity on measures of consolidation (percent forgotten) on any of the memory tasks.

Conclusion: We found no negative effects of epileptiform activity on measures of consolidation. However, the negative correlations between measures of acquisition on the one hand, and epileptiform activity during the day as well as under sleep on the other hand, may indicate a joint effect of EEG-pathology during the day and the *preceding* night, possibly including also a long-term effect of a history with ESES. Note that the majority of these children were only lightly to moderately affected by ESES.

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2. Larsson PG, et al., A new method for quantification and assessment of epileptiform activity in EEG with special reference to focal nocturnal epileptiform activity. Brain Topogr. 2009, 22 (1):52–9.

Abstracts

p756
NEUROPSYCHOLOGICAL ASSESSMENT OF EXECUTIVE FUNCTIONS IN CHILDREN AND ADOLESCENTS WITH FRONTAL LOBE EPILEPSY

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Purpose: Neuropsychological deficit related to frontal lobe epilepsy (FLE) in pediatric population has been poorly studied. The very few studies in children with FLE show deficits in attention, response inhibition, psychomotor speed, motor programming, and planning (Patrikelis et al., 2009). However, these studies only focused in some executive functions. The aim of this study is to assess executive function in children and adolescents with frontal lobe epilepsy through a comprehensive assessment.

Method: Participants were 8 FLE subjects (mean age = 13.85; SD = 2.85) and eight healthy control subjects (mean age = 14.02; SD = 3.08). Six FLE children were on medication. They all completed Verbal Working Memory Test of Siegel & Ryan, Digits Backward (WISC-IV), Trail Making Test, Control Oral Word Association Test, Stroop Test, Design Fluency subtest of the NEPSY and three test from the Cambridge Neuropsychological Testing Automated Battery (CANTAB): Intra-Extra Dimensional Set Shift, Stockings of Cambridge and Spatial Span reverse mode. These tests measure verbal and visual working memory, set shifting, cognitive inhibition, planning, verbal fluency, design fluency and mental flexibility. Data were analyzed using Student *t* statistics.

Results: Children with FLE performed significantly lower in verbal working memory, mental flexibility, design fluency and they were more sensitive to cognitive interference. There were no significative differences in spatial working memory, planning, set shifting and verbal fluency.

Conclusion: Results suggest some executive problems in FLE children. Frontal lobe dysfunction in these patients could be responsible of these findings. A bigger sample is needed in order to confirm these results.

p757
CHILDHOOD EPILEPSY: IDENTIFYING THE NEUROPSYCHOLOGICAL PROFILE AND SPEECH INTERVENTION OUTCOMES IN A RARE CASE OF LANDAU-KLEFFNER SYNDROME—FROM DIAGNOSIS TO 5-YEAR FOLLOW-UP

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Purpose: A rare case of Landau-Kleffner syndrome (LKS) was seen in a child and adolescent community mental health setting. This was written up as a single case study given the rare nature of this disorder. This was reported in an effort to contribute to the sparse literature particularly in relation to neuropsychological sequelae and long term follow up.

Method: Comprehension neuropsychological, speech and psychiatric assessments were conducted. Developmental and intervention outcomes were evaluated across a 5-year period.

Results: This young boy initially presented with language regression, then at 5-year follow-up was referred in relation to significant neuropsychological, and psychiatric sequelae including behavioral and socially inappropriate play, aggression, and self-harm in the context of difficulties in understanding, reduced self-esteem, lowered mood and bullying. Neuropsychological assessment also revealed a range of attention and executive deficits. The developmental trajectory together with management strategies are discussed and evaluated in relation to this case. Moreover, significant intervention related gains are highlighted in regard to his speech and language skills.

Conclusions: Subsequent to language regression, by age nine this child with LKS was consolidating the basics of speech and language at a time when his peers were developing the social elements of communication. This made him vulnerable to social and psychiatric difficulties. This was further contributed to by the identified executive dysfunctions and attentional problems. Therefore, intervention needed to shift from practical processes to the subtleties of pragmatic communication, theory of mind, executive cognitive skills and social development as well as psychiatric input.

p758
RIGHT TEMPORAL LOBE EPILEPSY AND SOCIAL COGNITION IN ADOLESCENTS

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Purpose: Social cognition refers to the ability of an individual to infer the emotional state of others and is crucial for successful social interactions. Social cognition deficits such as a diminished capacity for empathy may lead to the establishment of dysfunctional patterns of behavior (Matiack et al., 2009). The aim of this research was to examine the relationship between lateralization of brain dysfunction and judgment of social behavior in adolescents suffering from temporal lobe epilepsy (TLE).

Method: The subjects were 11 adolescents with left TLE, nine adolescents with right TLE and 13 matched controls. The research tool included 20 social interaction scenes each involving three participants: a person showing overt signs of distress, a person actively helping him and an observer. The subject was asked to judge the emotional state of each of the three participants by pointing to a ''smiley.''

Results: Patients with right TLE demonstrated a significantly lower level of social judgment compared to the NCs ($p < 0.01$) and to the patients with left TLE ($p < 0.05$). More interestingly, only the right TLE adolescents demonstrated a significantly lower level of inference of the emotional state of the observer, compared to the person in distress and compared to the active helper ($p < 0.01$).

Conclusion: Right temporal lobe dysfunction may disrupt the ability of social interaction in adolescents with TLE, particularly in situations where overt cues are absent and may result in emotional and behavioral problems requiring neuropsychological treatment.

p759
CORRELATION BETWEEN LANGUAGE IMPAIRMENT AND LOCOMOTION PROBLEMS IN CHILDREN WITH ROLANDIC EPILEPSY

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Purpose: An association between impaired school performance and rolandic epilepsy is frequently reported. Especially language outcome seems to be affected, although rolandic epilepsy originates from the motor-sensory cortex. In this study we assessed school performance of children with rolandic epilepsy as observed by the parents and by neuropsychological testing, to find a correlation between locomotion problems and language impairment.

Method: Noncontrolled open clinical cohort study of 48 children (mean age 115 months, SD 19.7) with diagnosed and reconfirmed rolandic epilepsy. All children had a 24-h electroencephalogram and a neuropsychological assessment. Semistructured interviews were given to the parents to measure problems on school performance.

Results: In children with rolandic epilepsy, parents reported that their children had language problems, i.e., reading, writing and perception and expression of language. There was a significant delay of the reading skills (6 months for reading of words (SD 11.9, $p < 0.002$) and 8.6 months for reading sentences (SD 12.7, $p < 0.001$), compared with the normal population. There was a significant correlation between parent reported problems in motor development and delays of the reading skills (reading words $r = -0.426$, $p = 0.006$; reading sentences $r = -0.343$ and $p = 0.03$).

Conclusion: Language and reading performance is impaired in children with rolandic epilepsy. Reading sentences is more impaired than reading words. There is a significant correlation between problems in motor development and language, which suggest an interaction of both on the level of the cortex.

p760
IDENTIFYING ANXIETY DISORDERS IN CHILDREN WITH EPILEPSY

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Purpose: Anxiety disorders are common in children with epilepsy with rates ranging from 13.0% to 48.5%. Parent and child self-report measures are often used to identify anxiety disorders. The purpose of this study was to assess the validity and clinical utility of two common self-report measures used in both research and clinical settings.

Methods: As part of a larger investigation of children with epilepsy, 69 participants aged 8–18 years and their parents underwent a standardized psychiatric interview using the Schedule for Affective Disorders and Schizophrenia (KSADS) to identify current anxiety disorders. The child completed the Multidimensional Anxiety Scale for Children (MASC) and the parent completed the Child Behavior Checklist (CBCL). We computed three diagnostic statistics based on clinical cutoff scores for each measure: sensitivity, specificity, and overall correct classification.

Results: Participants had a mean age of 14.3 years and a mean epilepsy onset of 11.3 years. Based on the KSADS, 19 (27.5%) children met criteria for an anxiety disorder. Three anxiety subscales of the CBCL were examined: internalizing problems (sensitivity = 0.375, specificity = 0.762, overall correct = 0.655), anxious/depressed (sensitivity = 0.250, specificity = 0.927, overall correct = 0.737), and anxiety problems (sensitivity = 0.125, specificity = 0.905, overall correct = 0.689). The total score for the MASC was also examined (sensitivity = 0.063, specificity = 0.857, overall correct = 0.655).

Conclusion: Both self-report measures have higher overall correct scores but their ability to identify children with anxiety (sensitivity) is quite low. Caution should be taken when using these measures and the clinical cutoff scores as screening tools for anxiety disorders in children with epilepsy.

p761
PSEUDOSEIZURES MONITORING IN PEDIATRIC POPULATION

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Purpose: Monitoring of patients with pseudoseizures in childhood. To determine the most frequent comorbidities in the study group. Recognize the value of in depth study of pseudoseizure for monitoring and family support.

Method: Retrospective observational study.

Monitoring of patients: Pediatric neurology consultation and child psychiatry. Evaluation of the pseudoseizure table: equal status better or worse. Applications on a global scale of child funtions.

Procedure: Monitoring was conducted on pediatric patients diagnosed with pseudoseizures at La fundacion Hospital de la Misericordia. The group was composed of pediatric neurology and child psychiatry patients, from January 2000 to December 2009 with a total of 50 children ($n = 50$ children).

Results: Of the 50 patients diagnosed with pseudoseizures, communication was achieved with 12 patients. Of these, five patients were diagnosed with pseudoseizures status, and antiepileptic agents. The remaining seven had epilepsy and pseudoseizures. The main psychiatric comorbidities presented were depression and anxiety disorder. The overall operating range evidenced a degree of dependence of patients on a caregiver was three patients (25%).

Conclusion: The findings about pseudoseizures can demonstrate the importance of timely diagnosis if suspected, this requires a multidisciplinary study and early diagnosis before the introduction of drug treatment. Biopsicosocial approach allowed us to determine the overall functioning level of the patient upon joining the network of support that is required in this population, in which psychiatric comorbidity is one of the diagnoses to be determined.

p762
DOES COGNITIVE FUNCTIONING INFLUENCE EPILEPSY OCCURRENCE IN CHILDREN DIAGNOSED WITH ADHD BY THE TIME OF ADHD ASSESSMENT?

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Purpose: To investigate the cognitive functioning influence of epilepsy in children with attention defict/hyperactivity disorder (ADHD) by the time of ADHD assessment. The cognitive levels, the intelligence quotient (IQ) were examined and compared in patients with and without previous history of epileptic seizures (ESz).

Method: Subjects were 607 (82.4% male), aged between 5 and 14 years, mean 9.4 + 2.5, who were diagnosed at our Hospital between January 2000 and December 2005. A previous history of ESz had 14 patients. Cognitive evaluation was made by means of the Wechsler Intelligence Scale for Children-Revised, the Norwegian version. All children were divided in two groups: normal cases with IQ >85 and mentally delayed cases with IQ <85 (including patients with mild mental retardation IQ<70, and borderline intelligence patients IQ <70 but <80).

Results: History of epilepsy was found in 14 (2.3%) children. Cognitive testing results were obtained from 549 patients (all 14 patients with and

535 without epilepsy). Of these with a history of ESz, 35.7% had IQ <85, and of those without ESz, 24.3% had IQ <85. When we excluded the patients with IQ <85, we found lower rate of epilepsy 1.9%, still different from the general population (1%).

Conclusion: A higher rate of epilepsy in children with ADHD was associated with lower IQ level of these patients. Excluding these cases, the epilepsy occurrence was still different. Children with ADHD had more often epilepsy than expected in the general population regardless of the lower cognitive functioning in some patients.

p763

ROLANDIC SPIKES AND BENIGN EPILEPSY WITH CENTROTEMPORAL SPIKES (BECTS) IN CHILDREN DIAGNOSED WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD)

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Purpose: This retrospective study investigated the frequency of rolandic spikes and BECTS in children diagnosed with ADHD, their relationships to ADHD types, and compared them with a historic control group of normal school-aged children.

Method: Subjects were 607 children with ADHD (82.4% male), aged between 5 and 14 years, mean 9.4 + 2.5, who were diagnosed at our Hospital between January 2000 and December 2005. At least one routine digitized EEG during wakefulness was performed on 517 patients. A previous history of epileptic seizures (ESz) had 14 patients.

Results: EA were recorded in the EEGs of 39 children (28 boys and 11 girls), 16 (41%) had ADHD-inattentive type. Of 39 cases with EA, 12 had previous history of ESz and of these 12 cases, 4 (33%) had ADHD-inattentive type. Rolandic spikes were registered in nine cases (1.7%; eight boys and one girl). It was not different than expected from control group in healthy children. Two patients had previous history of BECTS and both of them had ADHD-combined type. Of seven patients with rolandic spikes without previous history of ESz, 3 (43%) had ADHD-inattentive type.

Conclusion: Rolandic spikes and BECTS are common in children diagnosed with ADHD as in healthy children. ADHD children with EA had a larger proportion of ADHD-inattentive type independent of a history of epilepsy. The group with rolandic spike and previous history of BECTS had a trend toward ADHD-combined type, but group without previous history of ESz had more often ADHD-inattentive type.

p764

CERTAIN PECULIARITIES OF PHYSIOLOGICAL FUNCTIONING IN CHILDREN WHILE BENIGN EPILEPTIFORM DISCHARGES OF CHILDHOOD ARE BEING FORMED

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Purpose: Studying the link between development of BEDC in EEG on one side and cognitive deterioration on the other in children with and without brain organic lesion.

Method: The study enrolled 14 children aged from 2 years and 3 months old to 13 years old (average age is 6 years 8 months) with brain organic lesions and without such lesions. Male patients were numerously predominant. Nine patients had focal epilepsy. All patients also manifested various degrees of cognitive deficit. Abnormalities of intellect prerequisites (attention, memory and cognitive abnormalities) were diagnosed along with other dysfunctions. Behavioral abnormalities such as pathological impulsive reactions and affective fluctuations.

Results: Transitory complexes were found during dynamic EEG in all children participating in the study under the form of benign epileptiform discharges of childhood (BEDC).

We have noticed that the onset of these patterns coincides with clinical improvement in cognitive functioning and abilities (attention, psychic activity, speech production) in all children regardless of whether they had any brain organic lesion or not and the severity thereof.

Conclusion: 1. According to our data the dynamic changes in bioelectric brain activity in children with or without organic brain lesion under the form of BEDC accompany clinical improvement of cognitive functions.

2. BEDC within our study were transitory.

3. Supposedly BEDC do not lead to cognitive function degradation, however they serve as a prognostic factor for recovery of impairment of brain maturation in children.

Poster session: Neuropsychology/psychiatry V
Wednesday, 31 August 2011

p765

BIOLOGICAL FACTORS IN EPILEPSY CAUSING INTELLIGENCE DEFICIT

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Purpose: In a group of adult patients suffering from epilepsy, low intelligence quotient (IQ) levels, the cognitive deterioration rate as well as its relation to a number of biological variables are studied. The aim of this research is to determine the long term biological variables in order to reduce them.

Method: We used the IQ and Wechsler's Deterioration index (DI) to study 200 patients diagnosed with epilepsy. The patients were divided into two groups, a first group included those with IQ <89 and >90 and the second patients with or without a positive DI. These variables were analyzed according to different biological factors. Data was processed using different statistical methods.

Results: Out of the total of studied patients, 54.5% showed an IQ <89 and 50% a cognitive deterioration rate. Factors related to the patients with an IQ lower than 89 were among others the following:

The start of the seizures before the age of 15, having suffered from epileptic seizures for more than 15 years, a high frequency of seizures, and personal past history of status epilepticus as well as suffering from secondarily generalized partial epileptic seizures.

Patients suffering from generalized secondarily focal epileptic seizures show a higher cognitive deterioration than those suffering focal or generalized seizures, ANOVA p = 0.0029, which is highly meaningful.

Conclusion: Half of the patients show a normal-low IQ, as well as some cognitive deterioration. Although the deterioration detected by using WAIS was not evident, it is important to be aware of the fact that there are biological risk factors in order to be able to control them.

p766

AUDITORY AND VISUAL NAMING IN PATIENTS WITH LATERALIZED REFRACTORY EPILEPSY: INITIAL EXPERIENCE AT GHENT UNIVERSITY HOSPITAL

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Purpose: Patients with localized refractory temporal lobe epilepsy (TLE) enrolled in the presurgical workout protocol at Ghent University Hospital undergo, among many investigations, extensive neuropsychological assessment including auditory and visual naming tests. We developed dutch adaptations of these tests to presurgically asses visual object naming and auditory description naming in surgical candidates with lateralized refractory TLE. Both tests will eventually be adapted to be incorporated in the presurgical neurostimulation mapping protocol.

Method: Auditory and visual naming target words were matched controlling for word frequency and word length, resulting in two equally difficult naming tasks. Stimuli were based on Snodgrass and Vanderwart pictures and dictionary definitions. Both naming tasks were administered to left and right lateralized TLE patients and the performance of both groups in both tasks was compared.

Results: Patients with left lateralized focal TLE performed significantly worse on the auditory version of the naming task compared to the visual alternative. This pattern was also seen in the right lateralized group, but less pronounced. Also, the left lateralized group performed worse on the auditory naming test compared to the right lateralized group, while their results on the visual naming task were less differentiated.

Conclusion: The inclusion of auditory and visual naming tasks in presurgical neuropsychological assessment of refractory epilepsy patients is a valuable tool in the prediction of possible naming decline after surgical intervention. Particularly, the inclusion of an auditory naming task proves to be a valuable addition because of its unique capability to capture subtle naming deficits in patients with left TLE. Auditory naming characterizes and lateralizes left TLE-associated language dysfunction better, compared to the visual alternative.

p767

NEUROPSYCHOLOGICAL IMPAIRMENT IN PATIENTS WITH EARLY ONSET NOCTURNAL FRONTAL LOBE EPILEPSY

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Purpose: Aims of the study were to identify any neuropsychological deficits in patients with early onset nocturnal frontal lobe epilepsy (NFLE) and to verify a possible relationship between epilepsy features and cognitive impairment.

Method: Patients admitted to our Epilepsy Center from 1981 to 2007 with seizures onset within age 18, with a diagnosis of NFLE based on videopolysomnographic recording of one major seizure or at least two paroxysmal arousals were invited to participate. Clinical, electroencephalographical and neuroimaging data were collected. Patients underwent a neuropsychological assessment including evaluation of general intelligence (Wechsler Intelligence Scale for Children or Adults, Raven's Progressive Matrices), vigilance, attention, language, executive functions, visuospatial abilities, and psychomotor performances included in the FEPSY battery. Electroclinical and neuroimaging features were related to neuropsychological performances. Groups were compared using the Mann–Whitney nonparametric *U* test; the level of significance was set at 001.

Results: Twenty-two patients (12 males, 10 females, mean age: 29.3 years, SD = 6.2) were included. Eighty-one percent had at least one impaired test. IQ was impaired in three patients (14%) and borderline in one. Fifty-four percent showed deficits in attention tests, 41% in memory tests, 36% in vigilance, 36% in motor skills. IQ was lower in patients with diurnal and secondarily generalized seizures. Working memory was lower in patients with higher seizure frequency, secondarily generalized seizures, polytherapy with more than two drugs and ictal/interictal epileptiform discharges on EEG. Performance on the mental flexibility test was lower in patients with higher seizure frequency. Lower verbal fluency was detected in patients with ictal epileptiform discharges.

Conclusion: Vigilance, attention, memory, and motor skills are the cognitive domains most often impaired in patients with early onset NFLE. Cognitive impairment is significantly related to epilepsy severity at the time of examination.

p768

NEUROPSYCHOLOGICAL CHARACTERISTICS OF GEORGIAN-SPEAKING PERSONS WITH EPILEPSY OF DIFFERENT ETIOLOGY

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Purpose: Study aimed to investigate cognitive functioning among persons with epilepsy in Georgian-speaking population. Namely: (1) Influence of epilepsy etiology on cognitive functioning; (2) Difference in neuropsychological functioning between persons with epilepsy and non-epileptic seizures.

Participants and Methods: Six hundred twenty-two persons in two age groups (14–40; 41–65) were investigated. Among them were 218 healthy persons (control group), 139 with cryptogenic epilepsy, 35 with idiopathic epilepsy, 95 with symptomatic epilepsy and 135 with non-epileptic seizures. Benton Visual Retention Test and tasks from Luria's Neuropsychological Battery were used: 10 words verbal learning, hand motor program tasks, graphical sequence tasks, immediate and delayed recall of words' concurrent groups.

Results: 1. Persons with nonepileptic seizures differ significantly from healthy persons in all neuropsychological tasks (from $p < 0.05$ to $p < 0.001$), except graphical tasks in all ages.

2. The results of persons with nonepileptic seizures and persons with cryptogenic, symptomatic and idiopathic epilepsy differ reliably in first age group: persons with nonepileptic seizures showed better results in neuropsychological tasks in comparison to persons with cryptogenic and symptomatic epilepsy (from $p < 0.005$ to <0.001); but they had lower scores almost in all tasks despite graphical tasks in comparison to persons with idiopathic epilepsy who performed mostly on control group level.

3. By age the difference between persons with cryptogenic and symptomatic epilepsy and nonepileptic seizures was eliminated.

Conclusion: Neuropsychological investigation showed resemblance between cryptogenic and symptomatic epilepsies and this similarity is obvious with age. Some approximation in cognitive functioning by age between persons with cryptogenic epilepsy, symptomatic epilepsy and nonepileptic seizures was suggested.

p769

SPECTRUM OF ICTAL APHASIA IN TEMPORAL LOBE EPILEPSY

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Abstracts

Purpose: Ictal language abnormalities occur in language dominant temporal lobe epilepsy (TLE), but few data exist due to the difficulty of adequate ictal testing. We aim to describe ictal speech language disturbances in TLE and their anatomo-electroclinical correlations.

Method: Video-stereoelectroencephalography recordings of seizures of 10 patients with left-sided pharmacoresistant TLE were analyzed. Correlation between language disturbances and involvement of temporal lobe structures (hippocampus (H), entorhinal cortex (EC), temporal pole (TP), perirhinal cortex (PRh), posterior temporal superior gyrus (pSTG), fusiform gyrus (FG), was assessed.

Seizures were selected if: (1) ictal speech disturbance occurred; (2) conscious level permitted clinical evaluation and (3) detailed testing of language was available.

Results of ictal examination of oral and written comprehension, spontaneous speech, repetition, reading and naming were assessed where available.

Results: We analyzed 26 seizures. Oral comprehension was assessed in 73% and written comprehension in 19%. Poor fluency or speech arrest was observed in 53% and jargonaphasia in 34%. Naming was assessed in 46%, repetition and reading in 19% of seizures.

Three main patterns were observed: when mesial temporal structures plus TP were involved (9/26), no comprehension deficit was observed; anomia was constant (100%) and poor fluency occurred in 55%. When posterior temporal lateral structures were involved (pSTG) (8/26), comprehension was systematically altered and reading was preserved. When temporobasal structures were involved (FG and PRh), the main feature was jargonaphasia.

Conclusion: Different patterns of ictal aphasia in TLE were found. Impaired speech comprehension was associated with posterior lateral involvement, jargonaphasia with basal temporal involvement and anomia with temporopolar and rhinal structures involvement. Ictal examination of language function may contribute to the understanding of seizure organization.

p770
INFLUENCE OF CLINICAL AND DEMOGRAPHIC VARIABLES ON SHORT-TERM VISUAL MEMORY IN PATIENTS WITH EPILEPSY

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Purpose: Memory problems are the most widespread complaint in patients with epilepsy. The aim of the study was identification of variables influenced to short-term visual memory in Georgian population with epilepsy.

Method: In Total 506 persons, with age range 16–79 years (212 of them <30 years), admitted at Epilepsy Center of the Institute of Neurology and Neuropsychology for diagnosis of epilepsy were investigated and qualified as an having epileptic (n = 406; 186 male and 220 female; 328 with focal and 78 with generalized seizures; 102 untreated, 238 with mono- and 66 with poly therapy) or nonepileptic seizures (n = 101; 46 male, 54 female). All of them underwent neuropsychological assessment by Benton Visual Memory Retention Test (BVRT).

Results: In general, the patients with lower education level ($p < 0.01$), women ($p < 0.0004$) and patients with epilepsy ($p < 0.011$) had significantly lower BVRT scores and higher number of errors. The patients with late onset of focal epilepsy ($p < 0.0001$), patients with frequent and refractory seizures ($p < 0.01$), and subjects with longer duration of epilepsy ($p < 0.01$) had significantly lower scores in BVRT. Anticonvulsive treatment had no effect on BVRT scores.

Conclusion: Nonverbal memory deficit is often found in patients with epilepsy compare to patients with nonepileptic seizures. Focal epileptic seizures, late-onset of seizures, longer duration of epilepsy, seizures higher frequency, female gender, lower level of education are significant variables associated with short-term visual memory deficit. These criteria are considered as predictors of neuropsychological functioning of patients with epilepsy.

p771
COGNITIVE DEFICITS AFTER A FIRST UNPROVOKED SEIZURE: PRELIMINARY RESULTS

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Purpose: Several publications have indicated cognitive deficits in new-onset epilepsy. We set up this study to screen for cognitive deficits after a first unprovoked seizure and their association with cerebral lesions. Here we present the neuropsychological data of the first 25 patients.

Methods: This prospective study was approved by the local ethics board. Patients aged 18–70 years, who had a first unprovoked seizure, were tested using the Verbal-Learning-Memory-Test (VLMT), a visual learning and memory test (DCS) and a German version of the Stroop-paradigma (FWIT). Associations of pathological results with cerebral lesions in the MRI were tested for significance using chi-square tests.

Results: The first 25 patients (16 male, nine female) included in the study, were on the average 45.4 years old (SD 14 years). Twenty patients (=80%) had at least one pathological test result. Sixteen (=64%) had a pathological result in the VLMT, 8 (=32%) had a pathological result in the DCS, 5 (=20%) had a pathological result in the FWIT. Pathological results in the DCS were associated with right temporal lesions ($p = 0.04$), pathological results in the FWIT were associated with frontal lesions or subcortical arteriosclerotic encephalopathy ($p = 0.0005$).

Conclusion: Our preliminary data show that cognitive deficits are a frequent finding after a first unprovoked seizure. Three years later a catamnesis will show whether neuropsychological deficits after a first unprovoked seizure have any prognostic significance for recurrent seizures.

p772
PLEDS ON EEG DURING UNILATERAL SPATIAL NEGLECT: A CASE STUDY

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This study investigated the case of a patient showing unilateral spatial neglect (USN) with periodic lateralized epileptiform discharges (PLEDs) on electroencephalography (EEG).

Case Report: A 77-year-old right-handed man presented to the emergency unit in our hospital following a generalized tonic–clonic seizure. He was referred to our department the next day for clinical examination and interpretation of EEG results. Neurological testing, including confrontation test, yielded unremarkable results. Cognitive function was evaluated using the Mini-Mental State Examination, which provided a score 20. He could recall some items on this examination, and level of consciousness was recognized as largely clear. He could read aloud a booklet of medical information, which was not meaningful for him, but neglected sentences on the left side. In addition, when he was ordered to copy a picture of a flower, his drawing revealed left-side neglect. EEG performed at this time showed PLEDs over the right hemisphere. After 4 days, he could read the same booklet aloud without left-side neglect, and copy the flower nearly completely. PLEDs at this time had greatly reduced compared with the initial EEG. At 7 days after initial presentation, he could read and copy without PLEDs on EEG.

Discussion: To the best of our knowledge, this represents the first report of USN associated with PLEDs. Electrical stimulation of some cortical areas is known to potentially inhibit several cortical functions. In this

case, PLEDs on the right inhibited the ipsilateral area of the brain and resulted in neuropsychological deficit, in the form of USN.

p773
EXPLORING THE DIMENSIONALITY OF DIGIT SPAN

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Purpose: The Digit Span subtest from the Wechsler Scales is widely used in neuropsychological practice to measure Freedom from Distractibility or Working Memory. Some published research suggests that Digit Span forward should be interpreted differently from Digit Span backward.

Method: The present study explored the unidimensionality of the WMS-III Digit Span (forward and backward) items in a sample of heterogeneous neuroscience patients (n = 267) using confirmatory factor analysis (CFA) for dichotomous items. Unidimensionality is an assumption underlying the common practice of using parceled data, for example, subtest total scores, as the scores for factor analysis and clinical interpretation.

Results: Results suggested that four correlated factors underlie the Digit Span forward and backward items. The factors reflected presentation order and item difficulty. A simple distinction between forward and backward digit span was not observed. The model for Digit Span was then cross-validated in a seizure disorders sample (n = 223) including examination of metric invariance. Examination of invariance permits test of the precise numerical generalization of trait measurement across groups.

Conclusion: Results showed how item level modeling clarifies subtest trait composition, including the nature of hypothesized clinical dissociations and facilitates rational test scoring. The technique could be applied to unpack parcels and clarify trait composition in any neuropsychological test.

p774
NEUROPSYCHOLOGICAL TESTING IN GENERALIZED VERSUS FRONTAL EPILEPSIES

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Purpose: The difference between generalized and focal epilepsies shows a narrow border because generalized epilepsies may have EEG patterns showing frontal predominance, and frontal epilepsies may show bilateral secondary synchronies, that may look as generalized discharges. The neuropsychological assessment of both types of epilepsies may help to understand the brain dysfunction underlying epileptic condition. The aim of the study is to compare cognitive functions between patients clinically diagnosed of generalized epilepsies and patients with a clear clinical frontal onset of seizures.

Method: Twenty participants, 10 patients with focal epilepsy of frontal origin and 10 generalized epilepsy patients. Frontal epilepsies (6/4: M/F), middle age 42.3, generalized epilepsies (4/6 M/F), middle age 28.10. The studies performed were as follows: Logical Memory test I and II (WMS-III), Trail Making test A y B, Arithmetic (WAIS-III), Digit span test direct and inverse (WAIS-III), Spatial span (WMS-III), Block design (WAIS-III), Similarities (WAIS-III), STROOP test, The Wisconsin Card Sorting Test (WCST), Verbal Fluency test (phonemic and semantic).

Results: Generalized epilepsies showed significant differences in verbal and operative auditive memory, visual operative memory, auditive attentional spam, and learning tests memory subtests than the group of frontal epilepsies. For the rest of cognitive performance evaluated—Stroop test, TMTB, WCST, Verbal Fluency test (phonemic and semantic), Similarities (WAIS-III)—generalized epilepsies scored lower. The TMT-A and Arithmetic (WAIS-II were into normal range).

Conclusion: Study of neuropsychological profile in generalized epilepsies vs. frontal showed important coincidences in cognitive testing. Both epileptic group of patients performed poorly in executive function tests, but the frontal ones shower lower scores on those test, although there were no significant differences.

Poster session: Social issues/nursing I
Wednesday, 31 August 2011

p775
QUALITY OF LIFE IN EPILEPSY SUBJECTS AND THEIR CAREGIVERS – A STUDY OF 82 SUBJECTS

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Purpose: There are around 10 million subjects in India. Epilepsy may affect the quality of life of not only the subjects but also their caregivers thus causing enormous social burden. Study of quality of life in both may help in improving epilepsy care.

To study the quality of life among subjects with epilepsy as well as in their caregivers.

Method: This analysis was conducted in the ongoing study at G. B. Pant Hospital using a cross sectional design. Subjects with epilepsy of at least 1 year duration and their caregivers aged between 18 and 60 years were included. The subjects and their caregivers with co morbid neurological or premorbid psychiatric disorders, recent status epilepticus, stroke, and pregnancy, significant medical and surgical diseases were excluded from the study. Assessment was perfomed on adapted version of QOLIE 31 for epilepsy subjects and SF36 for their caregivers after obtaining permission from respective developers of these instruments.

Results: Eighty-two subjects and their caregivers were recruited. Males were 50 (61%) with mean age 25.10 years (±8.01 year). Mean seizure duration was 9.83 years. Forty-seven subjects were are on monotherapy and 35 on polytherapy. Positive family history was present in 11 Subjects. Thirty one were are students, 10 unemployed. Most common seizure type was GTCS (43 subjects) followed by partial seizure with secondary generalization in 24 subjects.

Conclusion: Polytherapy was found to be related to low QOLIE -31 score, low PCS and low MCS score.

p776
EPILEPSY IN THE ELDERLY: THE IMPACT OF EPILEPSY ON DAILY LIVING, FEARS, AND OVERALL QUALITY OF LIFE

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Abstracts

Purpose: Due to demographic change and high incidence of epilepsy in older people, the number of elderly with epilepsies is increasing. However, only few studies have investigated how epilepsy affects their quality of life (QoL) dependent on age at onset of epilepsy.

Method: In our prospective, multicenter, cross-sectional study the following groups were recruited from five centres:

Group A: 46 elderly with late onset of epilepsy (age ≥65 year, age at onset ≥65 year) Group B: 54 elderly with established epilepsy (age ≥65 year, age at onset ≤50 year) Group C: 40 younger adults with epilepsy (age ≤50 year).

Impairment in daily living, epilepsy specific fears, and overall QoL were assessed using a short questionnaire.

Results: Elderly with established epilepsy (B) reported the lowest QoL (A: 6.7, B: 5.5, C: 6.7; $p = 0.024$) and the strongest epilepsy specific fears, particularly with regard to rejection/social exclusion after seizures (A: 15.4, B: 36.6, C: 26.0; $p < 0.001$). Younger adults (C) reported a somewhat higher impairment in daily living (A: 17.9, B: 22.6, C: 27.2; $p = 0.084$) especially concerning employment ($p < 0.01$) and family/partnership ($p = 0.019$).

Stepwise regression analyses were performed to investigate how demographic variables (e.g. age), seizures (e.g. frequency) and epilepsy (e.g. age at onset) affect the aspects of QoL mentioned above. These analyses showed that postictal symptoms, seizure frequency, subjective efficacy and tolerability of antiepileptic drugs, and comorbidity were the strongest predictors. After including these predictors, age and age at onset of epilepsy had no significant or only a weak impact.

Further studies are necessary to investigate LQ in older people with epilepsy in more detail.

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p777

THE IMPACT OF SEIZURE CONTROL AND ADVERSE EVENTS OF ANTIEPILEPTIC DRUGS ON QUALITY OF LIFE IN PATIENTS WITH NEWLY DIAGNOSED EPILEPSY: A 1-YEAR OBSERVATIONAL STUDY

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Purpose: Seizure control and the adverse events (AEs) of antiepileptic drugs (AEDs) have been known as important factors to determine quality of life (QOL) in PWE. We examined the differential effects of seizure control and the AEs of AEDs on QOL in people with newly diagnosed epilepsy (NDE).

Method: We consecutively enrolled people diagnosed with epilepsy for the first time in our epilepsy clinic. We gave them several questionnaires, including Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Quality of Life in Epilepsy Inventory-31 (QOLIE-31), before AEDs intake and after 1 year of medication. Adverse Event Profile was given to measure the AEs of AEDs at 1 year. We observed the differences in QOLIE-31 overall scores with respect to seizure control and the AEs of AEDs. We also investigated the impact of affective symptoms on QOL.

Results: Sixty people with NDE completed the study. Twenty-eight people (47%) had seizure freedom during 1 year and 44 people (73%) experienced the AEs of AEDs. There were no differences of the scores of BDI, BAI, and QOLIE-31 except seizure worry between pre- and post-medication. The QOLIE-31 overall scores of people with seizure freedom were not different from those of people with no seizure freedom. On the other hand, the QOLIE-31 overall scores of people experienced the AEs of AEDs were significantly decreased compared with those of people experienced no AEs ($p = 0.003$). At the end of the study, people with affective symptoms at baseline were more likely to have poor QOL than those without affective symptoms.

Conclusion: Clinicians should concern the AEs of AEDs rather than seizure control to improve QOL in people with NDE.

p778

EMPLOYMENT OUTCOMES AFTER RESECTIVE SURGERY IN KOREAN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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Purpose: To assess the occupational outcomes of temporal lobe epilepsy surgery in Korean epilepsy patients.

Method: Adults who underwent resective surgery of the temporal lobe epilepsy between 1996 and 2006 in single tertiary epilepsy center were retrospectively identified. Change of occupational status and factors affecting employment outcome before and after surgery were analyzed in 84 patients.

Results: Thirteen patients (15.5%) were students at the time of surgery. More patients had full-time job after surgery than before (34, 47.9% vs. 50, 70.4%; $p < 0.001$). The number of jobless patients decreased significantly from the presurgery baseline (19, 26.8% vs. 9, 12.7%; $p = 0.037$). Factors that differed between patients with and without full-time jobs after the surgery were: ability to drive (38% vs. 9.5%; $p = 0.016$), education beyond middle school (80% vs. 57.1%; $p = 0.047$), postsurgical full scale IQ (103.38 vs. 89.67; $p = 0.03$), and pre- and postsurgical performance IQ (93.21 vs. 84.23; $p = 0.063$: 108.45 vs. 90.5; $p = 0.019$). None of the variables affecting postsurgical full-time job status were found to be significant upon multivariate analysis. Seizure freedom and discontinuation of antiepileptic drugs did not differ between those patients with and without full-time jobs after surgery ($p = 0.782$ and $p = 0.553$, respectively).

Conclusion: The employment status of Korean patients with temporal lobe epilepsy improved significantly after resective surgery. Work outcome appears to be related with pre- and postsurgical performance IQ, postsurgical full scale IQ, ability to drive, and education beyond middle school.

p779

MANAGING EPILEPSY WELL: SELF-MANAGEMENT NEEDS ASSESSMENT

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Purpose: Epilepsy self-management interventions have been investigated with respect to health care needs, medical compliance, depression, anxiety, employment, and sleep problems. Studies have been limited in terms of representative samples and inconsistent or restricted findings. The direct needs assessment of patients with epilepsy as a basis for program design has not been well-utilized as an approach to improving program participation and outcomes. This study investigated the perceived medical and psychosocial problems of people with epilepsy, as well as their preferences for self-management program design and delivery format.

Method: Mailed survey to 272 community-dwelling adults with epilepsy in the Pacific Northwest region of the United States.

Results: Survey response rate was 61%. The sample was primarily Caucasian and the majority of respondents reported postsecondary education attainment. Self-reported seizure frequency was high—38.5%

reported monthly or more frequent seizures. Self-reported seizure types varied, with 45% reporting generalized tonic–clonic and 35% reporting complex partial seizures. Results indicated a more psychosocially challenged subgroup of individuals with significant depressive and cognitive complaints. The issues rated highest as problems for respondents revolved around employment, seizures and stress, memory and word-finding, and sleep. The strongest predictor of psychosocial adjustment was depressive symptoms. A self-management program that involves face-to-face individual or group meetings lead by an epilepsy professional and trained peer leader for 60 min weekly was preferred. Eight sessions focused on diverse education sessions (e.g., managing disability and medical care, socializing on a budget, and leading a healthy lifestyle) and emotional coping strategies delivered on weeknights or Saturday afternoons was indicated.

Conclusion: Emotional self-management and cognitive compensatory strategies require special emphasis in self-management programs given the challenges of a large subgroup.

p780
THE IMPACT OF EPILEPSY ON THE QUALITY OF LIFE OF THE ADULT POPULATION IN IRELAND

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Purpose: To investigate the quality of life of adults with epilepsy in Ireland using the Quality of Life in Epilepsy-31-P (QOLIE-31-P).

Method: A postal questionnaire (QOLIE-31-P) along with information on the study and a preaddressed envelope were sent to 820 adults with epilepsy aged 18 years or older who are members of Brainwave, The Irish Epilepsy Association. Each questionnaire returned was scored using the scoring procedure for the QOLIE-31-P. The questions in each questionnaire were coded and computerized. Data was then entered and analyzed using the Statistical Packages for the Social Sciences 18.0 (SPSS 18.0). Descriptive statistics was used to describe and synthesis the data.

Results: The study comprises of responses from 350 (43%) adults with epilepsy in Ireland. There were more female than male respondents with the majority of women being in the age group 18–40 years and the majority of men in the age group 41–60 years. Following some exploratory analyses investigating the relationships between the various subscales of the QOLIE-31-P within this population, a statistically significant positive correlation was found between all the subscales examined for example Emotional Well-being and Medication Effects; Emotional Well-being and Overall QOL; Energy/Fatigue and Medication Effects. Stepwise multiple regression analysis found that the adults with epilepsy in Ireland who participated in this study felt that emotional well-being, social functioning, energy/fatigue and seizure worry were the areas which they felt most predicted their overall quality of life.

Conclusion: This study has created an awareness of the impact of epilepsy on the quality of life of adults with epilepsy in Ireland and has indicated a pressing need to explore preventative approaches to these impacts. The ability to live an independent life, to drive, to secure employment, to engage in social activities, to feel less anxious and psychologically well are all important aspects in the life of a person with epilepsy. Addressing the concerns of people with epilepsy would help improve the quality of life of adults with epilepsy in Ireland.

Poster session: Social issues/nursing II
Wednesday, 31 August 2011

p781
THE ATTITUDES AND PUBLIC AWARENESS TOWARD EPILEPSY IN GEORGIA

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Purpose: To assess the attitudes and public awareness towards epilepsy among adult population of Georgia.

Method: The study was conducted using a standard questionnaire "Survey of Public Awareness, Understanding and Attitudes Towards Epilepsy." Attitudes towards epilepsy and perception of epilepsy related stigma were assessed in relation to respondents' professional background, such as medical professions (physicians, nurses, pharmacists or medical students) and nonmedical professions.

Results: In total 1016 respondents (69% females; mean age – 37, SD – 14 years) were interviewed through face to face (n = 960) or online interview (n = 56). Ten percent of the respondents had medical, and the remaining respondents had a nonmedical professional background. Twelve percent of people with a medical background and 14% of those with a nonmedical background would object to their children having any relationship with a child with epilepsy. The majority of respondents from both groups would object to their children marry a person with epilepsy (82% and 79% respectively). Twenty-six percent of respondents with a medical and 19% with a nonmedical background considered epilepsy as a mental disease.

Conclusion: Epilepsy is a highly stigmatizing condition in Georgia. In some cases the attitudes towards epilepsy among medical professionals are more negative, than in other professional groups, which could be one of the major sources of epilepsy related stigma in Georgia. This underlines the importance of extensive educational activities on psychosocial aspects of epilepsy, especially among medical professionals.

p782
CLINICAL AND SOCIOCULTURAL ASPECTS OF EPILEPSY IN SIERRA LEONEAN AFRICANS

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Purpose: With an estimated 50,000 untreated people with epilepsy in Sierra Leone, the Epilspsy project was launched in 2010 to assess the clinical and sociocultural aspects of the condition in Sierra Leoneans and to offer treatment through dedicated epilepsy clinics (1).

Method: Three clinics in Freetown an nine outreach clinics countrywide have been started. Patients are seen by trained clinical personnel and a quesionnaire into demographic, clinical and sociocultural aspects completed. Patients are examined for physical and mental disability. Basic antiepileptic medication are provided and patients are reviewed at least monthly. Data on the first 980 patients seen are presented.

Results: There were 56% males and 44% females. The mean age was 22 years with 46% less than 18 years old. Mean age of onset was 12 years but in 76% of patients seizures started before 16 years. Mean delay in seeking medical care was 6.5 years with 56% presenting after 5 years of seizure onset. Forty-eight percent of school-going children discontinued schooling because of their epilepsy. Seventy-three percent of epilepsies were classified as symptomatic or probably symptomatic and 26% as primary. The etiology was unknown in 65% of cases but febrile convulsions, birth asphyxia and cerebral infections were important causes. Seventeen percent of patients had either physical or mental

disabilities. Fifty-four percent believed that epilepsy was caused by demons or witchcraft and over 75% had tried traditional treatment.

Conclusion: Epilepsy mainly affects young Sierra Leoneans and there is lack of knowledge about the condition and a reluctance to seek timely medical treatment. The belief in nonscientific etiology is probably the main barrier to access effective treatment. This has been noted elsewhere in Africa (2).

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p783
IS ATTITUDE TOWARD EPILEPSY CHANGING?

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Purpose: Epilepsy is not merely a medical illness. It is also a social stigma. We believe that a change in attitude towards epilepsy is needed for better management. We chose paramedical personnel of our hospital as a study group to see how they view epilepsy and whether their attitude towards the disease is changing.

Method: Eighty paramedical personnel (nurses, technicians and other caregivers). were selected randomly. A validated self-administered questionnaire was distributed via e-mail which tested the attitude towards epilepsy. The respondents were asked to fill the questionnaire anonymously and deposit in a drop box from where these were retrieved and the data analyzed.

Results: The mean age of the respondents was 27.9 years (Range 20–0 years). Thirty-three out of 80 responded. The male female ratio was 1:3.7. The respondents were mostly graduates. Majority (25) did not consider epilepsy to be a mental illness. Twenty-three out of 33 believed that persons with epilepsy can marry. If asked whether they would marry, or have their children marry a person with epilepsy, only 8 responded positively. Slightly more than half (18) would hire a person with epilepsy. Only 10 out of 33 felt that persons with epilepsy could be as successful as anyone else in their career.

Conclusion: The results show that attitude toward epilepsy is changing. Some wrong notions still persist. However, it must be borne in mind that the cohort studied consisted of educated young person working in a city hospital. So their beliefs may only be an indicator of the positive trend that will emerge in future and may not reflect the views of the whole society.

p784
A SURVEY OF PUBLIC AWARENESS, ATTITUDES TOWARD AND UNDERSTANDING OF EPILEPSY IN BULGARIA

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Some patients find that stigma, and discrimination against epilepsy are probably more devastating than the seizures themselves. Yet, little attention has been paid to tackle prejudice and improve the public knowledge regarding epilepsy in Bulgaria. In order to do this, the roots of the considerable social implications of the illness in Bulgaria need a better understanding. To gain the needed knowledge of the scope and nature of the misunderstanding of and prejudice towards epilepsy in the country, we conducted a nationwide representative survey of the awareness of, understanding and knowledge of epilepsy in Bulgaria.

The method was a self-administered questionnaire conducted across the country. The three areas that were investigated were:

1. ''Awareness and Familiarity.''
2. ''Attitudes (Prejudice) towards Epilepsy.''
3. ''Myths and Misunderstandings about Epilepsy.''

The findings of the study show that there is a very low level of familiarity with epilepsy. The general ignorance moreover, has become a basis for misunderstanding, myths and prejudice toward the illness amongst the population.

The research revealed a great need for a better education of the public on the nature of epilepsy, and the problems people living with the illness experience. The findings of the study will be used to inform an awareness-raising campaign in the media and schools, which the Association of Parents of Children with Epilepsy will initiate this year.

p785
FACTORS INFLUENCING MEDICATION PERSISTENCE AMONG PATIENTS WITH CONVULSIVE EPILEPSY IN RURAL AREAS OF WEST CHINA: A PROSPECTIVE STUDY

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Purpose: Interventions increasing the effectiveness of adherence may have a far greater impact on the health of the population than any improvement in specific medical treatments, especially in resource poor regions. We tried to find out factors that influence long-term medication persistence among patients with convulsive epilepsy (PWCE) in rural west China.

Method: PWCE were treated with phenobarbital in a management programme depending on local existing primary health services (Liu L et al., Epilepsy Behav. 2010, 17: 75–81). Demographic data and information on withdrawal of attendees were recorded prospectively from May 2005 to March 2010. Based on retention rate estimated by Kaplan–Meier analysis, factors influencing the persistence were analyzed with Cox's proportional hazard regression.

Results: 2,514 patients with active convulsive epilepsy were enrolled. Ninety-one patients died and 566 dropped out due to some other causes. The first three causes were migrating out of the study areas (29.5%), perception of inefficacy (26%), and nonadherence to doctor's prescription (21.4%). Nearly half of the withdrawal occurred within the first 3 months. PWCE who were aged between 15 to 30, with frequent attacks before enrollment, with poor seizure control during the study, and followed up by less experienced doctors, were at higher risk of withdrawal.

Conclusion: It suggested that in rural west China, special care should be targeted at the patients with less effective treatment, and the younger patients who were more likely to migrate out for jobs. There is also a pressing need to provide sustained supports to local health workers for the long-term management.

p786
WHAT HAPPENS IN YOUR BRAIN WHEN YOU SEE AN EPILEPTIC SEIZURE?

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Purpose: To identify brain areas activated with the visualization of a generalized tonic–clonic seizure.

Method: Six young women with a mean age of 26 years old from our lab participated in this study. We acquired fMRI images with a 3T MRI scanner (Philips, Achieva, Holland) using a TR = 2 s, TE = 30 ms, 40 axial slices, with a 3 mm slice thickness. We used a block paradigm

(four OFF = 10 s of a blank screen; and three ON = 69 s: video of a seizure). The fMRI statistical and analyses were performed using the Statistical Parametric Mapping (SPM8). All volumes were slice time corrected, realigned to the middle volume, corrected for motion artifacts, normalized into standard stereotactic space, and smoothed using an 8 mm full-width at half-maximum (FWHM) Gaussian kernel. The time series were high-pass filtered (filter width = 128 s) and adjusted for systematic differences across trials. Individual maps of activations were generated using voxel based analysis. Next, second-level analysis was used to generate maps of the group using one sample *t*-test, with p-value < 0.001.

Results: The group analysis showed significant difference between OFF and ON states in the limbic system, including amygdala, parahippocampal gyrus, cingulate gyrus; and frontal lobe, parietal lobe and insula. After the exam, five subjects stated that video caused an uncomfortable feeling.

Conclusion: Convulsion appears to have a negative emotional attribute with activation of limbic system including amygdala, which is related to the initial emotional response. This data reinforces that fear and be one of underlying stigma factors towards people with epilepsy.

p787
TOGETHER WE ARE STRONGER—COLLABORATION BETWEEN IBE AND ILAE LOCAL CHAPTERS IN RAISING AWARENESS ABOUT EPILEPSIES

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Purpose: Proper information about epilepsies should be available for citizens and the media by using modern technology.

Method: Finnish Epilepsy Association (FEA, Chapter of IBE) and Epilepsy Society (FES, Chapter of ILAE) enhanced collaboration in producing modern material to raise awareness. The role of FEA was to bring out the perspective of the person with epilepsy (PWE). The role of the FES was to provide up-to-date medical information and popularize scientific results.

Results: A TV documentary with three different stories of PWE. Besides the personal experiences facts about their epilepsy syndromes are described. The document has been disseminated to the epilepsy clinics to use in educating PWE/family members. The FEA use the document in voluntary activities. Five hundred copies of the document have produced. Three thousand citizens have seen the document. The aim is to show it in the Finnish National TV. The Finnish epilepsy portal (www.epilepsia.fi), launched in 2009, gathers basic information of the illness, care, support and aid available. In addition there is epilepsy news from Western Europe. The aim of the portal is to give information and support to PWE. Furthermore the portal is an electric channel for the FES to inform professional activities. The portal is an effective way to provide many sided epilepsy information to all 24/7. There was about 70 000 visits in 2010 in the portal. A facebook link was built 2011 and it further increased the visits and communication.

Conclusion: Unifying knowledge of the IBE and ILAE chapters strengthens both organizations as a part of civil society and their lobbying for equality of PWE. The document (subtitles in English) and the portal will be demonstrated in the poster presentation.

p788
E-MAIL PUBLICATION "EPILEPSY DISASTER" DURING THE FIRST 2 WEEKS OF THE CATASTROPHIC EARTHQUAKE AND TSUNAMI IN THE TOHOKU DISTRICT, JAPAN

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Purpose: A catastrophic earthquake and tsunami occurred on March 11 (Day 0) in the Tohoku district, on the northeast coast of Japan. Roughly 28,000 people are dead or missing, 3000 were injured, and 200,000 were obliged to move to evacuation centers. Many evacuated people with chronic diseases, including epilepsy, were abruptly deprived of their medications due to the sudden nature of the disaster, which occurred over a huge area including more than 600 km of coastline, and resulted in severe disruptions to the transportation system and critical shortages of gasoline. This report describes our use of e-mail bulletins to tackle the problems with the epilepsy treatment system during the first 2 weeks of the disaster.

Method: The Department of Epileptology, Tohoku University published 20 e-mail bulletins entitled "Epilepsy Disaster" from Day 6 to Day 14, which were sent to 239 subscribers including all members of the Tohoku Epilepsy Society, executive staff of the Japan Epilepsy Society (JES), some officials of the Ministry of Health, Labor and Welfare (MHLW), executive staff of pharmaceutical companies, and media representatives. The bulletins covered medical wish lists of hospitals in the devastated areas, summaries of daily briefings at the disaster countermeasures office in Tohoku University Hospital, daily reports from various disaster medical assistance teams, and official as well as unofficial comments from MHLW officials, JES executives, and pharmaceutical companies. All the information was freely and repeatedly transferred through the many subscribers and various types of media. The authors tried to select the topics carefully and to edit news accurately to encourage only positive responses.

Results: Quick matches were made between medical wish lists in the hospitals and drug providers. MHLW officials quickly issued several instructions to promote efficient drug delivery. Many antiepileptic drugs donated by JES member hospitals and pharmaceutical companies were delivered to the affected hospitals earlier than the recovery of the supply system of wholesale dealers. Consequently, only a few patients suffered status epilepticus in the affected area.

Conclusion: E-mail bulletins can be useful in medical emergencies caused by major and unprecedented disasters. Further verification will follow since this abstract was submitted on Day 20 after the disaster.

p789
TUMOR—A GRAPHIC NOVEL REPRESENTATION OF GLIOBLASTOMA MULTIFORME AND MULTIPLE SEIZURE TYPES

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Purpose: To review the representations of multiple seizures types presented as sequential art in the graphic novel *Tumor* (Fialkov, J. H. and Tazon, N., Archaia Entertainment, 2010).

Method: *Tumor* was a graphic novel published in 2010 in which a private investigator is diagnosed with a glioblastoma multiforme, while solving a crime, and presents with varied types of seizures and other associated symptoms, such as confusional state and space-time disorientation. All of these symptoms are presented in graphic form from the standpoint of the main character/patient, thus providing a layman's interpretation of seizure semiology.

Results: By analyzing the different seizure types graphically represented during the course of the story, reproduced with permission of the main author, one can have a portrait of semiologic features from the main character/patient's viewpoint. Seizure types include simple partial sei-

zures, complex partial seizures, jamais vu, uncinated seizures, secondarily generalized seizures, as well as other symptoms, such as time-space disorientation and confusion, among others.

Conclusion: In *Tumor*, a detective graphic novel, the main character is diagnosed with glioblastoma multiforme and throughout the story manifests with different types of seizures, which are graphically represented from a layman's perspective.

Poster session: Social issues/nursing III
Wednesday, 31 August 2011

p790
AN INVESTIGATION INTO THE PLACE OF MUSIC IN THE FIELD OF EPILEPTIC ART

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Purpose: To investigate the hypothesis that the artistic medium of music is highly underrepresente and researched in the field of epileptic art in comparison with other media.

Method: In researching the literature on epileptic art, several media were identified: painting and the visual arts, literature and choreography. Only two examples were found on music and epilepsy. Evidence was gathered from a geographically, culturally and socially diverse sample of theorists and practitioners in music, epileptic art, disability arts, and neurology. A body of source material was compiled for analysis in which the interaction of music and the epileptic experience was evident. Twenty three examples were identified.

Results: Music's lack of recognition as a medium for aesthetic expression of epileptic seizure and related issues was identified. Unlike the trend suggested in other epileptic art media, many of the musical examples were by nonepileptics, using epilepsy as a metaphor, rather than exploring personal experience. This outcome led to the composition of twenty musical pieces that directly communicate my own condition as an epileptic. In order to raise the profile of music as an epileptic art, these pieces were recorded as part of the *Ictal Variations Project* (Stoker, G. 2010), and a website constructed (Project MEA).

Conclusion: The initial hypothesis that the role and significance of music in epileptic art is undervalued was confirmed by the lack of comparative research to other media, and my own status as an epileptic artist was affirmed.

p791
EPILEPSY AND THE OLYMPICS

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Purpose: Little more than 30 years ago many physicians believed that epileptic patients should not be involved in any sport especially collision sports such as football and hockey. This was because epilepsy was regarded as an illness and all illnesses required rest!

Method: Many people with epilepsy are shown to have a poorer level of self-esteem leading to higher levels of anxiety and depression. In 1941 Lennox claimed that "Physical and mental activity seems to be the antagonist of seizures. Enemy Epilepsy prefers to attack when the patient is off-guard, sleeping, resting or idling."

In Africa and Asia there remains a stigma associated which prevents people from taking part in sports. This is due to fear of embarrassment if seizures were to occur in public places. In Malaysia recent studies showed that only 67% were willing to exercise together with a person with epilepsy.

In Norway studies showed that people with epilepsy exercised more in confined areas rather than in public places.

Results: There is a long way to removing these barriers but a periodic health evaluation (PHE) of elite athletes was published by the International Olympic Committee (IOC) in March 2009. This stated that the main purpose of the PHE was "to screen for injuries or medical condition that may place an athlete at risk for safe participation." The report regarding neurological conditions suggests that any athletes with a history or currently suffering from any symptoms of diseases of the nervous system must undergo an in-depth assessment.

The only sport restrictions on epilepsy are scuba diving, sky diving and possibly boxing and martial arts. Sports involving heights may require an individual assessment first.

Conclusion: There is no reason why a person with epilepsy should be excluded from the participation in sport as long as the necessary precautions and assessments are taken. Most sports and exercise have been proven to reduce seizure activity and improve the quality of life for many with epilepsy.

p792
DEATH AND RESURRECTION: THE PARADIGM OF EPILEPSY IN CHRISTIAN PAINTING

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Purpose: To show how the experience of—transient—death in epilepsy is viewed in Western cultural tradition and Christian painting.

Method: Evaluation of patients self-reports, philosophical background, arthistory and iconography based on search of the "Princeton Index of Christian Art."

Results: A transcultural approach shows that the epileptic seizure is in many different cultures linked to the idea of death. Death is perceived in indoeuropean tradition more as a stage than an end point. In Christian interpretation, one might be ressucitated after a seizure. This point of view is has its origins in the myth of Demeter and Persephone and, most importantly, in the destiny of Jesus Christ, being himself ressucitated. In Raffaellos last painting, the "Transfiguration," the individual destiny of the son of God and the epileptic boy in—figured in the shape of a chrismon—is presented by intermingeling their both, opposed and at the same time similar fate (death and resurrection).

Conclusion: In the "Transfiguration" culminates a longstanding iconographic tradition of the biblic gospel of the epileptic boy. In Raphael's vision of Italian renaissance, the young epileptic boy represents in his oscillatory relationship with Jesus a metaphor of the Passion, of the end and also of the resurrection of Christ. United in their opposed and yet similar fate, the son of God is tinted with human experience—and the epileptic son with a divine one.

p793
HAND OVER HAND: IMAGES OF ATHLETES AND PEOPLE WITH EPILEPSY

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For someone with epilepsy, the sporting achievement of a lifetime may be a personal best which others would hardly give a passing nod to. Imagine the elation of a young person with epilepsy who has held the hand of an Olympian. Imagine the hope for a young person with epilepsy who has not, but can see an Olympian's hand extended towards him and others like him.

The public image of epilepsy is often wide of the mark, mistakenly emphasizing its rarity and its negative traits of disability, social

exclusion, and educational, employment and sporting nonparticipation. The ILAE and IBE recently demonstrated how sport can educate as well as inspire (Press Book of the UEFA European Under-21 Football Championship Finals). The cooccurrence in London of the 2012 Olympics and the 2012 European Congress on Epileptology (ECE) offers an unrivalled opportunity to raise public awareness of epilepsy and to break down the barriers of the prejudice, ignorance and superstition surrounding epilepsy.

We plan to assemble high-quality photographs of young people with epilepsy in a sporting context with world athletes, to demonstrate the potential for full participation in sport by people with epilepsy. We are seeking the 2012 Olympic ''Inspire'' logo to support this work and expect to display the images at London's ExCel Centre—an Olympic venue and location of the 2012 ECE—during the 2012 Games and during the 10th ECE. These active sporting images have potential to make an unparalleled positive impact on the world public image of epilepsy.

p794
CHANGES IN KNOWLEDGE OF EPILEPSY AND ATTITUDES TOWARD PEOPLE WITH EPILEPSY IN ADOLESCENTS IN CROATIA

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Purpose: To survey changes in knowledge of epilepsy and attitudes toward people with epilepsy (PwE) in adolescents in Croatia.

Method: In 2010 the survey was carried out among students of IX. Gymnasium in Zagreb with the questionnaires which had already been used in 2002.

Results: In 2002, 227 high school students completed the questionnaire and in 2010 203 (mean age 17.34 ± 0.66 vs. 17.02 ± 0.74 years). In 2010, 6 months before the survey, 70.6% of respondents participated in the manifestations of Purple Day, which is dedicated to epilepsy destigmatization. The knowledge of epilepsy was evaluated on grounds of six questions with the correct and incorrect answers. The mean number of correct answers in 2002 was 4.54 ± 1.03 vs. 4.80 ± 1.02 in 2010 ($p < 0.05$). Attitudes toward people with epilepsy were examined in three categories: 1) their young relatives playing with children with epilepsy – without prejudice in 2002 97.4% vs. 98% in 2010 (NS), 2) marriage between their loved ones and PwE – without prejudice in 2002 86.3% vs. 94.1% in 2010 ($p < 0.05$), 3) ability of PwE in performing most of the jobs – positive attitudes increased from 68.1% in 2002 to 82.8% in 2010 ($p < 0.01$).

Conclusion: Our results indicate positive changes in knowledge of epilepsy and attitudes toward PwE during the period of the last eight years. We believe that these favorable changes might be influenced by intense media activities in this period as well by school activities during the manifestations of Purple Day performed 6 months before polling.

p795
EPILEPSY AND THE SCHOOL ENVIRONMENT

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Purpose: The proposed study examines the classroom experiences of students with epilepsy (SWE), prompted by common academic underachievement in the population. Research suggests that disorder characteristics are only partial predictors of achievement. Psychosocial effects of epilepsy, such as perceived stigmatization, have been investigated as potential predictors of achievement, but little research has directly examined the perceptions of SWE regarding educational or stigma-related experiences. This study begins to fill the research gap.

Method: We will examine the following research questions: How does perceived stigma relate to classroom interactions among SWE? To what extent are SWE experiencing their desired level of support and autonomy in the classroom? What is the relationship between solicited/unsolicited interactions, perceived autonomy and the reported effort and competency ratings of SWE?

To address these questions, we will collect quantitative and qualitative data from SWE using online questionnaires. One-time measures of perceived stigma will be captured initially, followed by 2 weeks of daily diary measures examining perceived classroom interactions and stigma.

Results: We anticipate that higher discrepancies between desired support and autonomy and actual experience will relate to lower reported effort and competency. Additionally, we expect those with higher discrepancies to report higher levels of perceived stigma. Reflective diary responses may highlight more nuanced relationships.

Conclusion: SWE often have the academic ability to succeed in school but do not fulfill their potential. This in-depth study may help to elucidate the needs of SWE in the classroom, and highlight avenues for improving their educational experiences and outcomes. Findings will be discussed at the conference.

p796
THE MANAGING EPILEPSY WELL (MEW) NETWORK

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Purpose: The Managing Epilepsy Well (MEW) Network is composed of individuals interested in the care of people with epilepsy. MEW Network members are representatives from universities in the United States, community-based organizations, and the U.S. Centers for Disease Control and Prevention. The mission of the MEW Network is to advance the science related to epilepsy self-management by facilitating and implementing research, conducting research in collaboration with network and community stakeholders, and broadly disseminating the findings of research.

Method: Consistent with its mission, MEW Network members from four universities in the United States (Emory University, University of Washington, University of Texas Health Science Center at Houston, University of Michigan) are developing and testing self-management models and tools appropriate for the full spectrum of epilepsy. Programs that are currently being tested include a community-based self-management program, a program to strengthen social support for people with epilepsy, and a decision-making support system for the clinical setting.

Results: The Network is currently disseminating an online epilepsy self-management tool (WebEase) and two programs for addressing depression in people with epilepsy (Project UPLIFT and PEARLS). Pilot testing of these programs has demonstrated improved medication adherence and a reduction in depression among people with epilepsy.

Conclusion: The MEW Network programs are increasing the number and variety of self-management support options available to people with epilepsy.

p797
HIPPOCRATIC CORPUS: ON THE SACRED DISEASE

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Purpose: The Hippocratic Corpus consists of approximately 60 medical texts. They are all written in the Ionian dialect and are attributed to the father of medicine, Hippocrates, and his students. ''On the Sacred Disease'' is considered to be the most interesting work of the collection. The present study aims to describe and analyze the Coan medical school

theory regarding the genesis, presentation and forms of epileptic seizures.

Method: Our effort is to provide insights into the concepts on epilepsy, as they are described in the ancient text and reflect the spirit of that distal era, which we consider remarkably similar to the modern perception of the condition.

Results: If someone does not take into consideration the theory on the etiology of the disease (theory of body humors) and the recent synthetic pharmaceutical products used for its treatment, the description of the epileptic attacks, their classification and the importance of heredity constitute real scientific facts, whose immense importance had been realized as early as Hippocrates' era and continue to be valued up to the present.

Conclusion: A distinction between religion, magic, and science has not always been recognized. ''On the Sacred Disease'' is considered to be a landmark in the history of medicine and European science, since it constitutes an expression ''of the constant battle of scientists against superstitions, moria and shameful fraud.''

p798

WHY ARE EPILEPTIC PEOPLE STIGMATIZED, REJECTED FROM SCHOOLS, AND CONSEQUENTLY DEPRIVED OF DECENT EDUCATION WHILE SPECIAL EDUCATIONAL NEEDS STUDENTS ARE ACCEPTED? ARE COGNITIVE PROBLEMS EASIER TO ACCOMMODATE IN SCHOOLS THAN EPILEPSY SEIZURES?

Al Assi N

Association for Care of People with Epilepsy in Lebanon, Saida, Lebanon

Purpose: To find solutions for a socially disadvantaged group.

Method: Action and field research.

Results: The current sources of income are not enough to support epileptic people we have reached, neither are they enough to launch a new project.

Conclusion: Without recognition from the Ministry of Education and without societal support, epileptic people will always be disadvantaged.

Abstract: The Association for Care of People with Epilepsy in Lebanon was established in 2001 and has ever since been run by the president and a team of volunteers. Characterized by openness, creativity and endless efforts, they tried a number of projects through which knowledge could be spread, funds raised and consequently epileptic people supported. In the first four years, the Association did research, started the handcrafts project, and could reach 521 epileptic individuals and support them medically. With time, experience and good assessment of the market needs, the Association decided that two projects be its basic sources of income and possible donations: (1) making accessories and (2) chocolate moulding and wrapping. Now, more socially acknowledged yet still not supported by the Ministry of Social Affairs, the Association's mission ''to do research, identify epileptic individuals, support them medically and spread knowledge about epilepsy'' has become ''to support epileptic patients medically, socially and technically so they would become independent and productive social entities, in addition to offering their parents training on handcrafts, offering jobs, and supporting them educationally and psychologically.'' The Association's three remaining problems are (1) lack of funds to complete the research and create a complete data bank about epileptic people in Lebanon to make the case stronger in the Ministry of Education, (2) lack of funds for awareness campaigns to spread knowledge more widely, and (3) society's and schools' persisting attitude toward epileptic people the thing that contributes to sustaining the stigma and depriving those individuals of decent education. What are the solutions?

Poster session: Drug therapy V
Wednesday, 31 August 2011

p799

EFFICACY AND SAFETY OF PERAMPANEL AS ADJUNCTIVE THERAPY IN ADOLESCENTS WITH REFRACTORY PARTIAL-ONSET SEIZURES: ANALYSIS OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE III STUDY

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Purpose: Adjunctive use of perampanel, an orally active, highly selective, noncompetitive AMPA receptor antagonist, in adolescents and adults with refractory partial seizures is under evaluation in multinational trials. We report efficacy and safety data for the adolescent subpopulation (<18 years-of-age) participating in a pivotal phase III study (Clinical Trials.gov identifier: NCT00700310).

Method: Patients aged ≥12 years with refractory partial seizures receiving 1–3 concomitant antiepileptic drugs completed a 6-week baseline period and were randomized to once-daily oral perampanel (2, 4 or 8 mg) or placebo (6-week titration; 13-week maintenance). Primary end point was percentage change in 28-day seizure frequency (double-blind phase vs. baseline). Other assessments included responder rates (patients with ≥50% reduction in seizure frequency) and adverse events (AEs).

Results: In the overall study intent-to-treat population (n = 693), median seizure-frequency change with placebo and 2, 4 and 8 mg perampanel, respectively, was −10.1%, −14.1% ($p > 0.05$ vs. placebo), −24.0% ($p < 0.001$), and −31.3% ($p < 0.0001$). In adolescents (n = 60), median changes were 4.6% (n = 14), 12.8% (n = 21), −23.9% (n = 13), and −34.6% (n = 12). Overall responder rates were 17.6%, 20.9% ($p > 0.05$), 28.6% ($p = 0.009$), and 34.9% ($p < 0.001$). Adolescent responder rates were 14.3%, 4.8%, 23.1%, and 33.3%. AEs were experienced by 64.3%, 71.4%, 61.5% and 58.3% of adolescents. The most common AEs in perampanel-treated adolescents were nasopharyngitis, dizziness and somnolence. Serious AEs and AEs causing discontinuation occurred infrequently in adolescents and were more common with placebo.

Conclusion: Perampanel was similarly efficacious in adolescents as in adults, although the adolescent sample size was small. Perampanel was well tolerated in adolescents. Further analyses using pooled phase III data are planned.

p800

EFFICACY AND TOLERABILITY OF LACOSAMIDE AS ADD-ON THERAPY IN PATIENTS WITH TREATMENT-RESISTANT EPILEPSY. PRELIMINARY EXPERIENCE AT A TERTIARY CENTER IN CYPRUS

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Purpose: To investigate the efficacy and tolerability of lacosamide as add-on therapy in Cypriot patients with refractory epilepsy.

Method: Thirteen adult patients with focal onset epilepsy, ages between 19 and 68 years, four males, nine females, were studied retrospectively for 6 months. Patients received lacosamide as add-on therapy to 2–5 (average 3) antiepileptic drugs (AEDs). Mean seizure frequency was compared for a 3-month period prior to and 6 months after lacosamide

introduction. All subjects had physical, neurological and hematological evaluations at entry and at 6 months after introduction of Lacosamide.

Results: One patient (7.7%) became seizure-free. Two patients (15.4%) had seizure reduction by 75% or greater. Three patients (23.1%) had seizure reduction by 50% or greater. Three patients (23.1%) had no significant change from baseline or became worse.

Four patients (30.8%) discontinued lacosamide treatment for lack of efficacy (15.4%), side effects (7.7%) or both (7.7%).

Reported side effects were: behavioral side effects (15.4%), insomnia (15.4%), ataxia (7.7%), tremor (7.7%), nausea/dizziness (7.7%) and headache (7.7%). No patient showed significant changes from baseline hematological, urinary or biochemical parameters.

Conclusion: Our study indicated that lacosamide was effective even in our selection of highly pharmacoresistant patients with focal onset epilepsy. 46.1% of our patients experienced seizure reduction of ≥50% sustained for 6 months, with 69.2% of patients continuing treatment. Lacosamide was also well tolerated by the majority of our patients. Further studies are needed in order to establish the long-term safety and efficacy of lacosamide in our population.

p801
EFFICACY AND TOLERABILITY OF ZONISAMIDE IN OUTPATIENT CLINICAL PRACTICE

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Purpose: The different pharmacological actions of zonisamide (ZNS) may contribute to reduced rates of seizures in clinical practice similar to those observed in controlled studies. We wanted to study the ability of ZNS to control refractory epilepsy and assess possible clinical factors related to treatment response.

Method: Prospective, observational study including outpatients with epilepsy drug-resistant. There were 106 patients (51 women, 55 men) with a median current age of 44.50 years and a median duration of epilepsy of 24 years.

Results: Ninety-one percent had focal seizures and etiology was symptomatic in 60% and probably symptomatic at rest. Treatment with ZNS, which remained a median of 20 months, seizure frequency was reduced by 50% over 58% of patients (30% noncrisis) and was similar or worse in the remaining 42%. Sixty percent stayed with ZNS at the time of the study and the rest had been withdrawn due to adverse effects (9%) or lack of efficacy (31%). We analyzed the relationship between any clinical variable and the better or worse response to ZNS. There was greater proportion of patients without seizures in patients over 60 years at onset of epilepsy (p 0.02) and those without risk factors for epilepsy ($p < 0.001$).

Conclusion: Zonisamide as adjuntive therapy is an effective, safe and well-tolerated long-term treatment in refractory patients. The onset of epilepsy after 60 years and absence of risk factors for epilepsy are good-prognostic factors.

p802
A CLINICAL STUDY METHOD USED TO EVALUATE THE EFFICACY AND SAFETY OF NOVEL ANTIEPILEPTIC DRUG ESLICARBAZEPINE ACETATE IN EPILEPTIC CHILDREN WITH PARTIAL-ONSET SEIZURES

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p803
EFFICACY AND TOLERABILITY OF ADD-ON LACOSAMIDE IN PATIENTS WITH CHILDHOOD ONSET PHARMACORESISTANT FOCAL EPILEPSY

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Purpose: To evaluate efficacy and safety of add-on lacosamide in patients with drug-resistant focal epilepsy with pediatric onset.

Method: In this retrospective, observational study we selected 12 subjects ranging 16–38 years (mean 20), with drug-resistant focal epilepsy with childhood onset. Lacosamide has been titrated up to 6.5 mg/kg/day, and all the patients have been followed up for 6 months. Patients have been considered responders if seizures frequency reduction was over 50%. Tolerability has been evaluated recording transient and persistent side effects, and eventual dropout.

Results: All subjects presented focal seizures with or without secondary generalization. Eight patients presented 2–4 seizures per week, while the other four subjects presented 1–3 seizures per day. Etiology remained unknown in five patients (41.7%). Sequelae of hypoxic-ischemic damage were present in three subjects (25%), focal cortical dysplasia in three (25%), and tuberous sclerosis complex in one (8.3%). All subjects but two, presented mental retardation: mild in 4, moderate in 5 and severe in 1. At the baseline all subjects were under antiepileptic polytherapy, which remained unchanged during the study course. After 3 months, responders were 66.7%; the total responder rate at 6 months was 45.4%. Fifty percent of patients experienced transient side effects (irritability, somnolence) in the titration period. These same adverse events persisted in four patients (33.3%). Treatment was discontinued due to lack of efficacy (six patients), or due to side effects (vertigo, nausea and vomiting).

Conclusion: Add-on lacosamide appeared to be efficacious and well tolerated in our group of patients with drug-resistant focal epilepsy.

p804
EFFICACY AND TOLERABILITY OF LACOSAMIDE AS ADD-ON IN CHILDREN AND YOUNG ADULTS AFFECTED BY DRUG-RESISTANT FOCAL EPILEPSY

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Purpose: Lacosamide (LCM) is a new antiepileptic drug acting on selective enhancement of slow inactivation of voltage-gated sodium channels. The aim of the study is to evaluate LCM in add-on in patients with drug-resistant focal epilepsy in terms of its effects on seizure control and tolerability.

Method: We enrolled 10 patients, between 6 and 29 years old, who had refractory epilepsy, due to hypoxic-ischemic encephalopathy, cortical dysplasia, tuberous sclerosis, Aicardi syndrome. Epilepsy type consisting of Lennox-Gastaut syndrome, focal symptomatic and cryptogenic epilepsy. Neurological examination, EEG, ECG, and plasmatic levels of AED were performed before and after beginning LCM treatment. The efficacy was calculated in relation to seizure frequency reduction using parents' diaries. Those patients only completing at least 3 months of LCM treatment (including titration) and kept a monthly seizure diary were included.

Results: LCM dose ranged between 200–400 mg in twice daily. The follow up ranged from 6 to 8 months. Diplopia, nausea and dizziness were side effects reported in two patients during the titration period in add-on with carbamazepine or oxacarbazepine. Side effects disappeared reducing the LCM dose or the associated AED. At the end of the follow up, seizure frequency reduction was of 75% in three patients affected by focal

symptomatic epilepsy and of 50% in four patients affected by cryptogenetic form. No clinical impairment was observed in the other patients.

Conclusion: Our preliminary data suggest that LCM in add-on is safe and efficacy in reducing seizure frequency in patients with refractory focal epilepsy.

p805
EFFECTIVENESS AND TOLERABILITY OF RUFINAMIDE IN CHILDREN AND YOUNG ADULTS WITH LGS: PRELIMINARY DATA IN KOREA

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Purpose: Rufinamide is a new antiepileptic drug (AED), which is known to be effective in the treatment of partial seizures and drop attacks of Lennox-Gastaut syndrome (LGS). The aim of this study is to evaluate the efficacy and tolerability of rufinamide in patients with LGS.

Method: Patients with LGS who had received rufinamide adjunctive therapy, between April 2010 and December 2010, were enrolled in this study. We retrospectively reviewed these patient's baseline clinical characteristics, reduction of seizure frequency after the use of rufinamide, and adverse events.

Results: Twenty-three patients (15 males and eight females, ages from 4 to 22 years) were enrolled in the study. All of the patients suffered from daily head drops and tonic seizures despite multiple antiepileptic drugs (mean 3.6 AEDs before the use of rufinamide). Twelve patients (52.1%) had history of epilepsy surgeries (nine callosotomy alone, three callosotomy as well as vagus nerve stimulation). After a mean period of 4 months of rufinamide, one patient (4.3%) achieved seizure freedom, 9 (39.1%) achieved a > 50% decrease in seizure frequency, and 6 (26.0%) patients achieved a < 50% decrease in seizure frequency. Adverse events were reported in four (17.3%) patients, which were aggressive behavior in one, aggravation of seizure in one, and somnolence in two patients.

Conclusion: Although it is a preliminary result, rufinamide was effective and well-tolerated in children and young adults with LGS.

p806
EVALUATION OF EFFICACY, TOLERABILITY AND ADVERSE EFFECTS OF THE ANTIEPILEPTIC DRUG LEVETIRACETAM IN CHILDREN AND YOUNG ADULTS

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Purpose: Levetiracetam is a relatively new antiepileptic drug. In Israel, it has been authorized for use as an add-on therapy for intractable epilepsy since May 2006. Adverse effects are mainly behavioral. The purpose of this study was to document the efficacy of Levetiracetam, facing its side effects profile, in a series of children and young adults with intractable epilepsy.

Method: This was a single-center, add-on, open label treatment study. We reviewed the medical files of 78 children and young adults aged 0.5–39 years (mean age 1.426 years) treated in the epilepsy clinic at Schneider Children's Medical Center for refractory disease. We also conducted telephone interviews and liaised with the caring physician. The study group was heterogeneous and included patients with partial epilepsy (67%) and generalized epilepsy (33%). Most of the patients (57%) had symptomatic epilepsy, 15% had idiopathic epilepsy and 27%, cryptogenic epilepsy. Levetiracetam was used as an add-on therapy in those who had failed to respond to at least three other antiepileptic drugs. Average age for first seizure was 4.1 years.

Results: Levetiracetam reduced seizures by half in 45% of patients. Complete remission was achieved in 11.5% of patients. There was a positive correlation between clinical and electroencephalographic improvement, which was statistically significant (p = 0.0012). The drug was well tolerated with a retention rate of 69% after one year. The most common adverse effect was nervousness in 32% of patients. Severe side effects (psychosis, confusion) was experienced in 6.4%.

Conclusion: Levetiracetam was found to be effective and tolerable in most patients who had not responded to at least three other antiepileptic drugs. Although the drug was well tolerated, a relatively large percentage of behavioral side effects was observed (6.4%), some requiring the cessation of treatment. Nevertheless, the retention rate at 1 year was high (69%). Levetiracetam is the treatment of choice for refractory epilepsy in children and adolescents.

p807
EFFICACY OF ADD-ON RUFINAMIDE IN CHILDREN AND YOUNG ADULTS WITH DRUG-RESISTANT FOCAL EPILEPSY

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Purpose: To evaluate efficacy and safety of add-on rufinamide in drug-resistant focal epilepsy beginning during childhood.

Method: In this observational, retrospective study we selected 40 patients, ranging 3–33 years of age (mean 10.7), with drug-resistant focal epilepsy with childhood onset. At baseline, 38 subjects were under polytherapy, monotherapy was present only in 2. Rufinamide has been titrated up to 20–40 mg/kg/day. Patients with seizure reduction over 50% have been considered responders. Side effects have been recorded to evaluate tolerability. All subjects underwent periodical clinical and instrumental assessments.

Results: All patients presented motor focal seizures; 31 of whom with secondary generalization (MFsG). Twenty-six patients presented one to three seizures per day, while 14 presented 2–5 seizures per week. EEG showed epileptiform abnormalities: focal in 23 patients, multifocal in 17. Fourteen patients presented cortical dysplasia, seven encephalitis sequelae, six porencephalic lesions, four chromosomal abnormalities, one hypothalamic hamartoma; in eight patients etiology remained unknown. Only five subjects were cognitively adequate. After 6 months four subjects were seizure-free (10.26%), with a total responder rate of 56.41%; while at 12 months follow-up three subjects (7.69%) were seizure-free, with a total responder rate of 46.15%. MFsG showed better results, while no efficacy was observed in myoclonic jerks. Four patients (40%) discontinued Rufinamide because of side effects: seizures exacerbation in two subjects, and vomiting and behavioral disorders in the other two.

Conclusion: Add-on rufinamide appears to be efficacious and well-tolerated in drug-resistant focal epilepsy, with a major efficacy in MFsG.

p808

EFFICACY, TOLERABILITY AND QUALITY OF LIFE IN ADD-ON TREATMENT OF ZONISAMIDE IN ADULTS PATIENTS WITH EPILEPSY

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Purpose: Noninterventional, multicenter, observational study to evaluate perceived efficacy, safety, patient satisfaction and titration schedules when starting zonisamide (ZNS) as adjunctive therapy in adult patients with partial epilepsy in a real life setting.

Method: Collection of clinical data of adult patients requiring treatment with ZNS using standardized questionnaires. Data on treatment history, titration schedule, dosing of different AEDs, most commonly expected adverse events, outcomes, information on patient's satisfaction and perceived efficacy after 3 months therapy were evaluated.

Results: Thirty-three women and 38 men (mean age of 41 years) with a mean epilepsy history of 22 years, receiving on average seven previous AEDs were enrolled. Most used AEDs before starting ZNS treatment were 59% lamotrigine (LTG), 39% valproic acid (VPA), 21% carbamazepine (CBZ) and levetiracetam (LEV). Mean daily ZNS dose (maintenance phase) was 254 mg (o.d. in 8%, b.i.d. in 92% of patients). Data on 49 patients (69%) were evaluable for a treatment period ≥3 months: 17 (35.4%) showed an amelioration of symptoms, ≥50% reduction in seizure frequency was achieved in 18 (37.5%), and seven patients (14%) were seizure-free. The frequency of adverse events did not increase after ZNS initiation. Patient satisfaction was improved in 29 (59%) patients, unchanged in 15 (31%), and worsened in 5 (10%). Forty patients (82%) continued ZNS treatment after 3 months.

Conclusion: Zonisamide as adjunctive therapy showed a favorable efficacy and tolerability profile, and improved patient satisfaction.

p809

EFFICACY, TOLERABILITY, AND PHARMACOKINETICS OF OXCARBAZEPINE ORAL LOADING IN EPILEPSY PATIENTS

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Purpose: The rapid achievement of therapeutic levels of antiepileptic drugs (AEDs) is required in epilepsy patients with a higher risk of seizures, and oral loading of AEDs may be an important consideration in these patients. We performed the present study to investigate the safety and tolerability of oral loading of oxcarbazepine in patients with recurrent seizures, or after temporary discontinuation of AEDs.

Method: We included 40 adult patients with recurrent seizures, or after temporary discontinuation of AEDs for diagnostic or presurgical evaluation of epilepsy. Oxcarbazepine was administered orally at a single loading dosage of 30 mg/kg. The plasma levels of oxcarbazepine and its active metabolite, 10,11-dihydro-10-hydroxy-carbazepine (monohydroxy derivative, MHD), were measured, and clinical assessment of adverse events was performed, 2, 4, 6, 8, 10, 12, 16, and 24 h after oral loading of oxcarbazepine.

Results: Approximately two-thirds of patients reached therapeutic levels of MHD 2 h after the oral loading of oxcarbazepine, and all patients reached therapeutic levels 4 h after loading. Most patients maintained therapeutic MHD levels for at least 16 h. Nearly half of the patients experienced adverse events, but all were mild to moderate in severity and resolved spontaneously within 24 h.

Conclusion: Our study showed that oral loading of oxcarbazepine is a well-tolerated and effective method for the rapid achievement of therapeutic levels of MHD in epilepsy patients. We suggest that oral loading of oxcarbazepine is a useful consideration in selected patients with recurrent seizures, or after temporary discontinuation of AEDs.

Poster session: Drug therapy VI
Wednesday, 31 August 2011

p810

A MULTICENTER TRIAL OF OXCARBAZEPINE ORAL SUSPENSION MONOTHERAPY IN CHILDREN WITH PARTIAL EPILEPSY

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Purpose: We conducted a prospective multicenter open label trial to evaluate the efficacy, tolerability, and safety of oxcarbazepine oral suspension (OXC) in newly diagnosed pediatric partial epilepsy patients.

Method: Children between the ages of 4–16 years were eligible for the study if they had been diagnosed with partial epilepsy and experienced two or more partial-onset or generalized tonic–clonic seizures during the preceding 6 months. OXC was introduced as monotherapy to previously untreated children and was titrated over 2–4 weeks to effective target doses, followed by maintenance for another 24 weeks. The primary outcome was measured by the seizure-free rate during 6 months of maintenance. Effectiveness of OXC was compared in intellectually normal versus impaired children (IQ <70).

Results: We enrolled 171 patients (mean age, 9.18 ± 2.69) including 99 boys and 72 girls. All types of partial epilepsy were included: 70 patients were affected by cryptogenic epilepsy, 64 by idiopathic epilepsy and 37 by symptomatic epilepsy. Maintenance dose of OXC was 24.92 ± 8.02 mg/kg/day. Out of the 171 patients enrolled, 122 completed the study and 91 patients (53.2%) became seizure-free after using the OXC treatment. In comparing the efficacy of OXC for intellectually normal and impaired patients, 76 (53.5%) of 142 intellectually normal patients and 15 (51.7%) of 29 intellectually impaired patients became seizure-free ($p = 0.779$). Adverse effects were reported in 56 (32.7%) of the patients and the drug was interrupted due to rashes in 16 (9.4%) cases. In comparing the adverse effects of OXC in intellectually normal and impaired patients, 46 (32.4%) of 142 intellectually normal patients and 9 (31.0%) of 29 intellectually impaired patients had adverse effects ($p = 0.677$).

Conclusion: OXC is effective and well tolerated as monotherapy in children with partial epilepsy. There is no difference of the effectiveness between intellectually normal and intellectually impaired children.

Abstracts

p811
RUFINAMIDE ADD-ON THERAPY IN REFRACTORY GENERALIZED EPILEPSY IN CHILDREN

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Purpose: This study was performed to evaluate the efficacy and tolerability of rufinamide as add-on therapy in children with refractory generalized epilepsy.

Method: Fifty-six children and adolescents (age range 2.3–17.3 years) with refractory generalized epilepsy, receiving 1–6 concomitant antiepileptic drugs, were included and treated with rufinamide. Baseline seizure frequency and type were determined during 1 month base-line period before the add-on of rufinamide. Responders were defined as those who showed more than 50% reduction in seizure frequency.

Results: After 3 months of therapy, 21 patients (21/56, 38%) showed more than 50% reduction in seizure frequency. While Lennox-Gastaut syndrome (12/29, 41%) and unclassified generalized epilepsy (6/15, 40%) patients revealed similar response rate, Dravet syndrome patients showed lower response rate (1/6, 17%). When analyzed by seizure types, axial tonic seizures (14/33, 42%), atonic seizures (6/14, 43%), epileptic spasms (4/10, 40%) responded better than myoclonic seizures (4/19, 21%). Adverse events were found in 15 patients (15/56, 27%). Common adverse effects were somnolence, poor oral intake and behavioral problems which were usually mild and transient. Seizure aggravation was suspected in seven patients and this tendency was more frequently found in Dravet syndrome patients (3/6, 50%). After 6 months of treatment, 26 patients (26/41, 63%) were still receiving rufinamide treatment. Thirteen patients (13/41, 32%) showed more than 50% reduction in total seizure frequency.

Conclusion: This study suggests that rufinamide could be effective and well tolerated in generalized epilepsies in children other than Lennox-Gastaut syndrome.

p812
CLINICAL EXPERIENCE OF RUFINAMIDE IN CHILDREN WITH SEVERE EPILEPSY

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Purpose: Rufinamide is a novel AED used mainly in refractory epilepsy in children. We retrospectively evaluated the efficacy and adverse events of children treated with rufinamide in our clinic.

Method: The study group consisted of 51 children, 27 boys and 24 girls. Their mean age was 9.3 ± 4.5 years (mean ± SD; range 1.7–17.9). All had pharmacoresistant epilepsy and had tried a mean of 8.5 (±2.4) AEDs. The number of concomitant AEDs was 1.9 (±0.7). The majority had a symptomatic etiology. The most common seizure type was tonic seizures. Efficacy was determined by change in seizure frequency before compared to 2–3 months after start of rufinamide. The children were categorized as having >50% seizure reduction, <50% seizure reduction or a seizure increase. Those with >50% seizure reduction were considered responders. The tolerability was assessed by evaluation of adverse events reported by parents and children.

Results: The rufinamide dose was mean 583.3 mg/day and 20.9 (±8.8 SD) mg/kg/day. Twelve children (24%) were responders. Thirty-seven children showed a slight improvement (<50%) or no change and two had increased seizure frequency. Thirteen children had Lennox-Gastaut syndrome and 4 (31%) were responders, which was slightly higher than the entire study group. Thirty-six children had tonic seizures. In this subgroup 9 (25%) were responders. There were no differences in relation to gender or epilepsy type. Side effects were found in 20 (39%) of 51 patients. The reported adverse events were fatigue in 12 children (24%), behavioral disturbances in 4 (7.8%), agitation in 3 (5.9%), sleep disturbances in 2 (4%), depression in 2 (4%), unsteadiness in 1 (2%) and vomiting in 1 (2%). Many of the adverse events were transient and they were generally mild in severity. No serious adverse events occurred.

Conclusion: Rufinamide may be a useful adjunctive AED in pharmacoresistant epilepsy in children especially in Lennox-Gastaut syndrome and side effects are relatively few and mild.

p813
CHALLENGES IN TREATMENT OF CHILD PHARMACORESISTANT EPILEPSY

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Purpose: We are assessing management of children with epileptic syndromes in order to identify pharmacoresistant seizures as soon as possible and reduce the risks and consequences of epilepsy.

Methods: Medical follow-up of over 80 children hospitalized at the ''Dr. V. Gomoiu'' Children Hospital – Bucharest, Romania, from 2007 to 2011 with epileptic syndrome; we have evaluated each patient with EEG, video-EEG and seric drug level (if possible) at every presentation. Brain MRI was performed when cognitive decline was noted, but not every time explainable by frequency of seizures.

Results: In our study almost one-fifth of children with epilepsy continued to have partial and generalized seizures, despite appropriate antiepileptic drug treatment, placing them at considerable risk of cognitive and psychosocial dysfunction; we present three cases of epileptic encephalopathies in children with minimal MRI-detectable lesions.

Conclusions: Identification of pharmacoresistancy in epilepsy is complicated by the variability of its appearance across different types of epilepsy and the variability of seizure control within a given patient over time; the main objective is to minimize seizures frequency in order to reduce the risks and consequences of epilepsy, including the cognitive and psychiatric comorbidities and even sudden death. Every case of epilepsy, inspite minimal MRI-detectable lesions, should be considered potentially pharmacoresistant.

p814
THE INCIDENCE, FEATURES, AND RISK PREDICTORS OF ANTIEPILEPTIC DRUGS-INDUCED CUTANEOUS ADVERSE DRUG REACTIONS IN CHINESE POPULATION

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Purpose: Preventing cutaneous adverse drug reactions (cADRs) is a major challenge in optimizing antiepileptic drugs (AEDs) therapy. Less study on the incidence, clinical features and risk predictors of AEDs-cADRs was performed in Chinese population. We aimed to investigate these issues under a prospective study.

Methods: From January 1, 2008 to December 31, 2010 all consecutive outpatients with newly diagnosis of epilepsy were recruited at the Epilepsy Center of Guangzhou Medical University. Each patient received individualized AEDs therapy with standardized titration methods. The demographics, dosage, duration of use, concomitant AEDs, skin manifestation and medical history were documented. HLA-B*1502 was genotyped in patients with an AED-cADR.

Results: Altogether 1841 patients were enrolled, of which 1.14% (21/1841) had an AED-cADR. The cADRs incidence of carbamazepine (CBZ), oxcarbazepine (OCBZ) and lamotrigine (LTG) was 2.9%, 2.3% and 1.6% respectively. Maculopapular exanthema (MPE) was the

majority type (81.0%, 17/21) and 8 (47.1%) was caused by CBZ. History of non-AED allergy appeared significantly more often in MPE patients than in non-cADRs patients (17.6% vs. 0.2%, p = 1.30'10^{-5}). Four patients were Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), and all were induced by CBZ. All CBZ-SJS/TEN (4/4) were positive for HLA-B*1502, compared to 12.5% (1/8) of CBZ-MPE (p = 0.023). Fevers were only seen in CBZ-cADRs (6/12) and none in other cADRs (p = 0.019).

Conclusion: The incidence of AEDs-cADRs is low under standardized titration methods in Chinese population, and CBZ is the leading cause. History of non-AED allergy is a high risk for MPE, while CBZ-SJS/TEN has a strong association with HLA-B*1502.

p815

A VALIDATED CHIRAL LIQUID-CHROMATOGRAPHY TANDEM MASS-SPECTROMETRY (LC-MS/MS) METHOD FOR THE SEPARATION AND QUANTIFICATION OF ESLICARBAZEPINE ACETATE AND ITS METABOLITES IN HUMAN PLASMA

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Purpose: This study aimed to develop and validate a sensitive and specific enantioselective liquid-chromatography tandem mass-spectrometry (LC-MS/MS) method, for simultaneous quantification of eslicarbazepine acetate (ESL), eslicarbazepine, oxcarbazepine (OXC) and R-licarbazepine in human plasma.

Method: Analytes were extracted from human plasma using a solid phase extraction. The chromatographic separation was achieved using a mobile phase of 80% of n-hexane and 20% of ethanol/isopropyl alcohol (66.7/33.3%, v/v). A Daicel CHIRALCEL® OD-H, (5 µm, 50 × 4.6 mm) was used with a flow rate of 0.8 ml/min, and a run time of 8 min. Analytes and the internal standard, 10,11-dihydrocarbamazepine, were quantified by positive ion tandem electrospray ionization mass spectrometry.

Results: The method was fully validated and it demonstrated accuracy, precision, linearity, and specificity. Linearity was proven over the range of 50.0–1000.0 ng/ml for ESL and OXC and over the range of 50.0–25000.0 ng/ml for eslicarbazepine and R-licarbazepine. The intra- and interday coefficient of variation was less than 20.0% and accuracy was between 80.0% and 120.0%. The lower limit of quantification (LLOQ) was 50.0 ng/ml for ESL, eslicarbazepine, OXC and R-licarbazepine in human plasma. Bench-top stability in plasma, freeze-thaw stability in plasma, frozen long-term stability in plasma, autosampler stability and stock solution stability all met acceptance criteria (% bias within ±15.0%).

Conclusion: This LC-MS/MS method can be used to monitor plasma drug levels of ESL and its metabolites in human plasma.

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p816

COMPLIANCE TO ANTIEPILEPTIC DRUGS IN EGYPTIAN EPILEPTICS

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Purpose: The present work aimed at studying the drug adherence in an Egyptian epileptic sample.

Method: All patients in Alexandria epilepsy center (from September 2010 to November 2010), who had been newly diagnosed as epileptics have been interviewed just before starting antiepileptic drugs, then 1 and 2 months after starting antiepileptic drugs. They answered a questionnaire (brief illness perception questionnaire [BIPQ]), in addition to other questions related to their adaptation to chronic diseases. Adherence to antiepileptic drugs was calculated as the number of pills taken by the patient/the number of pills prescribed percent. Moreover, drug level was drawn in the 2nd and 3rd visits.

Results: The mean adherence in the 1st month was 85.7 ± 15.5%, while the mean value for the 2nd month was 79.9 ± 24.3%. There was significant correlation between the serum level of the drug in the 1st month and 2nd month and the total score of BIPQ (r = 0.414 and 0.350 when P = 0.008 and 0.027 respectively). There was statistically significant difference between patients with different educational levels regarding both adherence and serum level in the 2nd month (F = 3.039, 3.070 when p = 0.023, 0.022 respectively). Regarding the 1st month, There was significant difference between the adherence of those who experienced side effect and others who did not (t = −5.36 when p = 0.001); but this was not valid in the 2nd month (t = −1.66 when p = 0.104).

Conclusion: The patient's perception of his disease is one of the most important factors that determines his adherence to the antiepileptic drugs. The patients' educational level is another important factor related to their compliance. The side effects of the drugs must be considered to achieve adequate patient compliance especially in the early course of the antiepileptic drugs.

p817

ADD-ON LACOSAMIDE IN BRAIN TUMOR–RELATED EPILEPSY; PRELIMINARY REPORT: EFFICACY AND TOLERABILITY

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Purpose: Patients with brain tumor–related epilepsy BTRE are forced to face a host of problems related to both epilepsy and the tumor itself. This presents a complicated therapeutic profile. For these reasons, the choice of the best AED must take into consideration the need to balance efficacy, potential side effects and drug-to-drug interactions. Lacosamide (LCM) is an antiepileptic drug (AED) that demonstrated a good efficacy in controlling seizures as add-on in adult epilepsy. To date there have been no studies on LCM in patients with BTRE.

Methods: To evaluate efficacy and tolerability of LCM as add-on in BTRE, we followed 14 patients suffering from BTRE who had already been treated with other AEDs and who had had not experienced adequate seizure control. Lacosamide was titrated according to the technical file as first to fifth add-on therapy at dosage variable from 200 to 400 mg/day.

Results: During treatment with LCM, 11 patients were undergoing chemotherapy, no patient underwent radiotherapy and nine patient died because of neoplastic disease progression Mean duration of follow-up was 5.4 months (min <1 max 10 months). Mean seizure number in the last month prior to the introduction of LCM had been 15.4. At last follow-up, the mean seizure number was reduced to 1.9/month. Lacosamide mean dosage was of 332.1 mg/day (min 100 max 400 mg/day). Responder rate was 78.6%. The difference in presence/absence of seizures between baseline and final follow-up was significant (p < 0.031). The difference in mean monthly seizure frequency between baseline and follow-up was also significant (p < 0.022). The median percentage seizure reduction was 79.8%. One patient discontinued LCM because of side effects. There were no other reported side effects.

Conclusions: Preliminary data on the use of LCM in add-on in patients with BTRE indicate that this drug may represent a valid alternative as add-on in this particular patient population. However larger samples are necessary in order to draw definitive conclusions.

Abstracts

p818
THE LONG-TERM EFFICACY AND SAFETY OF LEVETIRACETAM IN THE TERTIARY EPILEPSY CENTER

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Purpose: We evaluated the long-term efficacy and safety of levetiracetam based on the large population of patients in the tertiary epilepsy center.

Method: All patients who had been treated with levetiracetam at Seoul National University Hospital from 2007 to March 2009 were recruited. Electronic medical records were retrospectively reviewed. The follow up period was at least 18 months. Efficacy was measured during the last 6 month period of follow-up. Adverse events were also recorded. Retention rates at one year, two year, and three years were calculated.

Results: Total 567 patients were recruited including 68 generalized epilepsy patients. The 50% responder rate and seizure remission rate were 67.7% and 32.6% respectively. For 111 patients with monotherapy, the seizure-free rate was 66.7%. The number of prior antiepileptic drugs was inversely correlated with seizure-free outcome. The retention rates at 1, 2, and 3-year were 78%, 65%, and 61% respectively. One hundred and fifty-seven out of 567 patients were dropped out. The main reasons of discontinuation were lack of efficacy (75.8%) and emergence of adverse events (20.4%). There was a strong correlation between initial response and dose-up response. Tolerance was observed only in 31 patients. The commonest adverse events were irritability (9.1%), dizziness (4.1%), and somnolence (3.9%). For 27 juvenile myoclonic epilepsy (JME) patients, 16 became seizure-free and another 8 experienced only rare myoclonic seizures.

Conclusion: Levetiracetam was effective and safe on monotherapy as well as add-on therapy for partial and generalized epilepsies. The retention rates were well maintained up to three years.

p819
EFFECTS OF LEVETIRACETAM AS MONOTHERAPHY ON INTERICTAL ABNORMALITIES AND BACKGROUND ACTIVITY IN ADULT FOCAL EPILEPSY

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Purpose: Levetiracetam (LEV) is a relative new antiepileptic drug, well known for its efficacy, safety and tolerability in focal epilepsy. The purpose of this study is to investigate the changes occurring on EEG recordings of patients affected by focal epilepsy before and during LEV as monotherapy, in order to clarify some neurophysiological features of this drug.

Methods: Twenty-two patients with newly diagnosed focal epilepsy were enrolled in the study. They underwent 1-h EEG monitoring at baseline and after 6–8 month of stable treatment with LEV at the therapeutic dosage (range from 1000 to 3000 mg/day). We evaluated and paralleled the clinical outcome, the interictal abnormalities and the background activity, before and after LEV monotherapy. We enrolled a control group in order to compare qEEG measures obtained from epileptic patients.

Results: A High percentage of our patients (21/22 pts 95.4%) showed a noticeable reduction of the seizure occurrence and among them 59% were seizure-free. Computerized analysis of interictal epileptiform activity showed a marked reduction in particular of focal EEG abnormalities after LEV administration. EEG background activity did not reveal any meaningful change before and during LEV therapy and in comparison with the control group.

Conclusion: We confirmed the efficacy of LEV as monotherapy, treating focal seizures in patients affected by newly diagnosed focal epilepsy. The significant decrease of IEA suggest a role of LEV in regulating spike genesis. Moreover the lack of changes in the background activity is well related with the good cognitive profile of this drug.

p820
FIVE YEARS IN THE TREATMENT OF STATUS EPILEPTICUS WITH INTRAVENOUS LEVETIRACETAM

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Purpose: We assessed the efficacy of LEV IV in the treatment of various types of status epilepticus (SE).

Method: LEV IV was administered at dosages of 1000, 2000 or 3000 mg either as an infusion (1000 mg in 100 ml NaCl 0.9%, 15 min) or fractionated (500 mg in 20 ml NaCl 0.9%, 1–2 min). Termination of SE was the effectiveness criterion. Tolerability was assessed by evaluating adverse events (AEs).

Results: Since 2006, we have used LEV IV to treat 76 patients with various types of SE. In general, LEV was administered as second-line therapy, after benzodiazepines. Overall, LEV terminated SE in 55.3% of the patients (42/76). LEV was more effective in terminating simple partial SE (11/17, 64.7%) and complex partial (22/35, 62.9%) SE than nonconvulsive SE (5/11, 45.5%). LEV was most effective in the treatment of myoclonic SE (2/2, 100%) and subtle SE (2/3, 66.7%), but the number of patients in these types of SE was very small. For the treatment of (secondary) generalized tonic–clonic SE, LEV was not sufficient at a dosage up to 3000 mg (0/9, 0%), and the supposed faster effect of fractionated application was without benefit in these cases. Serious AEs were not reported. Prolonged somnolence (especially in elderly patients) was reported, but it was difficult to determine whether this was caused by LEV, benzodiazepines and/or postseizure twilight state.

Conclusion: LEV IV can be an alternative in the treatment of partial (simple and complex partial) SE.

p821
POPULATION PHARMACOKINETICS OF PERAMPANEL, A SELECTIVE, NONCOMPETITIVE AMPA RECEPTOR ANTAGONIST, IN PATIENTS WITH REFRACTORY PARTIAL-ONSET SEIZURES PARTICIPATING IN A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE III STUDY

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Purpose: To describe the population pharmacokinetics (PK) of perampanel as adjunctive therapy in patients with refractory partial-onset seizures.

Method: In a multicenter, double-blind, placebo-controlled phase III study (ClinicalTrials.gov identifier: NCT00700310), patients aged ≥12 years with refractory partial-onset seizures receiving 1–3 concomitant antiepileptic drugs (AEDs) were randomized to once-daily perampanel (2, 4 or 8 mg) or placebo (6-week titration period; 13-week maintenance period). Plasma samples were collected at treatment weeks 10, 14 and 19 and at the end of a 4-week follow-up phase (or study end). Population PK parameters were estimated by nonlinear mixed-effect modeling.

Results: Of 706 treated patients, 489 were included in the PK analysis (mean age 33.7 years; 51% female; 66% Caucasian, 19% Asian non-Chinese, 15% Chinese). Perampanel concentrations were described by a

one-compartment disposition model with first-order elimination. Apparent clearance (CL/F) was 0.719 l/h for a typical male patient with fat body mass (FBM) of 15.74 kg. A decrease in CL/F was observed with increasing FBM (by 7% when FBM doubled from 10 to 20 kg) and CL/F was 20% lower in females compared with males. Use of the CYP450 3A4-inducing AEDs carbamazepine, oxcarbazepine and phenytoin increased CL/F approximately 3-, 2- and two-fold, respectively. Perampanel CL/F was not statistically significantly affected by phenobarbital, topiramate, or any other AED studied, or by any of the other covariates, including race.

Conclusion: Perampanel PK was described by a one-compartment disposition model with first-order elimination. Carbamazepine, oxcarbazepine and phenytoin were found to increase perampanel clearance. These findings are consistent with earlier phase I and II studies.

Poster session: Drug therapy VII
Wednesday, 31 August 2011

p822
THE COGNITIVE AND LANGUAGE ABILITIES OF CHILDREN EXPOSED IN UTERO TO LEVETIRACETAM AND SODIUM VALPROATE: 3–4 YEARS OF AGE

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Purpose: To compare the development of children's cognitive and language abilities following in utero exposure to levetiracetam (LEV) or sodium valproate (VPA).

Method: Children exposed to LEV (n = 53), VPA (n = 45) and control children (n = 131) were assessed for development by the Liverpool and Manchester Neurodevelopment group between 2003 and 2010. The children were all aged between 36–54 months and completed the Griffiths Mental Development scale and the Reynell Language Scales.

Results: Children exposed to LEV scored significantly higher for gross motor skills ($p = 0.002$), comprehension of language skills ($p = 0.047$) and expressive language skills ($p = 0.005$), when compared to children exposed to VPA. Differences were not seen for other subscales. LEV exposed children did not differ significantly on any subscale when compared to controls apart from for expressive language skills whereby LEV exposed children scored significantly higher than controls ($p = 0.014$).

Multiple linear regression analysis revealed that VPA exposure and seizures during pregnancy were independent predictors of outcome for gross motor skills, personal and social skills, comprehension of language skills and expressive language skills. LEV exposure was not found to be predictive of outcome on any subscale.

Conclusion: Children aged 36–54 months exposed to LEV in utero did not differ from control children on any cognitive or language scores. The results support the notion that LEV may be a preferable alternative drug choice for WWE of childbearing age, in regards to cognitive and language outcomes in the child.

p823
ACADEMIC ACHIEVEMENT OF AUSTRALIAN CHILDREN PRENATALLY EXPOSED TO ANTIEPILEPTIC DRUGS

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Purpose: Exposure to some antiepileptic drugs in utero is known to increase the risk of major malformations, and recent publications have highlighted the potential for cognition and language to also be affected. We aimed to determine whether there is also an effect of prenatal antiepileptic drug exposure on children's academic skills.

Method: Participants were 106 school-aged children exposed to antiepileptic medications during pregnancy who took part in the Australian Brain, Cognition and Antiepileptic Drugs Study. Children with reported major malformations or epilepsy were excluded. Drug exposure information was obtained prospectively. The Wide Range Achievement Test-Fourth Edition was administered between 6 and 8 years of age. All assessors were blinded to drug exposure.

Results: Twenty-three children had a diagnosed learning disorder or condition likely to impact on learning (e.g., intellectual disability, autism spectrum disorder). Rates were highest in children exposed to valproate (7/26; 26.9%) and polytherapy that included valproate (8/15; 53.3%). Regression analysis incorporating maternal and demographic variables indicated that polytherapy exposure was associated with reduced reading and spelling achievement, and valproate exposure negatively impacted on mathematics performance ($p < 0.05$). First trimester folic acid supplementation had a protective effect on spelling performance ($p < 0.05$).

Conclusion: These findings are consistent with a growing literature suggesting that prenatal exposure to valproate or polytherapy can be harmful to brain development, and suggest that these children are also at increased risk of academic underachievement. It is important that exposed children are monitored from an early age to ensure those affected receive the additional support they require.

p824
PREGABALIN KINETICS IN THE NEONATAL PERIOD, AND DURING LACTATION

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Purpose: To investigate the kinetics of pregabalin (PBG) in the neonatal period and during lactation.

Method: PBG concentrations were measured in plasma and breast milk by using high-performance liquid chromatography (HPLC) in two women with epilepsy treated with PBG during pregnancy and in their infants. One mother-infant pair contributed with samples obtained at delivery and at breast-feeding and the other woman at delivery only.

Results: The umbilical cord plasma/maternal plasma ratios (mean values) of PBG were 1.3. PBG concentrations in the neonates declined to, on average, 14% of the cord plasma levels (range, 7–21%) at 48 h postpartum. The elimination half-life in the neonates was approximately 17 h. The milk/maternal plasma concentration ratio was close to one. The breast-fed infant had 2.7 μM plasma concentration of PBG and the plasma concentration in the breast-fed infant was about 8% of the mother's plasma level.

Conclusion: Our limited observations suggest free transfer of PBG over placenta and infants appear to have lower capacity to eliminate PBG than adults. The passage of PBG to breast milk seems extensive but low

concentration was measured in the breast-fed infant. No adverse effects were observed in the infant.

p825
SECOND GENERATION OF ANTIEPILEPTIC DRUGS (AEDS) DATA FROM THE AUSTRALIAN PREGNANCY REGISTER (APR)

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Purpose: A large number of new antiepileptic drugs (AEDs) have been approved since 1994, however published data on their role and use in pregnancy is limited. We analyzed data collected by the Australian Pregnancy Register (APR) over 11 years to provide information on the relative teratogenicity of new AEDs in pregnancy.

Methods: The database of the APR, containing pregnancy outcomes from 1317 women with epilepsy, was examined for the three most widely used new AEDs in pregnancy when used in monotherapy in the first trimester—lamotrigine, levetiracetam and topiramate. This was compared the outcomes of pregnancy women with epilepsy who were on monotherapy with three traditional AEDs, phenytoin, valproate and carbamazepine, and with those of untreated women

Results: The incidence of malformations associated with lamotrigine monotherapy during the first trimester was 12/231 (5.2%), with topiramate 1/31 (3.2%) and with levetiracetam 0/22 (0%). This compares with rates of 1/35 (2.9%) for phenytoin monotherapy, 35/215 (16.3%) for valproate monotherapy, 19/301 (6.3%) for carbamazepine monotherapy, and 6/116 (5.2%) for untreated women.

Conclusion: The new AEDS appear no more teratogenic than traditional drugs in monotherapy. There is no trend noted for facial abnormalities related to lamotrigine or topiramate, although the numbers of pregnancies exposed to monotherapy with these drugs is relatively small.

Acknowledgements: The study is approved by the Ethics Comittee, Royal Melbourne Hospital. Written informed consent obtained. Supported by RMH Neuroscience Foundation, Epilepsy Society and four pharmaceutical companies (UCB, Sanofi, Janssen, and Novartis.)

p826
EFFECT OF TOPIRAMATE AND CARBAMAZEPINE ON SEXUAL DYSFUNCTION IN WOMEN WITH EPILEPSY

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Purpose: To determine the occurrence of sexual dysfunction (SD) in women with epilepsy and to identify effect of topiramate (TPM) and carbamazepine (CBZ) on SD in women with epilepsy.

Method: Prospective open study using questionnaire, which included 28 married women with epilepsy, aged between 18 and 40 years, on antiepileptic monotherapy—TPM and CBZ, and a control group of healthy women. Sixteen patients had good seizure control (SC) (seizure-free in the last two years), and 12 patients had a bad seizure control (more than three primary or secondary generalized seizures in the last two years). All subjects were assessed for symptoms of SD with Female Sexual Function Index (FSFI), a 19-item questionnaire abouth sexual desire, arousal, lubrication, orgasm, satisfaction, and pain.

Results: All subjects were divided into three groups. The first group was consisted of 14 patients which were treated with TPM in average daily dose of 200 mg. The second group of 14 patients were treated with CBZ in average daily dose of 800 mg. The third control group was consisted of 14 healthy women. The mean value of FSFI score was 19.4 (12.8 with bad SC, 25.4 with good SC) in tne first group; 17.6 (11.4 with bad SC, 22.8 with good SC) in the second group and 27.4 in the third group. SD were increased compared to the population of women without epilepsy. SD was not statistically different between the first and the second group and correlated significantly with the control of epileptic seizures.

Conclusion: Women with epilepsy appear to have a higher incidence of sexual dysfunction than other women. Important predictors for sexual dysfunction is the control of epileptic seizure.

p827
DRUG-INDUCED METABOLIC ACIDOSIS: COMPARISON INDUCED OF TOPIRAMATE AND ZONISAMIDE

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Purpose: Both zonisamide (ZNS) and topiramate (TPM) share a mechanism of action, inhibition of carbonic anhydrase inhibition, which may cause metabolic acidosis. Although the side effect of metabolic acidosis by TPM is widely recognized, it is still not clear whether ZNS has similar effect on the acidosis. The aim of this study is to compare the side effect of metabolic acidosis in patients treated with TPM and/or ZNS.

Method: Fifty-seven patients who had venous blood gas (VBG) examination at Department of Pediatrics, Nagoya University Hospital from May 2009 to April 2010 were enrolled in this study. Blood examinations were performed as routine checkups, and all the patients showed no particular symptoms of acidosis. We divided the patients into four groups; group 1: with TPM and ZNS, group 2: with TPM, group 3: with ZNS, group 4: without TPM nor ZNS. We compared VBG parameters in these groups.

Results: Compared to group 4, pH is significantly lower in group 1 and 2, but not in group 3. Base excess is significantly lower in group 1, 2 and 3. Concentration of $HCO3^-$ is significantly lower, and Cl^- is higher in group 1, 2 and 3.

Conclusion: Patients with ZNS have subclinical metabolic acidosis as patients with TPM. VBG evaluation as routine checkups in patients with ZNS or TPM may be helpful to avoid the clinical adverse effect caused by metabolic acidosis.

p828
CARDIAC SAFETY AND RATES OF SUDDEN UNEXPLAINED DEATH IN PATIENTS WITH EPILEPSY TREATED WITH RETIGABINE (EZOGABINE)

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Purpose: To evaluate cardiac safety and sudden unexplained death in epilepsy (SUDEP) in patients treated with retigabine (RTG; ezogabine in the U.S. and Canada).

Method: Treatment-emergent adverse events (TEAEs) related to cardiac rhythm/conduction abnormalities, QTc prolongation and SUDEP were evaluated in all patients from 13 Phase II/III studies, including 3 pivotal controlled trials (PCTs; 205, 301 and 302) and 2 open-label extension studies (303 and 304; data through 2 October 2009).

Results: In the PCTs, patients (n = 813) were exposed to ≥1 dose of RTG with 211 patient-years of exposure. The frequency of cardiac-related TEAEs was similar for placebo (4%) and RTG (4.6%). The SUDEP rate was 4.7 for RTG versus 8.0 for placebo per 1000 patient-years. In the Phase II/III studies, patients (n = 1365) were exposed to ≥1 dose of RTG with 1420 patient-years of exposure. One hundred and sixteen (8.5%) reported cardiac rhythm/conduction abnormalities with no apparent pattern of time-to-onset. Arrhythmia (n = 22) and conduction (n = 9) TEAEs were reported. Serious TEAEs were experienced in seven patients (five chest pain, 1 arrhythmia/bradycardia with pauses in cardiac rhythm with a seizure, 1 syncope). Sixteen (1.2%) patients discontinued due to cardiac-related TEAEs, most commonly chest pain (n = 4) and palpitations (n = 4). The rate of SUDEP for RTG was 4.5 per 1000 patient-years.

Conclusions: TEAEs and QTc intervals evaluated from the PCTs and Phase II/III studies indicate no major effects on cardiac rhythm/conduction with RTG. The SUDEP rate in the RTG program is similar to rates reported for other drug-resistant epilepsy populations.

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p829
COGNITIVE ADVERSE EVENTS UNDER TOPIRAMATE IN PATIENTS WITH EPILEPSY AND INTELLECTUAL DISABILITY – FIRST RESULTS

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Purpose: Topiramate (TPM) is an effective antiepileptic drug. Cognitive adverse events (CAEs) have been described, particularly concerning executive functions, processing speed, and word finding. CAEs can easily be overlooked and misinterpreted in patients with intellectual disability (ID). Neuropsychological examinations are difficult to perform in these patients, because they often are not able to follow test instructions, and many neuropsychological instruments have been validated only for subjects with normal intelligence.

Method: Neuropsychological examinations were done before and after add-on or before and after withdrawal of TPM in 27 patients with epilepsy and ID. They were each examined with only part of the test battery. We assessed demographic, epilepsy-related and psychosocial data. Statistical analysis was done primarily with descriptive and exploratory methods. If pre-post values for a neuropsychological test were available for ≥6 patients, a Wilcoxon test was carried out.

Results: Cognitive speed (TMT scanning, n = 6, p = 0.063; TMT connecting numbers, n = 6, p = 0.031; TMT psychomotor, n = 7, p = 0.008), digit span forward (n = 14, p = 0.002) and verbal fluency (animal names, n = 20, p < 0.001; food, n = 13, p = 0.007) were more impaired with than without TPM. Two tests with n ≥ 6 showed no significant differences.

Conclusion: Despite some limitations (small sample size, considerable variation in the degree of ID, sometimes multiple changes of the therapeutic regimen, etc.) the results indicate that TPM can lead to similar CAEs in people with epilepsy and ID as in people with normal intelligence. An estimation of the prevalence of these adverse events cannot be made from this study.

p830
TEMPORAL CHANGES IN PLASMA TAURINE LEVEL IN PATIENTS WITH INFANTILE SPASMS TAKING VIGABATRIN

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Purpose: Although vigabatrin (VGB) is the first-line drug for infantile spasms (IS) in Europe, it has not been approved so far in Japan because of its irreversible constriction of the visual field. In 2009, the animal experiment was attributed the retinal cytotoxity of VGB to deficiency of taurine. In this study, we serially analyzed the plasma taurine concentration in IS patients during VGB therapy.

Method: Four patients with tuberous sclerosis whose IS were treated by VGB were recruited since 2009 to 2011. Monthly evaluation of plasma taurine concentration was done before and after taking VGB. Mean age at the study was 30 months old. Mean total dosage of VGB was 136.7 (50–200) g.

Results: Serial evaluation demonstrated that taurine level gradually declined during taking VGB in two patients. Taurine was supplemented (0.2–1 g/day) in three patients to sustain plasma taurine level during the VGB therapy. Thus taurine supplement was necessary before VGB therapy in two patients. In one patient, when VGB was reinitiated 2.5 months after the withdrawal of the first VGB, taurine was remarkably dropped. ERG at the end of VGB treatment was normal in all patients.

Conclusion: This is the first report showing gradual decrease of plasma taurine level in patients taking VGB. Only low amount of taurine supply was sufficient to maintain plasma taurine concentration. Neither obvious side effect nor ERG abnormality was recognized. Although the prophylactic effect of taurine for retinopathy still remains an open question, serial evaluation of plasma taurine is recommended in patients taking VGB.

p831
LONG-TERM COGNITIVE EFFECTS OF TREATMENT CARBAMAZEPINE AND VALPROATE

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Purpose: So far the information on cognitive effects of antiepileptic treatment is based on trials with an average duration of 12 weeks. The long-term effects have, as yet, not been studied. Moreover, information about the cognitive impact of AEDs is lacking in children. In this open clinical cohort study the long-term cognitive effects of monotherapy carbamazepine (CBZ) and valproate (VPA) were evaluated in children with epilepsy.

Method: All patients aged 6–16 years were included when assessed in the period August 2006 to February 2011. Patients were only included when they had been on monotherapy CBZ or VPA without any switch to other medication. So all patients had been on either CBZ or VPA from the onset of epilepsy. Outcome measures included Wechsler Intelligence Scale for Children-III (WISC-III) and cognitive tests (FePsy neuropsychological test battery).

Results: Thirty-five patients were included for CBZ and 46 patients for VPA. Average length of treatment in the CBZ group was 46.15 months (range 3–104) and for the VPA group 42.19 months (range 4–108). Both CBZ and VPA differed significantly from reference values on measures of attention and mental/psychomotor speed. On these measures CBZ did not differ significant from VPA. Patients on CBZ had lower scores on all intelligence values than patients on VPA (Figure 1). The two groups did not differ in type of epilepsy. There is a high inverse correlation between length of treatment and IQ scores only for CBZ (Figure 2).

Conclusion: Our study confirms the reported cognitive effects of CBZ and VPA. Both affect attention and psychomotor/mental speed to the same extent. This effect can be characterized as mild. In addition our

study shows evidence that at long-term CBZ may impact higher-order cognitive function and even intelligence: there is a significant impact of chronicity on IQ decline only for CBZ. The pathophysiological mechanism for our finding is unclear but our finding corresponds with a study of Piccinelli et al. and is predicted in some reviews (Hamed, 2009).

p832

AN INTEGRATED DATA ANALYSIS FROM THREE PLACEBO-CONTROLLED CLINICAL STUDIES ON OVER-READ ELECTROCARDIOGRAMS OF EPILEPTIC PATIENTS TREATED WITH ESLICARBAZEPINE ACETATE: ARE THERE ANY EFFECTS ON CARDIAC IMPULSE TRANSMISSION?

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Purpose: Eslicarbazepine acetate (ESL) is a novel once-daily voltage-gated sodium channel blocker approved in Europe for use in adults as adjunctive therapy for refractory partial-onset seizures with or without secondary generalization. ECGs from 3 phase III placebo-controlled studies of ESL at doses between 400 and 1200 mg/day were evaluated since ESL was associated with prolonging PR-interval.

Method: Paper tracing of 856 out of the 1049 patients' ECGs (81.6%) recorded at baseline and week-14 were successfully over-read by a cardiologist. Parameters including ventricular heart rate, ECG-intervals such as corrected-QT intervals according to Bazett's (QTc-B) and Fridericia's (QTc-F) formulae, were analyzed for the incidence of sponsor-defined potentially clinically significant (PCS) values and changes from baseline.

Results: Mean (SD) baseline QTc-B values for ESL 400, 800 and 1200 mg/day were 395.9 (22.90), 398.8 (25.42) and 397.6 (25.92) msec, respectively, similar to 397.0 (23.20) msec for placebo. No QTc interval exceeded 500 ms. Mean changes from baseline for each ECG parameter were similar to those observed in the placebo group, and not clinically relevant in any treatment group. Incidences of postdose PCS values were similar and did not exceed 1% in any group.

Conclusion: Although the use of ESL can be associated with PR-interval prolongation, no clinically relevant abnormalities of ECG-intervals were observed in association with ESL treatment despite the concomitant use of 1–3 antiepileptic drugs, in this large evaluated sample. There was no clinically relevant trend toward changes in parameters such as heart rate consistent with an earlier phase II study.

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p833

EFFECT OF LAMOTRIGINE ON MOTILITY AND CERVICAL MUCUS PENETRATION OF HUMAN SPERM CELLS

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Purpose: Several antiepileptic drugs (AEDs) may affect sperm motility in vitro. We previously demonstrated the ability of carbamazepine (CBZ), phenytoin (PHT), valproic acid (VPA) and topiramate (TPM) to decrease sperm motility and reduce sperm ability to penetrate cervical mucus (a functional test not studied before in relation to AEDs) in concentrations much higher than those in clinical use. In the presence study we investigated the effect of lamotrigine (LTG) on these parameters.

Method: Five mg of LTG were dissolved in 1.5% DMSO, and the solution volume was completed with 800 µl PBS. Normal semen from healthy human donors (sperm concentration >20 million/ml, >50% progressive motility) was incubated for 2 h with several dilutions of LTG. Parameters analyzed included sperm motility (% motile sperm), EC50, grade of motility (from 0 to 5, from immotile to good progressive motility, respectively) and the ability of spermatozoa to penetrate bovine cervical mucus after 10 min of contact (depth of penetration). Statistical analysis employed paired Wilcoxon signed-rank test or *t*-test with false discovery rate (FDR) correction for multiple comparisons.

Results: Sperm motility was significantly decreased with LTG concentrations ≥390 µg/ml ($p < 0.01$). Motility quality grade was significantly decreased with LTG concentrations ≥781 µg/ml ($p < 0.05$). Depth of mucus penetration was significantly decreased with LTG concentrations ≥195 µg/ml ($p < 0.001$). Motility quality grade in mucus was significantly decreased with LTG concentrations ≥390 µg/ml ($p < 0.05$). EC50 was not reached (LTG concentrations ≤6.250 µg/ml).

Conclusion: LTG impairs sperm motility, quantitatively and qualitatively, at concentrations much greater than the therapeutic range. At these concentrations it also impairs the ability of human spermatozoa to penetrate into bovine cervical mucus. Similar to our previous results with other AEDs (CBZ, PHT, VPA, and TPM), LTG also impaired the physiological function of spermatozoa at much higher concentrations relative to those in clinical use.

Poster session: Drug therapy VIII
Wednesday, 31 August 2011

p834

EFFECTS OF SODIUM VALPROATE ON NEUTROPHILS' OXIDATIVE METABOLISM AND OXIDANT STATUS IN CHILDREN WITH IDIOPATHIC EPILEPSY

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Purpose: To evaluate the influence of VPA treatment on neutrophils' oxidative metabolism and oxidant status in epileptic children.

Method: Ninety-eight patients with idiopathic epilepsy and 30 healthy children were included in the study. Patients were subdivided into four groups, 23 with newly diagnosed idiopathic epilepsy, 24 have been treated with VPA for half a year, 26 have been treated for 1 year and 25 for more than two years. The activation rates of neutrophils and stimulation indexes were detected in all the participants by flow cytometry with dihydrorhodamine as fluorochrome. The activities of myeloperoxidase (MPO) from neutrophils were also detected. Malondialdehyde (MDA) as an indicator of lipid peroxidation and antioxidant enzymes including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) were measured in plasma.

Results: The activation rates of neutrophils in patients treated with VPA were significantly higher while the stimulation indexes were lower than the control and untreated groups ($p < 0.01$). The plasma MPO activities and levels of malondialdehyde in VPA treated patients were also higher while the activities of SOD and CAT were significantly lower than the control and untreated groups ($p < 0.01$). GSH-Px levels

did not differ between the groups. Multiple linear regression analysis showed that the time of treatment and the activation rates of neutrophils were indicators which had positive correlation with the levels of plasma MDA.

Conclusion: VPA which is frequently used in childhood epilepsy may activate the neutrophils of patients and cause oxidative stress.

p835
EFFECTIVENESS OF LAMOTRIGINE IN EPILEPSY PATIENTS: A SINGLE-CENTER STUDY

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Purpose: In Japan, we have been able to prescribe lamotrigine (LTG) as the second choice to treat epilepsies for about two years because of insurance restrictions. Although the number of LTG prescribed patients was small, we have to evaluate the efficacy of LTG.

Method: From 2009, we retrospectively reviewed the charts of patients in our department. Eleven patients treated with LTG, but we analyzed eight patients since three patients did not have sufficient data.

Results: Four females and four males prescribed LTG. Seven patients were symptomatic partial epilepsies and one patient was Lennox syndrome. Mean age at the onset of epilepsy was 37 years (SD 24). Mean age at the first prescribed LTG was 42 years (SD 18). The mean number of prescribed anticonvulsants before using LTG was 1.6 (SD 1.3). There were no statistical significance between gender and ages. We had antiparallel correlations between the number of anticonvulsants and the age of epilepsy onset ($p < 0.01$), and between the range from the onset to the first using LTG and the onset age ($p < 0.05$). According to the ILAE commission report (Epilepsia 2001; 42:282–286), in the outcome, the number of class 3, 4, and 5 were 2, 4, and 2, respectively. We had antiparallel correlation between to the number of anticonvulsants before using LTG and the outcome ($p < 0.01$).

Conclusion: We suggest that to use LTG as soon as possible would be better for epilepsy patients. Now we have to investigate the efficacy of TLG as the first choice.

p836
ADJUNCTIVE LACOSAMIDE FOR PARTIAL-ONSET SEIZURES: PRELIMINARY OUTCOMES FROM AN EPILEPSY CLINIC

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Purpose: Lacosamide (LCM), licensed in the UK in 2008 for the adjunctive treatment of partial-onset seizures, exerts its effect by enhancing slow sodium channel inactivation. This audit examines everyday clinical outcomes with LCM.

Method: To date, 113 patients (57 M; 56 F, aged 18–74 years [median 39 years]) with uncontrolled partial-onset seizures (monthly frequency range 1–300; [median 4]) have started LCM. Patients took 1–4 antiepileptic drugs (AEDs), (median 1); having tried 1–12 (median 3). LCM was added with a target range of 200–400 mg/day. Review occurred until 1 of 4 end-points was reached: seizure freedom for ≥6 months; 6 months' ≥50% or <50% seizure reduction compared with baseline; withdrawal of LCM due to lack of efficacy, side effects, or both.

Results: An end point has been reached by 65 (57.5%) patients. Seventeen (26.2%) remained seizure-free on a median daily LCM dose of 100 mg (range 50–300 mg) (1 monotherapy). Six patients received traditional sodium blockers, and 10 took AEDs with other mechanisms. Seizure freedom was more likely when LCM was used as a first add-on (15 of 36, 41.7%), compared to a later treatment schedule (1 of 27, 3.7%; $p = 0.001$). A ≥ 50% seizure reduction occurred in a further 16 (24.6%) patients (1 monotherapy); 18 (27.7%) reported <50% reduction. Patients also taking traditional sodium blockers were as likely to remain on LCM (23 of 27, 85.1%) as those taking AEDs with other mechanisms (26 of 36, 72.2%). LCM was withdrawn in 14 (12.3%) patients (10 side effects [tremor and sedation were commonest, n = 3 each], 4 lack of efficacy). Of the 10 with side effects, only two patients took concomitant sodium blockers, but 8 received sodium valproate.

Conclusion: LCM is an effective and well-tolerated AED when combined with traditional sodium blockers as well as agents with other mechanisms. Seizure freedom was more likely when LCM was used as a first add-on compared to a later treatment schedule. The majority who discontinued LCM due to side effects were taking sodium valproate.

p837
RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE III STUDY OF PERAMPANEL, A SELECTIVE, NONCOMPETITIVE AMPA RECEPTOR ANTAGONIST, AS ADJUNCTIVE THERAPY IN PATIENTS WITH REFRACTORY PARTIAL-ONSET SEIZURES: EFFICACY BY SEIZURE TYPE

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Purpose: Perampanel is being evaluated as adjunctive therapy for refractory partial seizures. In a randomized, double-blind, placebo-controlled phase III trial (ClinicalTrials.gov identifier: NCT00700310), the efficacy of perampanel against different seizure types was investigated.

Method: Following a 6-week baseline, patients (≥12 years) with refractory partial seizures with or without secondary generalization receiving 1–3 concomitant antiepileptic drugs were randomized (1:1:1:1) to once-daily perampanel (2, 4, 8 mg) or placebo (6-week titration; 13-week maintenance). Seizure count/type were recorded daily. Secondary/exploratory end points included change (double-blind phase vs. baseline) in frequency per 28 days of (1) complex partial seizures plus secondarily generalized seizures (CPS + SGS) and (2 secondarily generalized seizures (SGS). CPS + SGS and SGS responder rates (patients with ≥50% reduction in seizure frequency; maintenance period) were also analyzed.

Results: Seven hundred six patients (90% with CPS; 38% with SGS) were randomized and treated. Median changes in CPS + SGS seizure frequency with placebo and 2, 4 and 8 mg perampanel were −17.6%, −20.5% ($p > 0.05$ vs. placebo), −31.2% ($p > 0.01$) and −38.7% ($p < 0.001$), respectively. CPS + SGS responder rates were 24.3%, 26.9% ($p > 0.05$), 36.3% ($p = 0.02$) and 39.6% ($P < 0.01$). Median changes in SGS frequency with placebo and 2, 4 and 8 mg perampanel were −35.8%, −28.0%, −49.6% and −69.2%. Responder rates for SGS were 44.9%, 44.1%, 49.3% and 62.9%. The differences in seizure frequency and responder rate for SGS were not significant compared with placebo.

Conclusion: Perampanel 4 and 8 mg/day significantly improved CPS + SGS end points. Patients showed decreases in tonic–clonic seizures (SGS), with an apparent dose-response trend for the perampanel 4 and 8 mg/day dose groups compared with placebo.

Abstracts

p838

PHASE III EVALUATION OF PERAMPANEL, A SELECTIVE, NONCOMPETITIVE AMPA RECEPTOR ANTAGONIST, AS ADJUNCTIVE THERAPY FOR REFRACTORY PARTIAL-ONSET SEIZURES: EFFECTS ON SEIZURE FREEDOM AND OTHER EXPLORATORY EFFICACY END POINTS

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Purpose: Perampanel demonstrated favorable efficacy and safety as adjunctive therapy for refractory partial-onset seizures in primary end point analyses in a phase III trial (study 306; ClinicalTrials.gov identifier: NCT00700310). We report the analyses of several exploratory efficacy end points.

Method: After a 6-week baseline, patients (≥12 years) with refractory partial seizures receiving 1–3 antiepileptic drugs were randomized (1:1:1:1) to double-blind treatment (6-week titration; 13-week maintenance) with once-daily perampanel (2, 4, 8 mg) or placebo. Exploratory end points included: change in number of seizure-free days per 28-days (maintenance vs. baseline); percentage of seizure-free patients during maintenance; categorized percentage changes in seizure frequency (25% increments from −100% to 100%); Kaplan–Meier analysis of time-to-first-50%-reduction in seizure frequency.

Results: Seven hundred six patients were randomized and treated. Mean (±standard deviation) number of seizure-free days increased by 1.0 ± 3.6 days with placebo, and by 1.6 ± 3.7 ($p > 0.05$ vs. placebo), 1.9 ± 3.9 ($p = 0.04$) and 2.3 ± 3.5 days ($p < 0.01$) with 2, 4 and 8 mg perampanel, respectively. Seizure-free rates during the maintenance period among patients who completed the study were: placebo 1.2%, 2 mg 1.9%, 4 mg 4.4% and 8 mg 4.8% (all $p > 0.05$). Seizure-frequency categorization showed that, compared with placebo, more patients treated with 4 and 8 mg perampanel experienced large percentage decreases in seizure frequency, while fewer experienced large increases ($p > 0.05$ and $p = 0.04$, respectively). Kaplan–Meier analysis of time-to-first-50%-response for each week demonstrated that overall, the percentage of patients achieving ≥50% seizure-frequency reduction was higher with 4 and 8 mg perampanel versus placebo ($p = 0.02$ and <0.0001).

Conclusion: Consistent with primary end point analyses, adjunctive perampanel (4, 8 mg) was superior to placebo in exploratory efficacy end points.

p839

SEIZURE FREEDOM ON MORE THAN ONE ANTIEPILEPTIC DRUG

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Purpose: Over the last 20 years, 10 new antiepileptic drugs (AEDs) have been licensed as add-on therapy for drug-resistant epilepsy in the UK. This audit ascertained the characteristics of patients registered with the Epilepsy Unit since 1982 who had been seizure-free on more than one AED for at least the previous 12 months.

Method: The database of all treated patients registered between 1982 and 2008 was interrogated.

Results: Of 2379 seizure-free patients, 486 (21–254% women, 232 men, aged 18–95 years [median age 49 years]) remained controlled on polytherapy. Epilepsies were localization-related in 309 (64%) and primary generalized in 177 (36%). Two AEDs were taken by 395 (81.3%) patients (64 different combinations). Sodium valproate with lamotrigine was the commonest successful duotherapy (n = 96, 19%). When used together, mean daily doses of both AEDs were lower (sodium valproate 1200 mg, lamotrigine 155 mg) compared with mean doses when sodium valproate was taken with carbamazepine or levetiracetam (n = 42; 1621 mg; $p < 0.001$), and lamotrigine was combined with topiramate or levetiracetam (n = 33; 430 mg; $p < 0.001$). The 10 most successful duotherapies all contained partners with differing mechanisms of action. Eighty-five (17.5%) patients were controlled on three AEDs (57 regimens), but only 6 (1.2%) remained seizure-free on four AEDs. Levetiracetam (n = 109) and topiramate (n = 81) were the most commonly represented of the newer AEDs in combinations.

Conclusion: One-fifth of seizure-free patients required AED polytherapy to maintain long-term control with the vast majority taking 2 or 3 AEDs only. The most common duotherapies comprised AEDs with different mechanisms of action, with lamotrigine and sodium valproate being the most successful combination. Mean daily doses of both drugs were significantly lower in this duotherapy, compared to when they were used with other agents, supporting synergism.

p840

EFFICACY OF THERAPEUTIC CHANGES IN PATIENTS ON ANTIEPILEPTIC POLYTHERAPY

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Purpose: To analyze the efficacy of different antiepileptic drugs (AED) combinations prescribed to epileptic patients taking at least three AED.

Method: Review of the the neurologic history of the last 668 patients attended in our Epilepsy Outpatient Clinic.

Results: The analysis involved 48 patients, all of them on three or more AED; 180 AED combinations from these patients were reviewed. Patients: females: 35.4%, males: 64.6%, age [mean (min-max)] 44.4 yo (20–67), history of epilepsy: 31.5 y (3–62); focal epilepsy 35 (72.9%), generalized epilepsy: 11 (22.9%), undetermined: 2 (4.2%); monthly seizure frecuency: 12.8 (0–100). AED combinations: number of drugs [mean (min-max)] 3.4 (2–6); the most frequent combination was carbamazepine + phenobarbital + phenytoin (2.7% of all AED combinations). The most commonly used drugs: carbamazepine (14.7%), phenytoin (14.1%), valproic acid (12.9%), phenobarbital (9.3%), topiramate (8.7%). In 135 AED combinations the reason of change was recorded: inefficacy: 53 (39.3%), improvement: 31 (23%, ussually the change tended to reduce de number of AED), adverse events: 28 (20.7%), worsening: 21 (15.6%), other: 2 (1.5%). The change in seizure frequency was 73.4% in cases of improvement and 58.3% in cases of worsening. In 8 AED combinations complete seizure control was achieved (4.4%).

Conclusion: In our series, changes in AED combinations in patients on AED polytherapy are well tolerated and tend to improve the seizure frequency.

p841

SODIUM VALPROATE TREATING EPILEPSY IN RURAL COMMUNITIES IN CHINA: AN EFFICACY AND SAFETY ASSESSMENT

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Purpose: Sodium valproate (VPA) is a broad-spectrum antiepileptic drug usually well tolerated. We conducted a study to assess the feasibility, efficacy and side effects of VPA in the treatment of epilepsy in primary care settings in rural China as an alternative to phenobarbital.

Method: People with epilepsy were identified at primary health care level and provided with VPA monotherapy. Community level physicians who were trained before the study identified patients, managed treatment, and followed with unified protocol for 12 months. All diagnoses were confirmed by senior neurologists. Efficacy of VPA medication was assessed by the percentage reduction in seizure frequency compared to baseline and by retention of treatment. Tolerability was assessed by reports of treatment-emergent effects and discontinuation rates.

Results: Six hundred seven people were enrolled of whom 579 completed the assessment. Four hundred ninety-five (85%) of people had their seizures decreased by at least 50% and among them 238 got seizure-free. The probability of retention was 95% at 1 year. Fifty-eight people (10%) reported adverse events which were mostly mild and transient, and did not necessitate drug withdrawal. Only two patients discontinued VPA due to side effects.

Conclusion: In the present study, VPA has favorable efficacy, few side effects and overall good acceptability, therefore might be an alternative to Phenobarbital as treatment of epilepsy in community level of rural China. VPA was also relatively inexpensive in China: one year's drug costing about 30 US Dollars and this was affordable by the patients.

p842
MULTICENTER SERVICE EVALUATION OF LACOSAMIDE

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Purpose: Lacosamide (LCM) was approved in the EU in September 2008 as an adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in epilepsy patients aged 16 years and older. No data have been published on the efficacy and tolerability of LCM as used in clinical practice.

Method: Preliminary data from 5/28 participating centres in this multicentre service evaluation are presented. Data was collected retrospectively from the clinical notes of 143 patients with simple partial (SPS), complex partial (CPS) or generalized tonic–clonic (GTC) seizures.

Results: Thirty-three percent with CPS, 32% with GTC and 32% with SPS experienced at least a 50% reduction in seizure frequency.

Twenty-four percent of patients with GTC, 15% with CPS and 11% with SPS achieved seizure freedom.

The retention rate for LCM was 60%. The most common reasons for discontinuation were side effects (44%), lack of efficacy and side effects (28%) and lack of efficacy (18%). The most common side effects were somnolence (31%), dizziness (28%), headache (15%) and double-vision (13%).

Conclusion: On average, patients were on 2.2 antiepileptic drugs when LCM was commenced, hence this is a difficult to treat sample with refractory epilepsy. LCM is demonstrated to be a useful add-on in controlling seizures. The discontinuation rate is comparable to that of other add-on drugs for treating refractory epilepsy. This is ongoing work and conclusions will be better reached when all data are collated.

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p843
ECONOMIC EVALUATION OF ADJUNCTIVE ESLICARBAZEPINE ACETATE IN PATIENTS WITH REFRACTORY PARTIAL-ONSET SEIZURES

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Purpose: To evaluate the cost-effectiveness of eslicarbazepine acetate (ESL) as adjunctive treatment for adult patients with uncontrolled partial-onset seizures compared to lacosamide (LCS) in Scotland.

Method: A model was developed to estimate costs and benefits of each treatment over a 2 year period. Patients were classified into health states according to treatment response. For efficacy in the initial 6-month period, an indirect comparison was performed based on clinical trials identified through a systematic literature search. ESL 800 mg/day and LCS 400 mg/day were selected as the doses for comparison on the basis of the identified studies. Long-term seizure control, life expectancy, utility, medical resource utilization and costs were obtained from the literature. Extensive sensitivity and scenario analyses were performed.

Results: Treatment with ESL and LCS resulted in comparable costs and quality adjusted life years (QALYs). Mean costs were £3943/patient (95% uncertainty interval (UI): 3091; 5028) and £3899/patient (UI: 3064; 4831) for ESL and LCS, respectively. ESL yielded 1.6559 QALYs/patient (UI: 1.2331; 1.7670) and LCS resulted in 1.6532 QALYs/patient (UI: 1.1892; 1.7682), corresponding to an incremental cost-effectiveness ratio of £16,300/QALY. The probability of ESL being the more cost-effective therapy is around 50%, independent of payer willingness to pay for QALY improvement. Results were not sensitive to the changes in key model inputs or assumptions.

Conclusion: ESL is a cost-effective alternative add-on therapy compared to LCS for adult patients with refractory partial onset seizures in Scotland.

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p844
EFFECTIVENESS OF CONVULEX IN THE TREATMENT OF NEONATAL SEIZURES IN CHILDREN WITH CONGENITAL HERPES-CYTOMEGALOVIRUS INFECTION

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Purpose: To study of the effectiveness of valproic acid (Convulex, Gerot Pharmazeutika GmbH) in the treatment of neonatal seizures in children with congenital herpes-cytomegalovirus infection.

Method: We studied 42 children with neonatal seizures on a background of congenital infection (boys – 26, girls – 16). Convulex was used as the starting anticonvulsant in 15 children (35.7%), and was appointed after unsuccessful treatment with barbiturates in 27 (64.3%) children. Convulex administered as monotherapy in the form of drops, the initial dose of 10 mg/kg/day in two divided doses. The maximum daily dose was 30 mg/kg. All patients underwent comprehensive clinical, laboratory and instrumental studies.

Results: Seizures were symptomatic. During the intake of Convulex coping with seizures was in 19 (45.2%) children and their less frequency occurrence by 50% or more was in 13 (30.9%) children, in 10 (23.8%) children a positive effect was not observed. The control electroencephalogram showed a decrease in the index and the prevalence of epileptiform activity in 47.6%, the blocking – at 19%. Side effects of Convulex occurred in three infants in the form of reduced muscle tone and lethargy (1), dyspeptic disorders (2).

Conclusion: Convulex showed a high efficiency (76%) in the treatment of symptomatic neonatal seizures. Along with clinical improvement a positive dynamics of the indices of electroencephalogram was observed. Side effects did not depend on the dose, were transient and did not require

discontinuation of therapy. Pharmacoresistance of seizures in 10 children was associated with early organic brain lesions on a background of congenital viral infection.

p845

TREATMENT OF INFANTILE SPASMS WITH VIGABATRIN AS THE FIRST DRUG

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Purpose: Vigabatrin was proved to be a promising drug for treatment of IS, with the response rate from 43% to 68%. We have conducted the single-center, prospective, observational, uncontrolled study of treatment of newly diagnosed patients with infantile spasms (IS) in order to assess the efficacy of vigabatrin.

Method: From September 1995 to the end of 2010 a total of 251 infants with IS were diagnosed in the Mother and Child Health Care Institute. We have included 176 previously untreated infants in the study. After two basal days for registering the spasms, vigabatrin was given according to the same protocol: 50 mg/kg one day, 100 mg/kg for 2 days, and 150 mg/kg for 7 days until 1999, and 14 days thereafter before assessment of the therapeutic response. Neurological status, psychometric testing, fundus oculi, metabolic investigation, CT or MRI of the brain were performed to reveal the etiology. EEG was done at admission, on 7th and 14th day.

Results: One hundred seven male and 69 female infants experienced the onset of spasms at 5.5 months – median (ranging from 10 days to 18 months). There were 138 infants with symptomatic, 25 with cryptogenic and 13 with idiopathic IS. Cessation of spasms and resolution of hypsarrhythmia was registered in 106 (60.2%) patients during 14 days, reduction of spasms for >50% in 35 (19.8%), reduction of spasms for <50% or persistence in 22 (12.5%), and worsening in 13 (7.38) patients. Good therapeutic response was registered in 74 (53.6%) patients with symptomatic, in 20 (80%) with cryptogenic, and in 12 (92%) patients with idiopathic IS ($p < 0.1$, P test). Worsening of IS during vigabatrin treatment and relapses after cessation of spasms were not registered in idiopathic group.

Conclusion: Vigabatrin demonstrated efficacy as the first drug in infants with IS, with the quick therapeutic response between 2nd and 14th day of treatment. Significantly more patients with cryptogenic and idiopathic IS became spasm-free as in other studies.

Poster session: Drug therapy IX
Wednesday, 31 August 2011

p846

EFFECT OF LEVETIRACETAM ON PILOCARPINE– AND COBALT-HOMOCYSTEINE–INDUCED STATUS RATS

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Purpose: As prolonged status epilepticus (SE) is refractory to the conventional antiepileptic drugs, antiglutamatergic drug like levetiracetam (LEV) will be helpful in treating SE. Recent researches showed effectiveness of LEV in SE, but experimental background of clinical usefullness is scanty.

Method: Fifty-four Sprague-Dawley rats were used in this experiment. Thirty rats were induced SE by pilocarpine and twenty-four rats were used in cobalt-homocysteine–induced SE. Every rats were implanted EEG electrodes before inducing SE. Rats were treated with diazepam alone or diazepam plus LEV (54 and 200 mg/kg) 30 min after the continuous spiking stage in pilocrpine-induced SE model, and just after the two discrete seizures in cobalt-homocysteine–induced SE model. EEG were continuously monitored in all rats during the SE and saved on compact disk and analyzed. End of SE was defined as less than one cycle per second epileptiform discharges after the stage of periodic epileptiform discharge (PEDs).

Results: Diazepam alone stopped SE in 71.4% of cobalt-homocysteine model and 88.9% of pilocarpine model. LEV did not increase success rate in pilocarpine model but shorten total SE duration more than 200 min (537.3 ± 116.7 min vs. 252.4 ± 72.7 in low LEV, 267.8 ± 113.4 in high LEV group, $p < 0.05$) and success rate in cobalt-homocysteine model was increased upto 100%.

Conclusion: LEV may decrease total duration of SE without sedative effects. The shortened duration of SE may decrease the complications frequently occur in patients. Also it may improve immediate anti-SE treatment in some types of SE.

p847

EFFECTS OF COMMONLY USED ANTIEPILEPTIC DRUGS IN THE MTLE MOUSE: A MODEL OF MESIAL TEMPORAL LOBE EPILEPSY TO EXPLORE NEW TREATMENTS FOR DRUG-RESISTANT EPILEPSIES?

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Purpose: Mesiotemporal lobe epilepsy (MTLE) is the most common form of epilepsy that is refractory to antiepileptic drugs (AEDs). The development of new efficient molecules needs the development of drug-resistant MTLE animal models. Recently, both morphological and electroclinical features of MTLE were shown to be mimicked following a unilateral injection of kainic acid (KA) in the dorsal hippocampus of adult mice. In addition we suggested that spontaneous hippocampal paroxysmal discharges (HPD) were not suppressed by classical AEDs.

Method: Here we further explored this hypothesis by testing the effects of seven AEDs with different mechanisms of action, at several doses, with acute or chronic administration protocols on the spontaneous occurrence of HPD by EEG in this MTLE mouse model.

Results: Injection of classical AEDs (valproate, carbamazepine and lamotrigine) fails to suppress HPD in a dose-dependent way. Indeed only high doses are effective (400, 100 and 90 mg/kg respectively) and are associated with modifications of the general behavior and/or EEG basal activity. A dose-dependent suppression of HPD was however observed with new AEDs: levetiracetam (100, 400, 800, 1000 mg/kg), vigabatrin (10, 50, 100, 200 mg/kg), pregabalin (10, 50, 100 mg/kg) and also with diazepam (0, 5, 1, 2, 3 mg/kg) without obvious behavioral or EEG side-effects. When diazepam or levetiracetam were administered daily (4 and 1600 mg/kg/day, respectively), their suppressive effects on HPD progressively vanished within 4 days.

Conclusion: Together these data show that this mouse model of MTLE displays immediate or acquired resistance to several AEDs and provides a critical tool to find new treatments with persistent effects.

p848

THE METABOLIC PROFILE OF PATIENTS WITH EPILEPSY TREATED WITH ESLICARBAZEPINE ACETATE: INTEGRATED ANALYSES OF PLASMA LIPID AND GLUCOSE PARAMETERS, AND DISTRIBUTION OF RELATED ADVERSE EVENTS IN PLACEBO-CONTROLLED PHASE III CLINICAL STUDIES

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Purpose: The antiepileptic activity of eslicarbazepine acetate (ESL) was demonstrated in three phase III randomized controlled studies of 12-week period in patients with partial-onset seizures unsatisfactorily controlled with ongoing antiepileptic therapy. In the pooled data of these studies, changes in metabolic parameters by body mass index and dose ranges, and related treatment emergent adverse events (TEAEs) were observed as surrogate cardiovascular metabolic markers in epileptic patients treated with different ESL doses or placebo as an adjunct to 1–3 concomitant antiepileptic drugs.

Method: The incidence of sponsor-defined potentially clinically significant (PCS) values of >300 mg/dl, >160 mg/dl, <30 mg/dl, >2.5 × ULN (upper limit of normal), and ≤40 or ≥175 mg/dl for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride (TRIG), and glucose, respectively, was analyzed by treatment group for the safety population (N = 1049) of subjects who received at least one dose of study medication. Mean changes from baseline were calculated, and related TEAEs were recorded.

Results: In ESL and placebo treated groups, the incidences of PCS values were 3.4% and 2.5% for TC, 20.3% and 20.8% for LDL-C, 1.3% and 1.4% for HDL-C, 1.7% and 1.4% for TRIG, 0.5% and 0.0% for hypo- and 1.2% and 1.1% for hyper-glycemia, respectively. Mean changes from baseline were not clinically significant for various parameters. The most reported relevant TEAEs for ESL were dyslipidemia (1.1%) and hypercholesterolemia (<1.0%), and for placebo, blood cholesterol increases (1.0%).

Conclusion: PCS values across treatment and dose groups did not demonstrate consistent clinically relevant patterns for metabolic parameters. The incidence of related TEAEs was similar across groups.

Supported by BIAL – Portela & Ca. SA.

p849
EFFECTS OF ESLICARBAZEPINE ACETATE IN THE AMYGDALA KINDLING MODEL OF TEMPORAL LOBE EPILEPSY

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Purpose: Eslicarbazepine acetate (ESL) is a novel once-daily voltage-gated sodium channel blocker approved in Europe for use in adults as adjunctive therapy for refractory partial-onset seizures. In contrast to carbamazepine and R-licarbazepine, ESL has the potential to delay kindling-induced epileptogenesis. The present study determines the effect of ESL in the mouse amygdala kindling model of temporal lobe epilepsy.

Method: Male NMRI mice were stimulated once daily via an implanted depth electrode until 10 generalized seizures were elicited. ESL (100, 200, 300 mg/kg) was administered intraperitoneally 15 min before stimulation. Each ESL experiment was preceded by a vehicle control experiment in the same group of animals.

Results: ESL dose-dependently increased the focal seizure threshold (ADT), with effects statistically significant ($p < 0.05$) at 200 and 300 mg/kg. In 1 out of 10 animals receiving 200 mg/kg and in 7 out of 13 animals receiving 300 mg/kg no seizure activity was observed until the maximum stimulation current of 1200 μA. In response to 200 and 300 mg/kg ESL, threshold increases reached >289% and >1319%, respectively. Seizure duration and after-discharge duration recorded at ADT were not significantly altered by ESL. ESL dose-dependently reduced seizure severity with a significant difference to the vehicle control experiment at 200 and 300 mg/kg.

Conclusion: In this study, ESL inhibited kindled seizures and protected against focal seizure activity in a kindling model. The effect of ESL on seizure severity suggests it may interfere with seizure progression by inhibiting propagation of activity from the focus.

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p850
EFFECTS OF ESLICARBAZEPINE ACETATE AND ITS METABOLITES IN THE CORNEAL KINDLING MICE MODEL OF EPILEPSY

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Purpose: Following oral administration eslicarbazepine acetate (ESL), a novel once-daily voltage-gated sodium channel blocker, undergoes rapid and extensive first pass hydrolysis to its major active metabolite eslicarbazepine. Approximately 4% of the parent dose circulates as ESL's minor metabolite R-licarbazepine. The present study was aimed to determine the effect of ESL, eslicarbazepine and R-licarbazepine on kindling epileptogenesis.

Method: NMRI female mice were kindled by bilateral corneal stimulation twice daily. The compounds ESL, eslicarbazepine and R-licarbazepine were administered intraperitoneally 15 min before each kindling stimulation. Three dosages of ESL were tested (10, 30 and 100 mg/kg). The control group received injections of the corresponding vehicle solution.

Results: At dosages of 30 and 100 mg/kg ESL, the average number of stimulations to reach a fully kindled generalized seizure was increased by 217% and 280%, respectively. Administration of eslicarbazepine also had an inhibitory effect on acquisition of kindling, whereas R-licarbazepine did not affect the number of stimulations necessary to induce a specific seizure stage, and did not exert any relevant effect on mean seizure severity during kindling progression.

Conclusion: These data provide evidence of the anticonvulsant effect of ESL on partial-onset seizures in a kindling model. However, disease-modifying effects may also be involved. ESL may not merely suppress seizure activity but may also inhibit the generation of a hyperexcitable network and therefore provide an antiepileptogenic effect.

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INHIBITORY EFFECTS OF ESLICARBAZEPINE ACETATE AND ITS METABOLITES AGAINST NEURONAL VOLTAGE-GATED SODIUM CHANNELS

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Purpose: Eslicarbazepine acetate (ESL) is a novel once-daily antiepileptic drug approved in Europe as adjunctive therapy for refractory partial-onset seizures in adults. ESL undergoes rapid and extensive first pass metabolism via hydrolysis to eslicarbazepine, its major active metabolite. This study was aimed to determine the effects of ESL, eslicarbazepine, R-licarbazepine (minor metabolite of ESL), oxcarbazepine (OXC) and carbamazepine (CBZ) on voltage-gated sodium channels (VGSCs).

Method: The whole-cell patch-clamp technique was used to investigate the effects of ESL, eslicarbazepine, R-licarbazepine, OXC and CBZ on

sodium channels endogenously expressed in N1E-115 cells. These compounds were tested at various holding potentials (−100 mV, −80 mV and −60 mV). The affinities of the test compounds (250 μM) for the resting (K_R) and inactivated (K_I) states were examined after 15 s conditioning prepulses ranging from −120 mV to −40 mV.

Results: The potency of inhibition was highly sensitive to the holding potential, increasing with depolarization. All compounds demonstrated a much higher affinity for the inactivated (K_I) state of the channel, but the affinity of ESL was approximately two-fold lower than that of CBZ whereas the affinities of eslicarbazepine and R-licarbazepine were approximately four-fold lower. The affinity of eslicarbazepine for VGSCs in the resting (K_R) state was about 15- to five-fold lower than that of CBZ, OXC and R-licarbazepine.

Conclusion: Eslicarbazepine demonstrated a greater selectivity for the inactive state of VGSCs, which is the common feature of the rapidly firing neurons, over their resting state as compared to CBZ, OXC and R-licarbazepine.

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EFFECTS OF ESLICARBAZEPINE, R-LICARBAZEPINE AND CARBAMAZEPINE ON NMDA AND AMPA RECEPTOR–MEDIATED CURRENTS

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Purpose: Altered glutamate-mediated excitatory neurotransmission may play a role in chronic experimental and human epilepsy. Eslicarbazepine acetate (ESL) is a novel once-daily antiepileptic drug approved in Europe for use in adults as adjunctive therapy for refractory partial-onset seizures. ESL undergoes rapid and extensive first pass hydrolysis to eslicarbazepine, its major active metabolite. This study determined the effects of eslicarbazepine, R-licarbazepine (a minor metabolite of ESL) and carbamazepine (CBZ) on submaximal NMDA and AMPA receptor–mediated currents.

Method: Human embryonic kidney (HEK) cells were stably transfected with human GRIN1 receptor (variant NR1-3) and transiently transfected with human GRIN2B receptor cDNAs and CHO cells were transiently transfected with GRIA1 cDNA. The modulatory effects of eslicarbazepine, R-licarbazepine CBZ and D-2-amino-5-phosphonopentanoate (D-AP5) (50–1000 μM, n = 3–5 cells) on submaximal NMDA receptor currents (short application of 30 μM NMDA/10 μM glycine) and NBQX, a negative allosteric AMPA-modulator on submaximal AMPA currents (short application of 50 μM AMPA) were measured in patch-clamped cells at a holding potential of −80mV; 0.4% DMSO was used as vehicle.

Results: Eslicarbazepine, R-licarbazepine, CBZ and D-AP5, a negative allosteric NMDA receptor modulator, inhibited NMDA receptor-mediated currents recorded in HEK cells transfected with GRIN1/2B with IC_{50} values of 1232, 2112, 214 and 7 μM, respectively. Eslicarbazepine, R-licarbazepine and CBZ did not significantly change AMPA currents, whereas NBQX reduced the currents with an IC_{50} of 19 μM.

Conclusion: Eslicarbazepine was more potent than R-licarbazepine although less potent than CBZ in inhibiting NMDA receptor currents. Neither compound affected AMPA currents.

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ESLICARBAZEPINE AND R-LICARBAZEPINE DO NOT HAVE EFFECTS ON ION TRANSMISSION THROUGH ALPHA1, ALPHA2, ALPHA3 AND ALPHA5 GABA CHANNELS

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Purpose: Carbamazepine (CBZ) aggravates absence seizures in ''generalized absence epilepsy rats from Strasbourg,'' possibly through its reported potentiation of $GABA_A$ currents. Eslicarbazepine acetate (ESL) is a novel once-daily antiepileptic drug approved in Europe for adjunctive treatment in adults with partial-onset seizures. This study was designed to determine the effect of ESL's major active metabolite eslicarbazepine, its minor metabolite R-licarbazepine, and CBZ on sub-maximal GABA currents in Ltk cells stably expressing a1b2g2, a2b2g2, a3b2g2 or a5b2g2 GABA-receptors.

Method: Cells were tested 24–48 h after transfection with human $GABA_A$ receptor cDNAs. GABA inward-currents were measured upon application of 1 or 2 μM GABA to patch-clamped cells (at an EC_5), which were voltage-clamped at a holding potential of −80 mV. Test compounds (eslicarbazepine, R-licarbazepine, CBZ, midazolam or bicuculline) were applied by perfusion with GABA.

Results: Eslicarbazepine and R-licarbazepine (50–500 mM) did not significantly change submaximal GABA currents recorded in Ltk cells stably transfected with the a1b2g2, a2b2g2, a3b2g2 or a5b2g2 GABA receptor. CBZ (50–1000 mM) increased in a concentration-dependent manner, sub-maximal a1b2g2 and a3b2g2 GABA currents by 50% and 66%, respectively. Midazolam increased submaximal a1b2g2 GABA currents by ∼80%. Bicuculline inhibited submaximal a1b2g2, a2b2g2, a3b2g2 and a5b2g2 GABA currents with IC_{50} values of 265, 170, 635 and 146 nM, respectively.

Conclusion: In this study, eslicarbazepine and R-licarbazepine, in contrast to CBZ, were devoid of effects upon submaximal GABA currents. Although further research is necessary, these results may translate into a reduced potential for ESL and its metabolites to aggravate absence seizures.

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THE EFFECTS OF ESLICARBAZEPINE, R-LICARBAZEPINE AND CARBAMAZEPINE ON ION TRANSMISSION THROUGH KV7.2 CHANNELS

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Purpose: Activation of voltage-gated potassium-channels (K_V7/M) during the initial stages of an action potential discharge suppresses later action potentials. Inhibition of channel activity strongly enhances repetitive firing. $K_V7.2$ knockout mice have a reduced electroconvulsive threshold and increased sensitivity to convulsing agents. The present study determined the effect of eslicarbazepine acetate's (ESL) major active metabolite eslicarbazepine, R-licarbazepine (a minor metabolite of ESL) and carbamazepine (CBZ) on $K_V7.2$ currents recorded from transiently transfected Chinese hamster ovary (CHO) cells.

Method: About 24–48 h following transfection with human KCNQ2 cDNA, cells were ready for electrophysiological experiments. As soon as a stable seal was established, $K_V7.2$ outward currents were measured at the end of a depolarizing pulse to +20 mV for 500 ms from a holding potential of −80 mV. This voltage protocol was run at intervals of 10 s until stabilization of evoked potassium currents.

Results: Eslicarbazepine had no inhibitory effect on human voltage gated $K_V7.2$ potassium channel transiently transfected in CHO-cells, whereas R-licarbazepine reduced the current amplitude of these currents

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at a holding potential of −80 mV. R-licarbazepine at 100, 250 and 500 μM significantly ($p < 0.01$) reduced the amplitude current amplitudes by 14.2%, 22.3% and 32.5%, respectively. IC_{50} values for CBZ and XE991 (K_V-blocker) were 571.8 and 1.3 μM, respectively.

Conclusion: These data demonstrated that eslicarbazepine differed from R-licarbazepine and CBZ by the lack of inhibitory effects upon $K_V7.2$ outward currents. Although further research is necessary, these results may translate into a reduced potential for eslicarbazepine to facilitate repetitive firing, which is apparently not the case with CBZ and R-licarbazepine.

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p855
EFFECTS OF TOPIRAMATE ON BODY WEIGHT AND SERUM LEVELS OF INSULIN AND LEPTIN IN YOUNG RATS FED A HIGH FAT DIET

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Purpose: Topiramate is an antiepileptic drug used widely in the treatment of epilepsy. It has also been reported to reduce body weight in humans and currently used for eating disorders and obesity: little is known about the mechanism by which this drug induces wight loss. This study was carried out to investigate the effects of topiramate on weight and serum levels of insulin and leptin in young rats fed high fat diet (HFD).

Method: Forty male Wistar rats (4 weeks old) were randomly divided into four groups; (1) HFD with placebo (n = 10), (2) HFD with topiramate (n = 10), (3) regular diet with placebo (n = 10), (4) regular diet with topiramate (n = 10). Topiramate (50 mg/kg/day) was orally administered via gastric gavage twice a day for 4 weeks. Food intake and body weight were monitored throughout the study. After 4 weeks, the plasma levels of glucose, triglyceride, free fatty acid, leptin, and insulin were determined.

Results: We found significant reduction in body weight gain after topiramate administration in HFD group (topiramate, 351.6 ± 28.6 g; placebo, 397.6 ± 28.4 g) ($p < 0.05$). Topiramate was able to reduce food intake in both diet groups ($p < 0.05$). Fasting glucose levels were significantly lower in both topiramate groups than placebo groups ($p < 0.05$), and serum leptin levels in the HFD group were decreased ($p < 0.05$).

Conclusion: Topiramate inhibited body weight gain by reducing food intake, especially in the HFD group and reduced serum levels of glucose in both diet groups and of leptin in the HFD group.

p856
EFFECTS OF VALPROATE AND TOPIRAMATE ON PANCREATITIS IN RATS

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Purpose: The importance of inflammation and apoptosis in acute necrotizing pancreatitis (ANP) is well known. Valproate (VPA) is an apoptotic agent and powerful histone deacetylase inhibitor. Its opposite, topiramate (TPM), is an antiapoptotic agent. This study investigated the apoptotic and necrotic effects of VPA and TPM on ANP induced by glycodeoxycholic acid in rats.

Method: Forty rats were divided into four groups of 10 animals each. Animals in group 1 received intraductal saline and intravenous saline infusion treatment. ANP was induced in the animals in group 2 (ANP with saline infusion). Groups 3 and 4 were given intraductal saline and intraperitoneal VPA (150 mg/kg in a total of six doses, twice a day, before pancreatitis induction. A further two doses were administered postpancreatitis induction) or TPM (40 mg/kg, twice a day, in a total of six doses (3 days), before pancreatitis induction. A further two doses were again administered postpancreatitis induction), respectively. Twenty-four hours after pancreatitis induction rats' cardiac and biochemical parameters were measured with bronchoalveolar lavage (BAL LDH) to the right lung. Pancreatic tissue myeloperoxidase and malondialdehyde activities were examined pathologically and immunohistochemically (for apoptosis TUNEL, TNFα, IL-1β and P53).

Results: ANP induction significantly increased mortality rate and pancreatic necrosis in pancreatic organs. It also increased levels of amylase and alanine aminotransferase (ALT) in serum, raised levels of urea and lactate dehydrogenase in BAL LDH, enhanced the activities of myeloperoxidase (MPO) and malondialdehyde (MDA) in pancreas and lung tissue, and reduced serum calcium levels. When edema, necrosis, inflammation, increased apoptosis, p53, TNFα and IL-1β in the ANP group were compared with the ANP + VPA and ANP + TPN groups, there was a worsening in pancreatitis in the ANP + VPA group and a significant improvement in the ANP + TPM group.

Conclusion: These results indicate that the effects of TPM were beneficial on the course of ANP in rats, while those of VPA were detrimental.

p857
INTERACTION OF THE ANTIEPILEPTIC DRUG ILEPCIMIDE WITH NA^+ CHANNELS IN MICE HIPPOCAMPAL NEURONS

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Purpose: Ilepcimide, 3, 4-methylene dioxy cinnamoyl piperidine, used to called antiepilepsirine (AES) is an effective Chinese antiepileptic drug. It was extracted from an effective traditional Chinese medicine prescription. Although its clinical treatment is effective, its antiepileptic mechanism is undefined. We intend to find the antiepileptic mechanism of ilepcimide.

Method: Brain sodium channels continue to be an important target of many antiepileptic drugs. We intend to find interaction of ilepcimid with Na^+ channels in mice hippocampal pyramidal neurons by whole-cell recording technique.

Results: In hippocampal pyramidal neurons, ilepcimide caused a tonic inhibition of Na^+ currents in a concentration-dependent and voltage-dependent manner. The half-maximal inhibitory concentration (IC_{50}) of approximately 8 μM was obtained at a holding potential (V_h) of −90 mV compared with an IC_{50} of 2 μM at a V_h of −60 mV. Ilepcimide (2 μM) caused a 8 mV negative shift in the voltage dependence of activation and a 15 mV negative shift in slow, steady-state inactivation curve, but had no significant effects on the delayed considerably the recovery from inactivation. Suggesting that ilepcimide acts mainly on the slow inactivated state. These results were consistent with the drug action being on firing properties of pyramidal neurons.

Conclusion: Ilepcimide produce a potent inhibition in those epileptiform bursts which caused cumulative inactivation of Na^+ spikes. Our data suggest that the inactivated channel is a primary target for ilepcimide action at therapeutic concentrations.

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THE EFFECTS OF ESLICARBAZEPINE, R-LICARBAZEPINE, OXCARBAZEPINE AND CARBAMAZEPINE ON ION TRANSMISSION THROUGH $CA_V3.2$ CHANNELS

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Purpose: Transcriptional induction of T-type calcium channels ($Ca_v3.2$) is a critical step in epileptogenesis and neuronal vulnerability. This study was aimed to determine the effect of eslicarbazepine (major active metabolite of eslicarbazepine acetate), R-licarbazepine, oxcarbazepine (OXC), and carbamazepine (CBZ) on $Ca_V3.2$ currents.

Method: The whole-cell patch-clamp technique was used to investigate the effects of eslicarbazepine, R-licarbazepine, OXC and CBZ on $Ca_v3.2$ calcium channels stably expressed in human embryonic kidney cells. Compounds were tested (0.3–1000 μM; n = 3–5 cells) on $Ca_V3.2$ currents upon depolarization of the cell membrane to −25 mV for 50 ms from a holding potential of −80 mV. $Ca_v3.2$ blockers valproic acid and mibefradil were used as reference.

Results: The observed inhibition was best fit using a two-site binding model with constant remaining current amplitude. A block of high affinity occurs with an IC_{50} of 0.43 μM, 6.54, and 27.10 μM for eslicarbazepine, R-licarbazepine and CBZ, respectively. A further block occurs at higher concentrations with an IC_{50} of 62.61 μM for eslicarbazepine, 883.10 μM for R-licarbazepine and 711.20 μM for CBZ. Up to 30 μM, OXC was devoid of effect on $Ca_V3.2$ currents. IC_{50} values for mibefradil were 143.7 nM; 1 mM valproic acid blocked calcium peak currents by 66.15 ± 2.05 (n = 8 cells).

Conclusion: These results demonstrated that eslicarbazepine effectively inhibits high and low affinity $Ca_V3.2$ inward currents with higher affinity than R-licarbazepine, CBZ or OXC. Although further research is necessary, this may translate into an enhanced potential for eslicarbazepine to elicit antiepileptogenic effects.

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p859
AMYGDALOHIPPOCAMPECTOMY: SURGICAL APPROACHES

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Between 2005 and 2010, 21 cases of mesial temporal sclerosis were diagnosed revealed by refractory epilepsy. Amygdalohippocampectomy was achieved through transylvian or transtemporal approach. The author's video presents the advantages and limits of each approach.

p860
SUDDEN UNEXPECTED DEATH IN EPILEPSY (SUDEP): PEDIATRIC CASES

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Purpose: To identify the rate and characteristics of SUDEP deaths in children identified from a large UK cohort safety study.

Method: A cohort study using the General Practice Research Database to assess mortality in children (aged 0–18 years) with epilepsy who were prescribed antiepileptic drugs. Between 1st January 1993 to 31st December 2005, there were 6190 subjects of whom 151 died. The cause of death was identified by an expert panel using patient profiles, GP questionnaires, postmortem reports, death certificates and hospital discharge summaries. SUDEP was defined based on Nashef's definition (1997). SUDEP was classified as ''definite,'' ''probable,'' or ''possible'' and the rate of SUDEP was calculated by dividing the number of cases of SUDEP by the person-years of the cohort (26,890 person-years).

Results: SUDEP was classified as a definite cause of death in two subjects (1%), probable in 3 (2%) and possible in 6 (4%). Incidence rate for SUDEP (definite and probable) was 1.9 per 10,000 person-years (95% CI 0.6, 4.3) and possible SUDEP rate was 2.2 per 10,000 person-years. Age range was 2–17 years, with more males (8) than females (3). Four subjects who died from SUDEP had no known underlying disorder; three of these subjects were treated with monotherapy, suggesting a milder form of epilepsy or better controlled epilepsy.

Conclusion: SUDEP occurs in children with epilepsy but the incidence is low. It is even lower in children with no other evident underlying disorder but can also occur in this group.

p861
THE PREDICTORS OF SEIZURE IN CEREBRAL VENOUS SINUS THROMBOSIS AND ITS PROGNOSTIC SIGNIFICANCE

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Purpose: There is paucity of information about the prognostic significance of seizure in cerebral venous sinus thrombosis (CVST). To evaluate the predictors of seizure in CVST and its influence in mortality and functional outcome.

Methods: Eighty-five consecutive patients with CVST were subjected to detailed history, clinical examination, and laboratory tests as per fixed protocol. The diagnosis of CVST was based on MR Venography (MRV). The MRI and MRV findings were noted. The occurrence and type of seizure at presentation and during hospital stay were noted. The patients were treated with low molecular or unfractionated heparin (LMWH/UFH) for 14 days followed by oral anticoagulation. Antiepileptic drugs (AEDs) were prescribed to the patients who had seizure. Hospital mortality and 3 month outcome based on Barthel index score was categorized into poor (BI < 12), partial (BI = 12–19) and complete (BI = 20).

Results: Their median age was 30 (6–76) years and 47 were females. 91.9% patients presented with headache, 53.5% focal weakness, 51.2% seizure and 53.5% altered sensorium. On univariate analysis, seizures were related to parenchymal lesion (p = 0.01) especially hemorrhagic infarction (p = 0.01) and raised intracranial pressure (p = 0.04). On multivariate analysis parenchymal lesion was independently associated with seizure (OR 0.02, 95%CI 0.07–0.60, p = 0.004). Five patients died, 6 had poor, 3 partial 68 had complete recovery. Mortality (p = 0.36) and 3 months functional outcome (p = 0.58) however were not related to seizure.

Conclusion: Seizures occur in half the patients with CVST especially in patients with parenchymal lesion. The mortality and 3 month outcome however are not dependent on seizure.

p862
COMPARATIVE STUDY OF CARBAMAZEPINE AND LEVETIRACETAM ON BONE MINERAL STATUS IN ELDERLY PATIENTS WITH EPILEPSY

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Purpose: Bone mineral status is important in elderly population while selecting antiepileptic drugs. The aim of this study is to do comparative study of carbamazepine and levetiracetam on bone mineral status in elderly patients with epilepsy.

Method: This prospective study was carried by department of Neurology, SMS hospital, Jaipur, India. We study bone mineral density (BMD) in 24 epileptic patients of age 60–75 years, 12 in each arm and compared with 15 controls. Patients were either taking carbamazepine or levetiracetam as monotherapy for more than 1 year.

Results: The mean age of patients was 65 ± 20 years. Mean duration of antiepileptic was 15 ± 3 months. Those patients on carbamazepine, Mean T score of forearm bone was −2.45, of hip −1.9 and of spine −2.4 which was significantly lower than control suggesting osteopenia. Those patients on levetiracetam, Mean T score of forearm bone was −1.15, of hip −1.2 and of spine −1.4. The Mean T score did not differ significantly between the patients on levetiracetam and control.

Conclusion: Elderly patients receiving carbamazepine as antiepileptic are at risk of osteopenia and should be offered bone densitometer. Routine monitoring of risk and consideration of prophylactic vitamin D supplementation is important in these patients. Levetiracetam does not significantly affect BMD and better alternative for elderly patients.

p863
THE RELATIONSHIP BETWEEN SLEEP AND EPILEPSY IN INFANCY AND CHILDHOOD

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Purpose: Part 1, to quantify the frequency and nature of sleep disturbances in epileptic children compared to nonepileptic children.

Part 2, to evaluate whether certain epilepsies have distinctive patterns of sleep disturbance.

Background: Sleep disturbance and epilepsy are disorders that when comorbid can potentiate each other. Sleep disturbance, epileptic discharges, nocturnal seizures and certain epileptic drugs, individually and collectively have a detrimental effect on cognition and behavior in children. Moreover, nocturnal and diffuse epilepsies, those occuring whilst awake and asleep, are especially prevalent in infants and children.

Method: A questionnaire-based study: The sleep disturbance scale for children (SDSC) was used. The SDSC contains 26 questions divided into five factors. Disorders of initiating and maintaining sleep, respiration, arousal and nightmares, sleep-wake transition, excessive somnolence and sleep hyperhydrosis.

The study population comprised; 100 children with epilepsy admitted to our hospital during a period of 1 year and 100 controls. Age range, 2–15 years. Exclusion criteria for the control group included; neurological illness or syndrome, ADHD or mental retardation. The epilepsy diagnosis was recorded for the epilepsy population.

Results: All statistical analyses performed using the program *Statistica*.

Comparisons of the item scores between the epilepsy and control group showed significant and robust results pertaining to 10 items. Six items related to: *disorders of initiating and maintaining sleep*: specifically, difficulty in falling asleep (at bedtime and after night awakenings), falling asleep anxiety, night awakenings and reduced sleep time. Other items that reached significance: nightmares, hypnic jerks, nocturnal hyperkinesia and sleep paralysis.

Conclusion: The preliminary results suggest that epileptic children have an increased incidence of disorders of initiating and maintaining sleep. The evaluation is continuing.

Reference: Bruni O, et al., The Sleep Disturbance Scale for Children (SDSC). J. Sleep Res (1996) 5. 251–261.

p864
NOVEL MUTATIONS IN THE *GLRA1* GENE ASSOCIATED WITH AN APPARENTLY SPORADIC CASE OF HYPEREKPLEXIA

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Hyperekplexia is a nonepileptic, paroxysmal disorder characterized by exaggerated startle responses to tactile, auditory or other stimuli. Infants with the major form of the disorder often present in the neonatal period with hypertonia and episodes of stiffening. Mutations of five genes have been associated with hyperekplexia. The majority of cases are caused by mutations in the alpha1-subunit (*GLRA1*) of the human inhibitory glycine receptor (hGlyR), located on chromosome 5 Q32. (Rees MI et al. Hum Mol Genet 2002;11:853–60.) While in familial cases of hyperekplexia a genetic mutation is often found, in sporadic cases, genetic mutations are rarely identified. (Rees MI et al. Hum Genet 2001; 109: 267–270) We report a case of apparently sporadic hyperekplexia with two novel, previously unreported heterozygous variants, resulting in the major form of hyperekplexia.

The infant, who had no family history of seizures or hyperekplexia, developed episodes of body stiffening and shaking at 2 days of age. Despite treatment with phenobarbital, the episodes persisted. At 47 days of age, video-EEG monitoring was performed, capturing numerous episodes without electrographic correlate. The infant manifested an exaggerated head-retraction reflex in response to tapping the tip of the nose, which did not habituate, and the diagnosis of hyperekplexia was suspected. *GLRA1* exon sequencing was therefore performed and was abnormal, with heterozygous variants identified in exons 4 and 7. These are previously unpublished variants, but in the context of the clinical symptomatology, they are felt to be pathogenic changes, resulting in the major form of hyperekplexia.

This case is unique both because of the novel mutations identified and because these were identified in a sporadic case of hyperekplexia.

p865
LEVETIRACETAM VERSUS LORAZEPAM IN STATUS EPILEPTICUS: A RANDOMIZED OPEN-LABEL PILOT STUDY

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Purpose: For the management of status epilepticus (SE), lorazepam (LOR) is recommended as the first and phenytoin or fosphenytoin as the second choice. Both these drugs have significant toxicity. Intravenous levetiracetam (LEV) has become available but its efficacy and safety has not been evaluated in comparison to LOR. To report a randomized, open-label pilot study comparing the efficacy and safety of LEV and LOR in SE.

Methods: Consecutive patients with convulsive or subtle convulsive SE were randomized into LEV 20 mg/kg iv over 15 min or LOR 0.1 mg/kg over 2–4 min. Failure to control SE after 10 min of administration of one

study drug was treated by the other. The primary end point was clinical seizure cessation and secondary end points were 24 h seizure freedom, hospital mortality and adverse events.

Results: Thirty-eight patients with SE were randomized to LEV and 41 to LOR. The baseline characteristics were similar between the two groups. In the first instance, the SE was controlled by LEV in 76.3% and by LOR in 75.6% (p = 1.00). In those resistant to above regimen, LEV controlled SE in 70.0% and LOR in 88.9% patients (p = 1.00). Twenty-four hours seizure freedom was also comparable; by LEV in 79.3%, LOR in 67.7% and combination in 75% (p = 0.38). LOR was associated with more frequent respiratory failure (10 vs. 5) and hypotension (8 vs. 2) compared to LEV.

Conclusion: For the treatment of SE, LEV is as effective as LOR and may be preferred in patients with respiratory compromise and hypotension.

p866
RETROSPECTIVE ANALYSIS OF MAJOR CONGENITAL MALFORMATIONS (MCMS) AND ORAL CLEFTS (OC) ASSOCIATED WITH IN UTERO TOPIRAMATE EXPOSURE

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Purpose: To examine the risk of major congenital malformations (MCMs), including oral clefts (OCs), among infants exposed to the antiepileptic drug (AED) topiramate in utero.

Methods: This is a retrospective analysis using data from Wolters Kluwer Pharma Solutions. Source LX Patient Longitudinal datasets from the United States followed patients' Pharmacy and Medical Claims (January 2003–December 2010) to identify women exposed to topiramate within 10 months of giving birth (n = 778). Probable exposure during pregnancy was refined using data on script fill date, days supply, infant birth date, and ICD-9 codes for birth term.

Two control cohorts were identified, one comprised of women exposed to other AEDs (n = 3431) during pregnancy and a second of women with a diagnosis of epilepsy (n = 2307). Topiramate use was excluded from both controls. In all cohorts known or suspected teratogens, including valproate, carbamazepine, and phenytoin were excluded. We calculated the unadjusted relative risk and 95% confidence intervals (95% CI) between topiramate and each control cohort.

Results: The frequency of OCs in topiramate exposed dyads was 0.26% compared to 0.20% in the AED control group and 0.30% in the epilepsy control group. For MCMs, rates were 4.11%, 3.50%, and 4.72% for topiramate, other AEDs, and epilepsy controls, respectively. Relative risk (95% CI) for TPM versus other AEDs for MCMs is 1.18 (0.80–1.72), with RR of OCs being 1.26 (0.26–6.05). For TPM versus the epilepsy control group, RR is 0.87 (0.59–1.28) for MCMs and 0.85 (0.18–4.07) for OCs. There were no significant differences in OC or MCM frequency between topiramate and controls.

Conclusions: These results do not support a significantly increased risk of oral clefts or major congenital malformations with topiramate exposure.

p867
ELECTRIC MODULATION OF ONGOING PHARMACORESISTENT FOCAL MOTOR SEIZURES BY SUBTHALAMIC NUCLEUS IN A PRIMATE MODEL

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Purpose: Epileptic seizures arise from pathological synchronization of neuronal ensemble. Those arising from primary motor cortex are often pharmacoresistent, and many times unsuitable for resective surgery because of location of epileptic focus in eloquent area. Basal ganglia play important role in seizure propagation. Microelectrode recordings performed during previous studies in our lab indicated that input structures of basal ganglia such as GPe, Putamen and STN are strongly modified during seizures. Pilot studies in humans have shown the possible effect of chronic DBS applied to STN to treat pharmacoresistant motor seizures. Our study was aimed at studying the therapeutic effect of electrical stimulation of input structures of basal ganglia.

Method: We generated and characterized a stable, predictable model of focal motor epilepsy by intracortical injection of penicillin in two primates and documented its pharmacoresistence. We then stereotactically implanted DBS electrodes in the Subthalamic nucleus (STN) and embedded stimulator at the back of the animals. In first set of 31 experiments in two animals Subthalamic nucleus subthreshold electrical stimulations at 130 Hz were applied.

Stimulator was turned ON when penicillin was injected. Sham stimulation at 0 volt was used as a control situation, each monkey being its own control. The time course, number and duration of seizures occurring in each epochs of 1 h were compared during ON and sham stim periods. Each experimental session lasted 6–8 h.

Results: The high frequency stimulation of Subthalamic nucleus was effective. The occurrence of first seizure was significantly delayed as compared to sham situation. And total time spent in focal seizures was significantly reduced by ≥60% on an average ($p \leq 0.05$) after STN stimulation.

Conclusion: This study provides initial original data in primates showing effects of electrical modulation by chronic HFS-STN DBS in focal motor seizures. Potential translational application to human disease condition is described.

p868
ANTICONVULSANT ACTIVITY OF ECLIPTA ALBA USING EXPERIMENTAL MODELS OF EPILEPSY

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Eclipta alba is reported with varied important activities in traditional system of medicine. In the present work, the extract of Eclipta alba leaves were studied for its anticonvulsant potential using Maximal electroshock (MES) and Pentylenetetrazole (PTZ) etc models of epilepsy. LD50 study was conducted and Eclipta alba was found to be safer upto 2000 mg/kg dose. Locomotor activity was carried out to understand the basic drug efffect. Three dose levels of extract were used. A decrease in duration of hindleg extension in MES model and delay in the onset of convulsion in PTZ model indicates anticonvulsant activity. Extract was found to posses anticonvulsant activity against both the models of epilepsy. Brain GABA and glutamate levels were estimated to study the effect of extracts on brain monoamine levels. GABA antagonist-picrotoxin had significantly inhibited the response of Eclipta Alba on guinea pig ileum and hence confirmed the involvement of GABA receptor. EEG recording is planned for neurological defect and epileptiform activity.

p869

COMPARISON OF ZONISAMIDE AND CARBAMAZEPINE MONOTHERAPY IN ADULTS WITH NEWLY DIAGNOSED PARTIAL EPILEPSY: PRELIMINARY RESULTS OF A PHASE III, RANDOMIZED, DOUBLE-BLIND, NONINFERIORITY TRIAL

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Purpose: To compare efficacy and safety of once-daily zonisamide (ZNS) and twice-daily controlled-release carbamazepine (CBZ) monotherapy in adults with newly diagnosed partial epilepsy.

Methods: Phase III, international, randomized, double-blind, noninferiority trial, in which 583 untreated adults (18–75 years) with newly diagnosed partial epilepsy received ZNS or CBZ. Following initiation (ZNS 100 mg/day; CBZ 200 mg/day) and up-titration (to 300 and 600 mg/day, respectively), patients entered 26–78-week flexible-dosing period (200–500 and 400–1200 mg/day, respectively, according to response/tolerability). Once seizure-free for 26 weeks, patients entered a 26-week maintenance phase. Primary end point was proportion of patients seizure-free for ≥26 weeks. Safety/tolerability evaluation included assessment of treatment-emergent adverse events (TEAEs).

Results: Overall, 161/282 (57.1%) patients randomized to ZNS and 192/301 (63.8%) patients randomized to CBZ completed the trial. Twenty-six-week seizure freedom rates were 79.4% (177/223) for ZNS versus 83.7% (195/233) for CBZ (Per Protocol Population). Adjusted absolute treatment difference was −4.5% (95% confidence interval [CI]: −12.2, 3.1). The lower CI limit narrowly exceeded the protocol-specified −12% margin, but lower CI limit of the relative difference (−14.7%) was within the ILAE-recommended margin (−20%). In majority of patients seizure freedom was achieved at first dose level (ZNS 300 mg; CBZ 600 mg). Incidence of TEAEs was similar for ZNS (60.5%) versus CBZ (61.7%), as was incidence of serious TEAEs (5.3% vs. 5.7%) and TEAEs leading to withdrawal (11.0% vs. 11.7%).

Conclusion: Both ZNS and CBZ demonstrated high response rates and were well-tolerated in newly diagnosed partial epilepsy patients.

Study supported by Eisai.

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PRELIMINARY RESULTS FROM 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: Zonisamide (ZNS) is currently licensed (USA, Europe) for adjunctive treatment of partial seizures in adults. This trial was conducted to assess the efficacy and safety/tolerability of adjunctive ZNS in pediatric patients with partial-onset seizures.

Methods: The CATZ Study was a Phase III, multicenter, randomized, double-blind, placebo-controlled trial in which 207 pediatric patients (6–17 years) with partial epilepsy, on 1–2 antiepileptic drugs, received either adjunctive ZNS or placebo. ZNS was initiated at 1 mg/kg/day, up-titrated to 8 mg/kg/day over 8 weeks (one down-titration permitted), and continued unchanged for 12 weeks. Primary end point was proportion of responders (≥50% seizure frequency reduction) after 12 weeks' maintenance treatment. Safety/tolerability evaluation included assessment of treatment-emergent adverse events (TEAEs).

Results: Overall, 93/107 (86.9%) patients randomized to ZNS and 90/100 (90.0%) patients randomized to placebo completed the trial. Responder rates were 50.5% for ZNS vs. 31.0% for placebo ($p = 0.0044$; ITT-LOCF). Overall incidence of TEAEs was similar for ZNS (55.1%) versus placebo (50.0%). There were low rates of serious TEAEs in the ZNS and placebo groups (3.7% vs. 2.0%), and TEAEs leading to withdrawal (0.9% vs. 3.0%). TEAEs reported more frequently with ZNS vs. placebo were decreased appetite (6.5% vs. 4.0%), decreased weight (4.7% vs. 3.0%), somnolence (4.7% vs. 2.0%), vomiting (3.7% vs. 2.0%) and diarrhoea (3.7% vs. 1.0%).

Conclusion: Adjunctive ZNS treatment was shown to be more effective than placebo in pediatric patients with partial epilepsy. ZNS was well tolerated and no new unexpected safety findings emerged in this population.

Study supported by Eisai.