

# Epilepsia

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## ASBTRACTS

# 30th International Epilepsy Congress, Montreal, Canada, 23–27 June, 2013

### Poster Session: Adult Epileptology A Monday, 24 June 2013

P073

#### SHOULD WE SUBSTITUTE ILAE CLASSIFICATION OF EPILEPSY FOR CLEVELAND CLASSIFICATION?

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**Purpose:** To determine the value of semiology and interictal perictal of seizures to estimate the location and laterality of the epileptogenic region.

**Method:** A descriptive cross-sectional multicenter double-blind to 142 patients referred for presurgical evaluation at the International Center for Neurological Restoration, the University of Antioquia and Neurological Institute of Colombia from the years 2007 to 2011. Underwent a structured interview and a video EEG, comparing the results obtained.

**Results:** Auras, focal seizures, dysphasia or ictal psychoses, postictal confusion, version of the head, migraine headache and amnesia preictal allowed to differentiate the origin of the crisis. The temporal and sequential order of appearance of the typical temporal auras, front focal seizures followed by focal or generalized Hemiconvulsion, or lower limb automatisms without automatic oroalimentary, together with confusion, depression, and the existence of a latency period can differentiate EAs clearly.

**Conclusion:** Symptoms Video perictales evaluated by EEG can be obtained by clinical interview, which the symptoms associated with interictal and analyzed in the temporal order in which they appear during crises for estimating the location and laterality of EAs with high sensitivity and specificity.

P074

#### EPISODIC EPIGASTRIC SENSATIONS AS SOLITARY MANIFESTATIONS OF TEMPORAL LOBE EPILEPSY

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**Purpose:** For adults, the paroxysm of abdominal symptoms is a highly frequent type of aura in medial temporal lobe epilepsy (MTLE). For the case of paroxysm of botanical nerves, by taking abdominal symptoms as the only clinical feature is extremely rare. Sometimes it may easily cause misjudgment. We would like to report an unusual case merely showing epigastric sensation without any abnormal motion symptoms or impairment of consciousness. One case of epigastric sensation, as the principal place for a year, has been made a diagnosis and gave pertinent medical treatments.

**Method:** A male patient aged 60 under health conditions before, who had been regularly suffering from episodic epigastric sensations six or seven times every day. Based on the patient's descriptions, "rising air" initiated epigastric ascending to his chest and terminated in the throat. Judging by the results of extensive gastrointestinal and cardiothoracic investigations, there was no abnormality, therefore, an underlying seizure disorder was suspected.

**Results:** Neurological examinations were normal. MRI imaging manifested right hippocampal sclerosis. Ictal v-EEG revealed that the seizure onset started with rhythmic theta activity associated with right anterior temporal leads and terminated with delta activity involved with right hemisphere leads. The patient was prescribed with low dose of carbamazepine of 100 mg twice daily. The episodic epigastric sensations disappeared utterly during a 2-month period of follow-up.

**Conclusion:** This case is peculiar for the following reasons: (1) The symptoms were confined to epigastric sensations. (2) Generally speaking, simple partial paroxysm of abdominal symptoms, as the clinical feature, is mainly showing by children and youth. But this case is unusual because the patient aged 60. (3) The patient was very sensitive to anti-epilepsy medications. Hence, for primary physicians, especially gastroenterologists should be acquainted with the manifestations of simple partial seizures to avoid any dispensable medical examinations, even mal-treatments.

P075

#### SEIZURE RELAPSES IN THE COURSE OF PARTIAL EPILEPSY WITH CONVULSIVE GENERALIZED SEIZURES IN ADULTS

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**Purpose:** Identify the dominant factor of relapse risk and relationship between length of remission and likelihood of relapse.

**Method:** Two patient groups of between the ages of 18 and 60 was studied. With a history of one or more relapses and patients in remission without a history of relapses. The research methods included retrospective and prospective observation. Groups were comparable with basic demographic and clinical data. The statistical methods were: The Fisher Chi-square test, tests of Mann–Whitney and Kaplan–Meier, the Cox-regression method, dispersive analysis. The statistical program used: SPSS for windows v.11.5.

**Results:** Following courses of disease were identified: (1) benign course (without relapses or with one relapse), (2) course with two or more relapses, (3) with serial seizures and status epilepticus, (4) pharmacoresistant course.

The difference in duration of the disease between the two groups was statistically significant  $19.57 \pm 9.12$  vs  $11.65 \pm 5.86$  years  $p < 0.001$ . In cases of the prolonged duration of the disease, there is a linear causal relationship between the duration of the disease and the logarithm of the relapse-free course of life, that is the likelihood of the epileptic relapse is similar for different patients and does not depend on the duration of the remission. We found out that there is no statistically significant relationship between the independent variables listed above and the risk of epileptic relapse. It appears that only the type of disease course is statistically significant as a risk factor of the relapse ( $p < 0.05$ ). We identified the likelihood of the relapse-free course of life in epileptic patients. The only factor that appeared statistically significant was the type of the remission ( $p = 0.026$ ).

**Conclusion:** The only statistically highly significant difference between groups with and without relapses is duration of disease. Among various

hypothetical risk factors, the type of the disease course, appeared statistically significant.

#### P076

##### VISUAL HYPERSENSITIVITY ATTACKS: AN ITALIAN CASE

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**Purpose:** Visual hypersensitivity attacks, sometimes accompanied by oculogyric crisis, are ictal adverse events of antipsychotic drugs, little known outside of the case studies in Japan, with possible implications in the differential diagnosis of seizure disorders.

**Method:** Description of a clinical case.

**Results:** A 46 year old woman, suffering from paranoid schizophrenia since the age of 30 years, is in chronic antipsychotic therapy, particularly with prescription over the last 3 years of paliperidone 6 mg daily associated with tetrabenazine 25 mg daily. Since she is taking this combination therapy, episodes appeared in the afternoon, with a frequency more than monthly, lasting from 15 min to a few hours, which begin with oculogyric crisis, associated with visual illusions (small spots, light and dark, overlap with what is present in the visual field), photophobia, anxiety and malaise, without alteration of consciousness nor triggering headache. The episodes occur more easily if the patient is outdoor and have gradual remission, facilitated by staying in dimly lit room. There are no interictal neurological or ocular abnormalities, not even there are pathological data at the ictal and interictal EEG. Previous neurological consultations required by the treating psychiatrist were not conclusive. The clinical picture is rather exactly matching to the visual hypersensitivity attacks described in Japanese patients treated with some antipsychotics.

**Conclusion:** The visual hypersensitivity attacks (otherwise known as paroxysmal perceptual alteration) are complications of antipsychotic drugs, little known in Europe, which should be considered in the differential diagnostic process of ictal disorders.

#### P077

##### THE THERAPEUTIC ROUTE OF THE EPILEPTIC PATIENT CONSULTED IN THE EPILEPTOLOGY UNIT OF ABIDJAN, COTE D'IVOIRE

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**Purpose:** To analyze the therapeutic route of the epileptic patients before the diagnosis and the starting of an antiepileptic treatment by the neurologist.

**Method:** A prospective and descriptive study realized in the epileptology units of the teaching hospitals of Cocody and Yopougon in Abidjan (Côte d'Ivoire), over a period of 8 months from August 2008 to March 2009 about 101 patients with epilepsy.

**Results:** 62.5% of patients had recourse to a traditional healer first. 13.3% saw more than 10 healers. 11.8% combined the medical and the traditional treatment. 27.7% consulted on the day of the first seizure in a health centre. In 37% of cases, the first health care facility was a dispensary. The first-line health professional was the male nurse (11.8%) or the general practitioner (41.7%). The average consultation period was equal to 2.16 years, that of the electroencephalogram performance was equal to 3.6 years and that of the prescription of antiepileptic drugs was equal to 3.64 years. The education level and the diurnal or nocturnal character of seizures affect the consultation period.

**Conclusion:** The intensification of awareness campaigns and the training of first-line health personnel can shorten the consultation period and improve the care.

#### P078

##### CORRELATION BETWEEN HIPPOCAMPAL VOLUME AND SLEEP QUALITY IN MESIAL TEMPORAL SCLEROSIS

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**Purpose:** We intended to demonstrate the association between sleep quality (SQ) and hippocampal volume (HV) in epileptic patients with mesial temporal sclerosis (MTS).

**Method:** Twenty-five patients diagnosed with temporal lobe epilepsy with MTS, on basis of video electroencephalogram and magnetic resonance imaging were consecutively enrolled. Volumetric measurement of each hippocampus was performed manually using Cavalieri's principle with coronal sections of 1 mm of thickness and regions of interest (ROIs) of 2 × 2 mm. HV was corrected by the volume of corresponding brain hemisphere, measured by the same method. SQ was evaluated through the Pittsburgh Quality of Sleep Index (PQSI). Variables were analyzed using Pearson's correlation and linear regression.

**Results:** Of the 25 patients, 13 had left and 12 right-sided MTS. There were no differences in atrophic hippocampal volumes between these groups. A negative correlation between the volume of the atrophic hippocampus and PQSI was observed ( $r = -0.60$ ,  $p < 0.01$ ). Bivariate linear regression also demonstrated that smaller hippocampi were associated with higher PQSI scores (therefore, worse quality of sleep), regardless of the side of MTS ( $R = 0.69$ ,  $R^2 = 0.48$ ,  $p < 0.01$ ).

**Conclusion:** These data suggest that structural alterations in hippocampus may be associated with SQ. During sleep, multiple neuronal circuits are integrated and the hippocampus performs a unique role in the interaction between cortical-subcortical networks. Disrupting the balance of this system may cause reduction in sleep efficiency. Further multidisciplinary structural, neuropsychological and polysomnographic studies are needed to assess the relationship of hippocampal atrophy and sleep in MTS.

#### P079

##### THE EPINET DATABASE: RESULTS OF A SURVEY OF EPINET INVESTIGATORS

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**Purpose:** The EpiNet database has been established to provide a platform to facilitate investigator-led clinical trials in epilepsy, and to simultaneously provide a clinically useful patient record. Investigators were surveyed to determine how the platform might be improved.

**Method:** All those who have used the EpiNet platform were circulated using the on-line tool, Survey Monkey. The survey was also sent to others who have expressed an interest in EpiNet.

**Results:** There was no significant difference in views between those who are already using the EpiNet platform and those who are not

currently investigators. Eighty six percent of respondents want to use EpiNet to participate in investigator led clinical trials, and 75% wish to enroll patients in prospective registries; 55% will use EpiNet as a personal database and/or to provide an individual patient record; 30% would like EpiNet to provide an on-line emergency management plan for others.

Eighty percent of respondents want EpiNet to collect information on surgical management of epilepsy, and 75% want it to collect information on Status Epilepticus. 80% would like a fully searchable on-line database, 67% would like to be able to link EpiNet with other clinical databases; 50% would like the ability to add documents to the EpiNet record.

The most common problems reported are that too much information is collected (30%), it takes too long to get patients' informed consent (30%), and that the website is too slow (27%).

**Conclusion:** Changes will be made to the EpiNet platform to improve its utility as a clinical tool, and to enhance its usefulness for trials. Forms will be added to collect information on status epilepticus and surgical treatment, and the data collection process will be made more versatile. An on-line search facility will be added. Other developments will be made as funding allows.

#### P080

##### LATE ONSET JUVENILE MYOCLONIC EPILEPSY: REPORT OF 13 CASES

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**Purpose:** To describe the clinical and EEG features of adult patients who presented for the first time with a history of seizures consistent with late onset juvenile myoclonic epilepsy (JME).

**Method:** Consecutive patients with diagnosis of seizures referred to a clinic for epilepsies during January 2006–December 2011 were evaluated. Diagnosis of JME was made based on clinical manifestations, history, EEG findings and normal brain MRI.

**Results:** Of a total 126 JME patients, 13 adult onset cases (10.3%; five males, eight females) were investigated. Mean age of JME onset and age at diagnosis were 43.4 years and 48.2 years respectively. All patients had myoclonic jerks, 12 patients had generalised tonic clonic seizures (GTCS) and two patients had absence seizures. The triad of absence seizures, myoclonic jerks and GTCS was seen in only one case while 12 cases had GTCS and myoclonic jerks. Myoclonic jerks were predominantly unilateral in eight patients (61.5%). Sleep deprivation was the most important precipitating factor (76.9%). Characteristic epileptic pattern of JME was found in 76.9% in the first EEG, which increased to 100% with repeat EEG. Positive family history for epilepsy was seen in 23% and 11 patients (84.6%) had comorbidities. The follow up period ranged from 1 to 7 years. 12 patients (92.3%) are seizure free on monotherapy.

**Conclusion:** JME can rarely begin in adulthood. It's diagnosis is essential to avoid antiepileptic drugs commonly used for focal epilepsy in this age group.

#### P081

##### CLINICAL FEATURES AND ELECTROPHYSIOLOGIC STUDIES OF TWO FAMILIES WITH FCMTE (FAMILIAL CORTICAL MYOCLONIC TREMOR WITH EPILEPSY)

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**Purpose:** To study the clinical features and electro physiologic characteristics of FCMTE.

**Method:** A clinical analysis on 15 patients with FCMTE in two families was conducted. Pedigree charts of the two families were drawn. Somatosensory evoked potentials (SEPs) and long latency reflex (C-reflex) were recorded in four patients, jerk-locked averaging (JLA) cortical potentials were analyzed in two patients.

**Results:** Pedigree chart of two families with FCMTE showed eight patients in three generations in family I and seven patients in two generations in family II. The proband of family I was a 45-year-old woman. Since age 34 she had noted static and kinetic tremulous movements of her hands and head, which was aggravated by emotional stress. Her first generalized convulsive seizure at age of 41. She also complained of migraine and hypomnesia. The seizures were decreased with Oxcarbazepine, her tremor was also attenuated. The proband of family II was a 58-year-old man. Since age 30, he complained of hand tremor when sleep-deprived or emotion stress. He had first seizure 4 years later. Valproate was effective for both symptoms. Giant SEPs were recorded at C3' or C4' by stimulating median nerve in four patients, and enhanced C-reflex was recorded from flexor carpi radialis simultaneously. Positive cortical potentials 15 ms before the gastrocnemius EMG bursts were recorded by JLA in two patients.

**Conclusion:** FCMTE is transmitted as an autosomal dominant trait with high penetrance. The main clinical features of FCMTE are tremor and seizures, which could be treated by anti-epileptic drugs. Electrophysiologic examinations including SEPs, C-reflex and JLA are helpful to diagnosis.

#### P082

##### CLINICAL UTILITY OF ICTAL EYES CLOSURE IN THE DIFFERENTIAL DIAGNOSIS BETWEEN EPILEPTIC SEIZURES AND PSYCHOGENIC EVENTS

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**Purpose:** To evaluate sensitivity, specificity and likelihood ratios (LR) of IEC in the differential diagnosis between psychogenic non-epileptic events (PNEEs) and epileptic seizures. Further studies evaluating the occurrence of IEC through direct observation by means of video-EEG recording and blind to both EEG tracings and patient diagnosis are therefore required to definitely estimate the diagnostic utility of this sign in the differential diagnosis between epileptic seizures and PNEEs.

**Method:** A systematic search of the literature was conducted to identify studies evaluating the presence of IEC in patients with epileptic seizures (all types) and patients with PNEEs using a video-EEG as a reference diagnostic standard. No age, race or gender restrictions were applied. Sensitivity, specificity, positive and negative likelihood ratios (pLR, nLR) with 95% confidence intervals (CIs) were determined for each included study and for the summary estimate of pooled analysis.

**Results:** Six studies (total of 1496 events; 1021 epileptic seizures and 475 PNEEs) were included. Pooled accuracy measures of IEC for the diagnosis of PNEE were: sensitivity 58% (0.579) (95% CI 0.534–0.623), specificity 80% (0.895) (95% CI 0.875–0.9131) %, pLR 5.524 (95% CI 4.546–6.714) and nLR 0.47 (95% CI 0.422–0.524). However, a sensitivity analysis including only the studies performing an IEC assessment blinded to the diagnoses yielded results indicative of a rather low diagnostic value of IEC (pLR 3.056) compared with the analysis including unblinded studies (pLR 12.754).

**Conclusion:** Further studies evaluating the occurrence of IEC through direct observation by means of video-EEG recording and blind to both

EEG tracings and patient diagnosis are therefore required to definitely estimate the diagnostic utility of this sign in the differential diagnosis between epileptic seizures and PNEEs.

### P083

#### IMPORTANCE OF CARDIOLOGICAL EVALUATION FOR FIRST SEIZURES

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**Introduction:** Long QT syndrome (LQTS) represents channelopathies of cardiac potassium/sodium ion channels. Channelopathies may present with seizures and/or risk sudden death because of ventricular dysrhythmia known as torsades de pointes (TdP).

**Cases:** *Case 1:* AB, a 24 year old Asian female, presented with post-partum suspected seizure. Investigation was negative and she was discharged. She re-presented with cardiac arrest and electrocardiogram (ECG) demonstrated TdP, necessitating an implantable cardioverter-defibrillator (ICD).

*Case 2:* CD, a 50 year old Caucasian male, presented with generalised seizure. Routine workup, prompted by experience with AB, confirmed LQTS provoking ICD insertion.

**Discussion:** Both patients presented with 'seizures'. AB was initially discharged with conservative management and LQTS diagnosed on representation. CD was diagnosed because of the experience with AB. LQTS crosses age, gender and racial boundaries (AB being a young Asian female and CD a middle-aged Caucasian male) demanding consideration of LQTS in all first seizures.

*Dobler v Halverson*, an Australian, NSW Court of Appeal case, involved LQTS in a young boy diagnosed by a neurologist as "syncope" without further investigation. Halverson was then managed by his general practitioner (GP), Dr Dobbler, without ECG. Halverson experienced cardiac arrest with severe brain damage and the GP found negligent for not performing an ECG [the role of the neurologist was not considered in this case].

These cases emphasise that first seizure or convulsive syncope presentation demand cardiological evaluation without which the clinician may be considered negligent. A high index of suspicion is mandatory to avoid subsequent catastrophe with personal and legal ramifications.

### P084

#### CASE REPORT: PREICTAL AND POSTICTAL PSYCHOSIS IN A PATIENT WITH PARTIAL COMPLEX SEIZURES WITH SECONDARY GENERALIZATION AND A FUSIFORM ANEURYSM OF THE INTERNAL CAROTID ARTERY

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**Aim:** To present a 46 years old female patient.

**Materials and Methods:** After a common cold, she became confused, oblivious, fearful, with perseverations. A psychiatrist prescribed anxiolytics, antidepressants and later neuroleptics. The patient started to experience fits of screaming, followed by tonic clonic shaking of the limbs.

One episode of unmotivated and uncontrolled laughing, followed by deviation of the head and the gaze to one side and one generalized tonic clonic shaking of the limbs in her sleep were registered. The patient was referred to the Clinic of Psychiatry where she was treated for psychosis with anxiolytics and neuroleptics. She was upset, confused, desorientated, screaming, with visual hallucinations. The fourth day of her hospitalization, the patient became febrile and unresponsive.

**Results:** Lumbar puncture was performed, with normal findings. Brain CT and CT angiography of the intracranial arteries showed giant fusiform aneurysm of the internal carotid artery. Then the patient was transferred to the Clinic of Neurology. On admission she was afebrile, agitated, aphatic. EEG showed one paroxysm of multiple spike wave complex and sharp waves in duration of 12 s. During the EEG, the patient had one partial complex motor seizure. After 2 days another complex partial motor seizure was registered. She was given Sodium valproate 2 × 300 mg, then 2 × 500 mg. The neurosurgeon suggested eventual surgical treatment when the patient recovers completely. Control EEG showed desynchronized background activity, with frequent theta waves bilaterally in the temporal regions. The following days the patient improved, she became aware, conscious and started to speak. No further epileptic seizures were registered during the stay. Antiepileptic drug level monitoring was in normal range. The patient was dismissed after 3 weeks in stable condition.

**Conclusion:** Recognizing a mental disorder that is related to epileptic seizures is crucial for providing an appropriate treatment and favours better outcome.

### P085

#### DIAGNOSTIC EVALUATION IN PATIENTS WITH INTRACTABLE EPILEPSY AND NORMAL MRI STUDY: A DECISION ANALYSIS AND COST-EFFECTIVENESS STUDY

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**Purpose:** Patients with focal intractable epilepsy and normal MRI frequently undergo further diagnostic test(s) to localize the epileptogenic zone. The aim was to determine the cost-effective diagnostic strategy that will identify the epileptogenic zone in patients with suspected focal intractable epilepsy and normal MRI using decision analysis.

**Method:** A Markov decision model was constructed using sensitivities and specificities of test strategies, seizure outcomes following surgical and medical treatment, costs, utilities, probabilities and standardized mortality ratios. Six diagnostic test strategies were compared: 2-[18F]fluoro-2-deoxy-D-glucose positron emission tomography (PET), ictal single photon emission computed tomography (SPECT) and magnetoencephalography (MEG) individually, and combinations of PET+SPECT, PET+MEG and SPECT+MEG. The outcomes measured were health care costs, quality adjusted life years (QALY) and incremental cost effectiveness ratio (ICER). One-way and probabilistic sensitivity analyses were conducted to adjust for uncertainties in model parameters.

**Results:** The two preferred strategies were PET+MEG and SPECT. The baseline strategy (PET+MEG) was estimated to cost \$95,612 with 16.30QALY gained. SPECT cost \$97,479 with 16.45QALY gained, and ICER of \$12,934/QALY gained when compared with PET+MEG. One-way sensitivity analyses showed the model's decisions were sensitive to variations in sensitivity and specificity of test strategies. Probabilistic sensitivity analysis showed when the willingness-to-pay was below \$10,000, PET+MEG was the favoured strategy, but SPECT became the favoured strategy when the willingness-to-pay was above \$10,000.

**Conclusion:** PET+MEG and SPECT were the preferred strategies in base case. The choice of test was dependent on sensitivity and specificity of test strategies, and willingness-to-pay. Further study with larger

sample size is needed to obtain better estimates of sensitivity and specificity of diagnostic tests.

#### P086

##### PREVALENCE OF RESTLESS LEGS SYNDROME AMONG THE EPILEPSY PATIENT WHO TOOK CARBAMAZEPINE OR VALPROIC ACID MONOTHERAPY

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**Purpose:** Restless legs syndrome (RLS) is a common sensory-motor disorder. RLS is characterized by intense restlessness and unpleasant sensation deep inside the legs. The aim of this study was to determine the prevalence of RLS among the epilepsy patient who took carbamazepine (CBZ) or valproic acid (VPA) monotherapy and the findings were compared normal subjects and general population.

**Method:** Patients who took VPA and CBZ monotherapy and followed up at least 6 months in our department were included in this study. The diagnosis of RLS was made according to the International Restless Legs Syndrome Study Group criteria. The finding was compared age-sex matched normal subjects and general population.

**Results:** Ninety-two patients were included in this study (fifty-seven of them taking VPA and the remaining thirty-five taking CBZ). We found RLS in two (2.2%) of them (one of them taking VPA, the other CBZ). The percentage of RLS in normal subject was 6%. However, this difference was not statistically significant.

**Conclusion:** We interpret this result as indirect evidence of treatment of RLS symptoms with CBZ and VA therapy when the finding was compared with general population and normal subject.

#### P087

##### OPERCULOINSULAR AUDIOGENIC PAINFUL SEIZURES

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**Purpose:** Audiogenic epilepsy is a rare form of reflex epilepsy in which seizures are triggered by sound or music. Painful seizures have never been reported with this type of epilepsy. Noninvasive studies of audiogenic epilepsy cases are reported with discordant results. In the few cases investigated with intracerebral electrodes, different temporal foci were found and the insular cortex was not sampled. We report a case of operculoinsular audiogenic painful seizures confirmed by invasive EEG monitoring.

**Method:** Case report.

**Results:** A 46 year-old right-handed man (left hemisphere dominance) with daily refractory nonlesional audiogenic painful seizures was

investigated by intracranial EEG to better delineate the epileptogenic zone. Diurnal seizures were characterized by pain over the right hemifacial area spreading to the right limbs for several seconds while nocturnal seizures frequently evolved into complex motor behaviours. A combination of depth and subdural electrode contacts were implanted sampling the left mesiotemporal structures, the insula, opercula and perisylvian region. Several seizures were triggered by loud noises (>80 db) irrespective of sound frequency, the emotional content of auditory stimuli, and type of ecological or musical stimuli. Electrically, seizures originated from the left parietal operculum-posterior insular area. Resection of the latter in addition to Heschl's gyrus led to seizure-freedom (FU 3 month).

**Conclusion:** Operculoinsular seizures can manifest as reflex audiogenic painful seizures.

#### P088

##### USABILITY TESTING OF THE CASES TOOL (WWW.EPILEPSYCASES.COM): AN ONLINE TOOL TO ASSIST PHYSICIANS IN IDENTIFYING PATIENTS WHO ARE CANDIDATES FOR AN EPILEPSY SURGERY EVALUATION

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**Purpose:** Guidelines recommend that surgery be considered in patients with drug-resistant epilepsy, yet epilepsy surgery is still underutilized. The CASES tool (Canadian Appropriateness Study of Epilepsy Surgery tool) is a web-based, evidence-informed clinical decision tool (www.epilepsycases.com) that was previously developed to assist physicians in determining which patients are appropriate for an epilepsy surgery evaluation. The purpose of the present study was to evaluate the usability of the CASES tool with the intended users.

**Method:** Usability testing was conducted with domain experts (2 neurology residents, 1 pediatric neurologist, 2 adult neurologists) and non-experts (2 family physicians, 1 family medicine resident) addressing barriers to using the tool. The users were asked to apply the CASES tool to five epilepsy cases. A "think-aloud" technique and some directed questions were employed to generate feedback about the usefulness of the website and the tool. Each session took approximately 1 h, was audio-recorded, transcribed, and thematically analyzed to identify recurring themes regarding usability difficulties of the tool and website.

**Results:** Six overall themes were identified: Clearly defining the target user, making the introduction more concise, clearly defining terminology, providing more response options, improving clarity of the final report, and providing guidance on next steps in the referral process.

**Conclusion:** This study provided guidance on how to improve the usability of the CASES referral tool for the target users. The themes and specific recommendations from this study will be incorporated into the tool to improve it, and the revised tool will subsequently be re-evaluated using focus groups.

#### P089

##### FEASIBILITY OF AUDITORY EVOKED MAGNETIC FIELDS IN ESTIMATION OF EPILEPTOGENIC SIDE IN MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** MEG for pre-surgical evaluation of mesial temporal lobe epilepsy (mTLE) is often confronted by fewer chances to detect spikes compared with long-term EEG monitoring. Some patients do not show any interictal spikes because of their rare occurrence during the MEG measurement. Auditory evoked magnetic fields (AEFs) are easily measured by MEG with high reproducibility. AEFs can assess the temporal lobe function, therefore we hypothesized that AEFs provided us to estimate epileptogenic side in mTLE.

**Method:** We measured AEFs in 12 preoperative patients (6 for each hemisphere) and 6 healthy subjects. Epileptogenic side was postoperatively determined and we compared the laterality of each component of AEFs with epileptogenic side in mTLE. A 500-Hz tone-burst stimulus of 100 ms duration was presented monaurally with intensities 50 dB SL and 100 responses were averaged for each side. Subjects were kept awake during the measurement, but no tasks were required in response to the stimuli.

**Results:** We found the significantly decreased amplitudes of N100 m on the epileptogenic side in the right mTLE patients, and there was also the same tendency for the left mTLE patients. Interestingly, we observed the significantly increased amplitudes of the late component (300–400 ms), which was also well concordant with the epileptogenic side in both mTLE groups. Source localization with the beamformer method revealed that the late component was localized in the mesial side of the temporal lobe on the epileptogenic side.

**Conclusion:** We propose that AEFs are useful for determining the epileptogenic side in mTLE.

## P090

### THE FREQUENCY AND REASONS OF SEIZURE-RELATED INJURIES IN A LARGE, OUTPATIENT CLINIC-BASED COHORT OF EPILEPTIC PATIENTS

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**Purpose:** The risk of injury is significantly higher in patients with epilepsy than in general population. Our aim is to investigate the type, frequency of trauma and related factors in patients with epilepsy.

**Method:** Seven hundred and sixty-three patients (368 males, mean age 32 ± 14) who visited the epilepsy outpatient clinic between September 2011 and February 2012 were interviewed face to face. Seventy-six patients with history of seizure-related trauma (44 males, mean age 35 ± 17) were evaluated for epilepsy syndrome, seizure type and frequency, besides severity and location of trauma. Quality of Life Scales EuroQol (EQ5D) and Quality of Life (QOLIE) were also performed to analyze the effect of trauma to social life.

**Results:** The seizure frequency was significantly higher in patients with trauma (p = 0.001). The most common seizure type and epilepsy syndrome were generalized tonic clonic seizures (51%) and symptomatic partial epilepsy (47%), similar to main group. 24% of the patients had

more than one trauma and total trauma number was 109. The head was the most commonly injured area (41%). The majority of injuries, especially burns had occurred at home (52%/87.5%). 57% of these injuries required treatment in hospital. The mean EQ5D score of patients was 65 ± 15.9 and the mean QOLIE score was 61 ± 15.6. 55% of the patients held the fear of being injured again.

**Conclusion:** The seizure-related trauma rate in patients with epilepsy is high (9.96%). Seizure frequency is the most common risk factor. The fear of being injured again is the most important worry leading to decrease in quality of life.

## P091

### FREQUENCY OF EARLY AND LATE-ONSET SEIZURE AFTER STROKE

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**Introduction:** Cerebrovascular diseases have an important role in the pathogenesis of symptomatic epilepsy, especially in older age. In this study, we aimed to evaluate frequency of early and late-onset seizures after stroke.

**Materials and Methods:** Data from 1789 patients with acute cerebrovascular disease were reviewed retrospectively and 188 patients with seizures were included in the study. The history of the disease, demographic features, age at stroke, stroke type, latency of the seizure, seizure type and antiepileptic treatment were recorded. Stroke types were classified as ischemic and hemorrhagic. Seizures after stroke were divided into two groups as early and late. Patients who had seizure within 15 days after stroke were considered as having early-onset seizure. Patients who had seizure later than that were considered as late-onset seizure group.

**Results:** Seizures occurred in 10.5% of the patients, including 9.6% of with ischemic stroke and 14.2% of with hemorrhagic stroke. Early-onset seizures developed in 5.1% and late-onset seizure developed in 5.4% of the patients. Early-onset seizures occurred in 4.6% and late onset seizures occurred in 5.0% of the of ischemic stroke. Early-onset seizures occurred in 7.1% and late onset seizures occurred in 7.1% of the hemorrhagic stroke.

**Conclusion:** Seizures after stroke occur frequently in patients older than 60 years. They can usually be controlled by antiepileptic monotherapy. Late-onset seizures after stroke are more common than early-onset. Hemorrhagic stroke seems to be more prone to seizures than ischemic stroke.

## P092

### EPILEPSY IN PEOPLE WITH INTELLECTUAL DISABILITIES OF DIFFERENT AETIOLOGIES: A SURVEY OF CARER-REPORTED SEIZURE PRECIPITANTS

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**Purpose:** Seizure precipitants are commonly reported in the general population of people with epilepsy. However, little is known about seizure precipitants for people with epilepsy and intellectual disabilities (ID). The aim of this research was to ascertain whether the number and nature of precipitants reported by carers differs depending on the aetiology of the ID of the person they support. Three groups were investigated: Rett Syndrome, Fragile X Syndrome, and a comparison group of other aetiologies.

**Method:** A carer survey was conducted using online and postal questionnaires, which were distributed by charities representing people with Fragile X syndrome, Rett syndrome and epilepsy.

**Results:** One hundred eligible responses were received. Respondents supported somebody with epilepsy and ID with either Rett Syndrome ( $n = 44$ ), Fragile X Syndrome ( $n = 25$ ) or other aetiology ( $n = 31$ ). Most were family members, and 98% identified at least one seizure precipitant for the person they support. Carers of people with Rett Syndrome and Fragile X Syndrome reported fewer precipitants than carers of people with other aetiologies ( $p = 0.014$ ). Illness was a commonly reported precipitant in all three groups and was the most commonly reported precipitant overall. The groups differed with regard to the relative prevalence of illness, tiredness, sleep deprivation and sleep (all  $p < 0.05$ ) as reported precipitants.

**Conclusion:** Differences were found regarding the nature and number of seizure precipitants reported by carers of people with ID of different aetiologies.

This research was funded by an Epilepsy Action studentship and approved by the University of Cambridge Psychology Research Ethics Committee.

### P093

#### DIFFERENTIAL DIAGNOSIS OF SEIZURES OF A PATIENT WITH ALCOHOL ABUSE: ABOUT AN EVENT AT THE CLINIC NEUROLOGICAL OF FANN

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**Introduction:** Alcohol abuse is associated with 40% of seizure that may be the primary cause or trigger.

**Aim:** This observation is to attract the attention of doctors on differential diagnoses of an epileptic seizure in the chronic alcoholic abuse.

**Observation:** Man, 47 years, alcohol abuse and smoking since 20 years, presented abruptly a generalized tonic-clonic seizure and repeatedly. The EEG was normal. The MRI found a large mass iso-intense T1 and T2 with strong enhancement after injection. It has a wide base of implantation of the clivus lateralized to the right coming into contact with the mammillary body and insinuating on the right temporal fossa coming into contact with the hippocampus ( $46 \times 30$  mm).

**Discussion:** The occurrence of seizures in alcohol abuse is so frequent that their etiology is systematically related. The discovery in our patient with a newly formed processes character strongly epileptogenic, shows the problem of exclusivity etiopathogenic seizures in the alcohol abuse. The issue has been studied in the literature in a paper entitled "Alcohol and epilepsy: A case report between alcohol withdrawal seizures and neuroborreliosis", etiology was infectious.

**Conclusion:** Every epileptic seizure in an alcohol abuser is not necessarily related to alcohol and/or is not solely because of alcoholism.

### P094

#### DURATION AND STRUCTURE OF ACCOMPANIED AND UNACCOMPANIED OUTPATIENT CONSULTATIONS IN A SPECIALIST SEIZURE CLINIC

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**Purpose:** Patients are routinely invited to bring along a companion to their appointments in a seizure clinic. However, the effect of the presence

of a third party on outpatient encounters between patient and doctor in such clinics has never been studied. This study was intended to explore differences in the duration and structure of accompanied (triadic) and unaccompanied (dyadic) initial outpatient consultations in a specialist seizure clinic.

**Method:** Forty-eight consecutive first appointments with three different neurologists were video- or audiorecorded. Eighteen patients were unaccompanied, 30 were accompanied (23 by seizure witnesses). Verbatim transcripts were produced. The contributions of all participants to the interactions were timed and the discourse space they occupied was measured (by counting the number of words contributed). The resulting numbers were compared and correlated.

**Results:** There was no significant difference in duration between dyadic and triadic interactions (22.9 versus 23.3 min,  $p = 0.589$ ). Patients occupied proportionally less discourse space in accompanied than unaccompanied interactions (56.9% versus 28.3%,  $p \leq 0.0001$ ). In accompanied interactions, there was a weak negative correlation between the discourse space of patients and that of doctors ( $r_s = -0.43$ ,  $p = 0.017$ ), and a moderately strong negative correlation between the discourse spaces occupied by patients and companions ( $r_s = -0.64$ ,  $p = 0.001$ ).

**Conclusion:** Whilst a seizure witness can clearly help with the process of formulating a diagnosis, the diagnostic value of the presence of a witness during an initial encounter in the a seizure clinic may be reduced by the more limited opportunity for patients to contribute their own seizure experiences. Our findings indicate that the presence of a companion reduces the opportunity for doctors to observe the interactional, linguistic and topical features in the talk of seizure patients, the differential diagnostic value of which has been described in a number of previous publications.

### P095

#### WHICH CLINICAL FACTORS PREDICT QOL IN JAPANESE PATIENTS WITH LOCALIZATION-RELATED EPILEPSY?

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**Purpose:** To explore the clinical factors affecting quality of life (QOL) in Japanese patients with localization-related epilepsy using multiple regression analysis.

**Method:** Subjects were 99 patients with localization-related epilepsy (median age, 39 years; female, 39; TLE, 61). QOL in the subjects was assessed using WHOQOL-26, a multidimensional measure for subjective assessment of QOL in general clinical setting which consists of four subscale domains. Fifteen clinical factors were also evaluated as the independent variables of regression analysis.

**Results:** Simple regression analysis showed that WHOQOL-26 score was significantly correlated with remission of seizures, the number of anti-epileptic drugs (AED), marriage status, current diagnosis of any psychiatric disorders established by Mini International Neuropsychiatric Interview (MINI), adverse effects of AED assessed using Adverse Events Profile (AEP), and Mini Mental State Examination (MMSE) score. Multiple regression analysis revealed that WHOQOL-26 score was independently correlated with diagnosis of any psychiatric disorders, AEP score, and MMSE score; the multiple regression coefficient, 0.53; the contribution ratio, 0.28. Interestingly, only AEP score was correlated with all subscale domains of WHOQOL-26.

**Conclusion:** Diagnosis of any comorbid psychiatric disorders, adverse effects of AED, and MMSE score predicted QOL in Japanese patients with localization-related epilepsy. Only adverse effects of AED were associated with all subscale domains of WHOQOL-26. The results suggest that reduction of adverse effects of AED may be most important to improve QOL and comprehensive psychiatric evaluation is necessary to evaluate QOL in patients with epilepsy.



## P096

**EARLY POST ACUTE STROKE SEIZURES: CLINICAL PROFILE AND OUTCOME IN A NIGERIAN STROKE UNIT***Imarhiagbe FA<sup>1</sup>, Ordia WC<sup>2</sup>*<sup>1</sup>*Department of Medicine (Neurology), University of Benin, Benin, Nigeria,* <sup>2</sup>*University of Benin Teaching Hospital, Benin, Nigeria***Purpose:** To describe the basic clinico-demographic profile and outcome of Early Post Acute Stroke Seizures (EPASS).**Method:** Two hundred and fifty-one patients admitted within 24 h of onset of stroke symptoms into the stroke unit of a tertiary care hospital were followed up for convulsive seizure(s) within 7 days of admission and for disease outcome in 42 days. Stroke subtype was defined by cranial CT and ictal phenomenon was as described by the stroke unit doctors. Stroke severity was by the Canadian Neurological Scale (CNS) and Glasgow Coma Scale (GCS). Seizures were characterized as partial or generalized or status. Stroke outcome was defined as discharge from in-patient care to follow-up or still in care and all cause in-hospital death.

Data was compared between the group with and without seizures. The effect of age, sex, blood sugar, GCS, CNS, and seizure type on stroke outcome and time to in-hospital death in EPASS was tested on logistic regression and Cox proportional hazard regression.

**Results:** EPASS occurred in 9.96% of subjects and intracerebral infarct was more associated with EPASS, a finding different from what is dominant in western literature.**Conclusion:** Profile of EPASS may appear different in terms of stroke subtype in Sub-Saharan African populations. Larger prospective studies may clarify the position better.

## P097

**COMPLICATIONS OF PROVOCATION OF SEIZURES BY REDUCTION OF MEDICATION AND SLEEP DEPRIVATION DURING LONG-TERM EEG MONITORING***van Regteren R<sup>1</sup>, van Hemert-van der Poel JC<sup>1</sup>, de Weerd AW<sup>1</sup>*  
<sup>1</sup>*Department of Clinical Neurophysiology, SEIN, Zwolle, the Netherlands***Purpose:** For patients eligible for epilepsy surgery video-EEG monitoring is a powerful tool to determine the epileptogenic zone. During this procedure seizures may be provoked by means of sleep deprivation or withdrawal of medication. It is unclear what is the risk of complications during these provocations and under which conditions they occur.**Method:** Files of patients with epilepsy who had a long-term video-EEG monitoring at our clinic from 2005 till 2011, were retrospectively studied. During these recordings the neurologist decided which method of provocation was used. Complications were defined as: tonic-clonic seizures in patients who did not have these regularly, clusters of seizures or status epilepticus during the recordings.**Results:** A total of 175 patients were included. The recordings revealed clinically relevant abnormalities in 141 (80.6%) of the patients. In patients using medication (167 (95.4%)) withdrawal of medication was used in 151 (90.4%). Sleep deprivation was applied in 85 (48.6%) of the patients. Complications occurred in 19 (10.9%) cases, all during partial (2) or total (17) withdrawal of medication, sometimes (11) in combination with sleep deprivation. Most complications occurred during reduction or stop of carbamazepine (7), lamotrigine (5) or oxcarbazepine (4).**Conclusion:** Complications occur in a limited number of patients during long term video-EEG monitoring despite the high yield in effectively

recorded seizures. Most complications occur when medication is stopped. Sleep deprivation is of minor impact.

**Recommendation:** Withdrawal of medication during long-term video-EEG monitoring is not standardized. World-wide protocols for withdrawal of medication are wanted.

## P098

**OBESITY AS A COMMON COMORBIDITY IN PATIENTS WITH EPILEPSY AND COGNITIVE IMPAIRMENT***Ladino LD<sup>1</sup>, Téllez-Zenteno JF<sup>1</sup>, Hernández-Ronquillo L<sup>1</sup>*<sup>1</sup>*Division of Neurology, Department of Medicine, University of Saskatchewan, Saskatoon, SK, Canada***Purpose:** Previous studies support the concept that obesity is a common comorbid condition in patients with epilepsy. In this study we described the body mass index (BMI) and data from a survey to assess physical activity in a sample of patients with epilepsy.**Method:** Thirty patients from an epilepsy clinic were included in this study. We obtained BMI, abdominal perimeter and information about physical activity using a standardized questionnaire. Clinic, electric and imaging parameters were collected.**Results:** Mean age of patients was 36 ± 14.3 (19–71). Sixty three percent were males. Fifty three percent had symptomatic epilepsy, 30% idiopathic and 17% cryptogenic. The distribution BMI in patients with epilepsy was as follows: underweight (BMI < 18.5) 6.7%, normal (BMI 18.5–24.9) 30%, over-weight (BMI 25–29.9) 16.7%, obese (BMI 30–34.5) 36.7%, and morbid obesity (BMI > 35) 10%. Factors associated with obesity were generalized epilepsy (p < 0.003), family history of epilepsy (p < 0.018), idiopathic etiology (p < 0.025) and cognitive impairment (p < 0.036). Additionally obese patients were younger at diagnosis of epilepsy (mean age 14.64) compared with non-obese patients (mean age 22.13). Factors associated with cognitive impairment were generalized epilepsy (p < 0.008), onset of seizures before the age of 15 (p < 0.024) and idiopathic etiology (p < 0.028). Leisure time habits were similar in patients with and without obesity. No association was found between physical activity and cognitive impairment and between antiepileptic treatment and the BMI index.**Conclusion:** The results suggest a significant association of obesity and cognitive impairment in patients with generalized epilepsy and idiopathic etiology.

## P099

**SIGNIFICANCE OF INPATIENT INTENSIVE SEIZURE MONITORING FOR EVALUATION OF ATYPICAL PHENOMENA IN CHRONIC EPILEPSY PATIENTS WITH MODERATE COGNITIVE IMPAIRMENT***Kirmani B<sup>1</sup>*<sup>1</sup>*Department of Neurology, Texas A & M University/Scott and White Neuroscience Institute, Temple, TX, USA***Purpose:** The objective of our study is to diagnose new onset frequent atypical events associated with change in typical ictal semiology prompting the need for frequent emergency room and hospital admissions.**Methods:** Retrospective chart reviews were conducted on patients with chronic epilepsy with moderate cognitive impairment who had increased incidence of new onset episodes different from the baseline ictal semiology. Data was acquired from patients admitted to Scott & White Hospital/Texas A&M Health Science Center, Temple, TX for intensive video EEG monitoring from 2008 to 2011. Approval for this retrospective analysis of patient records was given by the hospital's Institutional Review Board.

**Results:** We retrospectively analyzed three patients with an established diagnosis of epilepsy. Extensive chart reviews were performed with emphasis on type and duration of epilepsy, extent of interictal epileptiform abnormalities on EEG, failed and current treatment regimens, baseline frequency, semiology of baseline seizures and of new events. There were two men and one woman with moderate cognitive impairment. One subject had generalized epilepsy and other 2 had temporal lobe epilepsy. The patients were on an average of two to three antiepileptic medicines. The duration of follow up in our neurology clinic ranges from 9 months to 5 years. The occurrence of increased frequency of these events from the baseline associated with change in semiology of the seizures, despite therapeutic anticonvulsant levels, prompted the need for 5-day intensive video EEG monitoring. Atypical spells were documented in all three patients and were without any ictal correlate.

**Conclusions:** Our data analysis showed that intensive video EEG monitoring is an important tool to evaluate change in frequency and ictal semiology of seizures even in cognitively impaired patients with an established diagnosis of epilepsy for adequate seizure Management.

#### P100

##### EMERGENCY ADMISSION PATTERNS OF PATIENTS PRESENTING WITH PAROXYSMAL EVENTS

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**Purpose:** Patients with seizure disorder present a challenge to specialists both in diagnostic categorization and in further management. This study investigated the pattern of seizure-related emergency admissions to a specialized epilepsy centre and its role in differential diagnosis of paroxysmal events.

**Method:** All medical records of patients over age 10 admitted to the Epilepsy Unit at Sarajishvili Institute of Neurology & Neurosurgery during one calendar year were retrospectively reviewed. Statistical analysis was performed using chi-square trend tests.

**Results:** One hundred and thirty-four patients with clear discharge diagnosis were included in final analysis. Epileptic seizures were proven in 100 cases, in remaining cases no active epilepsy was found. Female/male ratio was 3:7 and 10:7 accordingly ( $p = 0.003$ ). Forty-six patients from a total number were urgently admitted within 24 h after symptoms onset. However, emergency medical services (EMS) for transportation to the hospital were used in 38 cases: among them 25 patients in whom epileptic seizures were detected and 13 – with non-epileptic seizures ( $p = 0.139$ ). In third cases of patients with epilepsy acute symptomatic seizures were the main reason for delivering by EMS. Only 9 out of 100 patients with epileptic and 3 out of 34 with non-epileptic seizures were managed in an intensive care unit. True status epilepticus was observed in six cases.

**Conclusion:** Emergency admission patterns did not significantly differ between patients with epileptic and non-epileptic seizures. The subgroup analysis revealed frequent EMS users in patients with acute brain and mental disorders. Further studies on large cohort should be performed to confirm the findings.

#### P101

##### FEBRILE SEIZURE AND EPILEPSY WITH HIPPOCAMPAL SCLEROSIS

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**Purpose:** To explore the clinical relationship between febrile seizure (FS) and epilepsy with hippocampal sclerosis (HS).

**Method:** A retrospective survey was made in 5572 epilepsy patients in Epileptic Center of Guangdong 999 Brain Hospital from October 2001 to December 2009. According to cranial MRI, 507 cases with hippocampal sclerosis were confirmed by neuroimaging specialists. We compared clinical features from 88 patients with FS with 419 patients without FS. We also conducted Fisher's exact tests and T tests to compare clinical features from different subgroups with different FS ages, which were FS age below 1 year and FS age between 1 and 5 years.

**Results:** Age at epilepsy onset was lower in patients with FS ( $t = 4.392$ ,  $p = 0.000$ ). Patients with FS were more likely to conduct operation than those without FS (likelihood ratio = 6.419,  $p = 0.013$ ). There were no statistical differences between two groups and two subgroups, in terms of gender and side of HS. Ages of FS had no means with age at epilepsy onset, interval time and whether to execute operation.

**Conclusion:** In the epileptic cases of 507 with HS, 88 of them experienced childhood FS. Age at epilepsy onset was lower in patients with FS and they were more likely to have operation.

#### P102

##### OUTCOMES IN A SINGLE SEIZURE CLINIC: A PROSPECTIVE CANADIAN STUDY

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**Purpose:** The assessment of patients with single unprovoked seizures should be done within two weeks of referral and the diagnosis should be confirmed ideally by a consultant with expertise in epilepsy. This study ascertains different clinical outcomes in a single seizure clinic.

**Methods:** We performed a 1 year prospective study including all patients who were referred to the single seizure clinic in Saskatoon, SK, Canada from November 2011 to December 2012. Three certified epileptologists and a registered nurse were responsible for the diagnosis and treatment of patients.

**Results:** Eighty patients were included in this study. The mean age of patients was 38.2 + 17.8 (range 14–84). Forty seven percent were females. The wait time from the spell to the assessment was 26 + 31 days (range 2–202). Patients were referred mostly for emergency room physicians (52%), 38% for family doctors and 10% by neurologists. The mean time from the spell to have an EEG was 30 days, for CT 12 and for MRI 54. Seventy five percent of patients had a final diagnosis in the first visit. The diagnoses were as follow: Epilepsy was diagnosed in 42.5% of patients. Twenty five percent of patients had syncope, provoked seizures in 12.5% (alcohol withdrawal, drugs use and hypoglycemia), single seizures in 11% and non-epileptic events in 9%. Medications more commonly prescribed were lamotrigine and topiramate.

**Conclusions:** Our clinic has produced a tremendous benefit for patients in our province providing the best care for patients. In all patients the assessment and conclusion was done in the next month after the spell.

#### P103

##### CLINICAL STUDY ON SEIZURE AFTER CRANIOPLASTY IN ADULT

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**Purpose:** To analyze seizure incidence rate and its risk factors and seizure prophylactic effect of anti-epilepsy drugs (AEDs) after cranioplasty in adults.

**Method:** To retrospectively collect 107 adults who underwent cranioplasty from March, 2007 to April, 2011, and statistics patients' general clinical feature, postoperative seizures, and prophylaxis using of AEDs, and statistics postoperative in-hospital days and later-onset postoperative seizure in patients with early-onset postoperative seizure after cranioplasty.

**Results:** There were 17 (15.9%) patients with early-onset postoperative seizures and 19 cases (17.8%) with later-onset postoperative seizures after cranioplasty. Patients with cranioplasties with autologous craniums presented less early-onset postoperative seizures compared with those with titanium meshes. Gender, age at surgery, history of skull defect, obvious cerebral atrophy or brain scar on magnetic resonance imaging, and intra-operative cerebral spine fluid leakage didn't rendered significant effect on postoperative seizure. Percentage of early-onset postoperative seizure was 23.5% in patients who didn't use AEDs after cranioplasty, which was significantly higher than the datum in those with AEDs ( $p < 0.01$ ), however, significant difference was not found in percentage of later-onset postoperative seizure between adults with or without AEDs after cranioplasty. Patients with early-onset postoperative seizure presented more postoperative in-hospital days and higher incidence rate of later-onset postoperative seizure than those without early-onset postoperative seizure.

**Conclusion:** There were high incidence rates of early and later-onset postoperative seizure after cranioplasty. Patients with early-onset postoperative seizure presented more postoperative in-hospital days and higher incidence rates of later-onset postoperative seizures. Prophylactic using AEDs could reduce early-onset postoperative seizure greatly.

#### P104

##### KEEP YOUR EYES OPEN! UNTREATED CO-MORBIDITIES IN ADULTS WITH EPILEPSY AND LEARNING DISABILITY

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**Purpose:** To determine the prevalence and nature of undiagnosed co-morbidities in new referrals to an epilepsy and learning disability service.

**Method:** Our clinical database identified new referrals with epilepsy and learning disability over a 12 month period. Ninety-three adults were referred. Patients with any previous contact with the service were excluded. 62 met the inclusion criteria. All patients were assessed by a Consultant Nurse with expertise in epilepsy and learning disability and a Consultant Neurologist. Medical records were reviewed to compare diagnostic and co morbidity information provided at the point of referral with that following detailed assessment. Co morbidities were treated within our Service or through appropriate specialist referral (who confirmed co-morbid diagnoses).

**Results:** Previously undiagnosed and untreated co-morbidities were identified in 58% of newly referred patients. Twenty-four separate health conditions were identified, including sleep disorder, drug toxicity, helicobacter pylori, seborrhoeic dermatitis, hypertension, lymphoedema, allergic rhinitis, hypothyroidism, tremor, hearing impairment, cataract, and reflux. 23% were vitamin D deficient.

**Conclusion:** We demonstrate the importance of a holistic approach to the assessment and treatment of patients with a learning disability presenting to an epilepsy clinic. A learning disability may mask co-morbid

conditions. We recommend a proactive and comprehensive approach to assessment. We find an integrated Neurology and Learning Disability Service beneficial.

Further study is required to determine why a high proportion of adults present with undiagnosed health needs despite a Primary Care health screening programme for adults with learning disability.

#### P105

##### KNOWLEDGE, BELIEFS, AND HEALTH CARE PERCEPTIONS OF EPILEPSY IN MINNESOTA'S NATIVE AMERICAN NATIONS

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**Purpose:** While epilepsy is a disease disproportionately affecting ethnic minorities, relatively little research has been conducted regarding factors and beliefs that impact associated care (Long et al., 2000), particularly among Native Americans (NA) Nations. For NA with epilepsy we hypothesized greater knowledge, heightened perception of stigma and care barriers, but less education, driving, marriage, employment and income. We explored these factors using a survey of Upper Midwestern Native Americans.

**Methods:** We surveyed 55 NA respondents, 23 with epilepsy and 32 without, recruited via Native and University clinics, tribal offices, and community centers, regarding demographics, epilepsy knowledge, care barrier and stigma perception, spiritual and other beliefs, education, income and insurance type. Fisher's exact test compared response differences between groups for categorical variables; t-tests for interval and aggregate variables (1- or 2-tailed by context). Significance is reported from  $p < 0.10$ .

**Results:** Respondents were significantly more female and urban. Age and etiological knowledge were not significantly different between groups. Affected had less accurate medication knowledge ( $p < 0.001$ ), viewed community seizure knowledge as lower ( $p < 0.05$ ), care providers fewer ( $p < 0.05$ ), aggregate barriers to good care higher ( $p < 0.10$ ) and had lower trust ( $p < 0.05$ ).

Both rated family contexts as least stigmatizing; affected rated work more ( $p < 0.05$ ) and school most stigmatizing ( $p < 0.001$ ). Educational levels did not differ significantly, but in affected unemployment was sharply higher ( $p < 0.01$ ), income lower ( $p < 0.05$ ; none >\$40K), and driving less ( $p < 0.01$ ). Affected had more hospital-based care ( $p < 0.05$ ) and insurance coverage.

**Conclusions:** Results suggest as needed for Upper Midwest Native Americans (1) additional education on epilepsy causes and management; (2) addressing stigma in schools and workplace; (3) correcting perceived care barriers including trust, and (4) addressing transportation and employment deficits impacting income. Respondents' gender gap indicates ongoing challenges for research and health care involving Native American males.

#### P106

##### STATUS EPILEPTICUS AS THE MAIN NEUROLOGICAL MANIFESTATION OF ANCA-RELATED VASCULITIS

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**Purpose:** Status epilepticus (SE) may occur in the setting of several internal or neurologic diseases. Vasculitis associated with

antineutrophil cytoplasmic antibodies (ANCA) are rare systemic autoimmune diseases affecting small to medium sized blood vessels.

**Method:** We report three patients with ANCA-associated vasculitis (AAV) with SE as main neurological manifestation.

**Results:** *Case 1:* A 44-year-old man with a previous diagnosis of autoimmune hemolytic anemia, came for partial SE requiring admission in intensive care unit for sedation and intubation. Serologic, histologic and neuroradiological examinations allowed to diagnose AAV. He was given rituximab along with antiepileptic drugs. Over the years he only presented three simple partial seizures when spontaneously reducing medications, with no further recurrence of systemic vasculitis.

*Case 2:* A 48-year-old man was admitted to our clinic due to generalized convulsive SE treated with iv lorazepam. A few months before, a diagnosis of glomerulonephritis had been posed and he had been given corticosteroid. Serologic, histologic and neuroradiological examinations allowed to diagnose AAV and he was given steroids. One month later he had a catastrophic evolution with multiple organ bleeding and death. *Case 3:* a 24-year-old girl presented at age 17 years, episodes characterized by visual hallucinations lasting a few minutes, followed by headache, along with short-lasting episodes of eyelid myoclonia. Two years later she was admitted to our hospital for occipital status epilepticus. The diagnosis of AAV was posed and treatment with cyclophosphamide was started. At 6-month follow-up, patients remains seizure-free.

**Conclusion:** Physicians should be aware that SE may represent the first or main neurologic manifestation of AAV.

#### P107

##### BRAIN TUMOR DEVELOPMENT AFTER DIAGNOSIS OF EPILEPSY

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**Purpose:** To study the risk of brain tumor development after new onset epilepsy in Taiwan.

**Method:** We extracted data from Taiwan National Health Insurance Research Dataset subset. All patients with epilepsy diagnosis (ICD-9-CM code 345.x) between January 1, 1997 and December 31, 2008 (n = 8,783) were selected. Patients with epilepsy before 1997 were excluded (n = 1,899). Patients whose brain tumor diagnosis (ICD-9-CM code 191.x and 192.x) prior to epilepsy diagnosis (n = 174) or in 30 days after epilepsy (n = 54) were excluded. As a result, 6,656 patients with epilepsy were included in the study. The end point of observation was assigned as the date either of brain tumor diagnosed or of last service visit if no brain tumor found. Seizure type, number of antiepileptic drug (AED) and brain image study were recorded. We tested the significance of explanatory variables by Pearson X<sup>2</sup> tests and estimated tumor free survival rate by Kaplan meier method.

**Results:** Of those enrolled patients (6656) with newly diagnosed epilepsy, 65 patients developed brain tumors (0.98%). Only older age (p = 0.0064) and tendency of AED to control seizure (p < 0.0001) were significant associating factors. No statistical significance was found in seizure type and in the rate of brain image study on epilepsy diagnosis. Survival analysis for brain tumor development after epilepsy diagnosis revealed turning point of decline of slope changing rate on 162th days.

**Conclusion:** Adult age and necessity of AED are the risks of brain tumor development after new onset epilepsy. Further brain image study should be arranged 6 months later if the initial one was negative.

#### P108

##### MUSICOGENIC EPILEPSY?

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**Purpose:** By definition, reflex seizures are reproducibly caused by a specific sensory stimulus. In practice, there may also coexist spontaneous seizures. In musicogenic seizures, dispute exists as to whether certain acoustic features of the music itself are triggering seizures or whether an emotional response to the music is responsible. We report a case of suspected reflex epilepsy and discuss the exams to clarify the nature of her clinical picture.

**Case report:** Our patient is a 52 year-old woman. At the age of 20 she started recurrent episodes of malaise followed by olfactory and auditory hallucinations, palpitations and inability to speak. They occurred when she was continuously hearing certain voices, lasted a few minutes and were followed by a brief period of excessive somnolence.

Recently, the episodes can also be elicited by certain songs, especially those with strident voices. Ictal semiology also changed: she has a psychic aura, less commonly an auditory one, with subsequent loss of consciousness and, sometimes, secondary generalization.

Brain MRI (1.5T and 3T) and routine EEG were normal. Video-EEG monitoring showed a normal baseline activity and two electroclinical seizures of the right temporal lobe when listening to two different songs by the same singer. There were also two clinically different events during two other songs by a different singer, interpreted as psychogenic non-epileptic seizures.

**Conclusion:** We report this case as an example of right temporal lobe epilepsy with seizures triggered by auditory stimulus and to illustrate the importance of video-EEG monitoring in diagnosing reflex seizures and to distinguish them from other clinical events.

#### P109

##### WAITING TIMES FOR ASSESSMENT AND TESTING IN PATIENTS WITH SINGLE UNPROVOKED SEIZURES FROM A SINGLE SEIZURE CLINIC VERSUS REGULAR EPILEPSY CLINIC

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**Purpose:** There is an urgent need to properly assess and manage patients after a single unprovoked seizure with the goals of establishing the diagnosis, determining if the patient has epilepsy, and determining the risk of recurrence

**Methods:** We compare the waiting time for medical assessment and testing in patients with single unprovoked seizures before and after the implementation of a single seizure clinic (SSC). We compared historical data of 50 patients who were referred to a regular epilepsy clinic (EC) because of single unprovoked seizures, with the data obtained from 80 patients who were assessed in a recently open SSC in the same hospital.

**Results:** Patients who were assessed to the regular EC waited to be assessed 142 ± 346 days (range 0–1945) vs. 26 ± 31 days (2–202) (p = 0.000) in the SSC. The median waiting time to have an EEG was 187 ± 631 days (range 0–4222) in the EC vs. 30 ± 34 days (range 1–202) (p = 0.000) in the SSC. Mean waiting time to have a CT scan was 54.4 ± 118 (range 0–484) days in the EC vs. 12.4 ± 27.5 days (range 0–161) (p = 0.000) in the SSC. Mean waiting time to have an MRI was 208 ± 231.5 days (range 4–1031) in the EC vs. 54.4 ± 42 days (range 0–168) (p = 0.000) in the SSC.

**Conclusions:** This study supports the notion that a SSC dedicated to diagnosis, management of patients with single unprovoked seizures improves the waiting times for assessment and testing.

## Poster Session: Basic Sciences A Monday, 24 June 2013

P110

### EPILEPTOGENESIS INDUCED IN RATS BY PERIVENTRICULAR NODULAR HETEROTOPIA CAUSED BY IMPAIRED EXPRESSION OF FILAMIN A

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**Purpose:** Malformations of the cerebral cortex represent a major cause of developmental disabilities, severe epilepsy and reproductive disadvantage. Among those, periventricular nodular heterotopia (PNH) characterized by the presence of nodules of neuron ectopically placed along the lateral ventricles walls results mainly from Mutations in *FLNA*, on Xq28 (in 100% of families with X-linked bilateral PNH and 26% of sporadic patients). The objective of this report was to develop an appropriate animal model of this condition to elucidate the pathophysiological basis of epilepsy linked to *FlnA* loss of function.

**Method:** The rat animal model was produced by RNA interference mediated *FlnA* knockdown expression in utero. The structural phenotype was investigated by immunohistochemistry. Epileptogenesis was evaluated by treating the animal with the convulsant agent PTZ. Susceptibility to develop seizures upon heat exposure was also investigated.

**Results:** *FlnA*-knockdown rats developed PNH with similar features than those observed in human patients. We demonstrate that the phenotype results from a disruption of the polarized radial glial scaffold in the ventricular zone altering progression of neural progenitors through the cell cycle and impairing migration of neurons into the cortical plate. We found that juvenile *FlnA*-knockdown rats are highly susceptible to seizures induced by Pentylentetrazole and that they develop "febrile-like" seizures.

**Conclusion:** We developed a unique model of PNH linked to *FlnA* loss of function confirming the link between PNH and epilepsy. This new animal model is particularly suitable for investigating the role of PH in the generation of seizures and therapeutic prospects.

P111

### VIEW AT THE CYCLIC GABA'S CONFORMER AND GLYCINE, AS AT NATURAL ENDOGEN AGONIST GABA-BENZODIAZEPINE'S RECEPTOR COMPLEX

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**Purpose:** It is known, that long using main's group anticonvulsants (Ac) lead to mental and cognitive reduction because all of them are artificial compounds, which are "xenobiotic". Search for the new Ac that could be devoid of the stated above disadvantages, that is so called "biotic", is still to be an actual and unsettled problem of the modern neuropharmacology. In the same time, creation of the any kind neurotropic compound implies resolve as minimum two problems: receptor's

affinity and possibility passing through GEB. In view of that this investigation has been turned out searching natural endogen agonists GABA-benzodiazepine's receptors and synthesis new Ac on the basis their similarity and also investigation mechanism their possibility to pass through GEB in the relationship with selectiveness membrane's cationic channel (Eisenman's rows).

**Methods:** (1) Molecular geometry of the benzodiazepine's pharmacophores, main GABA conformers) and glycine were studied in the approximation of molecular mechanics with the use of the MM2 force field. (2) Influence intraperitoneal injection different one-valence salts of glycine and GABA on the cerebral neurophysiological activity in white rats (taking of EEG) and their anticonvulsant activity using strychnine, picrotoxin, pentylentetrazol and maximal electro seizure models.

**Results:** (1) Molecular geometry derivatives of barbiturates, benzodiazepines and glycine in largest remind cyclic GABA-conformer. (2) It was founded good anticonvulsant activity Li salt of glycine, on the main convulsive models (pentylentetrazol and maximal electro seizure).

**Conclusion:** (1) Apparently, GABA-cyclic conformer and glycine are natural endogen agonists GABA-a-benzodiazepines receptor's complex in CNS, in that time barbiturates and benzodiazepines are their artificial agonists. (2) Elaboration of the new antiseizure drugs (like Li salt of glycine) with glycine pharmacophore in their structure could be perspective direction of antiepileptic neuropharmacology. (3) Probably, Li salt of glycine has possibility passing through GEB using channel with strong inside field (11-th Eisenman's row).

P112

### PRETREATMENT WITH CHLORPHENIRAMINE POTENTIATED THE HYPERTHERMIA-INDUCED CONVULSIVE BEHAVIORS AND IT CAUSED A MORE SEVER REDUCTION IN HISTAMINE BLOOD LEVELS IN INFANT RATS

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**Purpose:** This study investigated the effect of pretreatment with chlorpheniramine before hyperthermia (HT) on histamine blood level (HBL) and convulsive behavior in prepubertal rat.

**Method:** Twenty four rats aged 19–20 days divided into three groups (n = 8) namely control, hyperthermia and chlorpheniramine. In hyperthermia group, the rats were placed in the hyperthermic chamber for 30 min, and a warm air current was blown on them. In the chlorpheniramine group, the rats received intraperitoneal chlorpheniramine 4 mg/kg before the HT. The body temperature of the rats was continuously recorded via a rectal probe throughout the experiment. During 30 min of HT, behaviors of each rat was carefully observed and recorded. Finally, blood samples were obtained and were used to measure HBL.

**Results:** All the rats that exposed to HT showed convulsive behavior. Chlorpheniramine significantly potentiated seizure intensity, and it increased the rate of tonic-clonic (TC) seizure ( $3.82 \pm 0.75$  in chlorpheniramine and  $1.25 \pm 0.36$  in hyperthermia,  $p = 0.02$ ). HT decreased HBL, and chlorpheniramine potentiated this reduction ( $p < 0.001$ ). First TC temperature was significantly lower in chlorpheniramine treated rats than HT rats ( $p < 0.001$ ).

**Conclusion:** At least one way that in which HT leads to seizure is decreasing of HBL following HT. Since histamine has an anticonvulsant effect, reduction in HBL is one reason to hyperthermia-induced seizure. Pretreatment with chlorpheniramine potentiates the hyperthermia-induced reduction in HBL. Therefore, excitatory effect of chlorpheniramine on fibril convulsion may, in part, be mediated through reduction in histamine levels.

## P113

**ANISOPUS MANNII (ASCLEPIADACEAE) POSSESS ANTICONVULSANT EFFECTS THAT ARE INCREASED WITH PHYSICAL EXERCISE IN MICE***Ngo Bum E<sup>1</sup>, Assako N<sup>1</sup>, Bidias FC<sup>1</sup>, Vondou O<sup>1</sup>*<sup>1</sup>*Department of Biological Sciences, University of Ngaoundéré, Ngaoundéré, Cameroon*

**Purpose:** *Anisopus mannii* is a plant used empirically in traditional medicine in Cameroon to treat epilepsy and other brain diseases. The plant is found in Cameroon and many other countries in Africa. The aim of this study is to evaluate the anticonvulsant properties of *Anisopus mannii* and the influence of physical training in these anticonvulsant effects.

**Method:** In vivo mice models (Maximal electroshock, Strychnine, Pentylentetrazol, Picrotoxin) induced convulsions were used to evaluate the anticonvulsant activities of the plant decoction. In another set of experiments, maximal electroshock and Pentylentetrazol- induced convulsions were used to evaluate the anticonvulsant effects of *A. mannii* in mice that have been physically trained with the rotarod in order to look at the influence of the physical training on these anticonvulsant effects. Mice were divided in six groups in each test and received: Group I: distilled water, groups II to V: three doses of the plant, group VI: known anticonvulsant compounds.

**Results:** *A. mannii* protected 80, 80 and 80% of mice against STR, PTZ and MES- induced seizures, respectively. *A. mannii* also protected 100% of mice in PIC-induced convulsions. After physical training for 21 days in rotarod, *A. mannii* protected 100 and 100% of mice against PTZ and MES- induced seizures, respectively.

**Conclusion:** The effect of the decoction of *A. mannii* suggests the presence of anticonvulsant activities that might show efficacy against secondarily generalized tonic-clonic seizures and primary generalized seizures in humans. And physical training could increase these anticonvulsant effects of the plant decoction.

## P114

**THE ROLE OF THE INTERICTAL SPIKING ACTIVITY IN RAT'S FRONTAL CORTEX AND HIPPOCAMPUS IN FOCAL EPILEPSY MODELS***Denisenko KV<sup>1</sup>, Kashchenko OA<sup>1</sup>, Shandra OA<sup>1</sup>*<sup>1</sup>*Physiology Department, Odessa National Medical University, Odessa, Ukraine*

**Purpose:** The aim of our study was to investigate the involvement of development the regular interictal spikes (IS) in the generation ictal discharges in a chronic chemical kindling and in an acute penicillin cortex focus model.

**Method:** Experiments were performed in male Wister rats (n = 44), w = 180–220 g. Recording electrodes were implanted bilaterally into the frontal cortex and ventral hippocampus. Kindling was induced by repeated injections of a subconvulsant dose of pentylentetrazole (PTZ, 25 mg/kg, i. p.; 21 days). Intraperitoneal injections of 20 mg/kg isopicalon (IP) and 15 mg/kg carbamazepine (C) were made after formation epileptiform focus with IS-activity.

**Results:** The most commonly observed pattern in rat hippocampus and frontal cortex (67% – in kindling; 58% – in penicillin's cortex focus) was characterized by the appearance of regular IS, which shown a tendency to recur with a period of 9–20 s. Interspike period reduced immediately to 1–3 s and lasted a few 10 s after mioclonic jerks. Spiking was seen in EEG of all animals, but it was a rare event of interictal period of some rats (33%). In this case, single and non-regular IS progressed into generalized tonic-clonic seizures after fourteenth-seventeenth injection of PTZ. During this time of kindling procedure the development of severe generalized tonic-clonic seizures hasn't been found in rats with regular IS. At the

acute focal model the increasing of the cortical epileptiform activity was observed after injection of isopicalon only during depression of IS in the hippocampus. C. was demonstrated the reduction IS amplitude without changing frequency.

**Conclusions:** Results of this work show that the development of regular hippocampus IS interferes with the generation of severe clonic-tonic seizures in medium period of kindling and not accompanied with increasing cortical epileptiform activity in penicillin model.

## P115

**GENETIC EPILEPSIES AS PART OF THE NEURODISLOCATION SYNDROMES***Lakaye B<sup>1</sup>, Grisar TM<sup>2</sup>, Wolkoff N<sup>1</sup>, de Nijs L<sup>1</sup>*<sup>1</sup>*University of Liège, Liège, Belgium, <sup>2</sup>Department of Neurosciences-Neurology, University of Liège, Liège, Belgium*

**Purpose:** Heterozygous mutations in *Myoclonin1/EFHC1* co segregate with juvenile myoclonic epilepsy (JME) phenotypes. In adolescent JME patients they produce subtle malformations of cortical and subcortical architecture whereas homozygous F229L mutation in infancy induces severe brain pathology and death. However, the underlying pathological mechanisms for these observations remain unknown.

**Method:** We used classical cell biology and in utero or ex vivo electroporation to examine the role of epilepsy genes during early neuronal migration.

**Results:** We first demonstrated that EFHC1 is a microtubules-associated protein (MAP) involved in cell division and radial migration during cerebral corticogenesis. Next we show that JME-mutations, including F229L, do not alter the ability of EFHC1 to colocalize with the centrosome and the mitotic spindle but act in a dominant-negative manner to impair mitotic spindle organization. Using both in utero and ex vivo electroporation technologies, we also found that mutants EFHC1 expression disrupted radial and tangential migration by affecting morphology of radial glia and migrating neurons.

**Conclusion:** We hypothesize that heterozygous mutations of EFHC1 might lead to subtle deficits in the number, composition or positioning of glutamatergic and GABAergic neurons in the cortex that could explain the observed microdysgenesis and hyperexcitability in JME patients. Works in progress investigating new epilepsy genes involved in JME tends to support the concept that this particular form of epilepsy could be considered as a new neurodislocation syndrome.

## P116

**INTERNEURON PATHOLOGY ASSOCIATED WITH ARX MUTATION***Itoh M<sup>1</sup>, Goto Y<sup>2</sup>*<sup>1</sup>*National Center of Neurology and Psychiatry, Kodaira, Japan, <sup>2</sup>National Center Hospital, National Center of Neurology and Psychiatry, Kodaira, Japan*

**Purpose:** X-linked lissencephaly with abnormal genitalia (XLAG), showing severe neonatal seizure and developmental delay, is a rare disorder caused by mutations in the *aristless*-related homeobox (*ARX*) gene, located in Xp22.13. *Arx*-null mice for human XLAG model showed loss of tangential migration of GABAergic interneurons. However, GABAergic interneuron distribution of XLAG brain has never been reported. In the present study, we investigated subpopulation of GABAergic interneurons in the brain of an infant with XLAG, who had a nonsense mutation of the *ARX* gene, compared with those of age-matched normal control and Miller-Dieker syndrome.

**Method:** We performed immunocytochemistry for interneuron and migration markers.

**Results:** Glutamic acid decarboxylase (GAD)- and calretinin (CR)-containing cells were significantly very few in the neocortex and, interestingly, located in the white matter and neocortical subventricular zone, while neuropeptide tyrosine and cholecystokinin positive cells were normal. From previous rodent studies, the imbalance of GABAergic interneurons may be derived from the caudal ganglionic eminence tangential migration. Also, in the neocortical subventricular region, the GAD- and CR-containing cells had Mash-1 protein, like a radial migration marker, and nestin protein.

**Conclusion:** ARX protein controls not only tangential migration of GABAergic interneurons from the ganglionic eminence, but also may serve to induce radial migration from the neocortical subventricular zone.

## P117

### CORTICOSTEROID EXPOSURE INCREASES EPILEPTOGENESIS AFTER EXPERIMENTAL FEBRILE SEIZURES IN MICE

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**Introduction:** Stress is the most frequent self-reported seizure precipitant in patients with epilepsy, and a relation with early life stress has been suggested. Early life stress and stress hormones are known to influence seizure threshold in rodents, however effects on the development of epilepsy in later life (epileptogenesis) are yet unknown. The aim of this study was to investigate the effects of early life corticosteroid exposure on epileptogenesis.

**Methods:** At postnatal day 10/11, mice were exposed to hyperthermia-induced complex febrile seizures or normothermia. After two weeks of repetitive corticosterone or vehicle injections during the latent phase of epileptogenesis, three specific measures of epileptogenesis were examined: (1) excitatory postsynaptic currents, spontaneous (sEPSCs) and miniature (mEPSCs), measured by in vitro whole-cell patch clamp recordings of dentate gyrus granule cells; (2) synaptic plasticity (long term potentiation) determined by electrophysiological recording of medial perforant pathway evoked field excitatory postsynaptic potentials in the dentate gyrus; and (3) hippocampal mossy fiber sprouting, measured by Timm histochemistry in the dentate gyrus and hippocampal CA3 area.

**Results:** Repetitive corticosterone exposure in the latent phase after complex experimental febrile seizures increased the amplitude of sEPSCs and the frequency of mEPSCs. Also, mice exposed to corticosterone after febrile seizures showed modest, but significant, sprouting of mossy fibers into the stratum pyramidale and stratum oriens of the hippocampal CA3 area. No differences were found in synaptic plasticity.

**Conclusion:** Corticosterone exposure after experimental febrile seizures enhanced glutamatergic transmission in the dentate gyrus and induced mild mossy fiber sprouting. These functional and structural changes in the hippocampus suggest an increased epileptogenesis after exposure to corticosteroids, supporting the hypothesis that early life stress augments epileptogenesis.

## P118

### TOPIRAMATE IMPROVED THE PENTYLENTETRAZOLE-INDUCED LEARNING DEFICITS AND ATTENUATED EPILEPTIC BEHAVIORS IN PREPUBERTAL RAT

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**Purpose:** Animal models for seizures and epilepsy have played a fundamental role in advancing our understanding of basic mechanisms underlying epileptogenesis. Pentylentetrazole (PTZ) has been shown to induce seizure-like behavior, learning deficits, and even leads to death. This study investigated the effect of topiramate on PTZ-induced seizure and learning deficit.

**Method:** Thirty male Wistar rat aged 24, 25-day old divided into three groups (n = 10, each), namely control, saline, and topiramate. The rats in saline group received saline 0.5 ml; the rats in topiramate group received topiramate 20 mg/kg (in 0.5 ml) daily for 7 consecutive days. Control rats were used intact without any injection. Then, all the rats injected with PTZ 60 mg/kg intraperitoneally and epileptic behaviors monitored for 60 min. The seizure induction repeated 24 h later. The next day, the rats were tested concerning their learning capacity and memory in radial maze. Sixty minutes later, the rats anesthetized with ether, and their blood samples were obtained and were used to determine the corticosterone level.

**Results:** Our data indicated that topiramate suppressed seizure behaviors (p = 0.003), and improved learning ability (p < 0.001) in the rats treated with PTZ. Mortality rate was decreased significantly in topiramate treated rats comparing to saline, and control group (p < 0.01). Corticosterone blood level was significantly lower in topiramate treated rats (p < 0.03).

**Conclusion:** We concluded that pretreatment with topiramate may reduce stress level in rat, and leads to a decrease in corticosterone blood level and epileptic behaviors. It also improves learning ability and memory.

## P119

### EXPRESSION PATTERN OF SORTING NEXIN 25 IN TEMPORAL LOBE EPILEPSY: A STUDY ON PATIENTS AND PILOCARPINE-KINDLING RATS

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**Purpose:** There is evidence has shown that transforming growth factor  $\beta$  (TGF $\beta$ ) pathway involves in the epileptogenesis in the animal studies and human brain tissue study. Sorting Nexin 25 (SNX25), as a member of the SNXs which belong to The PX (phox-homology) domain family, has been recently proposed to modulate TGF- $\beta$  signaling via endosomal sorting of TGF- $\beta$  receptors for lysosomal degradation. The aim of the present study was to detect expression of SNX25 in human epilepsy and animal model of epilepsy.

**Method:** We investigated the expression of SNX25 in the brain tissues in the patients with temporal lobe epilepsy (TLE) and in the pilocarpine-induced rat model of epilepsy using western blotting, real time quantitative RT-PCR, and double-label immunofluorescence.

**Results:** The expression of SNX25 was significantly increased in the TLE patients compared to controls ( $0.21 \pm 0.07$  versus  $0.11 \pm 0.03$ , p < 0.05). In the pilocarpine-kindling rats, alteration of SNX25 had time phase property in the epileptic process. During acute and latent phases, no significant alteration of SNX25 occurred, and obviously increased in chronic phase of epileptic-model. Moreover, SNX25 located in both astrocytes and neurons.

**Conclusion:** Our results demonstrate that up-regulation of SNX25 may involve in the pathogenesis of temporal lobe epilepsy.

## P120

### DETECTION OF PROLIFERATING IMMATURE NEURONS IN EPILEPTIC HIPPOCAMPUS USING KI67, HU, PSA AND DOUBLECORTIN: DIFFERENCE BETWEEN CONTROL AND EPILEPTIC HIPPOCAMPUS

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**Purpose:** It is now well-known that human neurogenesis is detected even for the elderly. In the animal experiments, this neurogenesis is increased in epileptic animals. For medically intractable temporal lobe epileptic patients, the neurogenesis is not thoroughly studied until now. The authors studied the existence of hippocampal (dentate granule cell) neurogenesis in epileptic patients using PSA, Ki67, Hu, Doublecortin, and GFAP. The results in epileptic patients are compared with the findings of control human hippocampus (tumor and traumatic cases).

**Method:** Surgically resected hippocampus were transferred to the immunofluorescent staining using the above mentioned markers and analyzed by confocal laser scanning microscope.

#### Results:

- 1 Cell clusters of Ki67+/Hu+ cells are found in the human dentate gyrus (tumor control case).
- 2 Th proliferating neuronal precursor cells are detected in TLE patients.
- 3 Comparison between PSA+ immature cells and proliferating precursor cells: both in control and epileptic patients, these cells are detected, but no significant difference in number is observed between these two groups. (control group: Ki67+/Hu+/DCX+ cells 3/6 patients, and epileptic patients group: Ki67+/Hu+/DCX+ cells:5/11 patients).
- 4 In the epileptic patients group, there are two groups, hippocampal sclerosis group (5) and no hippocampal sclerosis group (6).
- 5 There is no difference between HS (+) and HS (-) group in terms of the existence of immature neuronal precursor cells, but the existence of abnormal bizarre PSA+ cells are only detected in HS group.

**Conclusion:** There is no difference of proliferating neuronal precursor cells between medically intractable TLE hippocampus and control hippocampus. In the hippocampal sclerotic dentate granule cells, there are abundant abnormal PSA+ cells, the role of such abnormal cells should be studied in future.

## P121

### BROAD BEHAVIORAL EVALUATION OF THE GAERS ABSENCE EPILEPSY MODEL: INCLUSION OF THE WISTAR STRAIN AS A SECOND CONTROL

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**Purpose:** In previous behavioral studies, GAERS were only compared to NEC (Non-Epileptic Controls) that were selected along with GAERS not to express any spike-and-wave discharge (SWD). Here we performed a comprehensive study of behavioral and cognitive performance of GAERS compared to NEC but also to their common strain of origin, Wistar rats.

**Methods:** Behavioral testing started at 3 months to ensure that all GAERS displayed SWDs. Several tests were used to evaluate locomotion (home-cage activity, coordination, habituation to a novel environment), anxiety, memory (long-term spatial memory, working memory and procedural memory), and attention. EEGs were performed to assess the presence of SWDs in all GAERS, their absence in NEC and their potential occurrence in Wistar.

**Results:** GAERS and NEC displayed lower nocturnal activity than Wistar. GAERS experienced delayed learning and less efficient working memory in the Morris water maze compared to NEC and Wistar. NEC had better attentional capacities than GAERS and Wistar. Likewise GAERS and Wistar displayed the same anxiety level that appeared higher than in NEC. All GAERS, 9/12 Wistar but no NEC displayed SWDs.

**Conclusion:** Our data indicate that GAERS and Wistar share a similar level of attention and anxiety while NEC differ from the other strains. This shows that including Wistar in studies on GAERS is critical for adequate data interpretation. In addition, absence seizures in GAERS are associated with some spatial learning and working memory impairments.

## P122

### SEEKING SEIZURES: ANALYSIS OF DEPTH ELECTRODE-RECORDED EEG IN EXPERIMENTAL POST-TRAUMATIC EPILEPSY

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**Purpose:** Post-traumatic epilepsy (PTE) accounts for 20% of symptomatic epilepsies. Animal studies have generally characterized PTE using EEG recordings from cortical screws or hippocampal depth electrodes, which may not accurately localize seizure onset and may miss some focal seizures. The aim of this study was to use more extensive EEG coverage to further characterize the location of seizure onset, latency, and rate of development of PTE.

**Method:** Twenty-three adult male rats underwent lateral fluid percussion injury (LFPI). Three rats were implanted with bilateral hippocampal depth electrodes, twenty had bilateral neocortical depth electrodes and screws plus ipsilateral hippocampal depth electrodes. Timing of electrode placement ranged from immediately post-injury to 9 months later, with some EEG recordings extending to 11 months post-injury. EEG recordings were visually reviewed for the presence of seizures and interictal discharges.

**Results:** Eleven animals (47%) developed recurrent seizures lasting  $\geq 10$  s, six (26%) had shorter duration seizure-like events, while the remaining six (26%) had interictal spikes. Seizure or seizure-like events occurred in 4/6 rats with mild injury (67%), 5/6 with moderate injury (83%), and 8/11 with severe injury (73%). In animals with a combination of neocortical and hippocampal electrodes it was determined that most seizures and seizure-like events had a focal onset in perilesional neocortex anterior to the site of injury (86%), with secondary involvement of the ipsilateral hippocampus in 63%, and secondary generalization in 45%. In the animals where the first appearance of spontaneous seizures was captured on EEG the average latency to seizure-like events was  $1.2 \pm 0.3$  months (n = 9), and latency to spontaneous seizures was  $2.8 \pm 0.6$  months (n = 6).

**Conclusion:** Intracranial EEG recordings demonstrated 74% of rats developed seizure or seizure-like events, occurring after all severities of brain injury. Posterolateral brain injury is associated with abnormal activity in both neocortical and limbic structures.



P123

### NEW IN VITRO PHENOTYPIC ASSAYS FOR EPILEPSY: FLUORESCENT MEASUREMENT OF SYNCHRONIZED NEURONAL CALCIUM OSCILLATIONS

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**Purpose:** The epilepsy field is moving from a primary focus on controlling seizures to the development of drugs able to address the disease pathology. This requires the adoption of resource and time-consuming chronic epilepsy animal models which are no longer able to sustain the testing of even moderate numbers of compounds. In vitro models of epilepsy largely rely on electrophysiological measurements of epileptiform activity which imposes significant throughput limitations, making these assays more suitable for compound mode of action studies than for compound identification or secondary screening. There is therefore a need for new in vitro functional assays of epilepsy able to provide a medium throughput while still preserving sufficient biological context to allow for the identification of compounds with new modes of action.

**Method:** Here we describe a robust and simple fluorescence-based calcium assay to measure epileptiform network activity using rat primary cortical cultures in a 96-well format. The assay measures synchronized intracellular calcium oscillations experienced by the population of primary neurons and is amenable to medium throughput screening.

**Results:** We have adapted two well-known cellular models of epileptiform activity to this assay format, the low magnesium and the 4-aminopyridine models, and confirmed the contribution of ion channels, AMPA, NMDA and GABA receptors to epileptiform activity in both models. We have also validated its translatability using a panel of antiepileptic drugs with a variety of modes of action.

**Conclusion:** Because of its throughput and translatability, the calcium oscillations assay bridges the gap between simplified target-based screenings and compound testing in animal models of epilepsy. This phenotypic assay also has the potential to be directly used as a functional screen to help identifying novel antiepileptic compounds with new modes of action as well as pathways with previously unknown contribution to the pathology.

P124

### CONVULSIVE AND NON-CONVULSIVE SEIZURES OBSERVED FROM AGING MICE FOLLOWING BRAIN ISCHEMIA EPISODES

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**Purpose:** Stroke is a leading cause of seizures/epilepsy in the aging/aged population, and seizure development after stroke is associated with poorer prognosis. Currently, seizure genesis after stroke is not well understood, and only limited information is available about post-stroke seizures in aging/aged animals. In particular, early-onset seizures that occur within 24 h post stroke remain to be examined in aging/aged animals. We thus attempted to model the early-onset seizures in aging mice.

**Method:** C57 black mice of 16–20 month-old were used. Unilateral hemispheric ischemia was induced by hypoxia-ischemia or middle cerebral artery occlusion (MCAO) models. The animals were under intensive behavioral monitoring and intracranial EEG recordings to detect post-ischemic seizures and then were euthanized for histological

assessments of brain injury. Exposure of mouse brain slices to hypoxia-hypoglycemia episodes were used as in vitro model of brain ischemia, and regional population activities were examined via extracellular recordings.

**Results:** Vigorous convulsive seizures were observed within 24 h following the hypoxia-ischemia or MCAO episode. These seizures were associated with EEG discharges in the brainstem regions but not in the hippocampal and neocortical areas. Development of these convulsive seizures correlated closely with extensive brain injury and poorer overall outcomes. In addition, non-convulsive seizures, characterized by hippocampal and cortical EEG discharges in the absence of convulsions, were observed following the MCAO episode and prior to the convulsive seizures. When examined in brain slices, seizure-like discharges were observed from the hippocampal CA3 area but not from the brainstem or neocortical area.

**Conclusion:** The early-onset seizures result from severe cerebral ischemia and brain injury. Generation of the convulsive seizures may involve deeper sub-cortical structures particularly the brainstem, and the non-convulsive EEG discharges may originate from the hippocampus. Our data may help understanding genesis of post-stroke seizures in the aging/aged population.

P125

### LOW FREQUENCY STIMULATION OF ENTORHINAL CORTEX INHIBITS HIPPOCAMPAL NEURONAL ACTIVITIES AND FAST KINDLING SEIZURES

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**Purpose:** The entorhinal cortex (EC) is a potential target for low frequency stimulation (LFS, 1 Hz) treatment of temporal lobe epilepsy (TLE). However, the neuronal basis of LFS at EC is unclear. Basing on the anatomy of entorhinal-hippocampal circuit, the present study was designed to determine whether LFS at EC interfere with hippocampal neural activities and seizures.

**Method:** The effects of LFS at EC on the neural activity of dentate gyrus (DG) were examined using single-unit extracellular recordings in anesthetized rats and mice. The effect of LFS at EC on hippocampal fast kindling seizures was tested.

**Results:** The spontaneous activity of the majority neurons (104/115 neurons) in DG were repeatedly interrupted as soon as LFS-on and quickly backed to baseline after LFS-off. EC stimulation pulse mainly induced two distinct types of neural response in DG: the commonly observed type (81/115 neurons) displayed a 179 ± 12 ms inhibition of neural firing 13 ± 2 ms after stimulation; the second type (23/115 neurons) firstly displayed an excitatory response and then a 130 ± 15 ms inhibition of neural firing 25 ± 5 ms after stimulation. This effect of EC stimulation on DG neural activities were mimicked by stimulation of the main projections from the EC to DG (perforant pathway, PP) or optogenetic selective stimulation of axonal projections in DG. LFS of EC also interrupted neurons in hippocampal CA3 and CA1 but not in substantia nigra. Furthermore, LFS of EC immediately after kindling stimulation but not after the cessation of afterdischarge interfered with kindling and kindled seizures.

**Conclusion:** LFS of EC directly interrupted the spontaneous activity hippocampal neural activities, which may through its axonal projections to the hippocampus; and LFS of EC interferes with hippocampal fast

kindling seizures in a time-dependent aspect. These results suggest EC is a promising target for closed-loop LFS treatment of TLE.

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#### P126

##### EFFECTS OF OXYTOCIN ON CARBACHOL-INDUCED OSCILLATIONS IN VENTRAL HIPPOCAMPAL SLICES OF RAT

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**Purpose:** To study the putative modulation of hippocampal oscillations by oxytocin under in vitro conditions.

**Method:** Horizontal slices (400  $\mu$ m) were prepared from 3 to 6 week old Wistar rats and incubated in a gas-liquid interface chamber at 28 C. Extracellular field potentials were recorded using glass electrodes (1 M $\Omega$ ) filled with artificial cerebrospinal fluid, positioned in CA1 stratum radiatum and in Entorhinal Cortex (EC) layer III. Fifty micromolar Carbachol (CCh) was used to induce oscillations in the slices and 0.4  $\mu$ M TGOT (oxytocin agonist) was perfused (i) during the start of CCh perfusion or (ii) during CCh induced oscillations.

**Results:** Application of CCh resulted in the rapid apparition of 30 Hz oscillations in CA1 (79  $\pm$  15 s, n = 18) that were replaced by an alternating 10 Hz/30 Hz oscillations within 5 min. Isolation of hippocampus (HPC) from the surrounding cortex revealed that 30 Hz oscillations were generated by the HPC whereas the 10 Hz oscillations were generated either within the HPC or in some cases, were propagated by EC. (1) Application of 0.4  $\mu$ M of TGOT along with CCh delayed the onset of 30 Hz oscillations (178  $\pm$  18 s, n = 4, p  $\leq$  0.05, unpaired, two tailed Students t-test). (2) Application of TGOT (60 s) on established CCh induced 30 Hz oscillations transiently reduced their amplitude (n = 2).

**Conclusion:** Oxytocin putatively by acting via CA1 interneurons seems to affect local synchronization by reducing the power of gamma oscillations. While the functional implication of this modulation still needs to be clarified, one could hypothesize that oxytocin can modulate epileptic and/or cognitive activities in the temporal lobe.

#### P127

##### EXPERIMENTAL STUDY ON THERAPEUTIC EFFECTS OF VAGUS NERVE STIMULATION FOR EPILEPSY

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**Purpose:** To improve the therapeutic effects and the making of VNS system by study the correlativity between the parameters of VNS and the frequency of epileptic discharge.

**Method:** Improved epilepsy model by injected 0.1% KA 5–10  $\mu$ l into the brain cortex of rabbit. Implanted the VNS system, which made in China, into the rabbit. Analyzed and evaluated the V-EEG of the epilepsy rabbit which treated with different parameter VNS.

**Results:** The EEG frequency of normal rabbit was 14–18 Hz, and the amplitude voltage is 20–50 mv. The epileptic discharge could be recorded after KA injection 30 min later. The frequency was 2–30 Hz. Different VNS parameters of treatment had varied different results in different frequency epileptic discharge. Lower frequency VNS had a better result to lower frequency discharge, and the same as higher frequency VNS to higher frequency discharge.

**Conclusion:** There were some pertinency between the parameters of VNS and the frequency of epileptic discharge. These results had directed significance to the choice of VNS parameters in clinical and the developing of new VNS device.

#### P128

##### THE GENERATIVE PROCESS OF EPILEPTIC HIGH-FREQUENCY OSCILLATIONS AS SHOWN THROUGH NEURONAL NETWORK SIMULATION OF THE RAT DENTATE GYRUS

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**Purpose:** The generative mechanisms of epileptiform discharges (EDs) in electroencephalogram (EEG), especially pathological high-frequency oscillations (HFOs), remain to be clarified. We aimed to illuminate the generative process through a realistic simulation of the sclerotic neural network with mossy-fiber sprouting in the rat dentate gyrus.

**Method:** The simulation, a modified version of that used by Morgan and Soltesz (2008), represented a three-dimensional structure of layers of neurons including 10,000 granule cells (GCs) and a corresponding number of various interneurons with a spatial extent of 1 mm in both the septotemporal and transverse axes. The sum of the field potential generated by the dipole moment of each neuron was recorded in simulation with a clinical macroelectrode with a surface area of 1 mm<sup>2</sup>.

**Results:** In the simulation, EDs with associated HFOs in EEG were provoked by means of perforant path stimulation. The generated HFOs had frequencies up to 280 Hz, and the spectral power of the HFOs tended to be augmented by progression of the degree of sclerosis and reduction of gamma-aminobutyric acid-ergic (GABAergic) inhibition. Each individual peak of an HFO in EEG apparently corresponded to a cluster of firing time-points of GCs.

**Conclusion:** Thus sclerotic changes, particularly the connections formed through mossy-fiber sprouting between GCs, were suggested to play a crucial role in the generation of EEG HFOs in the dentate gyrus.

#### P129

##### “SPASMOLYTIC POWDER” MAY BE AN EFFECTIVE ADD-ON DRUG FOR REFRACTORY EPILEPSY

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**Purpose:** The earliest records of traditional Chinese medicine (TCM) treatment of epilepsy dated back to the 5th -3rd century B.C. It is con-

firming that the famous TCM prescription “Spasmolytic Powder (SP)” was useful for refractory epilepsy as add-on treatment. So the objective of this study is to investigate the mechanism of SP against drug resistance.

**Method:** Repeated intramuscular injection of sub-threshold dose of CL into SD rat was used to establish the refractory epilepsy model. After respectively intragastric administration of low, middle, high-dose of SP, topiramate and verapamil for one week, changes of epileptic attack latencies and electroencephalograms of all groups were observed. RT-PCR and immunohistochemistry were respectively used to detect *mdr1* mRNA and Pgp expressions on hippocampus and temporal lobe in various groups.

**Results:** The epilepsy rat model was successfully established. Compared with the model group, epileptic attack latencies of high and middle-dose groups of SP and topiramate group increased significantly ( $p < 0.05$ ). From electroencephalograms, epileptic discharge frequencies and amplitudes of the three intervention groups were lower than those of model group, but there was no significant difference among the three intervention groups. Compared with model group, the low-dose group of SP had no significant changes of praxiology and electroencephalogram. For the *mdr1* and Pgp expressions on hippocampus and temporal lobe, high and middle-dose groups of SP and verapamil group were significantly less than model group ( $p < 0.05$ ), while compared with the control group, there was no significant difference. For the intracephalic *mdr1* and Pgp expression, there was no significant difference between low-dose group of SP and model group.

**Conclusion:** SP not only had an anticonvulsant effect, but also could inhibit intracephalic *mdr1* and Pgp expression of refractory epilepsy. Therefore, SP was expected to become an effective adjuvant drug for treatment of refractory epilepsy as a novel Pgp inhibitor.

### P130 INFLUENCE OF MYO-INOSITOL TREATMENT ON GABA-A RECEPTOR SUBUNIT CHANGES IN EPILEPSY

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**Purpose:** Epilepsy is a heterogeneous group of disorders. The most important challenge is to prevent the process of epileptogenesis. At present there is no anti-epileptic drug (AED) which would have such action. Identification of the compounds preventing the biochemical changes underlying the epileptogenesis is of great importance. We have previously shown that myo-Inositol (MI) daily treatment prevents certain biochemical changes triggered by kainic acid (KA) -induced status epilepticus (SE). The aim of the present work was to explore further influence of MI treatment on biochemical changes of epileptogenesis and focused on GABA-A receptor subunits:  $\alpha 1$ ,  $\alpha 4$ ,  $\gamma 2$  and  $\delta$  in the hippocampus and neocortex of rats.

**Method:** After SE one group of rats was treated with saline, whereas the second group with MI. Control groups that were not treated by convulsant, received either saline or MI administration. Each group was further divided in two subgroups according to the time of decapitation (the first or the 28th day after the start of experiment). The nuclear-free homogenate fractions from brain tissue samples were obtained and SDS gel electrophoresis and Western blotting analysis were carried out.

**Results:** Twenty-eight to 30 h after experiment (first day) decrease in the amount of  $\alpha 1$  subunit was revealed in the hippocampus and MI has not any significant influence on it. On 28th day of experiment the amount of  $\alpha 1$  was increased in both KA and KA+MI treated groups, whereas  $\alpha 4$  and  $\gamma 2$  subunits were strongly reduced in the hippocampus of KA treated

animals, but MI significantly halted this reduction. In the Neocortex on the 28th day after SE the decrease in the amount of  $\alpha 1$  was found, but MI treatment has no effect on it.

**Conclusion:** Obtained results indicate that MI treatment interferes with some biochemical processes of epileptogenesis.

### P131 WHAT CLINICAL EPILEPTOLOGISTS EXPECT FROM AN ANIMAL MODEL: AN EUROPEAN SURVEY

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**Purpose:** There is growing concerns about the adequation of currently used animal models to study the physiopathology of specific forms of epilepsy, in particular those that are drug-resistant. The aim of this study was to collect the opinion of clinicians on the most relevant features of four prototypical forms of epilepsies that should be considered in the modeling of epilepsy, in order to select or design appropriate animal models for the study of epilepsies and development of new antiepileptic drugs.

**Method:** Two hundred and fifty-four European clinicians expert in epileptology from 33 different countries were contacted via internet through e-mails and were invited to answer anonymously six multiple-choice questions on (i) the animal species and types of animal models and (ii) the most relevant features that should be considered to model idiopathic generalized epilepsies with convulsive seizures, absence epilepsy, focal epilepsy associated with cortical dysplasia or focal epilepsy associated with hippocampal sclerosis.

**Results:** A total of 83 clinicians completed the questionnaire. There was a clear preference for the use of rodent models with chronic seizures, and for in vitro preparations using slides from resection tissues. For each four types of prototypical forms of epilepsy, clinical epileptologists indicated that the most relevant features to be considered are specific EEG patterns observed during the seizures, similar behavioural changes and not necessarily convulsions, same brain structures and same reactivity to antiepileptic drugs.

**Conclusion:** This study confirms that several preparations appear not clinically relevant to study the physiopathology of epilepsies and suggests that animal models with chronic recurrent seizures that can be EEG quantified in similar brain regions as in human patients and with reminiscent behavioural changes should be preferred. It also asks the question of what type of model is really relevant for antiepileptic drug development.

### P132 THE ANTIDEPRESSANT SERTRALINE DIMINISH THE EXPRESSION OF IL-1 $\beta$ AND TNF- $\alpha$ MRNA INDUCED BY SEIZURES IN THE RAT HIPPOCAMPUS

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**Purpose:** The antidepressant sertraline is an effective inhibitor of Na<sup>+</sup> channels in vitro (Aldana and Sitges 2012), as well as of seizures in vivo (Sitges et al. 2012). Data of our laboratory show that anti-seizure drugs that inhibit Na<sup>+</sup> channels decrease the expression of important cerebral pro-inflammatory cytokines. Since several studies indicate that pro-inflammatory cytokines increase in the central nervous system by both, epilepsy and depression, in the present study a possible effect of

## Abstracts

sertraline on the rise in the expression of the pro-inflammatory cytokines IL-1 $\beta$  and TNF- $\alpha$  induced by seizures in the hippocampus was investigated.

**Methods:** The behavioral changes following administration of the pro-convulsive agent, 4-aminopyridine (2.5 mg/kg, i.p.) in control animals and in animals pre-administered either with one or with seven daily doses of sertraline (0.75 mg/kg, i.p.) were monitored. Then the hippocampi were dissected and the expression of the mRNA encoding for IL-1 $\beta$  and TNF- $\alpha$  determined by RT-PCR. Changes in these pro-inflammatory cytokines induced by the convulsive agent pentylenetetrazole (50 mg/kg, i.p.) in control and sertraline pre-administered (2.5 and 25 mg/kg, i.p.) animals were also determined.

**Results:** The administration of a single low dose (0.75 mg/kg) of sertraline decreased the baseline mRNA expression of both cytokines. However, the increase in IL-1 $\beta$  and TNF- $\alpha$  mRNA following 4-aminopyridine-induced tonic-clonic seizures was only overcome in animals receiving the low sertraline dose repeatedly (one daily dose for 1 week). The increase in cytokines mRNA following the dramatic tonic-clonic seizure induced by pentylenetetrazole was not significantly changed by sertraline at a dose of 2.5 mg/kg. Nevertheless a single dose of sertraline at a tenfold higher (25 mg/kg) concentration abolished the increase in pro-inflammatory cytokines induced by pentylenetetrazole.

**Conclusion:** Present findings strongly suggest that the reduction of brain inflammatory processes may contribute to the anti-seizure action of the anti-depressant sertraline.

## P133

## EFFECTS OF CYTIDINE 5'-DIPHOSPHOCHOLINE (CDP-CHOLINE) ON SEIZURE-INDUCED NEURON DEATH

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**Purpose:** To clarify the therapeutic potency of citicoline on seizure-induced neuron death, we used an animal model of pilocarpine-induced epilepsy.

**Method:** Temporal lobe epilepsy (TLE) was induced by intraperitoneal injection of pilocarpine (25 mg/kg) in male rats. Citicoline was injected into the intraperitoneal space 2 h after seizure onset. A second injection was performed 24 h after seizure. Superoxide production was detected by dehydroethidium at 3 h after seizure. Neuronal injury and microglia activation was evaluated at 1 week after seizure.

**Results:** Here we found that post-treatment of citicoline showed no difference of superoxide production but showed significant less neuron death and microglia activation in the hippocampus compared to vehicle treated group.

**Conclusion:** Taken together, these results suggest that neuronal membrane stabilization by citicoline can rescue neurons after severe seizure as seen in several ischemia studies. The present study suggests that citicoline may have a high therapeutic potential to reduce seizure-induced neuronal death.

## P134

## NEUROPROTECTIVE EFFECT OF LEVETIRACETAM ON HIPPOCAMPAL SCLEROSIS-LIKE CHANGE OF SPONTANEOUSLY EPILEPTIC RAT

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**Background:** Levetiracetam (LEV) is effective in inhibiting the seizures in kindled and genetic animals, and for the treatment of both primary generalized and partial epilepsy in humans. The spontaneously epileptic rat (SER) exhibits both tonic convulsion and absence seizures from the age of 8 weeks. Decrease of CA3 neurons, sprouting of mossy fiber, and hyper-expression of brain-derived neurotrophic factor (BDNF) observed in the hippocampus of SER. Our previous study of 5-day LEV administration to SER reported that significant inhibition of the seizures was detected 3–8 days, nevertheless serum LEV mostly disappeared less than 2 days after final administration.

**Objectives:** We examined if prophylactic administration of LEV prior to the exhibition of seizure protect the hippocampal sclerosis-like change which occurred in mature SER.

**Method:** LEV was administered for 28 days using osmotic mini-pump to SER at the age of 4-week. In Group A, LEV was administered at 420 mg/ml for 4 weeks, and in group B, LEV was given at 420 mg/ml and 840 mg for first and latter 2 weeks with consideration of the growth of SER. SER were sacrificed at 11–12 and 14–15 weeks of age. We studied cell count of CA3 neurons and the extent of sprouting of mossy fiber, and BDNF immunoreactivity expressed as the optical density.

**Results:** LEV administration prior to epileptic seizure dose-dependently reduced the decrease of CA3 neurons at 10- to 11-weeks-old, but did not inhibit at 14- to 15-weeks SER. Treatment of LEV suppressed sprouting of mossy fibers and decreased the expression of BDNF in inner molecular layer of dentate gyrus and CA3 of both 11- to 12- weeks and 14- to 15-weeks SER.

**Discussion:** Prophylactic treatment of LEV inhibited the hippocampal degeneration resembling to hippocampal sclerosis in SER, 4 weeks after finishing administration.

## P135

## TEMPORAL CHANGES IN THE IL1B MRNA LEVELS IN IMMATURE AND ADULT ZEBRAFISH BRAIN AFTER SEIZURE

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**Purpose:** Zebrafish was recently proposed as a model for epilepsy studies. Interleukin-1beta (*il1b*) gene has shown to be up-regulated in patients as well as in experimental rodent models; however, the profile of *il1b* in zebrafish brain after seizure is still unknown. We aimed to investigate the pattern of *il1b* transcript in immature and adult zebrafish brain after seizure.

**Method:** Adult and larvae (7 days post-fertilization) were separated in seizure (SG) and control (CG) groups. Animals from SG were individually exposed to 15 mM Pentylenetetrazole (PTZ). CG was handled in PTZ-free water. At 0.05 h and 6 h after seizure, animals were anesthetized and their brains were collected for total RNA extraction. Reverse transcriptase quantitative-PCR amplifications were carried out in triplicates with *bact* as endogenous control using TaqMan™ System (Applied Biosystems). The relative quantification (RQ) was calculated by the equation  $RQ = 2^{-\Delta\Delta C_T}$ . Statistical analysis was performed by Mann-Whitney test ( $p \leq 0.05$ ). This study was approved by animal ethical committee of our Institution.

**Results:** The mean  $\pm$  Standard Deviation results obtained were: (i) immature: CG<sub>0.05 h</sub>: 0.29  $\pm$  0.65; SG<sub>0.05 h</sub>: 0.50  $\pm$  1.12 ( $p = 0.0476$ ); CG<sub>6 h</sub>: 0.24  $\pm$  0.53; SG<sub>6 h</sub>: 0.47  $\pm$  1.05 ( $p > 0.05$ ) (ii) adult: CG<sub>0.05 h</sub>: 0.11  $\pm$  0.25; SG<sub>0.05 h</sub>: 0.39  $\pm$  0.87 ( $p = 0.0159$ ); CG<sub>6 h</sub>: 0.08  $\pm$  0.18; SG<sub>6 h</sub>: 0.18  $\pm$  0.40 ( $p = 0.0278$ ).

**Conclusion:** This is the first study using the zebrafish seizure model to investigate the neuroinflammatory response. Our data demonstrated that PTZ increased the *il1b* mRNA levels in immature and adult zebrafish brain, suggesting a similar pattern as observed in rodents. These results provide new insights about the zebrafish as a model for epilepsy studies.

### P136

#### INHALATION OF CO<sub>2</sub> SHOWS A POTENT AND FAST-ACTING ANTICONVULSANT EFFECT AGAINST SCN1A MUTATION-RELATED HYPERTHERMIA-INDUCED SEIZURES

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**Purpose:** The aim of this study was to assess the anticonvulsant effect of carbon dioxide (CO<sub>2</sub>) on Scn1a mutation-related febrile seizures.

**Method:** We examined physiological changes in the blood gas levels after the induction of hyperthermia-induced seizures (HISs), which were associated with the Scn1a missense mutation. We determined the efficacy of inhalation of 5% or 10% CO<sub>2</sub> to treat HISs. HISs were evoked in Scn1a mutant and wild-type (WT) rats by hot water baths. To determine the anticonvulsant effect of CO<sub>2</sub> inhalation, rats were placed in a chamber filled with air or mixed gas containing 5% CO<sub>2</sub> or 10% CO<sub>2</sub> for 3 min, immediately after the induction of HISs. We also analyzed the blood gas levels at the end of inhalation of CO<sub>2</sub>.

**Results:** Hot water bathing induced a significant reduction in the partial pressure of CO<sub>2</sub> (pCO<sub>2</sub>) and respiratory alkalosis in the WT and Scn1a mutant rats. HISs were evoked in 100% of the Scn1a mutant rats within 5 min, but in none of the WT rats. The Scn1a mutant rats demonstrated a higher HISs susceptibility associated with respiratory alkalosis than the WT rats. Inhalation of 10% CO<sub>2</sub> shortened the seizure duration from 62.6  $\pm$  12.1 s to 15.5  $\pm$  1.0 s. Blood gas analysis after the inhalation of 10% CO<sub>2</sub> demonstrated an elevated pCO<sub>2</sub> level and respiratory acidosis.

**Conclusion:** Inhalation of 10% CO<sub>2</sub> demonstrated a potent and fast-acting anticonvulsant effect against HISs.

### P137

#### FDG MICROPET STUDY OF CEREBRAL STRUCTURAL GLUCOSE UPTAKE IN CARISBAMATE TREATED RATS IN LITHIUM-PILOCARPINE MODEL OF EPILEPSY

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**Purpose:** The lithium-pilocarpine model of epilepsy in rats reproduces the main features of human mesial temporal lobe epilepsy. All adult animals become epileptic after lithium-pilocarpine induced status epilepticus (Li-Pilo SE). Carisbamate is to date the only drug able to prevent the course of epileptogenesis in part of these animals. Cerebral glucose

metabolic modifications that underlie the epileptogenic network are well documented by the <sup>14</sup>C-2-deoxyglucose autoradiography (2DG). This reference technique necessitates sacrificing the animals and does not allow a longitudinal study. Our goal is

To study by a non invasive technique, <sup>18</sup>F-fluorodeoxyglucose Positron Emission Tomography in small animals (FDG micro-PET), the modifications of cerebral structural glucose uptake at selected time points after lithium-pilocarpine SE.

To correlate carisbamate anti-epileptogenic effect to glucose cerebral metabolism.

**Method:** Thirty-one adults Sprague–Dawley rats were divided into three groups: controls (n = 10), submitted to lithium-pilocarpine SE followed by carisbamate treatment (n = 11) or not (n = 10). Video-monitoring permits to assess the occurrence latency of spontaneous recurrent epileptic seizures that define the chronic phase. Micro PET is performed 4 h, 2, 8 and 60 days after SE. Brain anatomic Magnetic Resonance Imaging (MRI) is performed at day 1 and 60. MicroPET and MRI are matched.

**Results:** After Li-Pilo SE, FDG micro-PET showed in vivo.

- 1 The transient early glucose hypermetabolism followed by late hypometabolism in para-hippocampal areas after lithium-pilocarpine SE. These results are in accordance with 2DG data.
- 2 The lessening of glucose metabolic modification by carisbamate, without significant difference between secondarily epileptic and non epileptic rats.

**Conclusion:** Our results validate FDG microPET to assess structural brain glucose metabolism in lithium-pilocarpine model of temporal lobe epilepsy. The epileptogenic outcome of carisbamate treated rats after Li-Pilo SE was not predictable by this technique.

### P138

#### UNILATERAL CORTICAL SPREADING DEPRESSION PRODUCES LONG-TERM CHANGES OF SPIKE-WAVE ACTIVITY IN WAG/RIJ RATS

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**Purpose:** Studies in genetic models of absence epilepsy (WAG/Rij and GAERS rats) show focal onset of spike-wave discharges (SWDs) in the somatosensory cortex. This study examined effect of transient unilateral physiological inactivation of the cortex on pattern and incidence of SWDs in WAG/Rij rats.

**Method:** A single unilateral wave of the cortical spreading depression (SD) was induced by injection of 5% KCl in the occipital cortex of awake WAG/Rij rats (n = 12). Each rat was equipped with six recording stainless-steel electrodes placed bilaterally over the frontal somatosensory and parietal cortex. Control rats received sham microinjections. EEG was recorded for 1 h after initiation of SD.

**Results:** A single cortical SD induced suppression of EEG for 2 min. A statistically significant ( $p < 0.01$ ) decrease in SWDs and increase in sleep spindles was found for 1 h after unilateral cortical SD. The first SWDs appeared earlier in somatosensory cortex (time delay was more than 50 ms). In all rats with SD SWDs were suppressed also on the opposite side following the unilateral decortication.

**Conclusion:** Our findings show that physiological inactivation of the cortex by SD produces long-term suppression of non-convulsive epileptic activity. These results confirm the crucial role of the cortex in

generation of SWDs. Increase in sleep spindles after cortical SD suggests that transient cortical inactivation leads to long-term predominance of thalamic rhythm.

### P139

#### CONSEQUENCES OF EARLY POSTNATAL DRUG TREATMENT ON THE EXPRESSION OF SPIKE-AND-WAVE DISCHARGES IN ADULT GENETIC ABSENCE EPILEPSY RATS FROM STRASBOURG (GAERS)

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**Purpose:** In GAERS, spike-and-wave discharges (SWDs) are only recorded after the 25th day of postnatal life. In this study, we treated GAERS during the neonatal period to verify whether targeting early neurotransmission systems or using antiepileptic drugs (AEDs) would affect the expression of SWDs in adult GAERS.

**Method:** One hundred and thirty-four male GAERS were injected once daily between postnatal day 7 (PD7) and PD25 with the following drugs: saline; NMDA receptor antagonists, PCP (5 mg/kg) or MK-801 (0.25 mg/kg); GABA<sub>A</sub> receptor agonist THIP (5 mg/kg) and antagonist picrotoxin (1 mg/kg); GABA<sub>B</sub> receptor agonist baclofen (4–10 mg/kg) and antagonist CGP 56999 (25 mg/kg). AEDs were also administered: valproate (200 mg/kg), vigabatrin (100 mg/kg), carbamazepine (20 mg/kg), phenytoin (80 mg/kg), ethosuximide (200 mg/kg) and lamotrigine (6 and 12 mg/kg). Rats were recorded at 4 months when seizures are stable in 100% of GAERS.

**Results:** While early baclofen ( $p < 0.05$ ), CGP 56999 ( $p < 0.01$ ), picrotoxin ( $p < 0.01$ ) and THIP ( $p < 0.05$ ) treatment increased seizure duration at 4 months, PCP ( $p < 0.05$ ) decreased duration and MK-801 had no effect. Valproate reduced seizure duration, lamotrigine 6 mg/kg had no effect, whereas vigabatrin, carbamazepine, phenytoin, ethosuximide and lamotrigine 12 mg/kg increased seizure duration.

**Conclusion:** This study suggests that early interference with GABAergic neurotransmission worsens SWD expression in adult GAERS, while acting on glutamate neurotransmission would alleviate seizure expression. Among AEDs, only early valproate treatment reduces SWD duration in adult GAERS while all other AEDs given before seizure occurrence, whether they are beneficial for or aggravate absences acutely, increase SWD duration in adult GAERS.

### P140

#### CONDUCTING EPILEPTIFORM DISCHARGE ACTIVITY TO EXTRA-CRANIUM IN RATS WITH TEMPORAL LOBE EPILEPSY

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**Objectives:** Most of current treatments of epilepsy aimed to remove epileptogenic zone, inhibit the propagation of epileptiform discharge, and/or improve the kindling threshold value, and the therapeutic theory for epilepsy is to inhibition seizure. We wanted to confirm that conducting the epileptiform discharge activity out of the cranium can prevent the seizure, and introduce the novel mini-invasive neurosurgical method in epileptic therapy.

**Methods:** To build temporal lobe epilepsy rats model with kainic acid, and divided them into three groups: control group, pseudo-conducting group, and conducting group. The self-made conducting electrode consisted of platinum silk with 1 mm in diameter and 20 mm in length which included 2 mm naked head and insulation lagging cov-

ered body, and a platinum patch 5 mm in diameter at the end of electrode, however, the pseudo-conducting electrode have only the platinum silk same as the conducting electrode. In the conducting and pseudo-conducting groups, the naked head of electrode was inserted into the CA1 area, and the patch (in leading group) or insulation lagging covered platinum silk (in pseudo-leading group) was put under partial region scalp. The epileptiform discharges were recorded by EEG with deep needle electrode for 2 h under anesthesia stage, and seizures were monitored by video for 24 h in waking stage. At last, the apoptosis ratio of hippocampus neuron was tested with flow cytometer.

**Results:** The mean times of epileptiform discharges in EEG in rats with temporal lobe epilepsy were  $7.27 \pm 2.25$  in control group,  $6.06 \pm 1.77$  in pseudo-conducting group, and  $1.94 \pm 1.93$  in conducting group respectively. Furthermore, the mean seizures times in 24 h were  $7.64 \pm 2.22$  in control group,  $7.79 \pm 2.48$  in pseudo-conducting group and  $2.44 \pm 1.84$  in conducting group. Significant differences were found in both epileptiform discharge and seizure times among three groups ( $p < 0.01$ ). Apoptosis ratio of hippocampus neuron was  $2.04 \pm 0.87\%$  in rats in conducting group, which was significant lower than  $6.33 \pm 1.59\%$  in control group, and  $6.25 \pm 1.46\%$  in pseudo-conducting group ( $p < 0.01$ ).

**Conclusions:** Conducting the epileptiform discharge activity out of the cranium can prevent the seizure and reduce epileptiform discharge and apoptosis ration of hippocampus in temporal lobe epilepsy rats with kainic acid.

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### P141

#### INTERICTAL EPILEPTIFORM ACTIVITY ORIGINATES IN THE NORMOTOPIC CORTEX AND SECONDARILY PROPAGATES TO THE HETEROTOPIC BAND, IN A RAT MODEL OF SUBCORTICAL BAND HETEROTOPIA

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**Purpose:** Subcortical Band Heterotopia (SBH) is a cortical malformation formed when neocortical neurons prematurely stop their migration in the white matter, forming a heterotopic band below the normotopic cortex, and is generally associated with intractable epilepsy. Although it is clear that the band heterotopia and the overlying cortex both contribute to creating an abnormal circuit responsible for the generation of epileptic discharges, it is less understood which part of this circuitry is most critical. Here, we sought to identify the origin of epileptiform activity in a targeted genetic model of SBH in rats.

**Method:** Rats with SBH (Dcx-KD rats) were generated by knocking-down the Dcx gene using shRNAs vectors transfected into embryonic day 15 neocortical progenitors of rat embryos. Susceptibility to pentylenetetrazol (PTZ)-induced seizures was assessed by electrocorticography in head-restrained non-anaesthetized postnatal day 15 (P15) rats. The origin, the spatial extend and laminar profile of bicuculline-induced interictal-like activity were analyzed by using multisite extracellular recordings from planar 60-channels microelectrode arrays on P15 acute neocortical slices.

**Results:** Dcx-KD rats were found to display an increased propensity for PTZ-induced seizures that were evoked with lower doses of PTZ and shorter latencies as compared to controls. Interictal-like activity on acute slices from Dcx-KD rats was mostly found to originate within the normotopic cortex, and rarely within the band heterotopia. However, the band heterotopia was always active during interictal-like activity.

**Conclusion:** These results are suggestive of a major role of the normotopic cortex over the band heterotopia in generating interictal epileptiform activity in SBH.

#### P142

### INTERACTIONS WITH IONOTROPIC GLUTAMATE RECEPTOR MAY EXPLAIN ANTICONVULSANT PROPERTIES OF *VALERIANA OFFICINALIS* ETHANOLIC EXTRACT IN *DANIO RERIO* (ZEBRAFISH)

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**Purpose:** Glutamate receptors (GluR) have an important role in seizure controls, but few drugs used it as pharmacological target. Natural product could be an alternative to treat epileptic people. *Valeriana officinalis* extract could have anticonvulsant properties. Also, interactions of *Valeriana officinalis* extracts with GluR have been shown [Del Valle et al. *Planta Med.* 2012;78:1719–1724.]. Our aim was to determine if the valerian extracts are anticonvulsant on *Danio rerio* (zebrafish). Interaction with glutamate GluR was tested as possible mechanism.

**Method:** Zebrafish were exposed to *Valeriana officinalis* ethanolic extracts (Val<sub>EIOH</sub>, 1 mg/ml) or selective ionotropic GluR antagonist (for AMPA or NMDA) or metabotropic GluR antagonist (CPGG or PHCCC) for 1 h. Seizures were induced with Pentylentetrazole (PTZ, 3 mg/ml) dissolved in water. The latency period was defined from the initial exposure to PTZ until the wild jumping immediately followed by the loss of posture.

**Results:** Val<sub>EIOH</sub> (1 mg/ml) significantly ( $p < 0.001$ ) increases the latency to PTZ (3 mg/ml). Zebrafish exposed to antagonist for AMPA or NMDA and then 1 h to Val<sub>EIOH</sub> the latency show a significant reduction ( $p < 0.01$ ) compared to those exposed to Val<sub>EIOH</sub>. Animals exposed to CPGG or PHCCC and Val<sub>EIOH</sub> do not show significant difference in the seizure latency compared to Val<sub>EIOH</sub>.

**Conclusion:** Selective interaction with AMPA and NMDA, GluR receptors could explain the anticonvulsant effect of ethanolic valerian extracts on zebrafish. However, extract interaction with metabotropic GluR was not demonstrated.

Approved by University of Puerto Rico-Medical Sciences Campus, UPR, Institutional Animal Care and Use Committee on June 1, 2010 (Proposal ID 3180110).

#### P143

### HIPPOCAMPAL SPIKE-AND-WAVE DISCHARGES IN THE GAMMA-BUTYROLACTONE RAT MODEL OF TYPICAL ABSENCE SEIZURES

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**Purpose:** Both typical and atypical absence seizures are generated by the interconnected circuitry of the thalamus and cortex. A fundamental distinction is a role of the hippocampal circuitry in atypical absence seizures, which is not thought to be involved in typical absence seizures. This study explores the interactions between the hippocampus and thalamocortical network, which may help to identify crucial neural networks as useful therapeutic targets for the elimination of seizure activity.

**Method:** Electroencephalography (EEG) was used to characterize neural activity between the thalamus, cortex and the hippocampus in the gamma-butyrolactone (GBL) rat model of typical absence seizures. Rats ( $n = 8$ ) were surgically implanted with depth electrodes in the medial parietal cortex, frontal cortex, visual cortex, hippocampus and ventrolateral thalamus. Following a week of recovery, rats were injected with 200 mg/kg GBL intraperitoneally and EEG was recorded continuously for 2 h.

**Results:** Within 9 min of injection, rats were completely immobile with a vacant stare. There was a simultaneous reduction in EEG frequency from a 5 to 6 Hz burst pattern to a continuous pattern of 4–6 Hz with an increase in power. Spike-and-wave discharges (SWDs) were recorded from all electrodes with the highest amplitude observed in the hippocampus.

**Conclusion:** The expression of SWDs in the hippocampus demonstrates an interaction between the thalamocortical and hippocampal circuitry and suggests an important link between the hippocampus and typical absence seizures.

#### P144

### ANATOMICAL CORRELATES OF LOW-VOLTAGE FAST-ONSET (LVF) VERSUS HYPERSYNCHRONOUS-ONSET (HYP) SEIZURES IN THE PILOCARPINE MODEL OF TEMPORAL LOBE EPILEPSY

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**Purpose:** Our study aim at looking if seizures with distinct onset patterns are related to different anatomical correlates.

**Method:** Sprague–Dawley rats (250–500 g) ( $n = 8$ ) were implanted with bipolar electrodes in the CA3 region of the hippocampus, entorhinal cortex (EC), subiculum, amygdala and dentate gyrus. Seizure onset zones were identified using EEG traces and frequency spectral analysis.

**Results:** Results showed that 81% (164/203) of HYP seizures originated from CA3 whereas 12.3 (25/203) % originated from the EC. On the contrary, 68.9% (51/74) of LVF seizures started in the EC and 27% (20/74) in CA3.

**Conclusion:** This study suggests that seizures with distinct onset patterns are related to different anatomical correlates and that seizures could be related to the pathological activity of distinct neural networks.

#### P145

### STATUS EPILEPTICUS-INDUCED PRECOCIOUS EXPRESSION OF KCC2 IMPAIRS EXCITATORY SYNAPSE FORMATION

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**Purpose:** Febrile seizures affect 5% or more of all children during a critical period of brain development. Atypical febrile seizures, particularly febrile status epilepticus, correlate with a higher risk of developing cognitive deficits and temporal lobe epilepsy as adults, suggesting that they may permanently change the developmental trajectory of neuronal cir-

cuts. However, the mechanisms underlying these effects are not clear. Cation-chloride cotransporter KCC2 decreases intracellular  $Cl^-$  levels and renders GABA responses hyperpolarizing. Recent data suggest that KCC2 also modulates excitatory synapse development. We investigated KCC2 expression and spine density in the hippocampus of a well-established rodent model of atypical febrile seizures, combining a cortical freeze lesion at post-natal day 1 (P1) and hyperthermia-induced seizure at P10 (LHS rats).

**Method:** We performed Western blot to quantify protein levels as well as patch clamp recording to measure KCC2 functionality and level of input. To measure spine density we used DiI labeling. Finally, to investigate whether KCC2 precocious overexpression plays a role in spine alterations, we mimicked it in hippocampal organotypic culture by biolistic transfection and in-vivo by in-utero electroporation.

**Results:** At P20, we found a precocious increase in KCC2 protein levels, accompanied by a negative shift of Egaba following high-frequency stimulation. In parallel, we observed a striking reduction in dendritic spine density and of mEPSC amplitude and frequency in CA1 pyramidal neurons. Lastly, overexpressing KCC2 in vitro and in vivo decreased spine density.

**Conclusion:** Increased KCC2 levels induced by early-life seizure could be responsible for alterations in spinogenesis and may be a contributing factor to the occurrence of hippocampal atrophy and associated cognitive deficits.

#### P146

##### P75 NEUROTROPHIN RECEPTOR MODULATION AND JAK/STAT INHIBITION: ROLE IN THE PROGRESSION OF EPILEPSY IN THE PILOCARPINE RAT MODEL

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**Purpose:** Following status epilepticus (SE), increases in BDNF regulate a wide variety of cell signaling pathways including the JAK/STAT pathway, in a receptor-specific manner. Recent studies have shown that inhibition of the p75 neurotrophin receptor (p75<sup>NTR</sup>) prevents BDNF-induced activation of the JAK/STAT pathway in cultured hippocampal neurons. To elucidate the role of p75<sup>NTR</sup>-mediated pSTAT3 activation in epileptogenesis, we examined the effect of p75<sup>NTR</sup> modulation (using LM11A-31) and of direct inhibition of STAT3 phosphorylation (using WP-1066) on SE-induced STAT3 phosphorylation and subsequent epileptogenesis.

**Method:** Rats were injected with 200 mg/kg of LM11A-31 or vehicle at time of pilocarpine injection and again at onset of SE then sacrificed 1 and 3 h later for tissue and plasma harvesting. A second set of animals received 50 mg/kg WP1066 at SE onset and the same dose 45 min later. Continuous video-EEG was recorded for 1 month from animals treated with drug or vehicle to evaluate effects on daily seizure frequency.

**Results:** LM11A-31 was present in brain at 1 h and less at 3 h after SE and produced a transient decrease in STAT3 phosphorylation in hippocampus 1 h after SE (approximately 75% inhibition (n = 5/group; p = 0.002), but not 3 h after SE (n = 4/group). WP1066 also significantly decreased pSTAT3 immunoreactivity by approximately 58% at 1 h after SE (n = 4/group; p < 0.0001). Neither treatment affected electrophysiological parameters of SE or seizure latency. WP1066 significantly reduced the daily seizure frequency over time (SE+vehicle,

n = 10–18/group; p < 0.001) while LM11A-31 treated rats showed no difference in cumulative seizure frequency compared to vehicle-treated rats (n = 6–7/group).

**Conclusion:** Despite early inhibition of STAT3 phosphorylation by both LM11A-31 and WP1066, only direct block of STAT3 phosphorylation with WP1066 successfully inhibited epilepsy progression. These findings suggest that the mechanism of JAK/STAT inhibition may be an important determinant of its disease modifying effects.

#### P147

##### INTERICTAL SPIKES AND HIGH-FREQUENCY OSCILLATIONS (80–500 HZ) DURING EPILEPTOGENESIS IN A MODEL OF TEMPORAL LOBE EPILEPSY

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**Purpose:** It was recently suggested that different types of interictal spikes may point to distinct neural mechanisms that occur during epileptogenesis (Chauviere et al. Ann Neurol 2012; 71: 805–814). In this study, we have analysed the evolution of interictal spikes (type 1 and type 2) and HFOs during the late latent (from 48 h before to first seizure occurrence) and early chronic periods (from first seizure occurrence to 48 h after).

**Method:** Sprague-Dawley rats (n = 8) were implanted with bipolar electrodes in the CA3 region of the hippocampus, after a pilocarpine-induced status epilepticus. Local field potential (LFP) recordings and video-monitoring were then performed starting from the 3rd to the 15th day after SE. Interictal spikes and HFOs were analysed during different time-periods: 48 h before first seizure occurrence, 24 h before, on the day of the first seizure, 24 h after and 48 h after.

**Results:** The analysis of interictal spikes showed that over time, rates of occurrence of type 2 spikes significantly increased before the day of the first seizure. The analysis of HFOs however showed that before the day of the first seizure, rates of occurrence of type 1 spikes with ripples significantly decreased over time whereas rates of occurrence of type 1 spikes with fast ripples significantly increased.

**Conclusion:** The results point to the importance of considering the different subtypes of interictal spikes and their associated HFOs during the latent period, as they may point to distinct underlying mechanisms that occur during epileptogenesis.

#### P148

##### ELECTROENCEPHALOGRAPHIC AND BEHAVIORAL EFFECTS OF GRAYANATOXIN III 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 (1). Mad honey poisoning caused by GTX causes dizziness, fatigue, excessive perspiration, hypersalivation, vomiting, paresthesia, seizures and convulsions in human. (2). We aimed to investigate the changes in the electroencephalographic (EEG) activities and accompanying motor movements of adult Wistar rats induced by intracerebroventricular (icv) administration of GTX III.

**Method:** Adult male Wistar rats were implanted with icv guide cannula and recording electrodes over the cortex (Ethics approval; 90.2010



March). After recording of baseline EEG, GTX III (100 ng/5  $\mu$ l, icv) was injected to rats (n = 6). EEG activities and motor movements were monitored for 3 h. Animals behavioral changes were evaluated based on the Racine's seizure scale.

**Results:** GTX III administration caused generalized cortical spikes in both hemispheres in EEG accompanied by behavioral changes in animals. Three out of six rats showed convulsive seizures throughout the observation period. The mean latency to the first generalized spikes in EEG was  $11.2 \pm 2.3$  min and mean latency to the first behavioral changes was  $22.7 \pm 2.5$  min after the injection.

**Conclusion:** These results suggest that the icv administration of GTX III can be a seizure model for understanding the mechanism of ictogenesis and epileptogenesis as well as the development of new target therapies.

#### P149

### PRESERVED HIPPOCAMPAL GLUCOSE METABOLISM ON $^{18}$ F-FDG PET AFTER HUMAN UMBILICAL CORD BLOOD-DERIVED MESENCHYMAL STEM CELL TRANSPLANTATION IN CHRONIC EPILEPTIC RATS

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**Purpose:** Medial temporal lobe epilepsy is a common type of medically resistant focal epilepsy. We evaluated the efficacy of human umbilical cord blood-derived mesenchymal stem cells (hUCB-MSC) transplantation in the lithium-pilocarpine rat model of chronic epilepsy using FDG PET serial monitoring.

**Method:** Ten weeks after status epilepticus (SE), rats with spontaneous recurrent seizures (SRS) were randomly divided into three groups: stem cell treatment (SCT, n = 8), sham control (ShC, n = 9), and positive control (PC, n = 9). Normal rats received stem cell transplantation were used as the negative control (NC, n = 7). PKH-26-labeled hUCB-MSCs were unilaterally transplanted into the right hippocampus of the each rat in SCT and NC groups, and the same procedures were performed on ShC rats using an equal amount of saline. FDG PET was performed three times: baseline, 1 week, and 8 weeks after treatment.

**Results:** Of 71 rats, 26 developed SRS. Bilateral hippocampal glucose metabolism at 8 weeks post-treatment was significantly higher in the SCT group compared with the ShC and PC groups (p < 0.01), however these did not return to normal. Histological studies indicated that the transplanted hUCB-MSCs in the SCT and NC groups survived in the ipsilateral and contralateral hippocampi but did not differentiate. Despite successful engraftment in SCT group, there were no significant differences in terms of seizure frequency among the groups at any time point.

**Conclusion:** These results demonstrate that transplanted hUCB-MSCs can be successfully engrafted and migrate to the damaged hippocampus and partially restore bilateral hippocampal glucose metabolism in a rat model of chronic epilepsy. Although such changes were not enough to alter the clinical course, the results suggest promising effect of hUCB-MSCs on repairing epileptic networks.

## Poster Session: Developing World Monday, 24 June 2013

#### P150

### EPILEPSY ASSOCIATION OF ZAMBIA SUCCESSFUL SCHOOL PROGRAMME

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**Purpose:** One of the objectives of the Association since inception has been to take back or enroll children of school going age into regular school schedule. If the condition of epilepsy is well controlled there is no reason why children and adolescents should not be able to receive the same schooling as other children.

**Method:** The clients are identified and enlisted for the programme during the usual clinical check up at the established special epilepsy clinics e.g. at the Chainama Hills College Hospital Tuesday weekly clinic.

**Results:** The school programme has been a great strength for the Association's existence and we proudly present four cases of success in summary as follows:

- 1 David Mwila – The Association began sponsoring David when he was in Grade Eleven at Kabulonga Boys High School. David completed his high school and is now studying Information Technology in Russia. Still sponsored by the Association.
- 2 Niggan Chibwe – Sponsored from Grade Eleven at Munali High School and completed his high school.
- 3 Rose Mwanza – Sponsored for Certificate in Secretarial Studies at the Lusaka Business Technical College and to continue with Advanced Secretarial Studies in 2013.
- 4 Cephas Phiri – Partial sponsorship for Medical Student at the University of Zambia. Cephas is a qualified young clinical officer who has shown great interest in caring for people with epilepsy and works closely with the Association Chairman regarding medical issues.

**Conclusion:** The Epilepsy Association of Zambia successful school programme has encouraged other parents/guardians to take their children to school despite living with epilepsy. We have seen other members of the youth group encourage one another to improve their capacity through education and we believe that with continued effort and a well-founded programme success is inevitable.

#### P151

### THE IMPACT OF ITINERARY CONSULTATIONS IN ISOLATED REGIONS OF MOROCCO ON THE MANAGEMENT OF EPILEPSY

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Morocco is experiencing a bad repartition of its neurologist, indeed, 90% of the 160 neurologist there is in our country are distributed in the small but central axis Rabat- Casablanca, leaving large areas (for example the south of our country) without any coverage. In another hand, it is estimated that up to 1% of our population (300,000 persons) suffers from epilepsy according to one study performed in our country. For these considerations the idea of developing itinerary consultations to rural and isolated areas comes to life. In accordance to this goal, we started in 2006 with the willingness and collaboration of the authorities of Ouarzazate and Kelaa the Sraghna to perform itinerary consultation to these two regions. The goal of this initiative was to offer specialized consultations in neurology for the population of these regions with a special focus on epilepsy. In the region of Ouarzazate, we found

interesting family cases of epilepsy giving the high frequency of consanguinity in this region, and important scientific studies are ongoing with the collaboration of an American team from San Diego.

Our initiative was very successful giving the dynamism of our team of neurologist from Mohammed VI university hospital in Marrakesh, but also thanks to the local authorities who gave us all the technical help to achieve this work. A thorough report of our achievements will be giving. Our main goal is to highlight the importance of such initiative in the management of epilepsy in our developing country and to encourage similar works in other regions of our country but also other developing countries facing the same challenges.

#### P152

##### POSSESSION BY JINN AS A CAUSE OF EPILEPSY (SARAA): A STUDY FROM SAUDI ARABIA

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**Purpose:** Explore if misconceptions such as possession by demons (Jinns) are still believed to be a cause of epilepsy among educated Saudi today.

**Method:** University-educated school teachers and undergraduate students were studied through structured questionnaire enquiringly about familiarity, source of knowledge and depth of knowledge about specific aspects of epilepsy.

**Results:** Three hundred and ninety-eight participants were included. Two thirds of them learned about epilepsy from friends and relatives. 172 (43.1%) believed that epilepsy is a psychiatric disease. 62 (40.3%) of the school teachers and 123 (50.4%) of the students in the study considered possession as a cause of epilepsy. The majority of the cohort believed medical treatment for the condition exists despite the fact that a significant number believed that faith healers and traditional medicine can be of help in the treatment of epilepsy.

**Conclusion:** Jinn possession is still believed to be a cause of epilepsy in Saudi society, even among educated people. This finding emphasizes the urgent need for public education campaigns at all level of education.

#### P153

##### ASSESSMENT OF THE AVAILABILITY OF ANTI-EPILEPSY DRUGS IN HARARE CITY COUNCIL CLINICS IN RELATION TO EPILEPSY MANAGEMENT NAME OF INSTITUTION: EPILEPSY SUPPORT FOUNDATION, HARARE, ZIMBABWE

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**Purpose:** To establish the availability of Anti-Epilepsy Drugs in Harare city clinics in relation to epilepsy management.

**Method:** Ten clinics were sampled from the city's forty clinics. The method of sampling was random. Data on number of epilepsy patients being catered for, drug availability and general comments was collected.

**Results:** Drug availability per product: Phenobarbitone – 100% Carbamazepine – 90% Phenytoin – 20% Sodium Valproate – Nil Despite all clinics having phenobarbitone, the available strength was not compli-

ant with the prescribing regimen in the country which poses a risk of breakthrough seizures. Both Phenobarbitone and Carbamazepine have been donated to Zimbabwe and are not registered with the Medicines Control Authority of Zimbabwe (MCAZ) which is responsible for ensuring that safe and efficacious drugs are dispensed. The two are not labelled in English (official language) and there is no name of manufacturer.

**Conclusion:** All the nurses interviewed in the clinics complained of the strength of Phenobarbitone which was presenting a challenge to them in terms of dispensing. The normal prescribing regimen in Zimbabwe is in multiples of 30 mg, so the 50 mg strength tablet was a real challenge. The same patient can access medication from either the government hospitals which have 30 mg tablets and then the following month, they go to their local clinic which dispenses 50 mg tablets which causes a lot of confusion to the system. It was concluded that management of epilepsy was not being prioritised as no one seemed to care what was really being given to the people. Survey conducted by Sr. Makoni (ESF) and Mrs. C.M. Chinyanya (ESF) on the 16th of August 2010 as an effort by the local chapter of the GCAE to appreciate what is actually going on at grassroots level.

#### P154

##### PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY PRESENTING WITH SEIZURES: A REPORT OF TWO CASES IN UYO, SOUTHERN NIGERIA

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**Purpose:** Progressive multifocal leuko-encephalopathy (PML) is an opportunistic infection of the central nervous system that occurs almost exclusively in the setting of immunosuppression. It is a fatal demyelinating disease caused by the polyoma JC virus that commonly presents with impaired vision, mental changes and motor weakness. few cases have been reported in Africa and seizures are a rare presentation. We report two cases that presented with seizures in Nigeria.

**Results:** Case 1: A 35 year old female nurse presented with seizures, loss of consciousness and weakness of the left side of the body. The seizures involved the left upper and lower limbs with tonic eye and neck deviation. The first ever episode of seizures was 5 days earlier. She had been HIV positive for 5 years but had not commenced HAART. CD4<sup>+</sup> count was 19 cells/ $\mu$ l. The brain CT scan showed a hypodense non-enhancing lesion in the right parieto-occipital region. A diagnosis of PML was made. Case 2: A 23 year old girl presented in status epilepticus. There was a preceding history of weight loss and headaches of 1 year duration. HIV screening was reactive. A brain CT scan showed multifocal non-enhancing deep white matter at the level of the midbrain, thalamus and left fronto-parietal lobes with a subsequent diagnosis of PML.

**Conclusion:** PML is also seen in African HIV patients. There is need for a high index of suspicion as the presentation may be unusual. Diagnosis has been improved by the availability of neuroimaging in our centers.

#### P155

##### INFLUENCE OF EARLY AND LATE TREATMENT OF EPILEPSY ON SEIZURE PROGNOSIS

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**Purpose:** To compare the seizure outcome in epilepsy patients, who were commenced on antiepileptic drugs early and those who had delayed treatment.

**Method:** Patients with epileptic seizures attending the neurology Medical outpatient clinic were evaluated using a standard proforma. Early treatment referred to patients that were treated within the first 2 years of seizure onset while delayed treated were those that were treated at 3 years or later. Outcome measure was the level of seizure control, patients were said to be seizure free after 1 year of complete absence of seizure while uncontrolled seizure described patients who are not seizure free for a year or more.

**Results:** Hundred and four patients were evaluated. Of these 62 (59.61%) patients were commenced on antiepileptic medication within the first 2 years of seizure onset while 42 (40.39%) patients commenced between 3 and 17 years after seizure onset. Of the 62 patients who were commenced on early treatment 33 (53.22%) were seizure free and 29 were uncontrolled. 25 (78.13%) of these achieved remission in the first 2 years. Of the 42 patients who started treatment late 12 were in remission giving a seizure remission rate of 28.6%. Factors responsible for delayed treatment are poor recognition of seizure, lack of access to medical care and the general misconception that seizures are spiritual attacks. Early diagnosis is associated with access to medical care and early generalized tonic-clonic seizure.

**Conclusion:** The result of this study suggests that early treatment is associated with better and earlier seizure remission rates.

## P156

### TREATMENT GAP REDUCTION IN PAKISTAN: SUCCESS OF PUBLIC AWARENESS CAMPAIGN

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**Purpose:** To assess the impact of epilepsy public awareness campaign on treatment gap in Pakistan.

**Study background:** According to 1987 population-based study epilepsy treatment gap was 86%; mainly because of poor knowledge and erroneous socio-cultural beliefs regarding the disorder (Aziz H et al. *Epilepsia* 1994; 35: 950-958). Countrywide public health education is ongoing since then; more intensive and sustained from 2001. Another population-based study was performed in 2006, part results of which are being presented.

**Method:** A door-to-door population-based epidemiologic study was conducted in urban and rural areas of Karachi, in southern Pakistan. Sample collection was done by random block selection method in proportion to the population structure of the area. Questionnaire based on ICBERG protocol (same as used in 1987 study) was applied.

**Results:** Of the 5379 people screened from urban and rural areas of Karachi, 23 had epilepsy (05 urban, 18 rural) and of these 09 (39.1%) were taking atleast one antiepileptic drug; 4 (80%) in urban and 5 (27.8%) in rural area.

**Conclusion:** A significant change in treatment gap status has been noted. There is an overall decrease from 86% to 60.9% (from 72.5% to 20% in urban and from 98.1% to 72.2% in rural area). This change in treatment gap status was achieved through >10 years of intensive and sustained epilepsy awareness campaign, countrywide whilst all other variables remained constant.

**Acknowledgement:** This study was planned and executed by Neurology Research and Patient Welfare Fund (NGO) with financial support from two donors who have no association, direct or indirect, with health care or pharmaceutical industry; hence no conflict of interest.

## P157

### MALNUTRITION IN YOUNG ADULTS WITH EPILEPSY AND NEURODISABILITIES

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**Purpose:** Nutritional deficiencies are common in people with epilepsy and other chronic neurologic conditions.

1. To explore the causes of nutritional problems in young adults prescribed nutritional supplements at a specialist centre.
2. To determine the effectiveness of supplements.
3. To investigate the extent of Vitamin D deficiency in this population.

**Method:** Retrospective review of case notes over a 3 year period at Young Epilepsy, a specialist residential unit in U.K. for young people with complex epilepsy and neurodisabilities. BMI was used as a marker of nutritional status to assess progress. Vitamin D levels were compared in the two groups: those with epilepsy versus those without epilepsy.

**Results:** Twenty young adults were started on nutritional supplements due to clinical indications. All had intellectual disabilities, 17 had epilepsy and 9 each had autism and behavioural problems. The cause for malnutrition was identified in 11 (55%). In four it was attributed to their eating habits, 3 had swallowing problems and in 2 each it was due to seizures or behavioural issues. 10 /20 (50%) was on anticonvulsant drugs (Topiramate and Levetiracetam), which might have contributed to weight loss.

There was significant improvement in their nutritional status following supplementation, with a mean BMI increase of 6.8% (p = 0.003). Thirty-four subjects with epilepsy and 11 without epilepsy had vitamin D results available. 33/34 (97%) of those with epilepsy versus 7/11 (63.6%) of those without epilepsy had severe or borderline Vitamin D deficiency.

**Conclusion:** Young adults with epilepsy and neurodisabilities are at high risk of nutritional deficiencies. The causes of malnutrition can be multifactorial in this population. Anticonvulsants are an important contributing factor. Supplementation significantly improved their nutritional status. Vitamin D deficiency is higher in those with epilepsy. Vulnerable subjects should be screened for Vit D deficiency and early supplementation should be considered.

## P158

### EVIDENCE-BASED RECOMMENDATIONS FOR THE ASSESSMENT FOR EPILEPSY SURGERY IN A DEVELOPING COUNTRY

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**Purpose:** This reliance on well-trained epileptologists and epilepsy neurosurgeons for the liable development of Epilepsy Surgery Program (EPC). And one essential question it is recognized the different candidates of surgical treatment.

**Method:** Our experience in training within the context of our own reality either exclusively or as a complement of training obtained in more developed centers. A possible scenario it is when the epileptogenic zone can be unquestionably localized, it will all depend on the ability of epileptologists and neuropsychologists using locally available technology. An other scenario exist when the available data is not enough, and further

refinement in localization would depend on additional complexity human and technology resources.

**Results:** In our experience, most of the patients reported were evaluated with the technology available in the 1990s, epilepsy monitoring unit, MRI imaging, operating theaters, and intensive care unit, may be thought of as the minimum requirement and is available at most incipient centers of the Third World. In the last time we introduced some news technologies, but it is indispensable in selected patients. One of most critical problem with adult patients, is the average duration of epilepsy before referral to surgery. It was over to 19 years, furthermore, almost 50% of patients were self-referred, and half of this group had been advised by their primary neurologist not to consider surgery.

**Conclusion:** These patients need to be identified early in life before the psychosocial consequences of prolonged disability prevent useful rehabilitation, even if the patient eventually undergoes epilepsy surgery and becomes seizure free.

The results obtained in our experience, not significantly dissimilar from results obtained of centers most experience in developed countries.

### P159

#### A VALIDATION OF A PAEDIATRIC GUIDELINE ON BASIC ELECTROENCEPHALOGRAM INTERPRETATION FOR CLINICIANS: A PILOT STUDY

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**Purpose:** To validate a paediatric guideline on basic electroencephalogram interpretation for clinicians.

**Method:** A prospective study was performed. Thirteen clinicians were recruited to report on twenty electroencephalograms (10 selected and 10 prospective). On completion of the pre-test electroencephalograms each participant was provided with a handbook on basic electroencephalogram interpretation. After 1 month participants were given another twenty electroencephalograms (10 selected and 10 prospective) to report. During the post-test, they completed in a survey of their opinions on the usefulness of the handbook.

**Results:** Eleven of the thirteen invited participants completed the study. Two failed to complete due to a busy schedule and delayed postage of the handbook. The pre-test results showed a median percentage of 50 with a minimum to maximum range of 0 (outlier) to 90%. The post-test results showed the median increase to 70% with the minimum percentage increasing from 0% to 45%. The p value of <0.06 supported a strong trend between the medians post-test compared to pre-test. Two participants declined in the post-test analyses. Comparison between the trained and not-trained shows the trained yielded a significant better outcome on all variables tested on EEG reporting and analysis of the survey.

**Conclusion:** There is statistical evidence on the trained post-test that supports the success of the handbook as a basic guideline to paediatric electroencephalogram interpretation.

### P160

#### FELT STIGMA AMONG MOTHERS OF CHILDREN WITH EPILEPSY

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**Purpose:** In resource limited settings, early child development and well-being is largely determined by the mother's resources and resilience. Little is known about the impact of epilepsy-associated stigma on the mothers of children with epilepsy (CWE).

**Method:** We surveyed 100 mothers of CWE receiving non-emergent epilepsy care at three Lusaka-based health centers. The survey assessed maternal knowledge, attitudes, and practices related to epilepsy; maternal felt stigma; mother's assessment of the child's stigma; and maternal anxiety/depression. Questions regarding child development, epilepsy characteristics, and family demographics were included. Approval was obtained from MSU Institutional Review Board and UNZA Research Ethics Committee.

**Results:** For CWE (mean 3.2 years; SD 1.9), seizure frequency and severity were high with 59% having  $\geq 1$  seizure/month and 76% with neurologic disability. Maternal education was relatively high (mean 9.7 years, SD 2.3), yet knowledge of epilepsy was limited (mean 3.6; SD 0.8; 7 max) with contagion fears and witchcraft beliefs common. 24% of mothers reported feeling stigmatized (mean 0.86; SD 1.1). Maternal stigma and child's proxy stigma were highly correlated ( $p < 0.00001$ ). Anxiety and depression symptoms were common among the mothers and were associated with greater stigma ( $p = 0.009$ ).

**Conclusion:** Mothers of CWE are at risk of felt stigma as well as anxiety disorders and depression. Educational efforts and screening evaluations are warranted. Improving mothers' well-being may also positively impact CWE.

### P161

#### DETERMINANTS OF TREATMENT GAP IN CHILDREN AND ADOLESCENTS WITH EPILEPSY IN A RURAL NIGERIAN COMMUNITY

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**Purpose:** Epilepsy management is hampered by the difference between those with the active disorder and those receiving appropriate treatment (treatment gap) in sub-Saharan Africa. The purpose of the study was to identify the determinants of treatment gap in children and adolescents (Subjects) with epilepsy in a rural Nigerian community.

**Method:** Subjects with epilepsy were identified through the assistance of village heads. Information obtained from Subjects and their care givers included: socio-demographic characteristics, type and frequency of epileptic seizures, current and past treatment options utilized, reasons for treatment option use, and treatment options utilized for other health complaints.

**Results:** A total of 23 Subjects (3.5 per 1,000 of community population) were identified as having epilepsy. Their age range was 4–19 years (mean  $14.3 \pm 4.7$ ). Most were males (19, 82.6%) and adolescents (18, 78.3%). Seizures were mainly generalized (22, 95.7%) and most Subjects (11, 47.8%) had a daily occurrence. Current treatment modalities were, use of traditional medication (23, 100%) and prayers (8, 34.8%). None was currently on orthodox medical therapy (Treatment gap 23, 100%). Only 5 (21.7%) had utilized orthodox medical therapy in the past. Reasons for utilizing the treatment options were cultural belief (23, 100%) and related to cost of accessing (20, 87%), failure of (5, 21.7%) and lack of knowledge about (4, 17.4%), orthodox medical therapy. Fever was the common-

est other health complaint and use of orthodox medical therapy was significantly ( $p < 0.05$ ) the main (16, 69.6%) treatment option utilized.

**Conclusion:** Cultural belief and financial constraints were the major determinants of epilepsy treatment gap. There is need to strengthen initiatives that enhance accessibility to standard epilepsy treatment.

## P162

### IMPACT OF EPILEPSY ON THE BIOPSYCHOSOCIAL STATUS OF ADOLESCENTS IN A RURAL NIGERIAN COMMUNITY: A CASE-CONTROL STUDY

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**Purpose:** Epilepsy is associated with impaired physical, psychological and social functioning. The purpose of the study was to assess the influence of epilepsy on the physical, psychological and social status of adolescents in a rural Nigerian community.

**Method:** Adolescents (Subjects) aged 11–19 years with epilepsy were identified through the assistance of village heads. Controls matched for age and sex were randomly selected from the community. Information obtained from the Subjects, controls and their care givers included: Socio-demographic characteristics, clinical features of epilepsy and its current treatment modality, school attendance and performance. The 2006 World Health Organization growth charts and MINI International Neuropsychiatric Interview modules were used in assessing growth and psychological parameters respectively.

**Results:** A total of 18 Subjects were identified with epilepsy (2.7 per 1,000 of community population). The mean age was  $16.7 \pm 2.6$  years and  $16.3 \pm 2.6$  years for the Subjects and controls respectively. Most were males (15, 83.3%) and all the females were married. All the Subjects had generalized epilepsy and were on traditional medication. None was currently on orthodox medical therapy though 3 (16.7%) had received such therapy in the past. There was no significant difference in the weight and height of the Subjects and controls ( $p < 0.05$ ). Epilepsy was significantly associated with school absence, poor school performance and rejection, family dysfunction, suicidality, stigmatization and discrimination ( $p < 0.05$ ).

**Conclusion:** Epilepsy had a negative impact on the psychosocial status of adolescents. The study highlights the need to provide comprehensive health and social services in epilepsy management.

## P163

### INTER-ICTAL MORBIDITIES IN ADULT EPILEPTIC PATIENTS ATTENDING THE LAGOS UNIVERSITY TEACHING HOSPITAL NEUROLOGY CLINIC

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**Purpose:** To identify inter-ictal morbidities in adult epileptic patients at the Lagos University Teaching Hospital Clinic and to determine their relationship to seizure aetiology.

**Method:** Patients with epileptic seizures attending the neurology Medical outpatient clinic of the Lagos University Teaching Hospital

were evaluated for inter-ictal morbidities using a standard pro-forma. The morbidities assessed are headaches, cognitive impairment (mental retardation and self-reported memory impairment), focal neurological deficits and behavioural abnormalities. Using the 2010 ILAE classification, aetiology of epilepsies was classified into genetic, structural/metabolic or unknown based on the presence of risk factors.<sup>1</sup>

**Results:** Out of the 104 patients assessed, 39 (37.7%) had inter-ictal morbidities: headaches 16 (15.38%), memory impairment 15 (14.42%), mental retardation 9 (8.65%), focal neurological deficits 8 (7.69%), behavioural problems 1 (0.96%). 65 (70.3%) had no inter-ictal morbidities.

Based on aetiology 61 (58.65%) had seizures of unknown aetiology, 38 (36.54%) had symptomatic epilepsy while 5 (4.8%) was possibly genetic due to a positive family history of epilepsy.

Of the structural/metabolic aetiology 16 (42.1%) had inter-ictal morbidities while 21 (34.42%) of patients with unknown aetiology had ( $p = 0.60$ ).

**Conclusion:** Although inter-ictal morbidities are common in patients with epilepsy, majority of the patients were normal in between seizures. Inter-ictal morbidities tended to be more common (though not significant) in patients with clearly symptomatic epilepsy. Patients with epilepsy should be evaluated for treatable interictal morbidities on routine follow up.

## P164

### TIME TO SPECIALIST EPILEPSY EVALUATION AND ITS RELATION TO SEIZURE CONTROL

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**Purpose:** The initial evaluation of a patient with seizures, which includes history, physical examination, EEG and neuroimaging, intends to diagnose an epilepsy syndrome and advise regarding need and choice of treatment. The ILAE-PECA program aims promote education and sustainable care for individuals with epilepsy. We compared patients in two disparate epilepsy clinics regarding time lag from the first unprovoked seizure to the completion of a basic epilepsy evaluation.

**Method:** We reviewed the medical records of patients seen on two adult epilepsy centers, in USA (center A) and in Brazil (center B), on 2 consecutive days. We identified individuals who had diagnosis of epilepsy and a minimum of two follow up visits. The reviewers collected demographic and clinical data, including seizure type, epilepsy etiology, seizure frequency, date of last seizure, age at first unprovoked seizure, date of first evaluation for seizure and date of EEG and MRI. The first 30 patients that met these criteria were included, fifteen in each center.

**Results:** The average time from first seizure to first specialist consultation were: Center B: 8 years, Center A: 0.5 years ( $t_{14}: 2.59, p = 0.02$ ). In Center B, 53% patients had their first EEG done within 1 year vs. 93% of Center A. MRI was performed in 66% in Center B and 33% had MRI in the first year of presentation. In Center A, 93% had MRI, 80% in the first year. Average number of seizures during the last 6 months: Center B: 16.2, Center A: 2.8 ( $t_{14}: 1.8, p = 0.08$ ). Drug resistant epilepsy: 46% in Center B and 6% in Center A.

**Conclusion:** Delayed specialist evaluation for epilepsy is a shared problem between both centers, however, if prolonged may contribute to low rates of seizure control. Early referral and increased access for all individuals with epilepsy is necessary to reduce the morbidity associated with DRE.

## P165

### ADHERENCE TO EPILEPSY QUALITY INDICATORS IN SPECIALIZED EPILEPSY CARE CENTERS: A COMPARISON BETWEEN DISPARATE HEALTH CARE SYSTEMS

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**Purpose:** There is substantial pressure to decrease the cost of health-care while improving quality. Specific quality measures are central to these efforts. For that reason, the Academy of Neurology (AAN)/American Epilepsy Society (AES) developed the Epilepsy Quality Measures (EQM). In order to begin to understand if the EQM are of generalized value, we applied them retrospectively to the care of patients at epilepsy centers in Rio de Janeiro, Brazil and Boston, Massachusetts.

**Method:** We reviewed 350 consecutive medical records starting on or after October, 2008 in adult epilepsy outpatient clinics at the Massachusetts General Hospital (center 1) and Hospital Universitario Pedro Ernesto (center 2). Seventy-six patients (Center 1:35, Center 2:41) who had an initial evaluation for epilepsy after that date and who had at least two follow-up visits were identified. A 15-item data extraction form was used to collect demographic data and documentation of EQM.

**Results:** At center 1, seizure type and epilepsy syndrome were documented in 100% of the records. Seizure frequency was documented in 94.2% and AED side effects in 94.2%. EEG was requested or reviewed in 97.1% and MRI was always reviewed/requested. Evidence that clinicians considered surgical approach was present in 50% of the 10 drug resistant cases. At center 2 there was documentation of seizure type in 78%, seizure frequency in 48.7%, epilepsy syndrome in 9.7% and AED side effects in 21.9%. Both EEG and MRI were requested/reviewed in 70% of the cases. Neither center effectively documented epilepsy safety or pregnancy counseling.

**Conclusion:** There may be many reasons for the differences between the centers. For example, center 1 uses an electronic medical record, has higher volume and offers more teaching conferences. Future research is warranted to understand these differences and whether these disparities truly reflect a difference in quality or potential flaws in the EQM.

## P166

### THE QUALITY OF LIFE OF PEOPLE WITH EPILEPSY TREATED WITH ESTABLISHED, NEWER OR A COMBINATION OF ANTI-EPILEPTIC DRUGS IN THE STATE OF QATAR

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**Purpose:** The aim was to study and compare the quality of life (QOL) in patients with epilepsy (PWE) treated with established (EAED), newer (NAED) or a combination thereof (CAED) in a developing Gulf state of a growing economy.

**Methods:** The study was carried on a prospective cohort of PWE attending the neurology clinic in Hamad General Hospital in Doha, Qatar between 15 October 2009 and 15 April 2011. Phenytoin, carbamazepine, sodium valproate, phenobarbitone, clobazam and clonazepam were the EAEDs and lamotrigine, topiramate and levetiracetam were the NAEDs drugs available for prescription in our hospital.

Epilepsy patients aged 13 year or more and on AED treatment for at least 6 months were provided with a self-completing 32-item questionnaire with graded scales and check-lists. Information collected from the questionnaire and the hospital clinical records was used to explore demographic characteristics, medication, seizure control, adverse effects of AED, physical harm, social and psychological impact of disease and stigmatization.

**Results:** Fifty-three males and 47 females completed the questionnaire. Their ages ranged between 13 and 65 years. 65% of the participants were below 35 years. Thirty-seven patients were on EAED, 33 on NAED and 30 on CAED. Patients on EAEDs were found to have better control of seizures but felt more drug side effects. Better psychological wellbeing, least stigmatization and fewer drug side effects were observed with NAEDs. More seizure, stigmatization and birth abnormalities occurred in patients treated with CAEDs. Good control of seizures was the main determinant of a favorable perception of QOL.

**Conclusion:** In our PWE NAED treatment was associated with less drug side effects and better psychological wellbeing. However, good seizure control was more important than the type of AED used in rendering improvement in QOL.

## P167

### IS NURSE-LED EPILEPSY FOLLOW UP CLINIC A FEASIBLE OPTION FOR INDIA?

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**Purpose:** To evaluate the feasibility of a nurse-led follow up clinic for epilepsy patients in India.

**Method:** Epilepsy patients following-up at AIIMS for  $\geq 6$  months were enrolled. A postgraduate neuroscience nursing student was trained by giving her 8 h of epilepsy lectures, an opportunity to observe 20 patients' follow-ups with a consultant and independently follow-up and then discuss with consultant 40 patients before start of study. For the nurse follow-up, a structured questionnaire was developed, validated and pilot-run. It was decided that feasibility of nurse-led clinic would be inferred if inter-rater agreement (kappa) between nurse and consultant was  $\geq 80\%$ . This agreement was specifically sought on five items: seizure/syndrome type, degree of seizure control, need for further investigations including pre-surgical evaluation, need to modify AED and recognition of AED side effects.

**Results:** One hundred and seventy-five patients (104 male), aged  $24.67 \pm 10.73$  years of which 65.1% came from rural communities were followed-up over a 6 month study period. The duration of epilepsy was  $<5$ , 5–10 and  $>10$  years in 26.9%, 36% and 37.1% patients respectively. An epilepsy risk factor or cause could be identified in 65.13% patients while 34.87 were labeled as idiopathic. Inter-rater agreement, measured as kappa, between the consultant and nurse was as follows: type of seizure/syndrome 86.34%, degree of seizure control 86.34%, need for further investigation 86.3%, need to modify AED 75.99% and recognition of side effects 94.3% ( $p < 0.0001$ ).

**Conclusion:** The study concluded that nurse-led follow up clinic could be a feasible option for epilepsy patients in India.

## P168

### KNOWLEDGE, ATTITUDES AND PERCEPTIONS OF EPILEPSY AMONG SECONDARY SCHOOL-TEACHERS IN NIGERIA: A COMMUNITY – BASED STUDY

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**Purpose:** The attitudes towards people with epilepsy are influenced by the degree of knowledge of the condition. The social problems encountered by schoolchildren with epilepsy as a result of negative attitude and beliefs are quite enormous. The study therefore looked at the knowledge, attitudes and perceptions of teachers, who see a lot of epileptics, relate to them on a daily basis and have influence on them.

**Method:** A cross-sectional survey, using a self-administered questionnaire obtained from the author of a similar study in the United States was carried out among 269 school teachers randomly selected from various secondary schools in Osogbo, the Osun State capital in South-West Nigeria. The questionnaire included the scale of attitudes towards persons with epilepsy and knowledge about epilepsy as well as demographic and teaching experience survey among others.

**Results:** Despite the high level of education of the teachers ranging from Masters Degree to National Certificate in Education, there were significant deficits in terms of general knowledge about epilepsy (70% of the respondents reported their general knowledge about epilepsy in the lower half of the scale). There was also poor knowledge of the first aids measures in the class-rooms. Below one-third (29.2%) felt it was contagious and 40% of respondents reported that sufferers should not be kept in regular classes. However, their attitudes towards epilepsy were generally positive.

**Conclusion:** We concluded that teachers need to have health education courses on common disease conditions such as epilepsy that are prevalent in school age; this might help to reduce the prejudice and increase the acceptance of epileptic individuals in the class-rooms. Also, generally public health campaigns should be encouraged in this field.

**Keywords:** Epilepsy, knowledge, attitudes and school teachers.

## P169

### EPILEPSY MONITORING UNIT IN GUATEMALA “OUR” EXPERIENCE

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Long Term Monitoring depends upon the purpose for which should be use (D.Velis et al 2007). There is no specific time for recording; even the shortest average time reported was 4.8 days in patients with Mesio Temporal Lobe epilepsy (MTLE)(Engel et al 1993; Fernandez Torre et al 1999). In developing countries this time increase the cost and makes difficult to pay it; we describe our work with less time of monitoring due to financial issues.

**Methods:** All the patients came from the national health system with the diagnosis of drug resistant epilepsy; we perform video eeg, 1–3 h, 4–8 h for all the patients and define long term monitoring like the monitoring more than 24 h (all the patients had TLE). For the patients under long term monitoring we reduce their medication 48 h before the start the medication. We collect 239 patients in 2012, 114 male and 125 female, the median age was 27.5 years, and range 1 month to 91 years old. We record at least one seizure in 35% of all the patients (n = 239), 33% in less of 3 h (n = 144) and 38% in 4–8 h of monitoring (n = 66), but in long term monitoring increase the sensitivity to 82% (n = 29). From those 29 patients, 14 were under surgery and remained seizure free 12 of them.

**Discussion:** Although we believe this time it's not the perfect time, it's an option for patients with TLE and lesional evidence in MRI for patients in developing countries

## P170

### AVAILABILITY OF THE NEWER GENERATION OF ANTI-EPILEPTIC DRUGS IN TWO TERTIARY REFERRAL EPILEPSY CENTERS

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**Purpose:** Despite choice of AED, the likelihood of achieving seizure freedom after the second or subsequent trial is low. Newer generation AEDs have found their place in the market because of lower side effect profiles. Economic disparity continues to dictate the availability of medications with a lower side effect profile. This study aims to compare the anti-epileptic drug therapeutic repertoire and AED side effect rates in drug resistant epilepsy (DRE) between two participating PECA centers.

**Method:** Retrospective cohort composed by 37 consecutive patients with DRE, currently treated at either Massachusetts General Hospital (Center A: 13) or Hospital Universitario Pedro Ernesto (Center B: 24); and a minimum of three visits over the last 5 years. Chart review included demographic data, epilepsy measures, AED history and side effects (SE).

**Results:** Both groups were comparable with regard to demographic, etiologic diagnosis and types of seizure. There was a significant difference in the number (center A mean four drugs, SD: 1.9 and center B mean two drugs, SD: 0.67;  $t_{13} = 3.8$ ,  $p = 0.001$ ) and type of AED prescribed between centers. Top 3 most frequently prescribed AEDs were; center A: levetiracetam, lamotrigine, carbamazepine; center B: carbamazepine, phenobarbital and phenytoin. Clonazepam was included in 66% of cases taking >2 drugs. Clobazam use exclusive to center B, whereas levetiracetam, lacosamide and zonisamide were only used in center A. Side effect rates were similar between our two centers (Center A: 53%, Center B: 50%), new generation AEDs were associated with less severe SE.

**Conclusion:** In DRE, number of available drugs, regardless its generation does not change likelihood of achieving seizure freedom. Side effect rates were similar between both newer and older agents used in our clinics; however less severe side effects were seen with newer generations AEDs.

## P171

### LIVING WITH EPILEPSY IN LUBUMBASHI (SOUTHERN DEMOCRATIC REPUBLIC OF CONGO): RESULTS OF A PATIENT SURVEY

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**Purpose:** To document the prevalence of epilepsy, as well diagnostic opportunities and access to antiepileptic treatment among patients with epilepsy in Lubumbashi, the Democratic Republic of Congo.

**Method:** A survey was conducted over a 12-month period (May 2010–April 2011) at a neuropsychiatry clinic in Lubumbashi. Data on demographics, education level, social status, characteristics of seizures, time to diagnosis, previous and current treatment were collected by physicians or nursing staff using a 64-item questionnaire.

**Results:** Of 3,540 patients presenting at the clinic with different neuropsychiatric conditions, 423 (11.9%) were diagnosed as having epilepsy. A total of 179 patients (aged ≥6 years) who provided informed consent

and completed a confirmatory EEG investigation were eligible to participate in the survey. Mean age was 21.5 years (range 6–106 years), 56.4% were male, 40.8% had no education or had completed primary education only, 38.0% were unemployed. Only 12.5% provided a good description of their condition, while 25.1% could not; 55.3% considered their condition to be of spiritual/religious origin and 6.7% confounded malaria with epilepsy. In terms of treatment, 33.0% were receiving antiepileptic drugs at initial visit (independent of adequate dosing and regimen), 30.2% had none, 36.8% had other treatment, including traditional (e.g., herbal remedies, prayers, rites). The mean interval between seeing traditional healers and the first consultation at the clinic was 15 months.

**Conclusion:** This descriptive epidemiological study shows a high prevalence of epilepsy among patients attending the centre in Lubumbashi, limited use of EEG for diagnostic purposes and a high proportion of untreated patients.

#### P172

### DIFFICULT-TO-TACKLE EXTRA-TEMPORAL EPILEPSY SURGERIES: IS IT WORTH PURSUING IN A RECENTLY ESTABLISHED COMPREHENSIVE EPILEPSY CARE PROGRAM?

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**Purpose:** To analyze the electrophysiologic and radiological features of difficult-to-tackle drug-resistant extratemporal epilepsies and their seizure outcome in a recently established Epilepsy Program in South India.

**Method:** Twenty-two consecutive patients with drug-resistant extratemporal epilepsy and were not straightforward to tackle through focal resections, underwent extensive evaluation through our surgical program between 2010 and 2012 were analyzed. Extratemporal epilepsies with a clear focal lesion and all electro-clinical data favorable for surgery were included. The postoperative follow-up ranged from 6 months–2 years. All patients underwent extensive pre-surgical workup with prolonged video-EEG; high resolution MRI, detailed neuropsychology, PET, SPECT, functional MRI, diffusion tensor imaging and/or WADA (if indicated). Postoperative seizure outcome was assessed using Engel's classification.

**Results:** The age at surgery ranged from 2 to 27 years ( $13.3 \pm 8.2$ ). Following investigations were performed: PET (n = 11), SPECT (n = 2), fMRI (n = 8) and WADA (n = 1) since the first-tier investigations failed to proceed with surgery. Four patients underwent invasive monitoring and cortical stimulation. The surgeries performed were lesionectomy in 8 (6 adjoining eloquent cortex and one with dual pathology underwent inferior frontal resection with anterior temporal lobectomy), quadrantotomy (posterior quadrantotomy-5, frontal disconnection-2), functional hemispherotomy in 1, hypothalamic hamartoma resection in 1, and callosotomy in 5 (one with refractory primary generalized epilepsy, four with Lennox Gastaut syndrome). Intraoperative corticography, stimulation and neuronavigation were used in five patients. Histopathology included gliosis, dysplasia, dysembryoplastic neuroepithelial tumor, porencephalic cyst, hypothalamic hamartoma, meningio-angiomas and polymicrogyria. During a median follow-up of 11 months, 13 patients had class I outcome and 4 had class II outcome. None of the patients after callosotomy had drop attacks. Transient hemiparesis occurred in two patients recovered completely at third month follow-up.

**Conclusion:** Good seizure outcome can be achieved in difficult-to-tackle extra-temporal epilepsy surgeries within the first 2 years of its inception in any centre with a dedicated team work approaching each case individually and utilizing modern investigations pragmatically.

#### P173

### EPILEPSY DISEASE, DISABILITIES IN POOR RESOURCE COUNTRIES: STIGMA AND DILEMMAS

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**Purpose:** Children with disabilities arising from Epileptic diseases have repeatedly highlighted their feelings of discrimination, stigma and exclusion in many domains of their lives. There is little research from Africa Countries addressing these issues. This study investigated the challenges encountered by these Children and the mechanisms of coping with these challenges while caring for them in a poor rural settings in Kenya.

**Background:** Thirty-five in-depth interviews were conducted on children with disabilities.

**Methods:** Ten unstructured observations were also conducted in home environments to observe mechanisms used in meeting the needs of the children with disabilities as a result of epilepsy. All interviews were tape-recorded, transcribed and translated from the local dialect. Note-taking was performed during all the observations. Data were stored in NVivo software for easy retrieval and management.

**Results:** The arrival of an epileptic disabled child severely impairs the expectations of parents. Hospital staff underestimate parent and guardian emotional distress and need for information. Fear for the future, stress, rumour-mongering and poverty are encountered by parents. As they grapple with lost expectations, they develop positive adaptations in the form of learning new skills, looking for external support and in some cases searching for cure for the problem. For their emotional stability, parents and guardians apply spiritual interventions and sharing of experiences.

**Conclusion:** Despite the challenges faced by the parent, values and priorities in adaptation to the challenges caused by the child's disability were applied. It is recommended that these experiences are considered as they may influence programmes that address the needs of children with disabilities.

#### P174

### STIGMA IN EPILEPSY: DEVELOPMENT AND VALIDATION OF A CULTURALLY RELEVANT INSTRUMENT IN INDIA

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**Purpose:** Epilepsy is a highly stigmatized condition world over. However, stigma is influenced by cultural factors and culturally sensitive tools are required. We adapted a published measure of stigma for the Indian setting using triangulation procedures and studied its psychometric properties.

**Method:** Qualitative procedures including Literature review, Focus Group Discussions and Semi-structured in-depth interviews with patients were carried out to identify the domains relevant to southern India. The resulting scale was translated from English to the local vernacular- Tamil and back-translated to ensure content validity and consisted of questions organized in five major domains- Work, Education, Family, Marriage and Social Interactions. The instrument was then administered to 105 patients with epilepsy attending the outpatient service together with the Hospital Anxiety and Depression Scale (HADS).

**Results:** The data was analyzed using SPSS, bivariate correlation analyses were performed with calculation of Cronbach's alpha and Pearson's correlation coefficients. The domains Work and Education displayed an 'Excellent' internal consistency ( $\alpha = 0.939, 0.953$ ), which reduced to 'Good' for Social Interactions ( $\alpha = 0.842$ ) and 'Questionable' for Family



and Marriage ( $\alpha = 0.683, 0.674$ ). The overall internal consistency of the new instrument was 0.561. Meanwhile, three domains (Family, Marriage and Social Interactions) showed significant Pearson's correlation (94–100%) to the HADS.

**Conclusion:** A new tool to measure Stigma in Epilepsy has been designed to suit the conditions of the Indian sub-continent. Sensitive areas like Family and Marriage have been identified as potential areas where stigma in epilepsy is felt or enacted. The results from this pilot study can be used to modify the sub-domains of the scale to increase the internal consistency and reliability.

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### LONG TERM OUTCOME OF PHENOBARBITAL TREATMENT FOR EPILEPSY IN RURAL CHINA: A PROSPECTIVE COHORT STUDY

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**Purpose:** To evaluate the long-term outcome of phenobarbital treatment for convulsive epilepsy in rural China, and to explore factors associated with overall seizure outcomes.

**Method:** We carried out follow-up assessments of people who took part in an epilepsy community management programme conducted in rural counties of six provinces in China. People with convulsive epilepsy who were previously untreated (or on irregular treatment) were commenced on regular treatment with phenobarbital. Information was collected using a standardised questionnaire by face-to-face interviews of the individuals. Information collected included treatment status, medication change, seizure frequency, and mortality.

**Results:** Among the 2,455 people who participated in the original programme, outcomes were successfully ascertained during the follow-up assessment in 1,986, of whom 206 had died. Information on treatment response was obtained in 1780 (56% male; mean age 33.9 years, range 3–84; mean duration of follow-up 6.4 years). Among them, 939 (53%) were still taking phenobarbital. The most common reasons for stopping phenobarbital were seizure freedom or substantial seizure reduction, socio-economic reasons, and personal preference. 453 (25%) individuals became seizure-free for at least 1 year while taking phenobarbital, 88% of whom did so at daily doses of 120 mg or below. 406 (23%) reported adverse events, which led to withdrawal of phenobarbital in <1%. The most common adverse effects were malaise/somnolence (7.4%), dizziness (3%) and lethargy (2.6%). At the follow-up assessment, 688 (39%) individuals had been seizure free for at least the previous year. People with persistent seizures had significantly longer duration of epilepsy and higher number of seizures in the 12 months before treatment.

**Conclusion:** We observed long-term benefits of regular treatment with phenobarbital for convulsive epilepsy in rural China. One hundred years after the discovery of its antiepileptic effect, phenobarbital is still playing an important role in the management of epilepsy.

P176

### SERUM TRACE ELEMENT LEVELS IN CHILDREN RECEIVING ANTIEPILEPTIC DRUG THERAPY: A CROSS-SECTIONAL STUDY

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**Purpose:** Few studies have evaluated the effects of antiepileptic drug (AED) therapy on trace element status in children and their results have been conflicting. The newer AEDs are considered to have a more acceptable safety profile, but this confidence is somewhat guarded in the absence of long-term data. This cross-sectional study was conducted to analyze the serum trace elements levels in epileptic children treated with conventional and newer AEDs and compare them with healthy controls.

**Methods:** The study included 92 epileptic children and 28 healthy controls. The participant distribution was as follows, Group I: Phenytoin (PHT) monotherapy (n = 35), Group II: Valproate (VPA) monotherapy (n = 30), Group III: Valproate plus Levetiracetam (VPA+LEV) (n = 27), Group IV: Healthy controls (n = 28). Serum levels of seven trace elements i.e. zinc, copper, magnesium, manganese, iron, selenium and strontium were determined using inductively coupled plasma-atomic emission spectrometry (ICP-AES).

**Results:** Phenytoin monotherapy was associated with increased copper (1568.8 µg/L vs. 1053.6 µg/L, p = 0.009) and strontium (37.0 µg/L vs. 30.7 µg/L, p < 0.001) concentrations & decreased manganese levels (1.5 µg/L vs. 1.9 µg/L, p = 0.04). Valproate monotherapy treated children had decreased serum zinc (1010.5 µg/L vs. 1242.9 µg/L, p = 0.01) and selenium levels (67.0 µg/L vs. 84.7 µg/L, p = 0.02) as compared to healthy controls. However, in VPA+LEV group no significant differences were observed in trace element profile as compared to healthy children.

**Conclusions:** A significant difference in trace element levels in VPA and PHT treated epileptic children as compared to controls suggests a possible association between AED therapy and trace element alterations. However, levetiracetam when used in combination with valproate was not associated with these alterations. These findings further support its favorable adverse effect profile as compared to conventional AEDs.

P177

### REPAIRED ABNORMAL PERFUSION FOCI IN CHILDREN WITH EPILEPSY THROUGH TRADITIONAL CHINESE MEDICINE COMPOUND DANSHEN DRIPPING PILLS ASSISTED WITH VALPROIC ACID (110 CASE): TO EVALUATE IN A NEW TREATMENT THROUGH INTERICTAL SPECT AND LONG-TERM V-EEG AND IMAGING

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**Purpose:** To investigate the new treatment of traditional Chinese medicine Compound Danshen Dripping Pills combined with Magnesium valproate sustained-release tablets (VPA) to repair the abnormal perfusion foci in childhood epilepsy.

**Method:** The 110 cases were classified according to the International Epileptic (2001). Compound Danshen dripping pills was used to repair abnormal perfusion foci in children with epilepsy after seizure was controlled by Magnesium valproate sustained-release tablets.

The interictal SPECT and long-term V-EEG and CT/MRI and TDM were performed before and after treatment.

**Results:** Male 79 cases and woman 31 cases. Age in 3–12 (average 7.85 years) and course average 4.6 years and the etiology 53.6%. Seizure type and syndrome in Generalized epilepsy 62 cases (GTCS 50 cases) and Focal seizures 48 cases and idiopathic epilepsy 42 cases and symptomatic epilepsy 54 cases and cryptogenic epilepsy 14 cases. CT/MRI abnormal 15.5%; Whole cases seizure of control average 30.2 month and VPA concentration in  $59.51 \pm 17.96 \mu\text{g}$ . SPECT abnormal in 77.3% and abnormal perfusion foci of 129 and Thirty-nine cases (35.5%) out of the abnormal perfusion foci showed changes after treatment, SPECT return to normal increase by 46 cases (41.8%,  $p = 0.00$ ) and abnormal perfusion foci to decrease 73 (56.6%) and temporal lobe abnormal repair rate in 62.3% and frontal lobe abnormal repair rate in 60.0%. The repair rate of abnormal perfusion foci in control group increase by 6.9%. Course and repair rate to <3 years 32.8%; (19/58) and  $\geq 3$  years 51.9% (27/52) and two groups of repair rate comparison ( $p < 0.05$ ). The long-term V-EEG abnormal 96.4% and after treatment V-EEG return to normal increase by 54.5% ( $p = 0.00$ ) and epileptic discharges before and after treatment 92.5% and decrease 52.7%.

**Conclusion:** The traditional Chinese medicine Compound Danshen dripping Pills and VPA had multiple mechanism to control seizures, increased the normal rate of abnormal perfusion foci in childhood epilepsy after repair was the ideal new treatment method and therapeutic areas in children with epilepsy.

#### P178 PHARMACOKINETICS, PHARMACODYNAMICS, AND SAFETY OF THREE DOSES OF USL261, A MIDAZOLAM FORMULATION OPTIMIZED FOR INTRANASAL ADMINISTRATION

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While not formulated for intranasal delivery, midazolam injection solution is often administered intranasally to treat intermittent bouts of increased seizure activity despite the availability of rectal diazepam gel (Diasat<sup>®</sup>; Valeant Pharmaceuticals). USL261 is a new midazolam formulation optimized for intranasal administration to treat this condition. The pharmacokinetics, pharmacodynamics, and safety/tolerability of three USL261 doses were compared with midazolam injection solution administered intranasally (MDZ-IN) and by intravenous infusion (MDZ-IV).

In this Phase 1, 5-way crossover, open-label study, 25 healthy adults (18–45 years) were randomized to receive 2.5, 5, and 7.5 mg USL261; 2.5 mg MDZ-IV; and 5 mg MDZ-IN in random order. For 12 h post-dose, blood samples were collected to determine pharmacokinetic profiles, and pharmacodynamic assessments of sedation and cognitive impairment were conducted. Safety/tolerability was evaluated by monitoring adverse events, oxygen saturation, and vital signs.

Increasing USL261 doses corresponded with an apparent linear increase in MDZ AUC and  $C_{\text{max}}$  with all doses demonstrating rapid  $T_{\text{max}}$  (10–15 min). Further, USL261 demonstrated increased absorption with a 134% relative bioavailability compared with an equivalent MDZ-IN dose. USL261 was associated with dose-dependent increases in sedation and psychomotor impairment ( $p < 0.05$ ); however, these effects lasted less than 4 h and generally did not differ from MDZ-IN or MDZ-IV at comparable doses. All treatments were well tolerated with no reports of oxygen saturation below 90%.

Compared with MDZ-IN, USL261 demonstrates improved midazolam bioavailability with similar pharmacodynamic effects and safety/tolerability profiles. Therefore, USL261 may provide an alternative to current treatment options for intermittent bouts of increased seizure activity.

Supported by Upsher-Smith Laboratories, Inc.

#### P179

#### USL255, EXTENDED-RELEASE TOPIRAMATE, DEMONSTRATES DOSE-PROPORTIONAL PHARMACOKINETICS AND TOLERABILITY OVER A WIDE DOSING RANGE IN HEALTHY SUBJECTS

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USL255 is a once-daily, extended-release formulation of topiramate intended for the treatment of epilepsy. Compared with immediate-release drugs, optimal extended-release formulations provide more consistent drug release over an extended dosing interval, maintain therapeutic concentrations over longer time periods, and display less inter-subject variability. The objectives of these analyses were to evaluate the pharmacokinetics and safety/tolerability of USL255 at doses from 25 to 1400 mg.

USL255 was evaluated in two single-dose, Phase 1 studies in healthy subjects: 1) an open-label, 5-way crossover study of USL255 25–400 mg in 30 subjects; 2) a randomized, placebo-controlled, double-blind, ascending, maximum tolerated dose study where 40 subjects received 600, 800, 1000, 1200, or 1400 mg of USL255. Post-hoc analyses evaluated dose proportionality and variability of AUC and  $C_{\text{max}}$  across the entire dosing range (25–1400 mg). Investigator-reported adverse event (AE) monitoring, electrocardiograms, and evaluation of clinical laboratory tests and vital sign measurements were obtained throughout the studies to establish USL255 safety/tolerability.

USL255 demonstrated dose proportionality in AUC from 25–1400 mg;  $C_{\text{max}}$  was proportional to dose from 50 to 1400 mg. Across the dosing range, consistent plasma topiramate exposure was observed with low inter-subject variability ( $C_{\text{max}}\%CV = 22\%$  [range: 14.5–33%];  $\text{AUC}\%CV = 20.2\%$  [range: 13.3–28.6%]). Additionally, USL255 was considered safe and well tolerated with dizziness, headache, and paresthesia being the most commonly reported AEs.

USL255 displayed dose-proportional pharmacokinetics with low inter-subject variability, consistent drug levels, and favorable safety and tolerability across a wide range of doses. Therefore, extended-release USL255 may provide a once-daily alternative to twice-daily immediate-release topiramate.

Supported by Upsher-Smith Laboratories, Inc.

#### P180

#### ANTIPSYCHOTICS AND AEDS: THERAPEUTIC DRUG MONITORING IN A MENTAL HEALTH CARE SETTING

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**Purpose:** A combination of valproate with an atypical antipsychotic provides synergistic mood stabilizing, anti-depressant and anti-psychotic action in bipolar and schizoaffective disorders. Reports of rare, but serious, adverse drug reactions occurring on the addition of valproate to olanzapine and quetiapine monotherapy indicate a possible drug-drug interaction (DDI). The aim of this study was thus to compare the plasma concentrations of quetiapine and olanzapine of patients concurrently taking valproate with that of patients on antipsychotic monotherapy.

**Method:** To achieve this aim, an HPLC-UV method for the analysis of quetiapine and olanzapine in human plasma was developed and used with a routine valproate therapeutic drug monitoring service. Bipolar disorder patients being treated with valproate/olanzapine, valproate/quetiapine or valproate/olanzapine/quetiapine monotherapy (controls) were recruited from mental health care setting. Plasma concentrations of the antipsychotics were measured and compared with those of patients not on the combination to assess the possible effect of valproate on quetiapine and olanzapine concentrations.

**Results:** Seventy-seven patients were recruited, 32 were included in the test groups and 45 in the control groups. An HPLC-UV method was successfully validated for the analysis of quetiapine serum concentrations. The comparison of quetiapine plasma concentrations between test and control groups did not reveal statistically significant results due to limitations in the methodology. However, clinical reviews of individual patients revealed low plasma concentrations of quetiapine and valproate in a patient not responding to treatment, while another patient on olanzapine/valproate developed neutropenia possibly due to a DDI.

**Conclusion:** The implementation of a quetiapine and olanzapine TDM service at Mount Carmel Hospital would provide a powerful tool to clinicians, enabling them to routinely monitor plasma concentrations of the antipsychotics.

### P181 ORAL LOADING OF OXCARBAZEPINE SUSPENSION IN EPILEPSY PATIENTS

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**Purpose:** Oral loading of oxcarbazepine tablet is effective and well tolerated to adequately achieve the therapeutic levels of its active metabolite, 10,11-dihydro-10-hydroxy-carbazepine (monohydroxy derivative, MHD) in epilepsy patients. The present study was performed to investigate the safety, tolerability, and pharmacokinetic profiles of oral loading of oxcarbazepine suspension in epilepsy patients with a high risk of recurrent seizures.

**Method:** Oxcarbazepine suspension was administered orally at a single loading dose of 30 mg/kg to 38 adult patients with recurrent seizures, who required rapid seizure control or temporarily discontinued antiepileptic drugs for diagnostic or pre-surgical evaluation. Plasma concentrations of oxcarbazepine and MHD were determined, and adverse events were assessed at 2, 4, 6, 8, 10, 12, 14, 16, and 24 h after oral loading of oxcarbazepine suspension.

**Results:** Thirty patients experienced  $\geq 1$  adverse event during the first 24 h after oral loading of oxcarbazepine (e.g., dizziness, transient diplopia, nausea or vomiting), most of which occurred within 4 h after loading, suggesting no temporal association with MHD plasma levels. Thirty-five (92.1%) patients were still compliant with a maintenance dose of oxcarbazepine after discharge from the hospital. Thirty-four (89.4%) patients reached the lower therapeutic level of MHD (12 mg/L) at 4 h after oral loading of oxcarbazepine suspension, which was lasted up to 24 h in most patients. No patient reached the supratherapeutic levels of MHD ( $>35$  mg/L) throughout the study. The mean plasma concentration-time curves and pharmacokinetic profiles of oral loading of oxcarbazepine suspension were similar to those of oral loading of oxcarbazepine tablet.

**Conclusion:** Oral loading of oxcarbazepine suspension followed by maintenance dosing is well tolerated and effective to steadily achieve the therapeutic level of MHD in selected patients with epilepsy.

### P182 DRUG-RESISTANT EPILEPSY

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**Background:** The persistence of some kind of epileptic seizures, sufficiently frequent and debilitating in a compliant patient for at least 2 years with antiepileptic therapy (combining two anti-epileptic drugs), has not been the subject of study in Guinea – Conakry.

**Methods:** The objective was to present the clinical and paraclinical characteristics of this particular disease. Our study was prospective. It took place from the 1st October 2008 to 30th September 2009, in the Neurology Department of the University Teaching Hospital of Conakry.

**Results:** We observed 36 cases of drug-resistant epilepsy during our study. With a sex ratio of 1.76 of male predominance. The age group most affected was that from zero to 19 years with 72.33% of cases observed. The extremes of age were five and 49 years. The most common etiology was infectious and parasitic diseases, 49.22% of cases. In women, malaria in pregnancy was the most common etiology. Partial seizures, secondarily generalized, were most frequent 38.88% of cases. The most refractory association was Phenobarbital and carbamazepine 30.55%. The limitations of our study were the lack of Magnetic Resonance Imaging, Positron Emission Tomography, Magneto-Electroencephalography and the dosage of carbamazepine.

**Conclusion:** Our results are similar to the studies already made on this subject, which state that 30% of epilepsies are refractory partial epilepsy.

### P183 THE INCIDENCE AND RISK FACTORS OF OXCARBAZEPINE (OXC)-INDUCED SYMPTOMATIC HYPONATREMIA

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**Purpose:** OXC is a new generation of AED and was recently approved for the treatment of seizures of partial onset. OXC-induced hyponatremia is mostly asymptomatic, its prevalence is highly variable and then estimated at 23–73.3%. But there is a limited available data about the incidence and risk factors of clinically more important OXC-induced severe and symptomatic hyponatremia. So, we conducted this study to examine the incidence of severe and symptomatic hyponatremia and to identify risk factors of developing them.

**Method:** We performed a retrospective review of the medical records about the patient's demographic and clinical data. The data was collected during a 10-year period. Inclusion criteria were (1) adult patients with epilepsy aged 18 years or older (2) had a past history of being prescribed OXC (3) whose serum sodium levels had been documented at least once after OXC therapy.

**Results:** Overall, we enrolled a total of 1,009 patients. In our series, 313 (31.0%), 112 (11.1%) and 69 (6.8%) patients were assigned to the hyponatremia group, the severe hyponatremia group and the symptomatic hyponatremia group, respectively. According to statistical analysis, significant severe hyponatremia risk factors were age ( $p = 0.014$ ), OXC combination therapy ( $p = 0.021$ ) and the number of patients who received a concomitant medication of diuretics ( $p > 0.001$ ) and symptomatic hyponatremia risk factors were age ( $p = 0.001$ ) and the number of patients who received a concomitant medication of diuretics ( $p = 0.035$ ). Of the total 313 patients with hyponatremia, 69 (22.0%) had symptomatic one. The distribution of onset of hyponatremic symptoms occurred in 50% of patients within 373 days after initial OXC treatment.

**Conclusion:** Our results indicate that clinicians should perform a serial monitoring of serum sodium levels for at least 1 year in elderly patients who are supposed to take OXC concomitantly with other AEDs or other drugs for medical diseases.

### P184 TOLERANCE OF ANTIEPILEPTIC DRUGS (AED) IN CHILDREN

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**Purpose:** To study frequency and nature of adverse AED reactions in children with epilepsy.

**Method:** There's been conducted analyses of 897 cases of prescribing AED in monotherapy to children at the age of 0–18 year as follows Valproate – 511, CRBM – 156, topiramate – 102, oxcarbazepine – 41, levetiracetam – 39, lamotrigine – 35, succinamide – 13. There were analyzed medical treatment records of patients to be registered in the Office of Epilepsy (Region Clinical Hospital #2, Tyumen, RF)

**Results:** On the whole adverse AED reactions have been revealed in 15% of the cases. At that adverse topiramate reactions revealed in 19% of the patients, lamotrigine – 19%, oxcarbazepine – 17%, Valproate – 16%, CRBM – 12%, succinamide – 8%, levetiracetam – 2.5%. The following adverse reactions appeared to be predominant (per cent of the total number of patients taken the drug of the type): Topiramate – sleepiness (3.9%), weight loss (5.9%), hyporexia, allergic reactions, shaky manner of walking and cognitive disorder (2%); Lamotrigine – dermatic allergic reactions (9%); Oxcarbazepine – sleepiness, headache, dyspepsia, allergic reactions (4.9%), retardation (2.4%); Valproate – dyspepsia (4.3%), weight gain (4.5%), thrombocytopenia (3.3%), sleepiness (2.7%); CRBM – sleepiness (4%), allergic reactions (4%), dyspepsia (3.2%); Succinamide – dyspepsia (8%), agitation and hallucinations (8%); Levetiracetam – sleep-onset disorder (2.5%). Predominantly to discontinue AED was a necessity due to allergic reactions and such dangerous adverse reactions as seizure aggravation (topiramate – 2%), toxic hepatitis (valproate – 0.4%, CRBM – 0.7%), trombocytopenia (less than  $90 \times 10^9/\mu$ , valproate – 0.6%), hallucinations (Topiramate – 1%, Succinamide – 8%, CRBM – 0.1%)

**Conclusion:** With extending of AED spectrum, the drug of new generation, tolerance of drug therapy has increased. Nevertheless, the issue of adverse reactions, especially in case of long-term drug intake remains relevant and requires further research

#### P185 EVALUATION OF ANTIEPILEPTIC TREATMENT FAILURE FOUNDATION CENTRAL LEAGUE AGAINST EPILEPSY (LICCE) IN THE CITY OF BOGOTA, DC

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**Proposal:** The control of epilepsy patients remains a challenge, in more than 30% is not achieved seizure control with one or two prescribed medications, which often involves the use of second-and third-line medications, some of them not included in the benefit plans.

**Objective:** To describe the pharmacological management of epilepsy during the first half of 2012 at the Foundation LICCE.

**Methodology:** Cross sectional observational study. We included the medical records of patients diagnosed with epilepsy during the first half of 2012.

**Results:** The most common diagnoses were secondary epilepsy focal complex III expression sequelar mild to catastrophic (54%) followed by primary epilepsy focal complex I expression cromosopatia mild to catastrophic (20%) and generalized epilepsy channelopathy elementary complexity I expression mild to catastrophic (19%). 74.6% was managed initially with valproic acid and / or carbamazepine, 8% was made with drugs not included in the benefit plan and 3% does not correspond to AEDs. It mentions a 100% treatment failure in first-line therapy and 12.4% of adverse drug reactions are the most common gastric intolerance and drowsiness 42.5% to 12.5%. Dosage forms for pediatric correspond to 13.6%, however this population is almost double (24.1%).

**Conclusions:** We found good adherence to clinical practice guidelines. There is a part of the pediatric population that has not suitable dosage forms. Concerns about the high percentage of therapeutic failure and adverse drug reactions not reported to the national pharmacovigilance program.

#### P186 INTRAVENOUS SODIUM VALPROATE FOR STATUS EPILEPTICUS

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**Purpose:** To determine whether intravenous sodium valproate was more effective or safer than other drugs in patients with status epilepticus, we performed a meta-analysis.

**Method:** A literature search was performed using Medline, Embase, the Cochrane Central Register of Controlled Trials CENTRAL. From 544 articles screened, 5 were identified as randomized controlled trials and were included for data extraction. Main outcomes were SE controlled, risk of seizure continuation. The meta-analysis was performed with the Random-effect model. The quality of the included studies was evaluated by Grade software.

**Results:** Five studies with 364 participants met the inclusion criteria. There was no statistically significance in SE controlled between Intravenous sodium valproate and Phenytoin (110/134 vs. 78/108 participants; RR 1.07 95% CI 0.91, 1.24). Compared with diazepam, sodium valproate had a statistically significant lower risk of time interval for control of RSE after giving drugs ( $8.8 \pm 7.4/20$  vs.  $26.6 \pm 26.7$  participants; MD  $-17.80$ , 95% CI  $-29.94$ ,  $-5.66$ ), however, there was no statistically significant difference in SE controlled within 30 min between the two groups (16/20 vs. 17/20 participants; OR 0.71, 95% CI 0.14, 3.66). There was no statistically significant difference in cessation from status between Intravenous sodium valproate and Levetiracetam (26/41 vs. 28/41 participants; OR 0.80, 95% CI 0.32, 2.01)

**Conclusion:** Intravenous sodium valprate was as effective as intravenous phenytoin for SE controlled and risk of seizure continuation

#### P187 PROSPECTIVE STUDY OF ANTIEPILEPTIC DRUGS WITHDRAWAL IN SEIZURE-FREE PATIENTS IN CHINA

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**Purpose:** The study aimed to assess the relapse rate and risk factors of seizure recurrence after discontinuing antiepileptic drugs (AEDs) in seizure-free patients in China, and to explore whether to reinstitute AEDs immediately after one single seizure happened after AEDs withdrawal.

**Method:** Patients with epilepsy, who were seizure-free for at least 2 years and decided to stop AEDs gradually, were followed up every 3 months for seizure relapse at the neurology department of West China Hospital, from March 2006 to October 2012. Patients who experienced first seizure after drug withdrawal were divided into two groups according to their willingness to reinstitute AEDs, and followed up for further seizure.

**Results:** A total of 162 patients were enrolled. The average time of follow up was 29.35 months. Until the end of the study, 37 patients (22.8%) relapsed and most relapsed within 12 months after withdrawal. The cumulative relapse rate was 16% at 12 months, and 20.2% at 24 months. The risk factors for seizure recurrence were

AEDs response time >1 year and multiple types of seizure. Most patients (73%) chose to reinstitute AEDs immediately after the first seizure occurred. Eight patients (8/32 = 25%) suffered seizure again within 1 year. No statistically significant difference was found between groups of reinstating AEDs or not.

**Conclusion:** The total recurrence rate after AEDs withdrawal was relatively low in China. Patients with long AEDs response time and/or multiple types of seizure were at higher risk of seizure relapse. First single seizure after drug withdrawal may need no AEDs reinstatement immediately.

## P188

### THE DIFFERENCE OF SIDE EFFECTS ACCORDING TO AGE DURING ACTH THERAPY

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**Purpose:** Adrenocorticotropic hormone (ACTH) therapy is used for infants with West syndrome. However, ACTH is also effective for older children with other types of seizures as atypical absence. To clarify the difference of side effects of ACTH therapy according to age, we investigated the incidence of side effects in patients of various age groups.

**Method:** We studied 70 children who underwent ACTH therapy between 2003 and 2012. ACTH therapy was performed 1–4 times in each patient (total 102 times). The age at ACTH therapy was from 3 months to 10 years (mean 10 months). The patients were divided into four groups according to age at the treatment as, (1) less than 1 year, (2) 1–2 years, (3) 3–4 years, (4) 5 years or older. We reviewed clinical charts to investigate the incidence of side effects in each group.

**Results:** While irritability is more common in younger patients (incidence in each group: 74.5%, 58.3%, 42.9%, 11.1%, respectively), lethargy is more frequent in older patients (9.1%, 8.3%, 64.3%, 55.6%). The incidence of increased appetite was similar in all groups. Infection (16.4%, 16.7%, 7.1%, 0.0%) and diarrhea (7.3%, 25.0%, 0.0%, 0.0%) were rare in older patients. Hypokalemia was more common in older patients (10.9%, 37.5%, 42.9%, 44.4%). Induced seizures were more frequent in older patients (0.0%, 4.2%, 14.3%, 22.2%).

**Conclusion:** The side effects of ACTH therapy were different depending on the age. We should pay attention to the difference when we perform ACTH therapy in older children.

## P189

### TRIAL IN PROGRESS: EXIST-3, A PLACEBO-CONTROLLED STUDY OF THE EFFICACY AND SAFETY OF TWO TROUGH RANGES OF EVEROLIMUS AS ADJUNCTIVE THERAPY IN PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX (TSC) WHO HAVE REFRACTORY PARTIAL-ONSET SEIZURES (POS)

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EXIST-3 is a 3-arm, randomized, double-blind, placebo-controlled study (NCT01713946) that will assess the efficacy and safety of two trough ranges of everolimus as adjunctive therapy in patients with clinically definite TSC who have refractory POS despite taking 1–3 antiepileptic drugs. Patients (estimated enrollment, n = 345) aged 1–65 years will be randomized 1:1:1 (stratified by age subgroup) to receive everolimus 3–7 ng/ml or 9–15 ng/ml, or placebo. Study phases include baseline (screening week 8 to randomization week 0), core (double-blind, titration period week 0 to week 6, maintenance period week 6 to week 18), and extension (week 18 until up to 48 weeks after the last patient has completed the core phase). The primary objective is to compare reduction from baseline in frequency of POS during week 6 to week 18 in the everolimus and placebo arms. Separate endpoints will be used for the European Medicines Agency (EMA) and for the US Food and Drug Administration (FDA) as requested by each. The primary endpoint for EMA is response rate (≥50% reduction from baseline in POS frequency) and for FDA, percentage reduction from baseline in POS frequency. Secondary endpoints include other measures of seizure frequency reduction, quality of life, neurocognition, pharmacokinetics, and safety. Prior studies in populations that manifest multiple seizure types have been confounded by irregularities in “seizure counting.” To minimize this factor, we are utilizing a novel strategy with centralized pre-screen seizure review to encourage only the counting of seizures for which the physician is highly confident of the diagnosis.

## P190

### EFFICACY AND SAFETY OF LEVETIRACETAM FOR EPILEPSY PATIENTS

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**Purpose:** Levetiracetam (LEV) is a newer anti-epileptic drug (AED) with over a 10-year history of US/EU approval. Its efficacy and tolerability have been shown in several studies as adjunctive therapy for partial and generalized epilepsy and as monotherapy for newly diagnosed epilepsy. In Japan, LEV has been authorized for use as adjunctive therapy for localization-related epilepsy since 2010, however, there is a lack of clinical report in Japanese patients. We evaluated safety and efficacy of LEV in our hospital database after the launch of LEV.

**Method:** The record of 243 patients aged ≥16 years receiving LEV were retrospectively evaluated with respect to classification of epilepsy, seizure outcome, efficacy with regard to the number of concomitant AEDs, adverse events and discontinuation of LEV.

**Results:** The populations were constituted of localization-related epilepsy (n = 186), idiopathic generalized epilepsy (n = 13), symptomatic generalized epilepsy (n = 19) and unknown classification of epilepsy or others (n = 25). Compared with pretreatment baseline, 74.2% of 179 assessable patients reduced ≥50% in seizure frequency (responders) and 41.3% of them became seizure free during the treatment period. The percentage of the responders for localization-related epilepsy during the treatment period was 68.2% for temporal lobe epilepsy (TLE) and 74.1% for frontal lobe epilepsy (FLE). Responder rates tended to be higher in the groups with less number of concomitant AEDs. Adverse events were reported in 23.4% of patients and caused discontinuation of LEV in 13.4%. As a result, 82.1% of the patients were able to continue LEV therapy.

**Conclusion:** LEV was well tolerated and efficacious as adjunctive therapy for Japanese epilepsy patients. In localization-related epilepsy, efficacy of LEV did not demonstrate an obvious difference between the patients with TLE and those with FLE. LEV may have some possibilities to give patients better outcomes if LEV is prescribed as the second or third AED.

#### P191

##### ORAL MEXILETINE FOR LIDOCAINE-RESPONSIVE NEONATAL EPILEPSY

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**Purpose:** Lidocaine has been used to treat seizures, especially in neonatal and patients with status epilepticus. Mexiletine hydrochloride is structurally similar to lidocaine and is used widely as a class Ib antiarrhythmic, also that has antiepileptic action. However, as lidocaine is not available as an oral drug, long-term treatment with lidocaine is difficult. Theoretically, mexiletine can be used as a substitute for lidocaine because it is active orally and its mechanism of action is similar to that of lidocaine.

**Methods:** After lidocaine infusion, we changed for oral mexiletine.

**Results:** The patient was a male neonate who had seizures since 2 days of age. Ictal EEG showed bilateral occipital-dominant rhythmic activity spreading to the left centro-temporal areas and lasting for about 60 s. The patient was diagnosed with focal epileptic seizures. While his seizures were refractory to phenobarbital, lamotrigine, vitamin B<sub>6</sub>, and midazolam, they were controlled by continuous lidocaine infusion. Oral mexiletine at serum levels of 0.2–0.4 µg/ml was used successfully for long-term treatment of his seizures. No delay in psychomotor development was observed at the last follow-up at 26 months of age. No mutation was identified in any of four genes: SCN1A, SCN1B, KCNQ2, and KCNQ3.

**Conclusions:** Our patient demonstrates that oral mexiletine can be useful for long-term treatment of patients with lidocaine-responsive epilepsy. Mexiletine was effective at serum concentrations below its antiarrhythmic effective level and was tolerated well.

#### P192

##### DEVELOPING A METHOD TO IDENTIFY MEDICINE NON-ADHERENCE IN A COMMUNITY SAMPLE OF ADULTS WITH EPILEPSY

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**Purpose:** The aim is to propose a simple way of identifying patients at risk of antiepileptic drug (AED) non-adherence during epilepsy review.

**Method:** A mixed methodology was developed in a nested study using a case record review to calculate the medicine possession ratio (MPR) from the AED medication records of a community sample, a literature review and a consensus panel to develop a questionnaire to address how people manage their epilepsy, particularly medicine management, and how to collect information about non-adherence through stated findings in keeping with non-adherent behavior.

**Results:** The literature review confirmed that adherence is a variable and dynamic behavior. There was also evidence to show that patient outcomes could be demonstrably improved by adhering to medication. Non-adherence is, however, a complex behavior, which can either be

intentional or unintentional and with conflicting evidence about the influence of patient demographics. A Cochrane review confirmed that non-adherence may be a problem in up to 50% of patients with long-term conditions and that no single intervention is effective in reducing levels of non-adherence. A combination of interventions may be more effective, but equally, there is a difficulty in measuring non-adherence. It was also shown that a medicine record can be used to estimate the MPR (<80% indicates non-adherence) and that an open and non-confrontational consultation style can be fostered by using key questions within the consultation to identify those at risk of both intentional and unintentional non-adherence by exploring patients beliefs and concerns about medicine and whether they have difficulty because of memory, cognition or dexterity.

**Conclusion:** There is no simple way of measuring medicines non-adherence, that it is a dynamic and variable behaviour and so the use of a multi-modal approach to the problem of non-adherence is necessary because of the limitations of any other method.

#### P193

##### LACOSAMIDE AS ALTERNATIVE THERAPY FOR NOCTURNAL FRONTAL LOBE EPILEPSY (NFLE)

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**Purpose:** Nocturnal frontal lobe epilepsy (NFLE) is a partial epilepsy syndrome for which sodium-channel mediating antiepileptic medications, particularly carbamazepine, are proven highly effective therapy for up to 70% of patients. Still, a substantial portion of NFLE patients fail to respond or have adverse events with standard medications, and might benefit from alternative agents. The objective of this report is to evaluate the potential value of a newer and different sodium-channel mediating agent, lacosamide, for treatment-resistant NFLE.

**Methods:** A retrospective analysis of all patients diagnosed with NFLE at the University of Maryland Epilepsy Center from 2008 to 2012 was performed. Patient response to current treatment was assessed and those who were treatment-resistant or had adverse effects from medications were offered alternatives, including lacosamide. Among patients given lacosamide, responses were evaluated.

**Results:** We identified 18 patients diagnosed with NFLE. Twelve (67%) reported satisfaction with seizure control and lack of adverse effects. For the remaining six patients, 4 chose to add lacosamide on as adjuvant therapy. Two patients discontinued lacosamide due to intolerable side effects. The other two patients reported improved seizure control and tolerability after 1 year follow-up, with one patient seizure-free and the other experiencing rare, mild episodes when sleep-deprived.

**Conclusions:** A substantial portion of patients diagnosed with NFLE and treated with standard medication report unsatisfactory seizure control or adverse effects warranting consideration of alternative treatments. Based on our preliminary experience, lacosamide, a new sodium-channel mediating agent, may be an alternative treatment for NFLE, and warrants consideration in future prospective studies.

#### P194

##### EFFICACY AND SAFETY OF CARBAMAZEPINE AND SODIUM VALPROATE AND QUALITY OF LIFE OF THE PATIENT WITH COMPLEX PARTIAL SEIZURE

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**Purpose:** To study and compare efficacy and safety of carbamazepine and Sodium Valproate and quality of life of patient with complex partial seizure.

**Methodology:** The research design and methodology is totally based on the patient reported outcomes (PRO). The patient who was clinically diagnosed with complex partial seizure including the EEG examination was randomly selected and prescribed carbamazepine and sodium valproate. The patients were assigned to follow up after 2 months of drug administration and interviewed in face to face interaction situation. Semi-structure Performa like QOLIE-31, QOLIE- 31P, QOLIE-AD- 48, SSQ, NARANJO ADR probability scale were used. Statistical analysis was evaluated by the use of Levene's test on SPSS.

**Results:** The results among 53 patients (30 sodium valproate users and 23 carbamazepine users) showed that the highly affected age group was 10–30 years of age. Female patients had lower QOLIE score. The older patients have low QOLIE score. Among sodium valproate user 63.33% are seizure free, remaining have average seizure severity 17.55% while in Carbamazepine user 52.17% are seizure free, remaining have average seizure severity 14.69%. A t test failed to reveal a statistically significant difference between the mean quality of life that used sodium valproate has ( $M = 631.80$ ,  $s = 63.459$ ) and that used carbamazepine has ( $M = 637.84$ ,  $s = 66.459$ ),  $t(51) = 0.326$ ,  $p = 0.738$ ,  $\alpha = 0.05$ . Incremental Cost Effectiveness Ratio is found as Rs. 8440 and Rs.7643 sodium valproate and carbamazepine respectively. The result has been found as 70.78% and 66.35% safe for sodium valproate and carbamazepine respectively.

**Conclusion:** Our current understanding of CPS is mostly of them have their seizure controlled with both drugs. Both of the drugs are effective and safe but Cost Effectiveness Analysis (CEA) shows that the carbamazepine has slightly more cost-effectiveness and quality of life (QOL) than sodium valproate.

### P195 RECOMMENDATIONS AND CLINICAL USE OF OXCARBAZEPINE FOR FOCAL EPILEPSY TREATMENT: MEXICAN NATIONAL SURVEY

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**Objective:** Report the use of Oxcarbazepine in newly diagnosed focal epilepsy in Mexico.

**Method:** A survey of 20 items was applied to 306 physicians (neurologists, pediatric neurologists, neurosurgeons, etc). Thirty-five cities divided in eight regions along the country were included. Eleven coordinators were selected to obtain the data for each region. Once the data was obtained this information was analyzed with descriptive analysis and graphic and tables.

**Results:** Twenty-one thousand four hundred and seventy-six patients with epilepsy were attended for physicians. 58% of patients had focal epilepsy. Adults were 36% of population and 64% children. The experience of 80% of physicians using oxcarbazepine between 5 and 15 years. Oxcarbazepine was the first option of treatment, followed by Carbamazepine and Valproic Acid. Initial used doses are 300–1,200 mg/day and for maintenance doses 600–1800 mg/day. Physicians don't ask for drug levels in 57.2% and crisis remission are between 50–75%. 33.7% of patients who fails to seizures control with previous antiepileptic drugs and switch to Oxcarbazepine obtained a 68.9% of control crisis. The most common adverse events founded were sleepiness (38.3%) and dizziness (21.6%). Hyponatremia was reported in a 9.2% and withdrawal was reported in a 5% of cases. Add on therapy most used with Oxcarbazepine was valproic acid.

**Conclusion:** The epilepsy in Mexico is the second cause of visits to neurologists. Oxcarbazepine is the first option treatment in newly

diagnosed focal epilepsy in Children and Adults. Adult the recommended dose 1,200–1,800 mg twice daily; in Pediatric patient 10–30 mg/kg/day. Screening of drugs levels is not necessary when manage as a monotherapy or add on therapy. Add on therapy is tolerable with Phenytoin, Phenobarbital and Lamotrigine. Adverse events were tolerable and just a minimal percentage of cases needs withdrawal of drug. Oxcarbazepine is a good alternative in Mexican neurologists' experience.

### P196 A COMPARATIVE OBSERVATIONAL STUDY OF EFFICACY OF OXCARBAZEPINE AND ZONISAMIDE AS MONOTHERAPY IN GENERALIZED TONIC CLONIC SEIZURES (GTCS) – IN DEVELOPING COUNTRIES – A GUIDELINE FOR ECONOMICAL TREATMENT

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**Purpose:** The major burden of cost of long term management of Generalized Tonic Clonic Seizures (GTCS), in economically strained countries, like India is heavy. Hence, information of an observational study between two commonly used drugs becomes essential, in the management of GTCS, economically. Both the drugs are used as monotherapy, to reduce cost, and complications.

**Method:** The present study is done to evaluate the efficacy of Zonisamide, and Oxcarbazepine in adequate therapeutic doses, rather than recommended dosage, as monotherapy, over a period of 1 year. 540 GTCS patients has been recruited, with proper inclusion and exclusion criteria, with the main parameters of control in EEG manifestations of seizure and clinical episodes of GTCS, between ages of 18 years to 36., both male and female. Proper monitoring of EEG and clinical evaluation were done every month, and seizure episode reduction and EEG normalization were taken as the criteria for the control of seizures. 270 patients were put on Oxcarbazepine on doses of 600 mg/day. The other 270 patients were on Zonergren 100 mg/day. The side effects, and other possible toxic reactions were evaluated.

**Results:** During the end of the study the efficacy and tolerability of both the drugs were studied. Student 't' test (Proportion) used in evaluating the results.

**Conclusion:** There is no statistical significance in the efficacy of both the drugs, i.e both drugs have more or less the same efficacy, thereby giving guidance to Neurologists in developing countries to choose an economical drug of the two of their choice towards affordability of their patients.

### P197 EFFICACY AND SAFETY OF ANTIDEPRESSANTS FOR DEPRESSION IN PEOPLE WITH EPILEPSY: A SYSTEMATIC REVIEW

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**Purpose:** Our aim is to assess efficacy and safety of antidepressants for depression in people with epilepsy.

**Method:** Randomized controlled trials or quasi-randomized controlled trials of antidepressants in patients with depression and epilepsy were

searched from Cochrane Epilepsy Group Trials Register; the Cochrane Depression, Anxiety and Neurosis Group Trials Register; the Cochrane Central Register of Controlled Trials; MEDLINE; the China Biological Medicine Database; and the Chinese National Knowledge Infrastructure full-text journal database. The selected trials' inclusion criteria, quality were evaluated. Data were extracted and a fixed-effects method was used to examine dichotomous outcomes.

**Results:** Four studies involving 197 patients were included, of which two trials were placebo-controlled, two others were open-controlled. Three studies, citaloram or venlafaxine, involving 158 patients, were included in the meta-analysis. In the pooled analysis, monotherapy with either antidepressant was found to be more effective than placebo by the end of follow up (OR 13.64, 95%CI 6.29–29.59). The majority of patients reported side effects, but generally mild and transient. Two of 158 patients (1.3%) experienced an increase in seizure frequency, but not significantly different from the placebo group.

**Conclusion:** Antidepressants, venlafaxine and citaloram, appear to be safe and effective for patients with epilepsy and depression. Whether amitriptyline or nomifensine is not more effective than placebo and no any antidepressant is more effective than another. Large-scale, placebo-controlled and properly randomized clinical trials are still needed to further address these questions.

#### P198 DESIGN OF A PROTOTYPIC TEST MODEL TO ASSESS STANDARDS OF GENERIC AND BRAND ANTIEPILEPTIC DRUG BIOEQUIVALENCE

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**Purpose:** The therapeutic equivalence of FDA approved generics antiepileptic drugs (AEDs) has been questioned by neurologists and patients with epilepsy based on reported adverse effects. The most common approach to evaluate bioequivalence (BE) is a two-treatment crossover pharmacokinetic (pK) study design in healthy adults, but BE is rarely assessed in patients under clinical conditions. Hence, a study design to assess BE in patients with epilepsy is warranted and needed. Lamotrigine (LTG) was selected here as study drug based on reported issues with its generic formulation.

**Method:** The study design considered typical elements of a conventional BE study in healthy adults. The approach also considered the unique aspect of performing a phase BE study in patients already taking LTG for epilepsy.. Feedback from the US Food and Drug Administration, the National Institutes of Health, and the Epilepsy Foundation were incorporated.

**Results:** A study is in process at our center. It is a double-blind, multiple-dose, full replicate design, pK study of LTG 100 mg tablets in patients with epilepsy. The 100 mg dose was selected due to most common usage. Rather than unblinded or double-dummy, over-encapsulation was selected as the method for blinding. White colored capsules are used for over-encapsulation, as patients surveyed most preferred this color. Subjects each receive the brand name and generic product twice, allowing for three switches between products. Each arm is to be about two weeks in duration to allow for steady-state to be achieved. The design also includes patient education for dosing compliance.

**Conclusion:** A study has been designed and initiated to evaluate the BE of generic and brand name LTG tablets in patients with epilepsy. Given

the lack of available prior study designs to assess BE in patients under clinical use conditions, this design may serve as a prototype for assessment of brand and generic equivalence.

#### P199 DOSE DEPENDENT LEVETIRACETAM INDUCED DE NOVO MAJOR DEPRESSION WITH SUICIDAL BEHAVIOR

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**Purpose:** Levetiracetam is a novel antiepileptic drug approved for adjunctive treatment of generalized and partial seizures. Levetiracetam has no clinically significant drug interactions with limited adverse effects which have led to levetiracetam being studied for off-label treatment of both psychiatric and pain disorders with mixed results. Recent reports suggest levetiracetam can induce de novo psychosis, affective disorder, aggression, and suicidal ideation. The authors report what is believed to be the first instance of de novo major depression following levetiracetam dose adjustment with near fatal suicide attempt.

**Method:** Case analysis with PUBMED literature review.

**Results:** Sixty-six year male with diabetes and hypertension had two seizures following an intracranial hemorrhage in 2007. He remained seizure free on levetiracetam 500 mg bid until hospitalized on 4/22/2012 with elevated CPK, hyperglycemia, and hypocalcemia. Routine EEG was normal and head MRI/CT revealed atrophy, small vessel ischemic disease, and old bilateral thalamic lacunar infarcts. He was stabilized and discharged on levetiracetam 500 mg bid only to be readmitted on 8/3/2012 following levetiracetam noncompliance with witnessed seizures. Levetiracetam was increased to 1000 mg bid (32.6 mcg/ml). Prior to levetiracetam increase, he had no history of psychopathology excluding alcohol abuse. Within 1 month, he developed a complete vegetative-affective cluster consistent with a major depressive episode and attempted a near fatal insulin overdose (field glucose 1). After psychiatric consultation and medical stabilization, he was transferred to an inpatient psychiatric hospital.

**Conclusion:** Levetiracetam may be associated with de novo depressive features in patients with epilepsy when dose is titrated. This near fatal overdose suggests the grave consequences of not monitoring for affective features in patients with epilepsy on levetiracetam.

#### P200 EFFICACY, TOLERABILITY AND RETENTION RATES IN 200 PATIENTS WITH EPILEPSY TREATED WITH LACOSAMIDE

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**Purpose:** We evaluated the effectiveness of lacosamide (LCM) for seizure control in the largest epilepsy cohort to date.



**Methods:** We analyzed charts of 213 patients prescribed LCM at Columbia or Yale Comprehensive Epilepsy Center. Endpoints included efficacy, retention and tolerability. Regression analysis and Fisher's test were performed to estimate associations between clinical factors and occurrence of remission or adverse effects (AEs).

**Results:** Of 213 patients, 150 were followed at Columbia and 63 at Yale. Most 187/213 (87.8%) had partial-onset epilepsy. Patients (mean age 39 year (SD 14.25) tried an average of 6.6 prior antiepileptic drugs (AEDs) before LCM. At last follow-up or discontinuation of LCM, mean duration of therapy was 11.6 months (SD 12.7, range 0–97). For estimation of efficacy, patients discontinuing LCM before 6 or 12 months for reasons besides inefficacy were excluded; 15/143 (10.5%) experienced 6 months and 3/104 (2.9%) experienced 12 months of seizure-freedom. For estimation of retention, patients still on LCM at last follow-up for less than 12 months were excluded; 78/149 (52.3%) stayed on LCM for at least 12 months. AEs attributed to LCM requiring lowering or discontinuation were present in 81/213 (38.0%), common symptoms included dizziness (10.3%), imbalance (10.3%), drowsiness (6.1%) and vision problems (6.1%). Presence of brain lesion was the only predictor of seizure-freedom ( $p < 0.008$ ), while concomitant use of other AEDs predicted AEs. Frequency of AEs among patients on LCM with AEDs that act on voltage-gated sodium channels was compared against that among patients on LCM with AEDs that do not act on sodium channels. Differences did not reach statistical significance.

**Conclusions:** LCM was well tolerated, half remained on it for more than a year, and 10.5% achieved at least 6 months of seizure-freedom. Polytherapy predicted AEs, though we could not identify a particular AED or class of AEDs that was predictive.

## P201 ANTIEPILEPTIC DRUGS WITHDRAWAL AFTER SUCCESSFUL EPILEPSY SURGERY: UTILITY OF POSTOPERATIVE EEG

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**Purpose:** Approximately one in three patients with a successful epilepsy surgery will have seizure recurrence following antiepileptic drugs (AED) withdrawal. A recent survey of Canadian epileptologists identified a negative EEG before discontinuation as the most important factor influencing the decision to attempt AED withdrawal (Télez-Zenteno et al. *Epilepsy Res* 2012; 102:23–33). The purpose of this study was to investigate the use of postoperative EEG at our institution as well as its value as a predictor of post withdrawal seizure recurrence.

**Method:** We performed a retrospective study of all patients who underwent epilepsy surgery at the Notre-Dame Hospital between 1986 and 2012. Patients who had a postoperative EEG before attempted AED withdrawal were included. We compared seizure recurrence rates between patients with a normal EEG and those showing interictal epileptiform discharges (IED).

**Results:** A total of 275 patients underwent epilepsy surgery during the study period (184 temporal and 91 extra-temporal). A favorable outcome (Engel I or II) was achieved in 218 (79.3%) patients. Of the 141 patients who attempted AED discontinuation, 44 (31%) had seizure recurrence. The mean follow-up after AED withdrawal was  $10.0 \pm 6.5$  years (range: 1–25). Only 49 (35%) of the 141 patients who attempted discontinuation of AED had a postoperative EEG. Sixteen (42.1%) of the 38 patients with a normal EEG had seizure recurrence, compared to 7 (63.6%) of the 11 patients with IED. This difference did not reach statistical significance ( $p = 0.208$ ).

**Conclusion:** The limited use of EEG before AED discontinuation at our institution contrasts with the self-reported practice described in the Canadian survey. Postoperative EEG was unable to predict post withdrawal seizure recurrence. These findings will be discussed in light of a systemic review we performed on the subject.

## P202 ANTI-SEIZURE EFFECTS OF PERAMPANEL IN COMBINATION WITH OTHER ANTIEPILEPTIC DRUGS (AEDs) IN A RAT AMYGDALA KINDLING MODEL

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**Purpose:** The AMPA receptor antagonist perampanel has demonstrated anti-seizure effects in preclinical epilepsy models and Phase III studies of patients with partial-onset seizures. It was not possible to study pharmacodynamic interactions between perampanel and other AEDs in the Phase III studies because most patients received >1 concomitant AED. Using a rat amygdala kindling model, we explored pharmacodynamic interactions between perampanel and the four most commonly co-administered AEDs in the perampanel Phase III studies.

**Methods:** A tripolar electrode was implanted into the basolateral amygdala of male Wistar-Kyoto rats (250–400 g;  $n = 45$ ), with a reference electrode placed on the contralateral cortex. Electrical stimulation was applied (500  $\mu$ A, 1 ms, monophasic square-wave pulses, 50/s for 1 s) until  $\geq 3$  Racine stage five seizures occurred. Perampanel, carbamazepine, lamotrigine, levetiracetam, and sodium valproate were administered alone or in combination intraperitoneally, at doses that increased the after discharge threshold (ADT), and a stimulation of three times the ADT was applied. Seizure severity, motor seizure duration, and electroencephalogram seizure duration were measured before and after treatment.

**Results:** Individually, perampanel 0.75 mg/kg, carbamazepine 20 mg/kg, lamotrigine 20 mg/kg, levetiracetam 50 mg/kg, and sodium valproate 200 mg/kg conferred modest reductions in seizure severity and duration. However, co-administration of perampanel with each of the other AEDs conferred synergistic improvements, with additional benefit at a perampanel dose of 1.5 mg/kg.

**Conclusions:** Combination of perampanel with other AEDs synergistically ameliorated efficacy parameters in a rat amygdala kindling model, at doses that had minimal anti-seizure effects when administered individually.

*Support: Eisai Co., Ltd.*

## P203 THERAPEUTIC TIME WINDOW OF PERAMPANEL FOR THE TERMINATION OF DIAZEPAM-RESISTANT STATUS EPILEPTICUS (SE) IN A LITHIUM- PILOCARPINE RAT MODEL

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**Purpose:** The AMPA receptor antagonist perampanel is approved in Europe and the USA as adjunctive treatment for partial-onset seizures in patients aged  $\geq 12$  years. Previously, perampanel terminated SE when administered 30 min after seizure initiation in a lithium-pilocarpine rat model, whereas diazepam only terminated SE when administered at 10 min (Ido & Hanada. Abstract 3.221, AES Annual Meeting 2012). Here, the same model was used to further explore the therapeutic time window of perampanel, and to evaluate another AMPA receptor antagonist, GYKI52466.

## Abstracts

**Methods:** An electroencephalography (EEG) electrode was implanted onto the primary somatosensory cortex of male Sprague-Dawley rats (250–450 g), with a reference electrode on the cerebellum. Lithium chloride 3 mEq/kg was administered intraperitoneally, followed 18–26 h later by scopolamine methyl bromide 5 mg/kg and pilocarpine 30 mg/kg. Perampanel 8 mg/kg or GYKI52466 50 mg/kg were administered intravenously 30 (GYKI52466), 60 (perampanel), or 90 (perampanel) minutes after seizure initiation (when the first EEG spike train occurred). Seizures were ‘terminated’ if SE-type high-frequency EEG spike activity was abolished within 30 min.

**Results:** When administered at 60 min, perampanel terminated seizures in 6/6 rats. Efficacy was reduced when administered at 90 min: 2/6 rats experienced seizure termination; 2/6 had EEG suppression with seizure recurrence; 2/6 did not achieve seizure termination. When administered at 30 min, GYKI52466 terminated seizures in 2/4 rats.

**Conclusions:** These data confirm observations that AMPA receptor antagonists terminate SE in a lithium-pilocarpine model, with a longer therapeutic time window than diazepam.

Support: Eisai Co., Ltd.

**P204**  
**ADJUNCTIVE PERAMPANEL DOES NOT INCREASE THE RISK OF CARDIAC ADVERSE EVENTS COMPARED WITH PLACEBO: A POOLED ANALYSIS OF THREE PHASE III TRIALS**

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**Purpose:** A pooled analysis of cardiac safety from three randomized, double-blind, placebo-controlled Phase III trials of adjunctive perampanel.

**Methods:** Patients (≥12 years) with partial-onset seizures despite treatment with 1–3 antiepileptic drugs were randomized to once-daily placebo, perampanel 2, 4, 8, or 12 mg. Studies included a 6-week Baseline Period, 6-week Titration Period, 13-week Maintenance Period, and 4-week Follow-up Phase. Treatment-emergent adverse events (TEAEs) were recorded and 12-lead electrocardiograms (ECGs) were obtained.

**Results:** In total, 442, 180, 172, 431, and 255 patients were randomized to placebo, perampanel 2, 4, 8, and 12 mg, respectively. The incidence of cardiac or ECG-related TEAEs was comparable between placebo-treated (n = 13, 2.9%) and perampanel-treated (n = 26, 2.5%) patients with no apparent dose relationship for any TEAE. Cardiac or ECG-related TEAEs occurring in >1 perampanel-treated patient or >1 placebo-treated patient were bradycardia (placebo n = 3; perampanel n = 4), tachycardia (placebo n = 1; perampanel n = 4), sinus bradycardia (placebo n = 3; perampanel n = 2), prolonged QT (placebo n = 0; perampanel n = 3), angina pectoris (placebo n = 0; perampanel n = 2), palpitations (placebo n = 2; perampanel n = 1), and decreased blood pressure (placebo n = 2; perampanel n = 1). Three patients discontinued due to cardiac-related TEAEs (palpitations [placebo], tachycardia [2 mg], and prolonged QT [8 mg]). There were no cardiac or ECG-related serious AEs or deaths and no clinically significant QTc results in any treatment group.

**Conclusions:** The incidence of cardiac or ECG-related TEAEs in three Phase III studies of adjunctive perampanel was comparable between perampanel and placebo-treated patients. These data suggest perampanel does not increase the risk of these events.

Support: Eisai Inc.

**P205**

**DISCONTINUATION RATES ACROSS THREE PHASE III TRIALS OF THE AMPA RECEPTOR ANTAGONIST PERAMPANEL AS AN ADJUNCTIVE TREATMENT FOR REFRACTORY PARTIAL SEIZURES**

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**Purpose:** We analyzed discontinuation rates, and reasons for discontinuation, across pooled data from three Phase III studies of adjunctive perampanel for refractory partial seizures (304 [NCT00699972], 305 [NCT00699582], 306 [NCT00700310]).

**Methods:** Patients (≥12 years), with partial seizures despite receiving 1–3 antiepileptic drugs, were randomized to receive once-daily placebo, perampanel 8 or 12 mg (304, 305), or placebo, perampanel 2, 4, or 8 mg (306) over a 6-week Titration (2 mg/week up-titration to randomized dose) and 13-week Maintenance Period. Discontinuations were assessed by randomized dose over the first and second halves of the Titration (≤3 and 3–6 weeks) and Maintenance Periods (6–13 and 13–19 weeks).

**Results:** Of 1478 patients in the pooled intent-to-treat analysis set (placebo, n = 441; perampanel 2 mg, n = 180; 4 mg, n = 172; 8 mg, n = 431; 12 mg, n = 254), 14.5% discontinued treatment (placebo, 11.1%; perampanel 2 mg, 4.4%; 4 mg, 8.1%; 8 mg, 14.8%; 12 mg, 24.0%). With placebo, there were similar rates of discontinuation (2.5–3.4%) and discontinuation due to adverse events (AEs; 0.5–1.4%) across the four time intervals. Rates of discontinuation and discontinuation due to AEs peaked at 3–6 weeks with perampanel 8 mg (5.4% and 2.8%, respectively) and 6–13 weeks with perampanel 12 mg (10.3% and 8.5%, respectively), but were similar across all groups by 13–19 weeks (1.3–4.4% and 0.0–2.5%, respectively).

**Conclusions:** Although assessed over uneven time intervals, discontinuation rates increased as perampanel dose was up-titrated to 8 mg and beyond, but, after titration, became similar across the placebo and perampanel groups during maintenance.

Support: Eisai Inc.

**P206**

**META-ANALYSIS OF OCT STUDIES FOR THE ASSESSMENT OF VIGABATRIN-ASSOCIATED RETINAL TOXICITY IN EPILEPSY**

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**Purpose:** Optical coherence tomography (OCT) can identify retinal abnormalities in people treated with vigabatrin (VGB) and it is particularly useful in those who cannot undergo perimetry. Loss of retinal nerve fibre layer thickness (RNFLT) has been described in recent studies employing small numbers of VGB-exposed individuals, even in those without VGB-associated visual field loss (VAVFL). We aim to quantify the mean RNFLT differences in VGB-exposed people with and without VAVFL that can be used as an alternative to perimetry.

**Method:** Literature search and meta-analysis of all published, prospective, observational studies in people with epilepsy with data on 1) the averaged thickness of peripapillary retinal nerve fibre layer measured by OCT and 2) visual fields assessed by perimetry in VGB-exposed people vs. controls (people with epilepsy not exposed to VGB, normal visual fields) [Clayton et al. 2012; Moseng et al. 2011; Lawthom et al. 2009; Wild et al. 2006].

**Results:** Pooled data from four studies showed a mean RNFLT in controls of 91.6  $\mu\text{m}$ . People with VAVFL (N = 70) had an average of 27.3  $\mu\text{m}$  (95% CL, 18–36) loss of RNFLT compared to controls (N = 121) ( $p < 0.00001$ ). In contrast, RNFLT loss in VGB-exposed people without visual loss (3 studies, N = 65) was 4.1  $\mu\text{m}$  (0.9–7.4) compared to controls (N = 114) ( $p < 0.012$ ).

**Conclusion:** VGB-exposed people with normal visual fields had only a mild proportional RNFLT reduction compared to controls (4%), while those with VAVFL had significant reductions (around 30%). These estimates may provide some clinical guidance for the assessment of individuals unable to undergo perimetry. However, results will need to be validated in future prospective studies.

## P207

### RATIONALE AND PROGRESS OF AN AUSTRALIAN CLINICAL TRIALS NETWORK: NEUROSCIENCE TRIALS AUSTRALIA (NTA)

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**Purpose:** Development of a neuroscience research organisation (CRO) to enable projects of all phases, including investigator-initiated and collaborative studies (therapeutic, device, allied health or clinical practice trials) to be undertaken. Triallists have access and support to generation and submission of data including feasibility, design and finalisation, budget negotiation, ethics preparation, trial management, contact with regulatory authorities, statistical analysis and report preparation.

**Method:** An approach to participants in all branches of neuroscience who agree to standardise procedures of clinical trials and support an operational infrastructure and expertise at a modest cost. Collaboration with other investigators and industry is promoted by attracting more neuroscience projects nationwide whilst avoiding the need of individual approaches to negotiate terms for participation in studies. The organisation is self funded through projects undertaken on behalf of various sponsors (pharmaceutical, biotechnology and device companies, collaborative groups and granting bodies e.g. NIH and the NHMRC (Australia)). NTA is not for profit and the surplus is earmarked for further research. The concept permits an improved level of expertise to be imparted to less experienced trialists and tends to select the most appropriate clinicians and scientists to collaborate.

**Result:** In excess of 30 projects have commenced in areas including epilepsy, stroke, MS, neurosurgery, Alzheimer's disease, mental health and spinal cord injury. NTA has been particularly successful in becoming the CRO of choice for academically- driven neuroscience trials in Australia.

**Conclusion:** NTA appears to be an excellent collaborative vehicle for combining neurological expertise and raising trial standards to global expectations.

## P208

### LEVETIRACETAM MONOTHERAPY IN YOUNG FEMALE PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY

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**Purpose:** Although valproate is a well-known first-line antiepileptic drug in juvenile myoclonic epilepsy (JME), valproate has a lot of tolera-

bility problems, especially in adolescence and women of childbearing potential. Levetiracetam (LEV) has been reported as one of alternative first-line antiepileptic drugs in JME. We want to describe our experience with LEV monotherapy in young women.

**Method:** We reviewed medical records of patients with JME treated with LEV monotherapy.

**Results:** Among seven young female patients [mean age 21.3 years (18–27)], LEV was initial monotherapy in 2, second monotherapy in 4, and third monotherapy in one patient. Four patients became seizure free and three patients had only myoclonic jerks. No patient had significant adverse events. All patients were subscribed as once-a-day schedule and the average daily doses were 678.5 mg (500–1000 mg). Minimum follow up duration was 18 months.

**Conclusion:** Our report demonstrates good efficacy and tolerability of LEV in young female JME patients and supports that LEV could be a first-line therapy in JME, especially in women of childbearing potential.

## P209

### PHARMACOTHERAPEUTIC EVALUATION OF PATIENTS TREATED WITH MAGNESIUM VALPROATE IN THE CITY OF BOGOTA

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**Introduction:** Epilepsy is a medical condition with neurobiological, cognitive, social psychological features secondary to this disease. Early diagnosis and early control will give the long-term prognosis. For this reason it is necessary to conduct studies to demonstrate the usefulness of magnesium valproate as initial monotherapy affecting their safety and effectiveness.

**Objective:** To identify and evaluate the clinical outcomes of a cohort of patients treated with magnesium valproate in various health institutions in the city of Bogota.

**Materials and methods:** Observational longitudinal study. We included all patients who request magnesium valproate scientific technical committee.

**Results:** Twenty-four patients who were prescribed with valproate magnesium were followed for 16 months. The average age was 8.8 years (SD = 4.5 years), and 58.3% were female. The two main diagnoses were idiopathic generalized epilepsy variable phenotype 33% (8) and focal symptomatic 29%. The 83.3% began with valproic acid and 29.2% required second-line drug. A cutoff date of the study, 37.5% of them are in polytherapy. The prescribed dose ranging was 8 mg/kg/day to 70 mg/kg/day without side effects. The average dose was 27 mg/kg/day. All patients were controlled. Among the problems encountered were: supply, adherence and some drug interactions that in all cases they were responsible for therapeutic failure or adverse reactions to the initial medication. The application of therapeutic failure algorithm proposed by INVIMA (Institute of Food and Drug Monitoring) shows that the main causes are related to drug usage and the intrinsic efficacy of valproic acid.

**Conclusions and recommendations:** Results show that it is a safe and effective antiepileptic, and broad spectrum of choice in epilepsy, possibly related to more predictable absorption and complete compared to valproic acid. Pharmaceutical care is recommended for patients with epilepsy and for identifying, preventing and resolving problems related to antiepileptic drugs.

## P210

### EFFECTIVENESS AND SIDE EFFECTS OF PERAMPANEL: A FIRST UTILIZATION STUDY

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## Abstracts

**Purpose:** Investigation of dose-related effectiveness and potential side effects of Perampamil (PER) in patients with refractory partial-onset epilepsy.

**Methods:** We retrospectively analyzed data of 19 patients (four women) who received PER since September 2012. We assessed outcome data by direct telephone interview after a mean follow-up of 3.7 months.

**Results:** The mean age was  $37.7 \pm 13.4$  years (range 20–60), mean duration of epilepsy was  $23.7 \pm 13.6$  years (range 8–56). Eighteen patients (94.7%) had a history of secondarily generalized seizures. Mean number of previous antiepileptic drugs (AED) was  $9 \pm 3.7$  (range 2–15). Mean number of concurrent AEDs was  $1.9 \pm 0.7$  (range 1–4). Nine patients (47.4%) received 8–12 mg PER/day at time of follow-up. Four patients (21.1%) stopped PER, two of them (10.5%) at a dose of 4 and 12 mg due to side effects such as depression, ataxia, dizziness, aggressiveness or agitation. One patient had to decrease dose from 10 to 8 mg because of dizziness. Side effects did not persist after discontinuation or reduction of PER. Twelve patients (63.2%) reported any side effects at all. No patient became seizure free. 26.6% of patients who continued PER had a decrease of seizure frequency >50%. They sustained a dose between 4 and 8 mg. 33.3% of the patients had a decrease of seizures frequency <50%, but still observed an effect.

**Conclusion:** Despite a small sample size our study shows a clear therapeutic benefit of PER and might be effective in difficult-to-treat patients. Side effects seem to be rare but might cause discontinuation.

## P211

### EFFICACY AND SAFETY OF THE COMBINED THERAPY OF HIGHER-DOSE LAMOTRIGINE AND VALPROIC ACID IN THREE CHILDREN WITH MYOCLONIC SEIZURE

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**Purpose:** To further understand the efficacy and safety of the combined therapy of higher-dose lamotrigine (6 mg/kg/day) and valproic acid (VPA) in children with myoclonic seizure.

**Method:** We prescribed lamotrigine to three children with myoclonic seizure who were taking VPA. Seizure decreased but still exist when the dosage of lamotrigine escalated slowly to 5 mg/kg/day. We tried carefully to increase the concentration to 6 mg/kg/day.

**Results:** Patients were seizure-free and did not have rash or other side effects after the dosage of lamotrigine escalated to 6 mg/kg/day. All patients' EEG were normal at months 3 of maintenance dose of lamotrigine at 6 mg/kg/day.

**Conclusion:** Administration carefully of the combined therapy of higher-dose lamotrigine and VPA is effective and safe.

## P212

### THE EFFECT OF CO-MEDICATIONS ON LAMOTRIGINE CLEARANCE IN JAPANESE CHILDREN WITH EPILEPSY

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**Purpose:** Lamotrigine was approved in Japan as an adjunctive therapy in 2008. Although it has been reported that some antiepileptic drugs have inducing or inhibiting effects on lamotrigine clearance, it has not been well clarified that they have same effects in Japanese epilepsy patients, especially in children. The aim of this study is to determine the effect of co-medication on lamotrigine clearance in Japanese children with epilepsy.

**Method:** We reviewed 152 routine serum concentration measurements of lamotrigine in 42 Japanese patients aged below 20 years. We calculated dose-corrected lamotrigine concentration, as [concentration]/[dose/(body weight)]. The dose-corrected lamotrigine concentration was compared with co-medication.

**Results:** Although drugs inducing glucuronic acid conjugation (phenytoin, carbamazepine, and phenobarbital) decreased the dose-corrected lamotrigine concentration, the effect of carbamazepine and phenobarbital was smaller than that of phenytoin. Valproate increased the dose-corrected lamotrigine concentration. There was little effect of the dosage or concentration of valproate and inducers within the dose of therapeutic range. While clobazam showed little effect on lamotrigine concentration when the concentration of lamotrigine was low, it tended to reduce the lamotrigine concentration when the lamotrigine concentration was high. Zonisamide had little effect on lamotrigine concentration when the concentration of lamotrigine was low.

**Conclusion:** Our study showed similar effects of co-medication on lamotrigine concentration to those of previous studies outside Japan. In addition, clobazam may reduce the lamotrigine concentration especially when lamotrigine is used in a high dose.

## P213

### OPTIMIZATION OF CARBAMAZEPINE THERAPY IN MONGOLIA FOR PEOPLE WITH PARTIAL EPILEPSY

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**Purpose:** The aim of the present study was to determine the effective dose of CBZ according to the serum level concentration, to indicate pharmacokinetic parameters of CBZ and effect of CBZ treatment by EEG control.

**Method:** Thirty patients with partial epilepsy: 14 males and 16 females included in the study. The average age was  $27.85 \pm 0.45$  (range 16–45) years. The mean duration of partial seizure was  $11.4 \pm 5.8$  years. All patients were using not appropriate doses of CBZ and most of patients were taking it irregularly. Patients were follow-uped during 3 months. Initial dose of treatment was  $7.27 \pm 2$  mg/kg,  $453 \pm 88$  mg/day. HPLC method was used to determine blood levels of CBZ. CBZ pharmacokinetic parameters volume of distribution (Vd), clearance (Cl) and half life ( $t_{1/2}$ ) were measured by the equations.

**Results:** The effect of CBZ monotherapy was 80%, seizure frequency reduced ( $t = 8.479$ ,  $p = 0.0001$ , CI 95%). Therapeutic effective serum level of CMZ in 18 (60%) seizure free patients was  $9.32 \pm 1.06$  µg/ml (range 6.89–10.77), daily dose was  $766 \pm 156$  mg ( $p < 0.01$ ) ( $11.23 \pm 2$  mg/kg). In 10 patients (50%) with serum level of CMZ  $7.3 \pm 1.5$  µg/ml (5.81–9.76) seizure reduced >75% ( $p < 0.05$ ). Adverse effects were observed in seven patients. Average side effects dose was  $1250 \pm 150$  mg ( $21 \pm 4$  mg/kg) ( $p < 0.01$ ). Vd was  $1.36 \pm 0.33$  L/kg, CI  $0.66 \pm 0.16$  ml/min/kg,  $t_{1/2}$   $23.78 \pm 0.12$  h. Non specific slowing and epileptic discharges significantly reduced in patients after the affordable medication. There were significantly decreased teta ( $t = 7.8$ ,  $p < 0.001$ ) and delta ( $p < 0.001$ ) waves by EEG spectral analysis.

**Conclusion:** Our result clearly demonstrates that is no difference of the response of Carbamazepine and Pharmacokinetic parameters of CBZ

between Mongolian patients and patients from other Asian and Western country.

## P214

### UTILIZATION OF GENERIC LACOSAMIDE IN SUPER REFRACTORY FOCAL EPILEPSY: A PROSPECTIVE CHILEAN EXPERIENCE

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**Purpose:** To show our results with the treatment of generic Lacosamide, as therapy add on, in adult patients suffering Super Refractory Focal epilepsy.

**Method:** We included adults patients suffering focal epilepsy (by semiology and EEG), with static or unknown etiology (by CT scan and/or MRI) without answer to conventional AEDs and at least 2 s generation AEDs. They did not suffer non-epileptic events and all them have normal hepatic and renal functions. We administrated Lacosamide, twice a day 25 mg per week in the first month until 100 mg. Then we increased 50 mg each month, with a maximum of 600 mg a day.

**Results:** Twenty-one adults' patients, age: 15–48 years old, average 30.5 Gender: male 7, and female 14. Duration epilepsy: 4–39 years, average: 20. Follow up: 4–21 months, average 10. Concomitant AEDs: 1–5, average: 2.7. Lacosamide dose. 150 mg to 600 mg/day, average: 270 mg. Seizures frequency: 1 without seizures, 7 decreased 75%, 9 decreased 50%, and 4 without change. In 12 patients the number and/or doses of concomitant AEDs were decreased. Adverse effects: Drowsiness (four patients) and acute dizziness (five patients) that disappeared when the dose was reduced, and the administration of Lacosamide, respectively, three times a day.

**Conclusion:** Generic Lacosamide is an alternative in adult's epileptics with super refractory focal epilepsy, with mild adverse effects. We suggest to administrate Lacosamide slowly.

Recalcine Laboratory kindly provided generic Lacosamide.

## P215

### COMPULSIVE GAMBLING POSSIBLY ASSOCIATED WITH ANTI-EPILEPTIC MEDICATIONS

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**Introduction:** Compulsive gambling is recognised with Parkinson's Disease treatment with dopamine agonists but has not been reported with anti-epileptic medications (AEMs) in epilepsy. This is the first report regarding possible compulsive gambling, provoked by AEMs.

**Case:** A 56 year-old female with tendency to excessive behaviour (shopping, drinking, exercising) had overcome these before presenting with epilepsy. Diagnosed with generalised seizures she trialled valproate (VPA), gabapentin (GBP) and levetiracetam (LEV) before commencing lamotrigine (LTG) in 2006. Following introduction of LTG, she initially lost \$4,000–\$5,000 gambling, which she could repay. She had, to this time, successfully concealed her gambling, but, with increased dosage of LTG, she lost \$50,000 of her family's assets thereby provoking serious consequences. At time of discovery, she was on LEV 500 mg II b.d. (blood level 31 mg/L, therapeutic) and LTG 200 mg I mane and II nocte (blood level 53.6 µM, therapeutic). She was not on dopamine agonists.

**Discussion:** GSK and UCB were contacted with GSK reporting intrusive repetitive behaviour (similar to punting) associated with

LTG but no reports of excessive gambling. LEV is recognised as associated with depression, but there are no known cases of obsessive behaviour nor gambling with LEV. To our knowledge, this is the first report of possible compulsive gambling associated with AEM therapy.

## P216

### HCN CHANNEL INHIBITOR GUANFACINE HAS A POTENTIAL OF A NEW ANTI-EPILEPTIC DRUG

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**Purpose:** HCN channel is one of the possible targets of anti-epileptic drug. Guanfacine, drug used to therapy of ADHD, can close HCN channel indirectly and pass through blood–brain barrier. In this study, we examined the effect of guanfacine on ADs induced by acute kindling of the rabbit hippocampus to reveal the contribution of HCN channel in epileptogenesis.

**Method:** We performed all experiments under appropriate conditions in accordance with the Guide for Animal Experimentation at Soka University. Four adult rabbits were used. Under deeply anesthesia, we delivered stimulations (1 ms biphasic pulse, 50 Hz, 1 s) with suprathreshold intensity for AD at 20-min intervals to the right hippocampus. Spectral analysis on each AD was performed with sampling frequency of 1 kHz by Power Lab (Chart, ADInstrument). The kindling stimulations were performed at least 30 times unless alteration of frequency component of ADs shown in chronic kindling experiment was found. After kindled, several doses (1 mM, 3 mM or 5 mM) of guanfacine were administered directly to the right hippocampus or injected intravenously, 5-min before the stimulation.

**Results:** In both cases of direct and intravenous administration, 1 mM guanfacine delayed the onset of AD occurrence, 3 mM guanfacine prevented AD occurrences to the level of 42.9% and 5 mM guanfacine prevented AD occurrences to the level of 21.1%.

**Conclusion:** Since guanfacine inhibited occurrences of AD with a dose-dependency, guanfacine could be a potent of a new AED. It is suggested that HCN channel might be involved in AD occurrence.

## P217

### EFFECT OF GABAB ANTAGONIST SACLOFEN 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 as well as acute hippocampal kindling of the rabbit and revealed that enhancement of the higher frequency band (HFB: 12–30 Hz) component is associated with classical kindling indexes including AD duration. In the present acute kindling experiment, we examined the effects of Saclofen on ADs to reveal the contribution of GABAB receptor in epileptogenesis with using spectral analysis.

**Method:** We performed all experiments according to the guidelines of Declaration of Helsinki and Animal Experimentation at Soka University. Four adult rabbits were used. Under deeply anesthesia, we delivered stimulations (1 ms biphasic pulse, 50 Hz, 1 s) with suprathreshold intensity for AD at 20-min intervals to the right hip-

pocampus. When HFB component in AD increased to the kindled level, 1 mm Saclofen was injected to the ipsilateral hippocampus with a rate of 100 µl/min, 5 min before stimulating. FFT analysis on each AD was performed with sampling frequency of 1 kHz by Power Lab.

**Results:** Saclofen injection significantly suppressed AD occurrence: No AD occurrences were found in six cases out of 24 trials ( $p < 0.01$ ). In the other weak AD occurrences, FFT analysis showed an increasing PSD ratio of the lower frequency band (LFB: 0–9 Hz) component ( $p < 0.01$ ).

**Conclusion:** Since Saclofen suppressed seizure occurrence and enhancement of HFB component, it is suggested that GABAB receptor contribute to the generation of high frequency seizure discharge.

## P218

### LONG TERM RETENTION OF LACOSAMIDE IN A LARGE COHORT OF PEOPLE WITH MEDICALLY REFRACTORY EPILEPSY: A SINGLE CENTRE EVALUATION

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**Purpose:** Lacosamide (LCM) is a recently licensed antiepileptic drug available in the UK since 2008. It is thought to act through modulation of sodium channel slow inactivation. Its efficacy and tolerability have been shown in several regulatory randomised controlled trials, but assessments of its performance in large naturalistic settings are rare.

**Methods:** We assessed a large cohort of consecutive people who started LCM at a single tertiary epilepsy centre, from June 2008 to June 2011.

**Results:** Forty-five percent of the 380 people included were still taking LCM at last follow-up, with estimated retention was 62% at 1 year, 45% at 2 years and 35% at 3 years. Eighteen percent reported a period of improvement in terms of significant seizure reduction or seizure freedom of at least 6 months duration whilst on LCM, of whom four people were seizure free for at least 1 year. Long term efficacy appears similar to zonisamide and pregabalin in previous retention studies from our centre. Adverse events were reported by 61%, CNS-related in the vast majority. Most clinical factors did not affect retention; withdrawal occurred more often because of inefficacy than because of adverse events.

**Conclusion:** Retention rates for LCM appear similar to lamotrigine, topiramate, pregabalin, zonisamide, higher than gabapentin, and lower than levetiracetam.

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## P219

### A POST-HOC EXPLORATORY ANALYSIS OF THE EFFECT OF ESLICARBAZEPINE ACETATE AS ADJUNCTIVE THERAPY IN ADULT PATIENTS WITH PARTIAL-ONSET SEIZURES AND COMORBID CLINICALLY RELEVANT DEPRESSIVE SYMPTOMS

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**Purpose:** To evaluate the efficacy and tolerability of eslicarbazepine acetate (ESL) as adjunctive therapy in adult patients with partial-onset seizures (POS) and co-morbid clinically relevant depressive symptoms.

**Method:** Data from two (BIA-2093-301 and -302) phase III multicentre, double-blind, randomized, placebo-controlled studies in adult patients with  $\geq 4$  POS per 4 weeks despite treatment with 1–3 antiepileptic drugs was pooled. ESL efficacy and tolerability was analysed in subjects with baseline Montgomery-Asberg depression rating scale score (MADRS)  $\geq 10$  and  $< 10$ .

**Results:** Safety population comprised 796 patients (MADRS  $\geq 10$ ,  $n = 325$ ; MADRS  $< 10$ ,  $n = 471$ ) and intention-to treat population included 751 patients (MADRS  $\geq 10$ ,  $n = 303$ ; MADRS  $< 10$ ,  $n = 448$ ). Compared with placebo, seizure frequency was significantly reduced with ESL 800 mg and 1200 mg both in patients with MADRS score  $\geq 10$  ( $p = 0.03$  and  $p = 0.004$ , respectively) and with MADRS score  $< 10$  ( $p = 0.0007$  and  $p = 0.0003$ , respectively). Responder rate was: MADRS score  $\geq 10$  group = 13% with placebo, 32% with ESL 800 mg and 35% with ESL 1200 mg; MADRS score  $< 10$  group = 23% with placebo, 39% with ESL 800 mg and 49% with ESL 1200 mg. Incidence of treatment-emergent adverse events was similar in MADRS score  $\geq 10$  group (55.8% with placebo, 63.4% with ESL 800 mg and 73.8% with ESL 1200 mg) and in MADRS score  $< 10$  group (45.6% with placebo, 69.2% with ESL 800 mg and 67.0% with ESL 1200 mg).

**Conclusion:** Once-daily ESL 800 mg and 1200 mg adjunctive therapy was significantly superior to placebo in reducing POS in adult patients with co-morbid clinically relevant depressive symptoms.

*These studies and post-hoc analysis were sponsored by Bial – Portela & C<sup>a</sup>, S.A.*

## P220

### A COMPARISON OF ANNUAL HEALTHCARE COSTS AND UTILIZATION BETWEEN ADULT PATIENTS WITH LONG AND SHORT ACTING ANTIEPILEPTIC MONOTHERAPY

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**Purpose:** Adherence to antiepileptic drugs (AEDs) is imperfect and AEDs of long half-life or duration of action (e.g., extended release) might mitigate the impact of missed doses. We compared costs and utilization between patients treated with long-acting (LA) and short-acting (SA) AED monotherapy.

**Method:** We conducted a retrospective claims database analysis of adults with  $\geq 1$  epilepsy diagnosis in 2010 and 2011, who used AED monotherapy and were continuously enrolled in 2011. Patients were excluded if they had  $< 2$  AED fills,  $< 9$  months of treatment, or a treatment gap  $> 60$  days. AEDs were classified as LA or SA. Medical utilization and cost were estimated using pharmacy and medical claims, with multivariate analyses adjusting for baseline differences.

**Results:** There were 4,058 (49.6%) LA vs. 4,122 (50.4%) SA users (mean age: 47.7 vs. 45.1 years, female: 47.6% vs. 57.0%, epilepsy-specific comorbidities: 19% vs. 25%; all  $p < 0.001$ ). Compared to SA users, LA users had lower mean overall (\$9,757 vs. \$12,689) and epilepsy-

related costs (\$3,539 vs. 5,279) and lower overall (8.7% vs. 10.8%) and epilepsy-related hospitalization (5.7% vs. 7.5%) (all  $p < 0.01$ ). After adjusting for baseline demographic and clinical characteristics, mean overall costs were lower by \$686 ( $p = 0.137$ ) and epilepsy-related costs by \$894 ( $p = 0.005$ ) in LA users vs. SA users.

**Conclusion:** LA AED monotherapy result in lower costs than SA AED monotherapy, indicating that AEDs with extended duration of action between doses decreased healthcare use and economic burdens. Future studies should examine the impact of LA AED in combination therapy.

## P221

### TWO-YEAR CLINICAL EXPERIENCE WITH ESLICARBAZEPINE ACETATE IN A TERTIARY HOSPITAL IN OPORTO, PORTUGAL

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**Introduction:** Eslicarbazepine acetate (ESL) is a new antiepileptic drug, approved in 2009 by the European Medicines Agency for adjunctive therapy of partial-onset epilepsy in adults. It is commercially available in Portugal since April 1st 2010. Despite good safety and efficacy shown in clinical trials, little is known about its efficacy and safety in clinical practice.

**Purpose:** Assess 2-year post-commercialization experience with ESL in our tertiary centre.

**Method:** All outpatients who initiated treatment with ESL between April 1st 2010 and March 31st 2012 were included, except those who had entered ESL clinical trials. We retrospectively collected data on demographics, clinical features, treatment response and side effects using a standardized data sheet.

**Results:** We included 154 patients, 79 (51.3%) women. Mean age at ESL initiation was 38.4 years-old (SD = 14.2), mean epilepsy duration 26.8 years (SD = 13.0) and median seizure frequency 10 seizures/month. At baseline, 57.8% of patients were taking  $\leq 2$  antiepileptic drugs (AEDs). Responder rates at 6, 12, 18 and 24 months were 31.8%, 34.1%, 28.8% and 25.8%, respectively. Favorable Global Clinical Impression rates at 6, 12, 18 and 24 months were 26.4%, 27.3%, 25.4% and 19.4% respectively. Retention rates at 6, 12, 18 and 24 months, were 83%, 69.3%, 57.8% and 32.4%, respectively. Fifty-one patients (33.6%) discontinued ESL, 30 (58.8%) due to side effects and 15 (29.4%) due to lack of efficacy.

**Conclusion:** Clinically relevant improvements were achieved in a significant proportion of patients. Global tolerability was good, with no severe side effects and no new safety issues observed. This study confirms ESL usefulness in a clinical setting.

## P222

### COMPARATIVE EFFECTIVENESS OF PERAMPANEL IN THE TREATMENT OF REFRACTORY PARTIAL ONSET SEIZURES RESULTS FROM BAYESIAN NETWORK META-ANALYSIS

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**Purpose:** Despite the availability of many anti-epileptic drugs (AED), one third of patients continues to have seizures and therapies that improve patients' outcomes are warranted. Primary objective is to compare the clinical efficacy and tolerability of perampanel relative to other recently approved AEDs (lacosamide, retigabine, and eslicarbazepine) for the adjunctive treatment of partial onset seizures. Secondary objective is to compare its efficacy among patients with secondary generalization.

**Method:** EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials from 1998 to September 2011, abstracts from selected 2010 and 2011 conferences, reference lists of included studies and unpublished study reports were searched. Odds-ratios for: ">50% reduction in seizure frequency", "seizure freedom" and "withdrawal due to adverse events" were estimated using conventional and network meta-analysis. Sensitivity analyses were performed to assess robustness of the treatment effect.

**Results:** For the primary objective, all AEDs performed significantly better than placebo for all outcomes with no significant difference between the AEDs when compared to each other. Sensitivity analyses for studies with patients who were heavily treated (>10% with  $\geq 3$  concomitant AEDs) and high baseline seizure frequency (>10/28 days) did not change the main results. For the secondary objective, data was only available for one comparator (lacosamide) and one outcome (">50% reduction in seizure frequency"). In this patient population, perampanel performed similar to lacosamide.

**Conclusion:** Compared with other licensed adjunctive AEDs, perampanel offers similar clinical efficacy and tolerability profile. This remained true for patients with secondary generalization and heavily treated subpopulations.

## P223

### ACSM 2A AND CPT 1A GENE POLYMORPHISMS ASSOCIATED WITH VALPROIC ACID-INDUCED HEPATOTOXICITY IN CHINESE PATIENTS WITH EPILEPSY

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**Purpose:** Mitochondrial  $\beta$ -oxidation (FAO) pathway accounts for more than 40% of the in vivo biotransformation of valproic acid (VPA). However, the effects of medium-chain acyl-CoA synthetase (ACSM) and carnitine palmitoyltransferase I (CPT I) polymorphisms, two rate-limiting enzymes in FAO pathway responsible for VPA metabolism, on the plasma concentrations of VPA or 4-ene-VPA and they induced hepatotoxicity have never been assessed. The present study is to investigate the expression and activity of ACSM and CPT I in VPA pharmacokinetics and hepatic functions in Chinese patients with epilepsy.

**Method:** Ninety-one Chinese patients with epilepsy who took divalproex sodium and eighty-seven Chinese healthy controls without taking any drug were recruited. ACSM2A and CPT 1A polymorphisms were genotyped and the plasma concentrations of VPA and 4-ene VPA were determined. In addition, the serum levels of ALT, AST, GGT and ALP were detected to evaluate the hepatic functions of all subjects.

**Results:** We found that variation of ACSM2A rs1133607 was significantly associated with the 4-ene VPA concentrations ( $p = 0.034$ ) and serum levels of ALT ( $p = 0.014$ ) and GGT ( $p = 0.027$ ) in patients. Furthermore, significant correlation was also observed between the variation of CPT IA rs597316 genotypes and VPA concentrations ( $p < 0.05$ ). However, no significant correlation was observed between the polymorphisms of ACSM2A and CPT IA and hepatic functions in healthy controls without VPA intake.

**Conclusion:** Determining the genotypes of rs1133607 and rs597316 is helpful to reduce the risk of toxicity and optimize VPA therapy in Chinese patients with epilepsy.

## P224

### CHILDREN (10–12 YEARS AGE) OF MOTHERS WITH EPILEPSY HAVE LOWER LANGUAGE PERFORMANCE

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**Purpose:** To compare the language function of children of mothers with epilepsy (CME) with that of children of mothers without epilepsy (CMO).

**Method:** CME (aged 10–12 years) under follow up in the Kerala Registry of Epilepsy and Pregnancy ( $n = 170$ ) were evaluated with Clinical Evaluation of Language Fundamentals version 4 and compared with 143 age and sex matched CMO drawn from schools in the same region.

**Results:** Maternal epilepsy was generalized (88), Localization Related Epilepsy (78) or Unclassified (20). Antenatal AED exposure was No AEDs for 14, monotherapy 100 (phenobarbitone 20, phenytoin 9, carbamazepine 36, valproate 33, others 2), polytherapy 56. Maternal IQ was comparable for the two groups ( $83.9 \pm 12.5$  vs  $81.5 \pm 11.7$ ). Core Language Standard Score (CLSS) for the CME ( $83.0 \pm 17.1$ ) was significantly lower than that of CMO ( $89.9 \pm 15.7$ ). The CME had significantly lower standard score than CMO for Receptive language ( $87.4 \pm 15.3$  vs  $91.7 \pm 14.0$ ), Expressive language ( $86.6 \pm 17.9$  vs  $95.0 \pm 17$ ), Language content ( $95.4 \pm 19.3$  vs  $101.7 \pm 17.2$ ), Language memory ( $76.4 \pm 16.8$  vs  $83.9 \pm 16.5$ ) and Working memory ( $85.3 \pm 15.6$  vs  $94.2 \pm 17.6$ ). The CLSS was significantly low for those exposed to phenobarbitone ( $79.9 \pm 19.0$ ) when compared to those exposed to other AEDs ( $85.7 \pm 15.4$ ). Polytherapy was associated with significantly low CLSS ( $79.5 \pm 16.5$ ) compared to monotherapy ( $86.0 \pm 16.5$ ). There was a significant correlation between the mental development quotient at 1 year of age and CLSS at 12 years of age for the CME.

**Conclusion:** CME had lower language performance than CMO and exposure to phenobarbitone or polytherapy was associated with significantly lower language scores.

## Poster Session: Epilepsy in the Elderly Monday, 24 June 2013

### P225

#### EPILEPSY EMERGENCY CARE IN THE ELDERLY: A PATIENT SURVEY

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**Purpose:** People with epilepsy over 50 years of age, require professional emergency care with expertise in this age group. Semiology, risks and treatment as well as co-morbidities are different in older compared to younger patients. Because of limited experience with emergency care in older epilepsy patients, a patient survey was performed.

**Method:** Patients older than 50 years were included. A special questionnaire was developed in order to explore patients' experiences and special needs during emergency situations.

The analysis of answers of 300 patients using internet online and paper pencil is intended.

The open and observational study was accompanied and supported by self help groups, NGOs and internet platform. The project started 2012 and will be finished in 2013.

**Results:** The first results of 31 patients – including the developed special questionnaire – of the ongoing study will be presented providing new insights in the epilepsy emergency care in patients older than 50 years. The average age is 60 years. 64.5% of the patients reported injuries suffered during a seizure. 81% of the patients were referred to hospital although they objected. 30% of the patients were admitted to a general hospital.

**Conclusion:** The results of the study can contribute to the better recognition of special conditions with regard to emergency treatment of elderly patients with epilepsies.

### P226

#### POST STROKE SEIZURES AND EPILEPSY: PREVALENCE AND RISK FACTORS IN A POPULATION BASED STUDY

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**Purpose:** To determine prevalence and risk factors for early-onset seizures (EOS; those occurring  $\leq 14$  days after a stroke), "late-onset seizures" (LOS; those occurring  $> 14$  days after a stroke) and post stroke epilepsy (PSE).

**Methods:** This study is part of a 2-year prospective community-based registry of all cerebrovascular events in the district of Udine (153,312 inhabitants), North-Eastern Italy, between 4-1-2007 and 3-31-2009. Multiple overlapping sources for case ascertainment were used, combining hot and cold pursuit. TIAs were excluded.

**Results:** Seven hundred and eighty-two cases of stroke (79.28% ischemic, 14.83% hemorrhagic, 3.20% subarachnoid hemorrhage and 2.69% undetermined) were identified. Prevalence of EOS, LOS and PSE was 5.10%, 3.14% and 2.22%, respectively. Hemorrhagic stroke, subarachnoid hemorrhage, stroke of undetermined origin and hyposodemia, represented risk factors for EOS ( $p < 0.05$ ). Within the subpopulation of ischemic strokes, EOS risk factors were: hyposodemia (OR = 4.00;  $p = 0.024$ ) and hemorrhagic infarction (OR = 3.12;  $p = 0.046$ ). The typical location of the hemorrhage was a protective factor for EOS within hemorrhagic strokes (OR = 0.16;  $p = 0.011$ ). LOS risk factors were younger age (OR = 0.96;  $p = 0.004$ ) and cortical location of stroke (OR = 4.05;  $p = 0.004$ ). Within ischemic strokes risk factors were youn-



ger age (OR = 0.96;  $p = 0.020$ ) and cortical location (OR = 9.68;  $p < 0.0001$ ). Within hemorrhagic strokes the only risk factor for LOS was the presence of a previous EOS (OR = 8.08;  $p = 0.017$ ). PSE risk factors were the same as for LOS [younger age (OR = 0.94;  $p < 0.0001$ ) and cortical location (OR = 5.05;  $p = 0.006$ ].

In addition, the secondary outcome of mortality at 1 and 24 months will be presented and discussed.

**Conclusions:** All acute and treatable conditions related to the occurrence of stroke are implicated in the pathogenesis of EOS, which is a risk factor for LOS only in the setting of hemorrhagic stroke. Therefore only in this situation and not when EOS are due to ischemic stroke, an early treatment with AED is needed.

## P227

### THE EFFICACY OF LOW-DOSE ADMINISTRATION OF LEVETIRACETAM FOR ELDERLY JAPANESE

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**Purpose:** Levetiracetam (LEV) was introduced to Japan in 2010 and recommended as an antiepileptic drug for partial seizures in the elderly. We evaluated the efficacy of LEV with both low- and regular-dose administrations.

**Methods:** The subjects were patients who visited our hospital with epileptic seizures and were prescribed LEV from September 2010 until October 2012. We investigated clinical information such as the age, gender, response to treatment, number of tried antiepileptic drugs or other medications, and adverse effects. Follow-up periods were over 3 months, and we judged subjects as <50% responders when the seizure frequency decreased to less than 50% or they were seizure-free.

**Results:** Sixty-two patients were administered LEV. Among them, 37 patients were elderly, aged 65 years of age or older ( $79.2 \pm 7.68$  years old). They consisted of 16 males and 21 females. Six patients were excluded because of their seizure diagnosis in three and death unrelated to seizures in three. The mean dose was  $945.9 \pm 482.8$  mg/day. In the low-dose group (14 patients,  $78.6 \pm 7.80$  years old, administered 250–500 mg/day), nine patients (64.3%) were <50% responders. In the regular-dose group (17 patients,  $78.8 \pm 7.65$  years old, 1,000–2,000 mg/day), 15 patients (88.2%) were <50% responders. Numbers of tried antiepileptic drugs (low-dose group:  $2.93 \pm 1.00$ , regular-dose group:  $2.88 \pm 1.32$ ) and other medications (low-dose group:  $3.21 \pm 2.78$ , regular-dose group:  $3.94 \pm 3.11$ ) did not show a significant difference. Adverse effects occurred and LEV was discontinued in 3 (21.4%) in the low-dose group and 2 (11.8%) in the regular-dose group because of drowsiness or aggression. Two patients discontinued LEV for economic reasons.

**Conclusion:** Levetiracetam was effective for epileptic seizures in elderly Japanese not only at regular but also lower doses. The efficacy should be evaluated from an economic point of view.

## P228

### TRENDS IN THE TREATMENT OF NEW-ONSET EPILEPSY IN THE ELDERLY

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**Purpose:** Newer generation anti-epileptic drugs (AED) have been recommended as first-line therapy of new-onset epilepsy in the elderly rather than first generation AED (Glauser T et al. *Epilepsia* 2006; 47: 1094–1120), mostly due to concerns over tolerability issues and potential

cognitive adverse effects. It is unclear how practice patterns have changed with these recommendations.

**Method:** We undertook a retrospective observational study to assess treatment patterns for patients 65 years or older diagnosed with new-onset epilepsy between 2001 and 2010 at a tertiary care Neurology Department in Sherbrooke, Canada. Charts from patients identified using an electronic database containing discharge diagnoses were reviewed. Patients with acute symptomatic seizures were excluded. The protocol received approbation from the local Research Ethics Committee.

**Results:** We present the results for 328 consecutive cases. Mean age was 77. There was a significant change in the proportion of patients receiving a suboptimal medication. From 2001 to 2005, this was the case for 121 out of 155 patients (78%, mostly phenytoin); from 2006 to 2010, this proportion fell to 49% (Khi-square;  $p$  less than 0.001). Levetiracetam was the most frequent AED in the last 3 years. Etiologies were: vascular 36%, tumour 15%, cognitive disorders 6%, trauma 4% and undetermined 39%. EEG was performed in 302 patients and revealed epileptic abnormalities in 40% of cases.

**Conclusion:** Our data indicate a trend towards the use of more appropriate medications for elderly patients in the years since the recommendations were published, but phenytoin remains widely used.

## P229

### EPILEPSY IN ELDERLY: EPIDEMIOLOGICAL FEATURE AT DOUALA LAQUINTINIE HOSPITAL

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**Purpose:** The aim of this study was to determine the prevalence and aetiologies of epilepsy in the elderly at Douala Laquintinie hospital, reference center in this town.

**Method:** A cross sectional, prospective and descriptive study was conducted at Douala Laquintinie hospital over a period of 7 months, from January to July 2012. Our study focused on epileptic patients of both sexes, who consulted neurologists for seizures. Among them we have sought those with age greater than 60 years and had at least two epileptic seizures in the past 12 months.

**Results:** Fifty patients were recruited, 26 male (52%) and 24 female (48%). The mean age of our study population was  $67.36 \pm 6.10$  years, with extremes of 60 and 84 years. The prevalence of epilepsy at Laquintinie hospital was 12.47%, and epilepsy in the elderly was 3.7% which represented 30% of epileptic patients. Stroke (38% of cases), were the leading cause of epilepsy in the elderly, followed by brain tumors (5%) and cerebral toxoplasmosis (3%).

**Conclusion:** The prevalence of epilepsy in the elderly in our study was 3.7% and represented 30% of epileptic patients. Aetiology was found in 50% of patients and stroke was the most frequent.

## P230

### EPILEPSY A POTENTIAL REVERSIBLE ETIOLOGY OF DEMENTIA: CASE SERIES FROM NAIROBI, KENYA

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**Purpose:** To determine the role of epilepsy on dementia.

**Method:** A review of case notes of patients with Dementia in a private neurology practice bias at the Agha Khan University Hospital in Nairobi, Kenya.

**Results:** Four patients with dementia and epilepsy were seen over the past 1 year. Three males and one female. Mean age of 77 years, mean age of onset 74 years. All the four patients suffered stroke and were reported to have hypertension. Two of them had vitamin B 12 and vitamin D deficiency. On average, their MSE score was 9/30. Neuroimaging revealed that all the four patients had atrophic changes with absent alpha on EEG. All of them were on cholinesterase inhibitors and no major side effects noted. They all remained on follow up some reporting improvement or stability in symptoms. They all were dependent on activities of daily living.

**Conclusion:** Dementia, an age related non communicable chronic disease, is among the major causes of death and disability in developed countries however its incidence is on the rise in developing world in tandem with the ageing society. Might epilepsy be associated with dementia and cognitive impairment? We present data on 4 well documented patients with dementia and cognitive impairment from a private referral neurological practice in Kenya, with epilepsy being a potential reversible cause of dementia among them. However, basic science investigations are greatly needed to determine the influence of epilepsy on brain degeneration and cognitive impairment. Study of the effects of epilepsy on the brain in relation to dementia may create a window for providing an avenue for future interventions. In addition, the interesting clinical material available for research and the gnawing need for epilepsy and cognitive disorder service will be highlighted as will the need for locally appropriate screening and specialized care.

## Poster Session: Epilepsy Surgery A Monday, 24 June 2013

### P231

#### HEMISPHERIC DISCONNECTION FOR INTRACABLE EPILEPSY

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**Purpose:** The aim was to introduce the seizure outcomes and neurological deficits on hemispheric disconnection treatment for intractable epilepsy caused by hemispheric lesions; Surgical indications were described as well.

**Method:** We retrospectively studied eight cases of refractory epilepsy treated with multi-lobe disconnection of the cerebral hemisphere from 2009 to 2011. Every patient had an extensive lesion in hemisphere, while the motor and sensory functions of the Rolandic region were remained. The operation was intended to preserve the Rolandic region and its connections with the thalamus, basal ganglia and internal capsule. Other links across the frontal, temporal, parieto-occipital lobes and anterior and posterior parts of the corpus callosum were disconnection. Data collection included seizure outcomes: Seizure frequency was determined using the modified classification of Engel and colleagues; and neurological deficits. The follow-up duration was from 6 months to 2 years.

**Results:** At the end of follow-up, five cases achieved Engel I class, three cases were Engel II class. Especially, two cases seizure accompanied with reflection seizure were seizure free after operation. Three patients did not show any new neurological deficit postoperatively, three cases showed starting difficult in move and indifference. They were recovered 3 months later. Two cases persisted muscle weakness.

**Conclusion:** The multi-lobe disconnection of the cerebral hemisphere can effectively treat the patients with refractory epilepsy caused by severe hemispheric lesions. This operation is particularly indicated to the patients with hemispheric lesion, but without the deficit of the motor, sensory and language functions of the hemisphere.

### P232

#### SURGICAL TREATMENT STRATEGY FOR DRUG-RESISTANT EPILEPSIES: CHRONOTOPOLOGY OF NEUROPHYSIOLOGIC INDICATORS OF EARLY AND LATE EPILEPTOGENESIS

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**Purpose:** To research neurophysiologic mechanisms of epileptogenesis and to optimize adequate surgical treatment in drug-resistant temporal epilepsy.

**Method:** Electroclinical examination and surgical treatment results in over 200 drug-resistant temporal epilepsy patients aged 19–50 were analyzed. Algorithm including neurophysiologic (monitoring EEG, ECoG, SEEG with topographic brain map via deep electrodes) and visualizing (MRI, SPECT) technologies to study dynamics of epileptogenesis in the process of epileptic syndrome forming has been elaborated.

**Results:** A strict-indications protocol to surgical patient selection was developed. Based on critical chronotopology of electrographic trait-markers particularities of preclinical (initial), early (temporal) and late (extratemporal) epileptogenesis were depicted reflecting clinical-neurophysiologic forms of focal and multifocal temporal epilepsy. Monotemporal epileptogenesis is characterized by peculiar localization of the epileptic focus: in our series ECoG-SEEG studies revealed a combined neocortical and limbic (hippocampus, amygdala) damage in 79% of patients. This optimizes technology of open surgical treatment (anterior temporal lobectomy) with additional use of multiple subpial transection in eloquent cortex. Morphofunctional basis of extratemporal links of epileptogenesis is amounted by integral brain systems: according to EEG-SEEG data limbic-brainstem pathways of epileptization were followed-up – hippocampus and amygdala via thalamic nuclei are involved in cyclic Papez, Nauta and Livingston-Escobar-Yakovlev systems, forming multifocal forms, which is of importance in neuromodulating interventions.

**Conclusion:** Our results show that neurophysiologic indicators appear a reliable method to evaluate regularities and chronotopology of epileptogenesis at the cortical, limbic and brainstem structure levels. The dynamics of epileptogenesis optimizes strategy of differentiated surgical treatment of drug-resistant focal and multifocal temporal epilepsy.

### P233

#### RESECTION OF FRONTAL LOBE EPILEPTOGENIC FOCI IDENTIFIED AFTER CORPUS CALLOSOTOMY: LONG TERM RESULTS

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**Purpose:** To analyze the results of resective surgery in patients in which it was possible to identify a frontal epileptogenic zone after corpus callosotomy.

**Method:** We prospectively reviewed data from drug resistant epilepsy patients who showed persistence of disabling seizures after performing a corpus callosotomy and posteriorly were treated with frontal lobe resective surgery. There were evaluated classifications according the Engel's scale before and after each surgery and the percentage of seizure reduction. Additionally the satisfaction of family members with surgical outcomes was also assessed.

**Results:** Eleven patients were identified. After a mean follow-up of 6.2 years, 63% of patients showed improvement of seizures as classified

in the Engel's scale, 27% remained unchanged and one worsened. A patient was categorized into class I, eight in class II, one in class III and one in class IV. The percentage of seizure number reduction was higher than 90% in 55% of the patients, between 50% and 90% in 36% and less than 50% in 9%. Family satisfaction was esteemed good or excellent in 91% of cases.

**Conclusion:** Besides providing a better seizure control, corpus callosotomy appears also to be a diagnostic tool that allows the identification of potential targets for resective surgery and therefore should be especially considered when there is a suspected frontal epileptogenic focus that could be surgically treated.

#### P234 THE SURGICAL TREATMENT OF HEMISPHERIC LESIONAL EPILEPSY

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**Objectives:** Retrospectively analyze the surgical treatment of 25 cases with hemispheric lesional epilepsy to explore its surgical strategy.

**Methods:** Between March 2005 and July 2012, there were 25 cases met the selection criteria among all patients admitted to our department. There were 16 males and nine females, ranging in age from 4 months to 29 years (mean 11.61 ± 7.84) with average onset age of 4.76 ± 4.70. Preoperative IQ was 56.1 ± 11.8 (except 4 uncooperative cases).

**Results:** There were 17 cases with epileptogenic zone in the left hemisphere and the rest eight cases in the right. Twelve cases without main neurological function in lesional hemisphere (motor and language); in contrast, six cases probably had those main neurological function and rest seven cases definitely had, in the lesional hemisphere, and cortical electrical stimulation was performed during surgery on these 12 cases to mapping eloquent areas. Hemispherectomy was performed in 17 cases, and rest 8 had combined operations with rolandic area preservation. Following up of those patients for 3–90 months (mean 44.8 ± 27.1 months) indicated the seizure control conditions were Engel I 22 cases (88%) and Engel II 3 cases (12%), and respectively, the patients performed hemispherectomy were Engel I 16 cases (94.1%) and Engel II 1 case (5.89%), and patients performed combined operations with rolandic area preservation were Engel I 6 cases (75%) and Engel II 2 cases (25%). Furthermore, postoperative IQ of those patients was 63.6 ± 16.1, and their character changed in better way like more docile and obedient.

**Conclusion:** For patient with hemispheric lesional epilepsy, medical treatment is disappointed, while surgery treatment is effective. Hemispherectomy is more effective in seizure control than combined operations with rolandic area preservation. For selection of surgical strategy, except the nature of lesion, the remained function of the lesional hemisphere is a vital factor.

#### P235 BILATERAL COAGULATION FOR TEMPORAL LOBE EPILEPSY: A PATIENT RESEARCH

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**Purpose:** To search a method for treatment of bilateral temporal lobe epilepsy.

**Method:** One case which was confirmed as bilateral temporal lobe epilepsy by video scalp EEG recordings, dipole source localization and

intracranial depth electrodes recordings, experienced radiofrequency thermocoagulation of the bilateral amygdalohippocampals under the navigation of depth electrodes recordings. Neuropsychological examinations were performed before, 5 days, 18 months, 30 months, and 49 months after the operation subsequently.

**Results:** No seizure occurred in the follow-up period of 49 months. No long term memory and intelligence deficits correlated with coagulation were found except for a transiently decline 5 days after operation and a significantly improvement during 18 months.

**Conclusion:** Since the severe damage of memory in resective surgery, stereotactic radiofrequency thermocoagulation of bilateral amygdalohippocampals under the circumstances of limited lesions should be considered as a possible approach to treat bilateral temporal lobe epilepsy for seizures control.

#### P236 STEREOTACTIC TREATMENT FOR BILATERAL TEMPORAL LOBE EPILEPSY

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**Purpose:** To evaluate the effects of seizure control and neuropsychological affections of bilateral amygdalohippocampotomy for the treatment of bilateral temporal lobe epilepsy.

**Method:** Twelve patients with bilateral temporal lobe epilepsy, which diagnosed by intracranial depth electrodes recordings, were analyzed retrospectively. Stereotactic radiofrequency amygdalohippocampotomy (SAHE) was performed under the deep electrode guidance in all these patients. Neuropsychological examinations with Wechsler Adult Intelligence Scale-Revised (WAIS-R) and Wechsler Memory Scale-Revised (WMS-R) were performed before, 5 days and 6 months after operation subsequently.

**Results:** The patients were followed-up for 12–49 months, five patients were assessed as class I, 2 as class II, 3 as class III and the other 2 as class IV respectively according to Engel's classification. Postoperatively MRI showed no severe structural damage in the areas of bilateral amygdalohippocampal complex. No long term memory and intelligence deficits correlated with the coagulations were found except for a transiently decline in 5 days after operation but significantly improved after 6 months.

**Conclusion:** The resection surgery is unsuitable for bilateral temporal lobe epilepsy, while stereotactic surgery can reduce seizures and not result in severe neuropsychological dysfunction under the circumstances of limited lesions, thus being worthy attempted for the treatment of bilateral temporal lobe epilepsy.

#### P237 DOES THE LOCALIZATION OF THE EPILEPTOGENIC ZONE DETERMINE CLINICAL COURSE AND CLINICAL FACTORS OF INTRACTABLE EPILEPSIES: A RETROSPECTIVE INVESTIGATION OF SURGICALLY TREATED PATIENTS

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**Purpose:** Epilepsy surgery provides an effective method to achieve seizure freedom but is often delayed due to intermittent remissions in the course of disease. The aim of our study was to investigate the influence of localization of the epileptogenic zone on the course of disease and time to refractoriness.

**Method:** Retrospective, hospital-based study on 200 pts. with focal epilepsy who had received epilepsy surgery between 1998 and 2009. We grouped the pts. into temporal lobe (TLE) and extratemporal lobe epilepsy (ETE). Clinical factors and the course of disease were extracted from patients' charts, intractability was defined according to four definitions (Surgery definition, Connecticut definition, Canada Definition, ILAE definition).

**Results:** One hundred and seventy-four points (median age 45.2 years, range 15.2–57.3) met the inclusion criteria (86 W, 49.4%), 148/174 pts. (85.1%) with TLE and 26/174 pts. (14.9%) with ETE. Median time to refractoriness as defined by four different definitions was 10 years (range 0.4–53.0) in pts. with TLE and 8.6 years (range 0.8–28.9) in those with ETE ( $p = 0.560$ ). Median time to surgery was 23.1 years (range 1.0–57.8) in pts. with TLE and 18.9 (range 1.2–53.1) in pts. with ETE. Intermittent remissions ( $\geq 1$  year) occurred at least once throughout the course in 86/174 pts. (49.4%) (TLE 48.0% vs. ETE 57.7%,  $p = 0.640$ ). Surgical outcome in 70.6% (123/174) (Engel class I) and 74.1% (129/174) (Wieser class I). The presence of localized spikes and sharp waves ( $p = 0.002$ ), as well as detection of ictal pattern ( $p = 0.015$ ) in routine EEG occurred more frequently in patients with TLE.

**Conclusion:** Intermittent remissions occurred in at least half of the patients prior to surgery. The results underline the assumption that the localization of the epileptogenic zone is not a major determinant for the clinical course and time to refractoriness in this sample of surgically treated patients.

## P238

### EPILEPSY SURGERY IN A 4-YEAR OLD WITH IDIOPATHIC INFANTILE SPASM: A CASE REPORT

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Seizure has become a classic topic for neuropediatrician. Infantile spasm is a catastrophic childhood epilepsy syndrome with its associated mental retardation. Its resistance to pharmacotherapy results to a massive drain on health care resources. Epilepsy is a diverse condition with only a subset of epilepsy syndrome being amenable to neurosurgical treatment. Surgical candidacy and subsequent seizure control is determined by identification of "epileptogenic zone." Clinical history coupled with further presurgical diagnostic evaluation of a particular candidate for surgery should be made before subsequent planning of surgical strategy.

We reviewed a case of intractable idiopathic infantile spasm in a 4-year old patient and collectively summarized the interesting features from the onset of epilepsy syndrome and preceding surgical treatment. The challenge in this case is the absence of localized lesion and with generalized ictal patterns on pre-operative evaluation. This limitation of the role of surgery in this patient was overcome by implantation of subdural electrodes to precisely define the region of epileptogenicity.

## P239

### FINALLY SEIZURE-FREE AFTER EPILEPSY SURGERY: RUNNING DOWN PHENOMENON OR POSITIVE INFLUENCE OF POST-OPERATIVE ANTI-EPILEPTIC DRUG (AED) TREATMENT CHANGES

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**Purpose:** Epilepsy surgery offers a real chance of seizure freedom in thoroughly pre-selected patients with drug resistant epilepsy. While most of the patients get immediately seizure-free after surgery, seizures may persist in some patients in the first post-operative years. We investigated if delayed seizure remission might be due to changes of post-operative AED treatment.

**Method:** We assessed the long-term post-surgical follow-up as well as information about pre- and post-operative medical treatment of 340 adult patients of the Kork Epilepsy Centre. By means of this data collection we were able to identify patients with the so called running down phenomenon.

**Results:** Thirty-nine (11.5%) of 340 patients still had experienced frequent seizures including auras during the first years after surgery whereas no seizures were reported anymore at the time of the last recent observation for more than two consecutive years. Thirty-three (85%) of these 39 patients had undergone temporal lobe resections. AED treatment was changed post-operatively in 17 of those patients. Thirteen patients received levetiracetam additionally to their pre-operative AEDs or in exchange with one of the pre-operative AEDs. In four further patients other AEDs than levetiracetam were contributed. Otherwise 16 patients remained on their pre-operative AED treatment and in six patients AEDs had even been tapered or discontinued before they became completely seizure-free.

**Conclusion:** Post-operative AED changes, as the administration of levetiracetam might have a positive impact on the long-term outcome. Other factors previously described in the literature such as the size of the epileptogenic zone may also contribute.

## P240

### LONG-TERM ANALYSIS OF POST-OPERATIVE HIPPOCAMPAL VOLUME ON NON-EPILEPTIC SIDE USING MR VOLUMETRY IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Magnetic resonance (MR) volumetry studies have showed longitudinal decreases of the hippocampal volume (HV) in patients with newly diagnosed focal epilepsy. We examined the long-term hippocampal volume (HV) changes after contralateral hippocampectomy in patients with mesial temporal lobe epilepsy (MTLE) to elucidate if non-epileptic hippocampal damage was progressive after surgery.

**Method:** We measured HV on 1.5 Tesla-MR according to the Wu's method (AJNR, 2005) in 10 patients with typical MTLE and anterior temporal lobectomy (ATL). Serial MRI studies were followed-up at post-operative 1 and >2 years. HVs of patients were compared with those of age-matched controls ( $n = 14$ ), and the results were subjected to neuropsychological examination.

**Results:** No difference in age was observed between controls ( $35 \pm 11.3$  years; mean  $\pm$  SD) and patients ( $36.7 \pm 8.2$  years) at surgery. The seizure duration ranged from 15 to 37 years (mean: 27.5 years). The preoperative epileptogenic HV ( $0.97 \pm 0.34$  cm<sup>3</sup>) was significantly ( $p < 0.01$ ) smaller than the non-epileptic HV ( $1.61 \pm 0.40$ ). The preoperative non-epileptic HV was not significantly different from

HVs of controls (right:  $1.58 \pm 0.25$ ; left:  $1.54 \pm 0.21$ ). During the follow-up (15–40 months), HVs of patients decreased at postoperative 1 ( $1.55 \pm 0.37$ ) and >2 ( $1.41 \pm 0.33$ ) years. There was a significant difference ( $p < 0.05$ ) between preoperative and postoperative (>2 years) HVs. All patients experienced no seizure after surgery. Neuropsychological examinations revealed a decline of memory function and/or intelligence in three of four patients with left MTLE and unchanged neuropsychological functions in six patients with right MTLE during the follow-up, and in fact improvements were observed in one patient.

**Conclusion:** The above findings suggest that achieving a good seizure control with surgery may not completely prevent further progressive hippocampal damage, although excessive seizures have once affected the non-epileptic hippocampus for an extended period before surgery. However, the extent of the volume decreases was not enough to affect the neuropsychological findings in this study.

#### P241 SURGICAL TREATMENT OF HYPERMOTOR SEIZURES ORIGINATED FROM TEMPORAL LOBE

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**Purpose:** To describe the characteristics of electro-clinical manifestations in patients with hypermotor seizure (HMS) which originated from temporal lobe.

**Method:** We retrospectively reviewed the data of patients who received surgical treatments to select the patients with HMS originated from temporal lobe. We systematically reviewed their seizure histories, imaging findings, video-EEG monitoring data, operative records and pathology findings.

**Results:** Eight of the nine patients experienced auras. The ictal behavior showed marked agitation in five patients and mild agitation in four patients. All the nine patients showed stiffness or dystonia of the upper limb or contralateral limbs during the ictal behaviors. Seven of the nine patients received intracranial recording. Totally, 23 seizures were recorded by the cortical electrodes, at least three seizures for each patient. The intracranial recordings showed ictal activities originated from mesial temporal in 6 and lateral temporal lobe in one patient. The time interval of ictal propagation from temporal to frontal lobe was  $15.0 \pm 8.3$  (3–28) seconds. The time interval from EEG origination to the beginning of hypermotor behavior was  $21.0 \pm 8.1$  (7–38) seconds, and from the frontal lobe involvement to the beginning of hypermotor behavior was  $6.0 \pm 6.8$  (0–22) seconds. In the recording, seven patients showed certain behaviors before the burst of hypermotor. MRI showed hippocampal sclerosis in 3, neoplastic lesion in 1, and normal images in other five patients. The pathology examination showed hippocampal sclerosis in 4, hippocampal sclerosis plus focal cortical dysplasia (FCD II) in 1, FCD or heterotopias in 3, ganglioglioma in one patient. The patients were followed up 1–5 years, and 7 of them were seizure free.

**Conclusion:** Some HMS can originate from temporal lobe. Though the complex functional network participated is not clear, frontal lobe may be involved. In carefully selected patients, surgical resection can have good outcome.

#### P242 MODIFIED FUNCTIONAL HEMISPHERECTOMY, A NEW SURGICAL CONCEPT FOR THE TREATMENT OF HEMIMEGALENCEPHALY IN OHTAHARA SYNDROME

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**Purpose:** Ohtahara syndrome or early infantile epileptic encephalopathy is a severe refractory to medical treatment epilepsy. Advocated surgical treatment for this condition did not prove its efficiency. We present a modified surgical technique for functional hemispherectomy to preserve motor function.

**Method:** We are reporting a 6 months old boy diagnosed to have tonic spasms since birth that starts in the left hemibody and then became generalized. Brain MRI showed right hemimegalencephaly. EEG showed burst suppression pattern predominant in the right hemisphere. The boy was operated for resection of his hemimegalencephaly. Surgery consists of temporal lobectomy with resection of supplementary motor area and callosotomy of the anterior two third of the corpus callosum.

**Results:** Seizure stopped after surgery. The infant motility was preserved in the left hemibody. He presents good eye contact and vocalization. Axial tone improved dramatically and he is able to maintain his head appropriately.

**Conclusion:** This is the first report of surgical resection of supplementary motor area for the treatment of hemimegalencephaly. We consider that resection of supplementary motor cortex is less harmful and have less burden on patients motor function. We hypothesize that temporal lobectomy; anterior callosotomy with supplementary motor area resection provides promising results in term of epilepsy control and preservation of motor function in previously intact patient.

#### P243 CLINICAL UTILITY OF VAGUS NERVE STIMULATION FOR PROGRESSIVE MYOCLONIC EPILEPSY

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**Purpose:** Progressive myoclonic epilepsy (PME) is a group of disorders in which myoclonus, mental retardation, cerebellar dysfunction and epileptic seizure are major components. The epileptic seizure is usually medically and open surgically resistant. The purpose of this study is to evaluate VNS efficacy for PME.

**Method:** Patient 1 is a 16 year-old right hand dominant man with mitochondria encephalomyelopathy with ragged-red fibers (MERRF). He had exhibited myoclonus and epileptic seizures since 12 years old. His seizure frequency was weekly. He also had been suffered from status epilepticus. He underwent VNS. Patient 2 is a 20 year old woman with Gaucher's disease type III. She has started exhibiting hands and face myoclonus and generalized seizure at the age of 13 years old. Her seizure frequency was daily. She also had been suffered from status epilepticus monthly. She underwent VNS.

**Results:** Patient 1 was followed up for 2 years. He has been free from seizure. However VNS did not work for cerebellar dysfunction and mental retardation. Patient 2 was followed up for 1 year and 10 months. Her seizure frequency has reduced gradually. She has become status epilepticus free after VNS. Her mental retardation and cerebellar symptoms have shown no remarkable change postoperatively.

**Conclusion:** VNS has efficacy for epileptic seizure and status epilepticus in patients with PME. However, VNS may not control myoclonus, cerebellar symptoms and mental retardation. As the epileptic seizure and status epilepticus reduce patients' quality of life, VNS can be one of the treatment options for medically intractable epilepsy in PME.

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### LOCATION DIAGNOSIS AND SURGERY FOR MEDICALLY REFRACTORY EPILEPSY: METHODS AND OUTCOME

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**Purpose:** To obtain further security and validity of epilepsy surgery by discussing the methods and outcome of location diagnosis and surgery for 255 patients.

**Method:** Located the epileptogenic cortex by long time V-EEG monitoring and MRI, PET, or MSI scans of brain. If scalp EEG monitoring failed to determine the location of the epileptogenic cortex, placed electrodes directly on the brain surface (subdural electrodes) or in the brain (depth electrodes). Electrical brain stimulation identified the location of vital brain regions (function mapping). Then some removed surgery was operated.

**Results:** Location diagnosis for most of the patients are accurate and the effects of surgery were good. The efficiency rate was 94.12%.

**Conclusion:** Long time V-EEG monitoring with MRI can accurately locate the seizure focus of most of the patients. For seizure focus in function area, using cortex electrodes monitoring can mostly excise the seizure focus and protect the function of the brain.

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### THE DYNAMIC CHANGES OF CSF AFTER TEMPORAL LOBE EPILEPSY SURGERY

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**Purpose:** To investigate dynamic changes of intracranial pressure, cell counts and biochemical components of cerebrospinal fluid (CSF) after temporal lobectomy or selective amygdalohippocampectomy. We try to summarize the relationship between cerebrospinal fluid composition and postoperative fever.

**Method:** Twenty-eight patients who underwent temporal lobe epilepsy surgery in Peking Union Medical College Hospital from April 2012 to August 2012 got fever >38.5 centigrade were made the lumbar punctures to test the intracranial pressure, the cell counts and the biochemical components of the CSF.

**Results:** Fluctuation curve of intracranial pressure, cerebrospinal fluid cell count and some biochemical compositions such as protein and sugar after temporal lobe epilepsy surgery were obtained.

**Conclusion:** The postoperative fever of temporal lobe epilepsy was caused mostly by bloody CSF, but not due to infection; Intracranial pressure after temporal lobe epilepsy surgery is usually mild increased and intracranial pressure lowering drugs were not necessary. To evacuation the bloody CSF through the lumbar punctures was favourable for fever releasing.

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### LESIONAL ETIOLOGY AND YOUNG AGE: FAVOURABLE PREDICTORS FOR LONG TERM FOLLOW UP IN VNS TREATED EPILEPSIES

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**Purpose:** The results of vagus nerve stimulation (VNS) for the treatment of drug-resistant epilepsies are highly variable. Defined patient's selection criteria are lacking and the follow-up (FU) of published studies is generally short. In this study we report the outcome of VNS in a series of patients with long FU and investigate the role of some factors in determining the prognosis.

**Method:** We reviewed the data of 53 patients (33 M, 20 F). Mean FU was  $55.96 \pm 43.53$  months. The monthly average seizure frequency for each patient at baseline, 3, 6, 12 months and each year until the latest FU after implant was measured. We identify patients as "responders" when the decrease of seizure number was at least 50%. We also calculated the response time (RT) as the period of time from the device implant to the 50% decrease of seizures. Finally, we investigated the potential prognostic role of these factors: age of onset of epilepsy, pre-implant epilepsy duration, etiology, age at implant.

**Results:** Globally, 40% of patients responded to VNS (mean RT was  $14.85 \pm 16.85$  months). Lesional etiology ( $p = 0.0179$ , log-rank test), particularly ischemia ( $p = 0.011$ , Fisher exact test) and tuberous sclerosis ( $p = 0.0229$ , Fisher exact test), and age at implant <18 years ( $p = 0.0242$ , log-rank test) were associated to better response to VNS. In the lesional subgroup the best results were observed in patients with a pre-implant epilepsy duration <15 years ( $p = 0.0204$ , log-rank test) and an age at implant <18 years ( $p = 0.0187$  log-rank test).

**Conclusion:** The best candidate to VNS seems to be a patient with lesional etiology epilepsy (particularly post-ischemic and tuberous sclerosis) and a short duration of epilepsy who undergo VNS younger than 18 years.

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### LONG-TERM OUTCOME AFTER FUNCTIONAL HEMISPHERECTOMY

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**Purpose:** Hemispherectomy is the largest neurosurgical procedure available; the results regarding seizures and development are among the best considering all cortical resection. We describe our series of patients submitted to functional hemispherectomy.

**Method:** Ninety-two patients were submitted to functional hemispherectomy from 1996 to 2012. Twenty-six patients had Rasmussen's syndrome, 47 patients had hemiplegic syndrome (HHE), five patients had Sturge-Weber syndrome and 14 had cortical dysplasia. Age ranged from 2 months to 42 years (45 males). Mean post-operative follow-up was 7.2 years. All patients were submitted to functional hemispherectomy.

**Results:** Eighty-eight percent of the patients with Rasmussen syndrome remained seizure-free. This was also true for 87% of the patients with HHE, all patients with Sturge-Weber and 65% of the patients with cortical dysplasia. There was no worsening of motor function in patients who were previously hemiplegic. Gait actually improved in most of the patients who were previously hemiplegic. Cognitive improvement was noted in all patients with Sturge-Weber, in all but one patient with HHE, and all but two patients with Rasmussen's syndrome and in 8 out of 14 patients with cortical dysplasia. Seventy-eight patients presented with a transient (mean duration = 9 days) post-operative febrile syndrome (aseptic meningitis).

**Conclusion:** Hemispherectomy is a very effective and highly underused procedure, especially in kids with HHE syndrome. It can be performed safely in specialized centers. A very high rate of seizure-free patients and a high number patients with some degree of cognitive and motor improvement might be expected.

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### HIPPOCAMPAL DEEP BRAIN STIMULATION (HIP-DBS) IN PATIENTS WITH TEMPORAL LOBE EPILEPSY (TLE) AND NORMAL MRI FINDINGS OR MESIAL TEMPORAL SCLEROSIS (MTS)

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**Purpose:** We present our experience with Hip-DBS, a non-resective technique, in patients with temporal lobe epilepsy.

**Method:** Nine patients with temporal lobe epilepsy were studied. Three had normal MRI, 4 had bilateral MTS and 2 had unilateral MTS. Seven patients were implanted bilaterally in the hippocampus, and 2 unilaterally, using a Kinetra device. The electrodes were inserted along the axis of the hippocampus through a posterior approach; the most anterior contact was positioned in the head of the hippocampus. Pre-, intra- and post-stimulation scalp EEG recordings were obtained in all patients intra-operatively. Continuous stimulation was carried out using 300  $\mu$ s, 130 Hz, 2–4 V pulses.

**Results:** In six patients, an increase in temporal lobe spiking was noticed unilaterally at the time of electrode insertion. In all patients an ipsilateral temporal lobe recruiting response was noted during low frequency acute stimulation. In six patients, high frequency intraoperative hippocampal stimulation reduced or abolished interictal spiking. Seven patients received unilateral and 2 bilateral stimulation (1 with normal MRI and 1 with bilateral MTS) so far. Two patients with unilateral stimulation are seizure free and the other five had at least 90% reduction in seizure frequency. The two patients with bilateral hippocampal stimulation were non-responders. There was no memory decline in patients submitted to bilateral hippocampal stimulation. Mean follow-up time was 30 months.

**Conclusion:** Hippocampal stimulation seems to be an effective and safe non-resective technique in this patient population. Memory decline did not occur with bilateral hippocampal stimulation suggesting that Hip-DBS did not lead to complete inactivation of the hippocampus.

P249

### POSTERIOR FOSSA HAMARTHOMA AND GANGLIOGLIOMA: EPILEPTIC SYNDROME AND OUTCOME AFTER SURGERY

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**Purpose:** An increasing (though very small) number of kids with posterior fossa lesions and seizures have been reported in the literature. Their epileptic syndrome has not been clearly defined and the pathological substrate was heterogeneous, although hamarthomatous lesions prevailed. We report 2 such kids submitted to surgery.

**Method:** One kid was 5 (Patient 1) and the other 6 year-old (Patient 2) by the time of surgery. Both had daily, frequent seizures, beginning in the first days of life. Patient 1 had bilateral symmetric tonic seizures prevailing during sleep (but not exclusively). Ictal video-EEG monitoring showed bilateral diffuse recruiting rhythms. MRI showed a discrete, rounded lesion above the left facial colliculus. Patient 2 had motor simple and complex partial seizures that sometimes resemble facial tics. MRI showed a 3 cm lesion occupying the middle cerebellar peduncle. Ictal video-EEG showed a bilateral slow spike-and-wave pattern.

**Results:** Patient 1 was submitted to complete removal of the lesion; pathological examination showed hamarthoma. He has been seizure-free since surgery; a post-operative EEG was normal. Patient 2 was submitted to partial removal of the lesion; pathological examination showed ganglioglioma. There was 90% improvement in seizure frequency. Post-operative EEG showed rare spiking, with the same morphology as preoperatively.

**Conclusion:** As seen in patients with hypothalamic hamarthoma, surface EEG was false-positive and epileptogenesis is very likely related to the posterior fossa lesion. Although focal, these lesions led to generalized epileptic syndromes. Complete resection of the lesion might lead to seizure freedom; partial removal would very unlikely be successful regarding seizure control.

P250

### RESULTS OF SURGERY FOR EXTRATEMPORAL REFRACTORY EPILEPSY

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**Purpose:** This paper reviewed a series of epileptic patients submitted to extra-temporal lobe resective surgery in the MR era.

**Method:** Four hundred and sixty-two patients submitted to extra-temporal epilepsy surgery from 1996 to 2012 were studied. Mean age at surgery was 18 years. Mean postoperative follow-up period was 5.7 years. One hundred and eighty-seven patients were submitted to temporal lobe, 187 to frontal, 70 to rolandic, 69 to posterior quadrant, 26 to parietal, 12 to occipital and 6 to insular cortical resection. Ninety-two patients were submitted to hemispherectomy.

**Results:** Eighty-two percent of the patients submitted to hemispherectomy have been rendered seizure-free. Ninety percent of the patients with MRI-positive frontal lobe have been rendered seizure-free; 61% of the patients with MRI-negative frontal lobe epilepsy have been rendered seizure-free. All patients submitted to occipital, parietal and insular resections were MRI-positive; 85%, 80% and 100% of them, respectively, have been rendered seizure-free after surgery. Sixty percent of the patients submitted to posterior quadrant resections were MRI-positive; 83% of them have been seizure-free after surgery. MRI-negative patients submitted to posterior quadrant resection did somewhat worse (67% seizure-free). Four patients died: one patient had SUDEP immediately before leaving the hospital, 1 had malignant hyperthermia, 1 had malignant propofol syndrome, and 1 had malignant visceral phenitoin syndrome.

**Conclusion:** Better outcome was seen in patients with MRI-defined lesions. Morbidity was low, and those patients' deaths could not probably been prevented (1 SUDEP and 3 idiosyncratic syndromes). Overall, extra-temporal resection might be regarded as safe and effective.

P251

### RESULTS OF SURGERY FOR REFRACTORY EPILEPSY: HIGHLIGHTS FROM A SERIES OF 1696 PATIENTS SUBMITTED TO SURGERY

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**Purpose:** This paper reviewed a series of epileptic patients submitted to surgery in the MR era.

**Method:** One thousand six hundred and ninety-six patients submitted to epilepsy surgery from 1996 to 2012 were studied. Mean age at surgery was 16 years and follow-up period was 6.6 years. 919 patients were submitted to temporal lobe, 187 to frontal, 70 to rolandic, 69 to posterior quadrant, 26 to parietal, 12 to occipital and 6 to insular cortical resection. Ninety-two patients were submitted to hemispherectomy and 190 patients to callosotomy; 102 patients were submitted to VNS and 23 to DBS.

**Results:** Overall, 81% of the patients submitted to temporal lobe resection were seizure-free after surgery, as did 82% of the patients submitted to hemispherectomy. 72% of the patients with frontal lobe have been rendered seizure-free. Patients submitted to occipital, parietal and insular

resections were seizure-free in 85%, 80% and 100% of them, respectively. Eighty-three percent of the patients submitted to posterior quadrant resections were seizure-free postoperatively. There has been an 88% reduction in the generalized seizure frequency in those patients with Lennox-Gastaut syndrome submitted to callosotomy. Overall, 51% of the patients submitted to VNS had at least a 50% reduction in seizure frequency; best results were obtained in kids with Lennox-Gastaut syndrome. Among the DBS patients, although targeted for different syndromes, the best results were obtained with hippocampal stimulation.

**Conclusion:** Patients with MRI-defined lesions had better seizure-outcome. There is a clearcut trend towards operating at a younger age, and discontinuing the use electrocorticography, awake-craniotomy and Wada's testing. Neuromodulation is very likely to be increasingly used in these patients.

## P252

### TECHNICAL ASPECTS IN DEEP BRAIN STIMULATION FOR EPILEPSY

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**Purpose:** We had been using centro-median (CM), anterior nucleus (AN) and hippocampal (Hip) DBS over the last 6 years; this paper discusses technical aspects related to the procedures.

**Method:** Twenty-three patients with refractory epilepsy were submitted to DBS: 7 in CM, 7 in AN and 9 in Hip. Patients submitted to CM had generalized epilepsy, those submitted to AN had fronto-temporal epilepsy or failed prior temporal lobe resection, and those submitted to Hip-DBS had temporal lobe epilepsy.

**Results:** The hippocampus was targeted using intra-operative CT/MRI fusion with direct visualization. The more distal electrode was aimed at the head of the hippocampus, and oriented at the axis of the hippocampus itself with an occipital entry point. Thalamic nuclei were targeted initially based on the proportional coordinates. During AN, the visualization of the mammillo-thalamic tract was also a useful landmark. In CM, the more distal electrode was aimed at the level of the posterior commissure point. During thalamic low-frequency stimulation recruiting responses after unilateral stimulation were always bilateral and diffuse, prevailing over the stimulated side. Low frequency stimulation of the hippocampus generated localized recruiting responses. High frequency stimulation led to DC-shifts after thalamic stimulation, without modification of the cortical epileptic discharges. High frequency hippocampal stimulation led to spike frequency reduction in two thirds of the patients; no DC shift was noted.

**Conclusion:** As DBS is used in an increasing frequency to treat epilepsy, targeting definition and intra-operative technique should be standardized. Biomarkers for adequate electrode positioning and their relationship to outcome need to be further studied and refined.

## P253

### VAGUS NERVE STIMULATION (VNS) IN REFRACTORY EPILEPSY

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**Purpose:** We report the results regarding seizures obtained in our VNS series.

**Method:** Ninety-seven patients were studied (mean age = 18.6 years). Forty-seven had secondary generalized epilepsy (SGE; Lennox and Lennox-like syndromes), 11 were temporal lobe resection failures, 11 had frontal lobe epilepsy, 10 had posterior quadrant epilepsy and 21 had non-localized epileptic foci. Final standard parameters were 2.5–3.5 mA,

500  $\mu$ s and 30 Hz (30 s “on”, 5 min “off. Mean follow-up time was 4.7 years.

**Results:** Three patients had to be explanted due to infection. Ninety-percent of the patients with SGE got at least 50% seizure frequency reduction. Only one patient who failed temporal lobe surgery benefit from the procedure; 50% of the patients with frontal or posterior quadrant epilepsy did so. Attention level and cognitive improvement was noted in 60% of the patients but did not strictly correlate with seizure outcome. There was an immediately postoperative period (generator “off”) of seizure frequency reduction (“honeymoon phase”) in 50% percent of the pediatric patients (not noted in adults). Sixteen percent of the kids presented seizure frequency worsening when stimulation current was set higher than 2.5 mA.

**Conclusion:** VNS was effective in both adults and kids. The pediatric population appeared to represent a set of patients with better seizure and cognitive outcome after VNS. Children might be at higher risk for seizure frequency worsening at higher stimulation currents when compared to adults. Patients who failed temporal lobe resection did not benefit from the procedure.

## P254

### EPILEPSY SURGERY IN DRUG-RESPONSIVE CHILDHOOD FOCAL EPILEPSY

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**Purpose:** To discuss the opportunity to perform early surgery in children suffering from focal symptomatic epilepsy even if drugs are effective.

**Method:** We present two cases of epilepsy surgery in childhood symptomatic focal, non drug-resistant, epilepsy. The first one is a 6 year-old female, starting with a focal status epilepticus, stopped by benzodiazepines and subsequently controlled by carbamazepine. The first MRI during the status, showed a hyperintense lesion (probably a Focal Cortical Dysplasia, FCD) located in the right gyrus rectus. Six months later, she performed a second MRI, showing a doubtful hyperintensity in the same region. She was seizure-free since the onset. According with the parents we performed a simple lesionectomy (January 2012) and the histological diagnosis was FCD type IIb. She was seizure-free since the surgical procedure and the pharmacological treatment was stopped (January 2013). The second case was a 2 year-old boy, starting with focal seizures at 1 year. MRI showed a probable FCD in the right frontal pole. Seizures remain extremely infrequent, with a carbamazepine treatment. A lesionectomy was performed at 2 years (April 2009), and he was seizure-free since then. The pharmacological treatment was stopped (August 2010). Neuropsychological examination in both patients was absolutely normal, before and after surgery, with high cognitive performances.

**Results:** A simple lesionectomy was performed to cure the two paediatric patients. The total duration of the illness was 20 months in the first case, and 3 years in the second one.

**Conclusion:** The two cases suggest that surgical choice, also in patients non drug-resistant, may be an option to take into account especially in the paediatric population, in which the presence of an anatomical lesion obliges a long-life therapy, and the possibility of AED side-effects and cognitive decline, beyond a high risk of seizure recurrence.

## P255

### NOVEL TECHNOLOGY OF SURGICAL TREATMENT OF SYMPTOMATIC EPILEPSY IN PATIENTS WITH BRAIN ARTERIOVENOUS MALFORMATIONS

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**Purpose:** The main type of cerebral AVMs clinical course is an epileptic syndrome (symptomatic epilepsy). The aim of this study is to determine the efficiency and risk of treatment of epileptic syndrome in patients with cerebral arteriovenous malformations based on the modernized standard method of endovascular surgery under EEG-control.

**Method:** Forty-seven patients (17–62 aged) with AVMs manifesting epileptic syndrome (discirculatory epileptic encephalopathy) were included in the analysis. All the patients received active endovascular superselective embolizations of AVMs using HepaSphere<sup>®</sup> microspheres (BioSphere Medical, France) loaded with anticonvulsant (Diazepam). The treatment involved neurophysiological control of dynamic EEG-monitoring in all stages.

**Results:** Sixty-three surgeries in 47 patients were performed on the same technology. Total and subtotal AVM embolization was achieved in 31 patients and partial in 16. Electroclinical observations with catamnesis to 3 years showed a positive postoperative adaptive dynamics of the epileptic syndrome with a distinct tendency toward inhibition of epileptic manifestations. All the patients had a significant decrease in the frequency and severity of epileptic seizures, 29 (62%) patients had the attacks completely stopped (Engel class I). EEG proved full regression of paroxysmal activity with a tendency toward normalization of the spatial bioelectrical pattern.

**Conclusion:** Creative technology of active surgical treatment of symptomatic epilepsy in patients with cerebral AVM is proposed. New way to deliver AEDs directly in the brain with continuous release of anticonvulsant direct into the regions of the brain responsible for seizures is prospectively. Embolization of AVMs with drug-loaded microspheres is save and effective.

#### P256 STEREO-EEG (S-EEG) IN THE COURSE OF PRE-SURGICAL EVALUATION: RESULTS OF THE FIRST 23 IMPLANTATIONS IN A DUTCH COMPREHENSIVE EPILEPSY CENTER

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**Purpose:** To evaluate clinical characteristics, results and complications in the first 24 SEEG procedures in the period 2008–2011 in a patient cohort with epilepsy.

**Methods:** Decisions to perform S-EEG were made in the comprehensive epilepsy surgery workgroup. Data from all patients in whom S-EEG was performed were prospectively obtained and analyzed. Electrode implantation was performed in Maastricht University Medical Center. Recordings and stimulations were done in Kempenhaeghe, Heeze.

**Results:** Twenty-four implantations were performed in 23 patients, resulting in 17 resections. 71% of the resections led to freedom from epileptic seizures. One of these patients developed non-epileptic seizures. 18% of the resections led to a significant (>50%) reduction of seizure frequency. In one patient follow up after resection is too short to make a valid statement. In five procedures (21%) temporary complications were noted. Two complications without direct relation to the S-EEG: one patient with hoarseness due to intubation and one patient with ulnar nerve compression neuropathy. S-EEG related complications were present in three cases (13%): one patient with paresis due to post-implantation edema, one patient with a small amount of subarachnoidal blood in the right Sylvian fissure on the postop CT-scan and skin irritation in one patient. All these complications completely resolved.

**Conclusion:** S-EEG is a valuable addition to the invasive presurgical analysis in epilepsy surgery candidates with a very acceptable low complication rate in a starting center. It makes surgery available for some epilepsy patients who would otherwise be rejected.

#### P257 SEIZURE CONTROL FOLLOWING THE IMAGE-GUIDED RESECTION OF CEREBRAL GLIOMAS

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**Purpose:** Seizures are common presenting symptoms of supratentorial gliomas and play an important role in postoperative quality of life of patients who undergo the surgical resection. The factors positively associated with postoperative seizures are pathological diagnosis, preoperative seizure control, and disease duration. Of the treatment-related variables, the strongest predictor of seizure freedom after surgery was gross-total resection. Image-guided resection (IGR) can maximize the extent of resection. We retrospectively analyzed seizure control following IGR of gliomas.

**Method:** Between May 2006 and December 2008, 76 adult patients with a supratentorial glioma undergoing primary resection of IGR were retrospectively reviewed. Preoperative data included date of seizure onset, type of seizure, other presenting and patients' use of antiepileptic drug (AED). Seizure control was evaluated at 6 and 12 months after surgery.

**Results:** Of the 76 patients, histological diagnosis included glioblastoma in 22 patients, anaplastic astrocytoma in 10 patients, astrocytoma in nine patients, oligodendroglioma in 25 patients. The mean tumor volume was 57.1 ± 41.7 ml; 33 of the tumors involved frontal lobe, 16 temporal lobe, 1 parietal lobe, 3 occipital lobe, 18 others. Forty-one patients (53.9%) had preoperative seizures. Twenty-eight patients presented with simple partial seizure, 25 patients secondary generalized, 10 patients complex partial seizure. Gross total resection was achieved in 52 cases. The mean resection rate of tumor was 98.8% and median survival was significantly longer, compared with that of 24 patients undergone conventional resection. Fourteen patients presented with postoperative seizure and six seizures were associated with the tumor progression. For the cohort of patients that presented with seizures, 12-months or until tumor progression- outcome after surgery (Engel class) as follows: seizure free (I) 89.3%, rare seizure (II) 8.5% and meaningful seizure improvement (III) 2.2%.

**Conclusion:** IGR could improve clinical outcome and gross total resection appeared to be associated with a favorable prognosis for seizure control.

#### P258 POSTERIOR TEMPORAL INTERICTAL EPILEPTIFORM ACTIVITY ON SCALP EEG: SIGNIFICANCE AND CORRELATION WITH CLINICAL OUTCOMES IN TEMPORAL LOBE EPILEPSY SURGERY

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## Abstracts

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**Purpose:** To analyze whether posterior temporal interictal epileptiform discharges (IEDs) on scalp EEG imply a reduced chance of seizure freedom following temporal lobe surgery.

**Methods:** Twenty-two patients with pharmacoresistant temporal lobe epilepsy (TLE) were included. Video-EEG monitoring documented IEDs maximal at T5/T6/P9/P10 or equipotential between T3-T5/T4-T6/T9-P9/T10-P10 (along with independent anterior temporal IEDs). Intracranial EEG used temporal subdural strip and depth electrodes. Surgery comprised standard anterior temporal lobectomy/amygdalohippocampectomy (ATL/AH), selective AH or neocortical resection tailored to intracranial EEG recording with or without ATL/AH.

**Results:** MRI was normal in ten patients, revealed mesiotemporal lesions in ten (hippocampal sclerosis – 7, cortical dysplasia – 1, other – 2) and purely neocortical lesions in two. Of the patients with mesiotemporal lesions, eight underwent resection (standard ATL/AH – 4, tailored ATL/AH – 3, selective AH – 1) with 1-year seizure outcome of Engel 1 in seven (88%) and Engel 4 in one (12%). Of the ten MRI-normal patients, five went on to resection (tailored ATL/AH – 3, purely neocortical – 2) with 1-year seizure outcome of Engel 1 in two and Engel 3 or 4 in three. One of the two patients with a neocortical lesion underwent lesionectomy with ATL/AH and the other did not proceed to resection. Intracranial EEG demonstrated exclusively posterior temporal neocortical ictal onsets in only four patients, three of whom underwent resection. Two of these four had mesiotemporal pathology (one underwent tailored ATL/AH with Engel 1 outcome) and two had normal MRI (both underwent neocortical resection, one with Engel 1 and one with Engel 4 outcomes).

**Conclusion:** Posterior temporal IEDs do not portend a poor chance of seizure freedom in the context of mesiotemporal pathology. However, in MRI-normal TLE, the chance of not proceeding to resection after intracranial EEG was high and seizure outcome after resective surgery was relatively poor.

### P259 THE UNFINISHED SURGICAL ADVENTURE OF WILDER PENFIELD: INSULECTOMY FOR REFRACTORY EPILEPSY

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**Purpose:** Wilder Penfield was the pioneer of insulectomies for refractory epilepsy, notably when electrocortigraphy performed after temporal lobe removal disclosed insular spikes. However, this approach was abandoned because of poor results and complications. With technological advancement in seizure focus localisation and microsurgery, it is time now to reassess the surgical outcome of insulectomies.

**Method:** All patients with intracranial insular recordings and all patients who had an insulectomy for refractory epilepsy at the Université de Montréal were reviewed. Insular surgeries for tumors and vascular lesions were excluded.

**Results:** Thirty patients had intracranial insular recordings. Five had electrode placement by stereotaxy and 25 by direct implantation after microsurgical opening of the Sylvian fissure, including 10 with the Hybrid Operculo-Insular Electrodes. No patient had complications with permanent consequences. Twenty-one patients had an insular resection, combined with an opercular resection in 19. Seven insulectomies were performed on the dominant hemisphere. Pre-operative insular MRI was normal or non specific in 14/21 patients (67%). Engel class I seizure outcome was achieved in 18/21 patients (86%) (Mean follow-up 4 years, range 0.1–14). No new permanent deficits were detected.

**Conclusion:** Intracranial EEG sampling of the insula and insulectomy for refractory epilepsy are safe procedures. Good seizure control is now a reachable goal.

### P260 MANAGEMENT OF ANTIEPILEPTIC DRUGS FOLLOWING EPILEPSY SURGERY: A META- ANALYSIS

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**Purpose:** No consensus exists regarding the management of antiepileptic drugs (AEDs) after successful epilepsy surgery. We performed a meta-analysis of the evidence on this topic. Our aim was to provide evidence-based estimates of results on AEDs discontinuation after epilepsy surgery.

**Method:** We performed a comprehensive search for articles published from 1980 to 2012 using Medline, Embase, Index medicus, Cochrane database and bibliographies of pertinent reviews and original articles. Of 257 citations identified, 57 potentially eligible articles were reviewed in full text, and 25 fulfilled eligibility criteria and were included in the analysis. Two investigators independently extracted data, resolving disagreements through discussion.

**Results:** Twenty-five studies with 3,850 patients were included. Fifteen (60%) studies were in adults, 6 (24%) in children, and 4 (16%) mixed. Twelve (48%) studies involved the temporal lobe, 1 (4%) the extra-temporal lobes, and 12 (48%) both. The majority of the studies were retrospective cohorts. The mean period for drug withdrawal was started at 12.95 months from surgery. Recurrence occurred in 25% of patients during or after withdrawal, and in 47% of patients who continued taking medication. Following seizure recurrence 70% of patients regain seizure freedom with AEDs.

**Conclusion:** There is substantial variation in outcomes among studies. Surprisingly seizure recurrence was higher for patients without AED modification than in the withdrawal group of patients. This may be explained due to selection of patients for AED discontinuation. Although seizure breakthrough is possible, restarting drugs is likely to restore seizure control.

### P261 HEMISPHERECTOMY IN ADULTS PATIENTS WITH SEVERE UNILATERAL EPILEPSY AND HEMIPLEGIA

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**Purpose:** To Study postoperative seizure control of hemispherectomy in adult with epilepsy, and evaluate the changes of movement and speech function, and changes of intelligence quotient (IQ) and quality of life (QOL) after hemispherectomy.

**Method:** To Study postoperative seizure control of hemispherectomy in adult with epilepsy, and evaluate the changes of movement and speech function, and changes of intelligence quotient (IQ) and quality of life (QOL) after hemispherectomy.

**Results:** Nine functional hemispherectomies and 16 anatomy hemispherectomies were performed. The percentages of seizure-free were 92%, and 8% researched Engel II grade seizure control. Factor on seizure control was not found. Movement function impairment was presented in 9 (36%) adults' upper limbs and 5 (20%) patients' low limbs. The patients with age at seizure onset  $\leq 3$  years rendered improvement of mean motor function of upper limb. Speech function impairment

presented in seven patients with left hemispherectomies. Mean aphasia quotient improved totally, and significant difference was found in change of aphasia quotient between patients with different onset age. All of the patients' postoperative scores of overall QOL, full IQ, verbal IQ and performance IQ improved compared with those pretreatment scores respectively, and those improvements not associated with patient's age at seizure onset and surgical approach. However, significant difference was found in change of verbal IQ between patients with right hemispherectomies and those with left hemispherectomies. Surgical complications included 1 hydrocephalus, and 6 transient complications.

**Conclusion:** Hemispherectomy presented good seizure control and improvement in QOL and IQ, and impairment on motor and speech function were mild, furthermore, and patients with early seizure onset could reach movement function of upper limb and speech function improvement. Therefore, it is worth pursuing hemispherectomy in well-selected adults with severe unilateral epilepsy and hemiplegic.

## P262

### “NOCTURNAL SEIZURES ONLY” POST TEMPORAL LOBECTOMY: CHARACTERISTICS OF AN UNUSUAL OUTCOME GROUP

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**Purpose:** Following temporal lobectomy, a phenomenon of exclusively nocturnal seizures has been recognized but not widely studied. Here we analyse such a patient group to try and understand factors that determine this unusual outcome pattern.

**Method:** Among 476 patients who underwent temporal lobectomy between 1978 and 2007, 18 patients were identified with exclusively nocturnal seizures occurring for  $\geq 5$  years post surgery. They were compared with 20 controls matched for histology (majority hippocampal sclerosis) and seizure frequency.

**Results:** The age at seizure onset was significantly older in the cases (mean 15.6 years) compared with the controls (mean 5.6 years,  $p = 0.001$ ). Presence of febrile seizures, presence of generalised seizures pre-op and concordance of supporting investigations (MRI/ EEG/ Ictal SPECT/Ictal PET) did not differ significantly between the groups.

Seventy-eight percent of cases and 65% of matched controls experienced seizures within the first post operative year. All the cases experienced a reduction in seizure frequency postoperatively; seizure frequency plateaued by the second year post surgery in 13 of the 18 (72%) cases. The majority experienced infrequent ( $\leq 1$ /month) seizures, though seizures were bilaterally convulsive in at least half of patients. The mean duration of follow up was 16.8 years, demonstrating long term stability of the “nocturnal seizures only” pattern.

**Conclusion:** Patients who experience exclusively nocturnal seizures following temporal lobectomy appear to be older at seizure onset compared with controls of similar pathology and (daytime) seizure frequency. Seizures are infrequent and although not formally assessed here, nocturnal only seizures appear to be associated with improved quality of life, including the ability to drive.

## P263

### IS THE PATENCY OF THE POSTERIOR COMMUNICATING ARTERY DURING THE INTRACAROTID WADA TEST IN EPILEPSY SURGERY CANDIDATES, RELATED TO MEMORY PERFORMANCE OF THE WADA?

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**Purpose:** Due to anatomical differences in the circle of Willis, variability of distribution of sodium amobarbital during the WADA procedure might occur between patients. This might lead to differences in delivery of sodium amobarbital to the medial temporal lobe structures, especially the (posterior) hippocampus, which plays a crucial role in memory function. Since the posterior cerebral artery is often responsible for supplying the posterior hippocampus, patency of the posterior communicating arteries (PCom) might influence cognitive functioning during the WADA test. The current study was conducted in order to investigate the contribution of PCom patency to anesthetizing the posterior hippocampus and memory scores during the WADA test.

**Method:** Forty-five Patients who were eligible for medial temporal lobe resection in order to treat drug-resistant epilepsy underwent a WADA test to evaluate memory (besides language) functions (25 females, mean age 38.4, SD 12.1). The angiographies were obtained during the WADA and divided into two PCom patency groups; with contribution of PCom patency (N = 21) and without contribution of PCom patency (N = 24). Furthermore, WADA memory scores and WADA memory story scores were collected to evaluate memory functioning during the WADA test.

**Results:** No significant differences were found in memory scores between both PCom patency groups. ANOVA analyses revealed no effect of PCom patency on WADA memory, ( $F_{1,43} = 2.58$ ,  $p = 0.12$ , and WADA memory story scores,  $F < 1$ ).

**Conclusion:** Variations in PCom patency do not seem to affect WADA memory scores. Whether the delivery of anaesthetics to the hippocampus is influenced by variations in PCom patency remains unclear. Recommendations for future research are given.

## P264

### EPILEPSY SURGERY: BETTER OUTCOME IN THE LESS THAN 5 YEARS-OLD CHILDREN AFTER STEREO-EEG EXPLORATION

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**Purpose:** We report a paediatric series of post-operative outcome in less than 5 year-old patients (group 1, n = 21) presenting with intractable epilepsy.

**Method:** Children were explored with stereo-EEG monitoring before surgery in the past 2 years in our institution. We compared them to more than 5 year-old children (group 2, n = 44) explored during the same period of time.

**Results:** In group 1, the mean age was 39 months (range 20–60 months), including five children with infantile spasms and 6 with bilateral EEG abnormalities. The exploration was extended as electrodes were

implanted in at least three lobes, and up to 4/5 lobes in 76%. In group 2, 70% of the children had 4/5 lobes explored. In group 1, 2 patients were turned down for surgery after stereo-EEG; type 2 dysplasia was found in 57% of the patients versus 42% in group 2, DNET was found in 9.5% of the children versus 18.2%, hippocampal sclerosis in 9.5% versus 6.1% in group 2, hypothalamic hamartoma in 1 child in each group. After surgery the follow-up lasted 16 months on average. The outcome in group 1, was Engel 1 in 76% of the children, 14% were Engel 2/3 and 1 was Engel 4. In group 2 only 59% of the patients were Engel 1 and 15% Engel 2/3.

**Conclusion:** Our results show that after careful exploration, children younger than 5 year-old have better outcome after epilepsy surgery than the older children. Suitability of stereo-EEG and more frequent MRI abnormally in youngest patients allow a better guidance of the surgical planning.

## P265

### INDICATION OF VAGUS NERVE STIMULATION AND CALLOSOTOMY: A RESULT OF SINGLE NEUROSURGICAL UNIT

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The vagal nerve stimulation (VNS) and corpus callosotomy (CC) can reduce the frequency and severity of seizures in the patient with intractable epilepsy. Both procedures are palliative treatment for the multifocal epileptic case that cannot recommend the resection of epileptogenic lesion. It is still unclear to indicate two procedures for refractory generalized seizures. We had strategy of decision of CC in the patients with bi-frontal epileptic lesion confirmed by scalp electroencephalogram (EEG), symptom, video-EEG and magnetoencephalogram (MEG). The other criteria cases were chosen VNS. We evaluate the effect of VNS and CC in a single neurosurgical unit of Kinki University Hospital. Twenty-eight patients (nonrandomized) who underwent a VNS placement or corpus callosotomy procedure for refractory generalized seizures between 2010 to 2012 at our institute. Twenty cases were operated VNS system (Cyberonics). Other eight cases had CC procedures. There were no mortality and mobility in both groups. In the patients with CC, there were transient side effects such as mutism, difficult to take orally at early postoperative periods. In all cases with CC, the frequency and strength of the seizure were decreased in an immediate postoperative period. At follow-up periods, the type of seizure alternated in all cases. In fourteen of twenty cases with VNS, the reduction of frequency of seizure was observed at a period after 3–6 months starting a VNS. Six cases had no obviously the decrease of seizure. A tonic seizure was decrease in all cases.

Both CC and VNS resulted in a significant improvement in seizure control.

**Keywords:** Vagus Nerve Stimulation, Callosotomy, Intractable epilepsy.

## P266

### THE EFFECT OF AGE ON ATTITUDES TOWARD EPILEPSY SURGERY

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**Purpose:** A recent survey of unselected adult patients with epilepsy demonstrated widespread reluctance to accept Epilepsy Surgery (ES). However, after reading “informative” statements contained in the questionnaire, many subjects shifted from unfavorable to more favorable atti-

tude (Epilepsy & Behavior 24 (2012) 352–358). In this report, we compare responses of the adult population with those of adolescents.

**Method:** The same ad hoc questionnaire, adapted for age, was submitted to 43 random adolescents (15–18 year old; 26 females). Forty two% had generalized epilepsy; 58% focal epilepsy (64% in remission; 36% with active seizures). Their responses were compared to those of four older age groups (19–29 year; 30–39 year; 40–49 year; >50 year) of similar size.

**Results:** Initial reluctance to undergo ES was highest among adolescents (75% “against”; 25% “in favor”). As for the older groups, attitude was independent of seizure control and clinical characteristics. After completing the questionnaire, adolescents’ attitude shifted to 46.2% “against”, and 53.8% “in favor”. Compared to the adult groups, change rate toward “favorable” was greatest, and toward “unfavorable” was smallest, among adolescents. Those who remained “unfavorable” were mostly adults (79.7% of those originally unfavorable) and least frequently adolescents (58.6%) (p = 0.03).

**Conclusion:** Patients of all ages tend to reject ES. While initially adolescents are more often “against”, a greater portion is receptive to reverse their negative attitude. Our data suggest that ES may be more acceptable and therefore, when indicated, easier to perform in the younger population.

## P267

### CORPUS CALLOSOTOMY FOR PEDIATRIC INTRACTABLE GENERALIZED EPILEPSY ASSOCIATED WITH CEREBRAL INFARCTION: TWO CASES REPORT

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**Rationale:** Cerebral infarction in childhood is rare in comparison with adulthood. Most seizures associated with cerebrovascular disorders are late seizures, which become intractable more easily than early seizures. We reported two surgical cases with pediatric intractable generalized epilepsy after cerebral infarction.

**Method:** We reviewed seizure outcomes in two pediatric patients who underwent corpus callosotomy against their intractable generalized epilepsy associated with cerebral infarction.

**Result:** *Case 1:* The patient is currently a 10-year-old boy with Down syndrome and moyamoya disease. He had cerebral infarction over whole territory of the left middle cerebral artery and right temporal tip at the age of 2 years. He presented with intractable seizures consisting of head nodding and atonic spells since 3-year-old. He had dozens of clinical seizures a day. He underwent total corpus callosotomy at the age of 8 years. He has had no clinical seizures for 2 years post surgery.

*Case 2:* The patient is currently a 14-year-old girl with a history of renal transplantation. She had cerebral infarction over whole territory of the left middle cerebral artery and right middle-posterior cerebral artery watershed boundary at the age of 1 year. She presented with intractable seizures consisting of blank stares and motionless spells since the age of 6 years. She had different types of seizures consisting of head nodding followed by extension and elevation of the right arm, drop attacks and atonic spells since 10-year-old. She had more than 10 clinical seizures a day. She underwent partial corpus callosotomy at the age of 13 years. She has had no drop attacks and atonic seizures for a year post surgery.

**Conclusion:** Corpus callosotomy succeeded in controlling drop attacks and atonic spells in our cases. It is suggested that corpus callosotomy is effective for intractable generalized epilepsy associated with extensive or multiple cerebral infarction in childhood.

P268

### PEDIATRIC EPILEPSY SURGERY USING INTRA-OPERATIVE 3-TESLA MRI AND NEURONAVIGATION: THE MONTREAL CHILDREN'S HOSPITAL EXPERIENCE

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**Purpose:** Modern epilepsy surgery, involving tailored resections of specific epileptogenic foci and functional disconnection procedures, requires highly detailed imaging. In recent years at the Montreal Children's Hospital we have been using 3-Tesla intraoperative MRI (iMRI)-based neuronavigation for such procedures. The purpose of this study was to investigate the role of this technology in pediatric epilepsy surgery.

**Method:** We conducted a chart and imaging review of all epilepsy cases performed in this setting from September 2009 to September 2011, such that we would have at least 1 year post-operative epilepsy follow-up on these patients.

**Results:** The iMRI neuronavigation suite was used in a total of 25 epilepsy surgeries during this period, and an iMRI was performed in 22 of these 25 (88.0%) cases. In 20 cases where an epileptogenic lesion was well delineated on pre-operative imaging, a complete resection was achieved in 85.0% of these operations. In seven cases (35.0%), further surgery was performed because of residual lesion found on iMRI, and in five of these cases complete resection of the lesion was achieved. Of 16 patients that have had at least 1-year follow-up, 81.3% are seizure free after surgery.

**Conclusion:** We feel that 3-Tesla iMRI has been very beneficial in tailored epilepsy surgeries. Further follow-up studies will be needed to assess if this translates into durable, long-term freedom from seizures for these patients.

P269

### UTILITY OF THE INTRACRANIAL VIDEO-EEG MONITORING IN PRESURGICAL EVALUATION OF PATIENTS WITH REFRACTORY EPILEPSY

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**Purpose:** Patients with refractory epilepsy are potential candidates for epilepsy surgery. Precise preoperative identification of the epileptogenic focus is crucial for the outcome.

**Method:** Sixty-two patients had long-term video EEG monitoring in an attempt to identify the epileptogenic focus or to recommend invasive diagnostics i.e. implantation of intracerebral, subdural or foramen ovale electrodes. Decision on location of the electrodes was based on semiology of the seizures and lesions displayed in an MRI brain scan. Intraoperative corticography was carried out before and right after excision of the focus.

**Results:** In 43 patients the focus was mapped yet on video EEG recordings. The remaining 19 (31%) had to undergo invasive diagnostics: 10 (53%) had intracerebral depth electrodes, 6 (31%) depth and subdural and 3 (16%) in foramen ovale. Ictal intracranial video EEG recordings (SEEG) showed focal seizure onset in all patients. There were: 10 in mesial temporal structures, 4 in accessory motor area, 3 at the base of the frontal lobe and 2 in epileptically silent cortex. There was one case of asymptomatic intracerebral haematoma at the electrode. All patients

were subsequently operated on. Location of the focus was confirmed by means of intraoperative corticography. In 54 (87%) cases the seizures subsided (follow-up 6 month–3 years), in 8 (13%) their frequency and intensity decreased.

**Conclusion:** Video EEG monitoring is very useful in presurgical evaluation in refractory epilepsy. Once a focus in the hippocampus, insula or in the basal parts of the frontal lobe is suspected, the SEEG is required.

P270

### EPILEPSY OUTCOME AFTER CEREBRAL CAVERNOUS MALFORMATIONS SURGICAL TREATMENT

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**Purpose:** Cerebral cavernous malformations (CCMs) are commonly associated with seizure disorder. In this study, we analyze the predictors that might have an impact on the chance of seizure freedom after CCMs treatment.

**Method:** Subsets of 19 patients with CCMs and medically intractable epilepsy were retrospectively analyzed. Seizure frequency pre and post-treatment was measured. The magnetic resonance imaging (MRI) features were assessed in terms of CCMs location, size, and hemosiderin thickness around the lesion. In addition, the extent of surgical resection was analyzed.

**Results:** The group of patients includes 11 females and eight males ranging between 5 and 62 years old (mean 29.2, SD 12.3). The mean duration of epilepsy was 12.6 years with a range between 4 and 36 years. CCMs were located in the temporal lobe in four patients, perirolandic area in five, multiple in four, and other locations in five. The average CCMs size was 2 cm with average hemosiderin thickness of 3 mm. Thirteen patients underwent surgical resection (lesionectomy, lesionectomy plus extensive corticectomy, and lesionectomy with temporal lobectomy). Two patients underwent radiosurgery using Cyberknife with limited benefits. Overall, eight patients became seizure free (8/13, 61%), three showed partial improvement, and two suffered worsening of seizure frequency. The important factor associated with seizure freedom is lesionectomy with extensive corticectomy or lobectomy. Temporal and perirolandic location was associated with more intractable epilepsy.

**Conclusion:** Lesionectomy with extensive corticectomy or temporal lobectomy was found to be an important factor for seizure freedom after CCMs treatment.

P271

### VAGUS NERVE STIMULATION FOR EPILEPSY: A COMPARISON OF OUTCOMES AT 1- AND 2-YEARS INTERVALS

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**Purpose:** Vagus nerve stimulation (VNS) therapy reduces seizures in certain patients with pharmacoresistant epilepsy who are not candidates for resective surgery. This study was conducted to compare the outcome of VNS therapy at 1-year and 2-year intervals.

**Method:** A retrospective analysis of 28 patients who received VNS therapy was conducted. Seizure frequency was measured before therapy, after 1 year of therapy, and after 2 years of therapy using a seizure diary. There were no changes in antiepileptic regimen after VNS implantation. VNS programming was standardized for all patient groups with adjustment based on tolerance and side effects. The response to VNS was defined as >50% reduction of baseline seizure frequency.

**Results:** A group of 20 adults and eight pediatrics were identified. At 1 year of VNS therapy 35% (n = 10) were considered responders (>50% reduction of seizure frequency). At 2 years of VNS therapy 43% (n = 12) were considered responders. None of the patients developed worsening of seizure. One patient underwent device removal after 19 months of therapy due to no benefit and patient request. Overall, the adverse effects (hoarseness, coughing) induced by stimulation are mild.

**Conclusion:** VNS therapy has a more significant effect on seizure reduction at 2 years of therapy. This indicates an accumulative effect of chronic neurostimulation on epilepsy.

#### P272 EPILEPSY SURGERY IN 57 CHILDREN AND ADOLESCENTS WITH BENIGN TUMORS

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**Purpose:** To report tumor characteristics, methods of investigation and postoperative seizure outcome in a large cohort of pediatric patients with epilepsy in association with benign tumors.

**Method:** Analysis of the medical charts of children and adolescents with epilepsy in association with benign tumors operated on between 09/1998 and 06/2012.

**Results:** Fifty-seven out of 368 operated patients (=15%) included; 28 females, 29 males; average age at onset of epilepsy 4 year 8 month; average age at operation 10 year; average follow up 67 months (range 6 m–153 m). Tumor localization: temporal 28, "temporal plus" 16, frontal 4, par.-occ.3, centro-par.3, occipital 2, parietal 1, central 1. suspicion of FCD type IIIb on MRI in 53% of the patients; exact figures by neuropathology pending histology: ganglioglioma 40, DNET 9, astrocytoma I 4, other I; type of preoperative evaluation: non-invasive plus ECOG 50, invasive 7; postoperative seizure outcome (Engel's Class.) Class I 44 (88%), Class II 4 (5%), Class III 1, Class IV 1, pending 7; reasons for outcome other than class I: incomplete resection because of overlap with eloquent areas 3, incomplete resection of FCD IIIb 2, unknown 1.

**Conclusion:** The excellent overall result in terms of postoperative seizure outcome is by and large in line with figures as they have been reported in several other studies dealing with epilepsy surgery for children with benign tumors. Invasive recordings is needed in special situations only but ECOG is highly recommended as further corticectomies because of remaining spikes beyond the preliminary margins of resections as outlined on the basis of MRI and the results of non-invasive investigations were necessary in a considerable no in this cohort of patients.

#### P273

#### THE SURGICAL RESULTS, IMAGING, EEG AND PATHOLOGICAL FEATURES OF THE INTRACTABLE EPILEPSY SECONDARY TO ULEGYRIA

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**Object:** To demonstrate that the intractable epilepsy secondary to ulegyria is a surgically remediable syndrome and ulegyria is a distinctive kind of epileptogenic lesion.

**Methods:** Forty-five patients who underwent surgery for the intractable epilepsy secondary to ulegyria and were followed up for more than 2 years were included. All patients underwent comprehensive presurgical evaluations. Thirty-five patients underwent intracranial electroencephalography (EEG) study. The ulegyria cortex including the magnetic resonance imaging (MRI) lesion was resected totally or subtotally in all patients. Postoperative follow-up period was 2–10 (mean 4.4) years.

**Results:** Thirty patients had a history of perinatal distress including prolonged labor, postterm delivery, asphyxia, or hypoglycemia. Age at seizure onset was 1–22 years with the average onset age 8.4 years. Ulegyria was unilateral in twenty-five patients and bilateral but unilateral-predominant in twelve patients. In most of the cases, the lesions were in the posterior cerebral artery area or the watershed area between middle cerebral and posterior cerebral arteries. There were 35 patients who underwent intracranial EEG. Postoperative seizure outcome was Engel's class I in 33 cases, and class III in three cases. Fifteen of eighteen patients whose lesions were subtotally resected achieved class I outcome. Five of eight patients with bilateral symmetric lesions achieved class I outcome.

**Conclusion:** Intractable epilepsy with ulegyria may be included in the category of surgically remediable syndromes. Ulegyria due to perinatal distress is a major cause of posterior cortex epilepsy. Long-term postoperative seizure outcome is favorable and stable. Resection of MRI lesion is important for seizure relief. Subtotal resection of lesion also can acquire a satisfactory postoperative epilepsy control result. Bilateral symmetric lesions should not be excluded from surgical indication. The usefulness of intracranial EEG may be limited.

#### P274

#### OUTCOME PREDICTORS FOR SURGICAL TREATMENT OF TEMPORAL LOBE EPILEPSY

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**Purpose:** To study long-term postoperative course and identify predictors for postoperative seizure control in patients with medically intractable temporal lobe epilepsy (TLE).

**Method:** One hundred forty-three patients with TLE, who underwent anterior temporal lobectomy (ATL) were included. Predictive value of gender, duration of epilepsy, febrile convulsion history, absence of secondarily generalized tonic-clonic seizures (SGTCS), unilateral interictal epileptiform discharges (IED), hippocampal atrophy (HA) on MRI, hypometabolism on Florodeoxyglucose positron emission tomography (FDG)-PET, postoperative histopathological data and operation side were evaluated. Surgical outcomes were classified using with Engel's classification at 1, 2, 4 years and latest follow up after surgery.

**Results:** The seizure-free rate was 83.2% at latest follow up. By univariate analysis, febrile convulsion history, unilateral IED, HA on MRI, unilateral hypometabolism on PET and hippocampal sclerosis in pathology were significant association with seizure-free outcome at 2 and 4 years. Multivariate analysis revealed that some variables lost their predictive power except febrile convulsion history, unilateral IED and hypometabolism on FDG-PET.

**Conclusion:** Many factors that have been previously described to predict favorable outcome after outcome after epilepsy surgery in TLE. Our results suggest that febrile convulsion history, unilateral IED and hypometabolism on FDG-PET were most significant positive predictors of seizure-free outcome.

## P275

### OUTCOME OF EPILEPSY SURGERY IN FOUR PATIENTS WITH TUBEROUS SCLEROSIS AND PHARMACORESISTANT EPILEPSY

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**Purpose:** Tuberous sclerosis (TSC) is a leading cause of pharmacoresistant epilepsy. Epilepsy surgery has emerged as a potent treatment, but determining which patients will make good surgical candidates remains challenging. Therefore, we wanted to describe our center's experience with epilepsy surgery in patients with TSC.

**Method:** We identified patients with TSC who underwent epilepsy surgery at our center after 2005 and retrospectively reviewed their charts. These patients were also enrolled in a larger, multi-center cohort study on epilepsy surgery in TSC (REST: Resective Epilepsy Surgery for Tuberous sclerosis). Our institution's research ethics committee approved this study.

**Results:** Four patients (one male, three female) were included. Epilepsy onset was between 1 and 5 months of age in three patients and at 8.5 years of age in the fourth. Average age at epilepsy surgery was 55 months (range: 20–142 months).

Three patients had infantile spasms. Two patients had multiple seizure semiologies and two patients had only one seizure type, excluding infantile spasms. Prior to surgery, our patients had between one and five seizures per day despite antiepileptic treatment.

For these patients, electroencephalographic and imaging data pointed toward a dominant epileptogenic focus. The epileptogenic zone to be resected was delineated using invasive electrocortical monitoring in all patients. Postoperatively, two patients remained seizure-free at their last visit, while two had a significant reduction in seizure frequency (Engel class II and III) (follow-up: 12–21 months).

**Conclusion:** Epilepsy surgery appears to be an effective treatment for TSC patients with different clinical characteristics.

## P276

### TEMPOROPARIETOOCIPITAL AND PARIETOOCIPITAL DISCONNECTION IN PATIENTS WITH INTRACTABLE EPILEPSY

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**Purpose:** To investigate the surgical techniques and surgical outcomes of Temporoparietooccipital (TPO) and parietooccipital (PO) disconnection in the treatment of intractable epilepsy.

**Method:** The authors conducted a retrospective review of clinical, neuropsychological, EEG, imaging data in 20 patients with intractable epilepsy who underwent temporoparietooccipital and parietooccipital disconnection between April 2008 and June 2012. Of the 20 cases, 14

were males and 6 were females. The age of seizure onset was from 0.1 to 27 years (average 7.6) and disease duration of 0.1 to 18 years (average 7.7). The surgery was performed between the age of 3 and 37 years (average 14.5). 11 patients underwent temporoparietooccipital disconnection, seven patients parietooccipital disconnection and two patient parietooccipital disconnection and temporal lobotomy.

**Results:** After a mean follow-up of 1.8 years (range 0.5–4.5 years), 15 patients (75%) had seizure free, two patient had Engel Class II seizure outcome and three patient had Engel class III outcome. Two patients exhibited severe brain swelling and one of the two patients were performed the second resective operation and recovered beneficently. None of the patients developed new motor deficits postoperatively and no death case in this study.

**Conclusion:** Temporoparietooccipital and parietooccipital is a safety and effective epilepsy surgery procedure for patients with epileptic zone localization to the posterior quadrant on one side. The results of surgical disconnection for posterior quadrant epilepsy have yielded excellent seizure outcomes in 75% of the patients in the series with no mortality or major morbidity.

## P277

### SURGICAL TREATMENT OF PATIENTS WITH RASMUSSEN ENCEPHALITIS

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**Purpose:** To describe the clinical, electrophysiologic, neuroradiologic, and histologic findings of our patients with Rasmussen encephalitis (RE) and to evaluate the outcome of their surgical treatment.

**Method:** Thirty-six patients were identified by criteria of RE. Surgery was conducted in the left hemisphere in 14 patients and in the right hemisphere in 22 patients. The mean age at surgery was  $7.90 \pm 4.92$  years. The surgical methods included anatomical hemispherectomies (AH, 9 cases), functional hemispherectomies (FH, 19 cases), hemispherotomy (six cases), bipolar electro-coagulations of functional cortexes (BEFC, one cases), and selective resection guide by intracranial electrode monitoring (one cases). Surgical treatment and presurgical evaluation including semiology, magnetic resonance imaging (MRI), video-electroencephalography (VEEG) were analyzed retrospectively.

**Results:** The mean follow-up period was 4.35 years (range 1–8 years). After surgery, 29 patients (80%) were evaluated as being Engel Class I, 1 patient was Engel Class II, three patient had a significant decrease in seizure frequency (Engel Class III), and three patient had no change in seizure frequency (Engel Class IV). One patient presented contralateral seizure after AH and was diagnosed with bilateral RE. All of the patients excepting the one bilateral RE had increases in cognitive abilities after the surgery. After surgery, most of the patients could walk independently, but the fine movement of the hands was lost. The main early complications were aseptic meningitis (40%) after hemispherectomy and hemispherotomy. Postoperative hydrocephalus was observed in two patient after AH, and there were no death in this series.

**Conclusion:** Hemispherectomy and hemispherotomy were both confirmed as beneficial procedures in controlling seizures and improving quality of the life in cases with RE.

## P278

### DEXMEDETOMIDINE ANESTHESIA DURING INTRA-OPERATIVE ELECTROCORTICOGRAPHY (ECOG) RECORDING: PROMISING, SAFE AND ENHANCES SPIKE GENERATION

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## Abstracts

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**Purpose:** Effect of dexmedetomidine sedation on intraoperative ECoG spike generation during epilepsy surgery was studied.

**Methods:** In this prospective study, dexmedetomidine was administered during ECoG to 30 patients (M:F = 20:10, age = 29.9 ± 11.2 years; duration of epilepsy = 15.2 ± 9.2 years) during anterior temporal lobe resection with amygdalo-hippocampectomy for drug-resistant mesial temporal lobe epilepsy (Right:18, Left:12). Ethical approval was obtained. Anesthesia was induced with thiopental/propofol and maintained with oxygen-N<sub>2</sub>O-isoflurane. During ECoG recording, (15 min after MAC of N<sub>2</sub>O and isoflurane was decreased to 0) background anesthesia was maintained with O<sub>2</sub>:air (50:50), fentanyl (1 µg/kg, a dose that did not influence ECoG significantly) and vecuronium. ECoG was recorded using a 4-contact strip electrode for: a) 2 min prior to dexmedetomidine (PreDEX), b) 5 min during dexmedetomidine infusion (DEX) and c) 5 min after stopping it (PostDEX). Cardio-respiratory parameters were monitored. The spike rate was manually counted in all the channels. For each phase, spike rate in the channel with maximum spikes was normalized to 3-min duration. RM-ANOVA was used to compare the spike rates across the three stages. A p value of <0.05 was considered statistically significant.

**Results:** The normalized mean spike rates were 89,111 and 94 in pre-DEX, DEX and PostDEX phases respectively (p = 0.02). Spike rates during dexmedetomidine infusion were higher compared to preDEX (p = 0.009) and PostDEX (p = 0.015). The spike rate increased in 18 patients decreased in 9 and didn't change in 3 from preDEX to DEX. From DEX to PostDEX, the spike rate decreased in 15 patients, increased in 14 and didn't change in 1. Hemodynamic parameters were stable throughout the procedure.

**Conclusion:** This is the biggest cohort wherein the effect of dexmedetomidine on ECoG spikes was analyzed. The results suggest that dexmedetomidine can be used during intra-operative ECoG recording since it enhanced epileptiform activity in the majority of patients and didn't cause any untoward effects.

## P279

### RESECTIVE SURGERY FOR DRUG RESISTANT TUMORAL EPILEPSIES: SEIZURE OUTCOME AND ITS PREDICTORS

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**Purpose:** To study a large cohort of patients with "long-term epilepsy associated tumors" (LEATs) who underwent focal resective surgery.

**Method:** Between 2005 and 2011, 105 patients (64 males) with LEATs underwent surgery in our center. We utilized their data to evaluate their long-term seizure outcome.

**Results:** Out of 105 patients (aged 3–50 years), the mean age at surgery was 20 years and mean pre-surgical duration of epilepsy was 10.9 years. 82 patients had temporal, 23 had extra temporal tumors and 4 had associated hippocampal sclerosis. Lesionectomy and/or adjoining corticectomy/temporal lobectomy was done. Ganglioglioma was the most dominant pathological substrate in 61 (58%). During a mean follow-up of 7.52 years (range 2–16 years), 78 patients (78%) were seizure-free and 45 (57.4%) were totally off drugs. Presence of secondary generalized seizures (SGTCS) (p 0.02) and temporal location of tumor (p 0.008) were the pre-operative factors and spikes in 3 month post-operative EEG (p 0.03) were associated with unfavorable seizure outcome. The hazard of seizure recurrence was thrice if the patient had SGTCS prior to surgery (p 0.02). A pre-surgical duration of epilepsy of 6.6 years was the most specific and sensitive cut-off time beyond which the seizures tended to recur despite adequate resection.

**Conclusion:** Early excision of the tumor and the adjoining epileptogenic tissue renders favorable seizure outcome in LEATs. Presence of SGTCS and temporal location of tumor caused a less favorable outcome. A waiting period of more than 5–6 years for surgery is likely to cause less favorable seizure outcome.

## Poster session: Pediatric Epileptology A Monday, 24 June 2013

## P280

### AN INTERVENTION TO IMPROVE ACADEMIC SKILLS IN CHILDREN WITH EPILEPSY

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**Purpose:** Academic achievement measures were administered as part of an epilepsy-specific tutoring program to determine (1) participants' academic needs and (2) whether participants improved those academic skills.

**Method:** Fifteen students in grades 1–10 participated in a tutoring program for students with epilepsy and learning difficulties. The intervention lasted for 8 months and students attended once a week for 1.5 h. All students were diagnosed with epilepsy and experienced (1) generalized seizures, (2) partial seizures, or (3) generalized and partial seizures. All students except one characterized their seizure control as good and all students used anti-epileptic medication. Prior to and following the intervention, students completed Reading (Phonemic Awareness, Nonsense Word Decoding, Letter/Word Recognition, and Reading Comprehension), Math (Concepts & Applications, Computation), and Writing (Written Expression, Spelling) subtests of the Kaufman Test of Educational Achievement- 2nd edition (KTEA-2). Results were compared using a paired-samples t-test and effect sizes were calculated.

**Results:** Students scored significantly higher (p < 0.05) on all subtests post-intervention as compared to pre-intervention, with the exception of the Phonemic Awareness subtest (please note: data was only available for six students for this subtest). Effect sizes for these were either small-medium or medium. Overall scores for Reading, Math, and Writing were also compared and post-intervention scores were also significantly higher than pre-intervention with small-medium effect sizes for Reading and Math and a medium effect size for Writing.

**Conclusion:** Students with epilepsy face unique academic struggles. This tutoring program helped students improve their reading, math, and writing skills.



P281

**QUALITY OF LIFE OF FILIPINO CHILDREN WITH EPILEPSY AGED 5–12 YEARS OLD USING PEDS<sub>Q</sub>L™ 4.0***Obiigar PDP<sup>1</sup>*<sup>1</sup>*Child Neuroscience Center, Philippine Children's Medical Center, Quezon City, Philippines***Purpose:** This study aims to assess the health related quality of life among children with epilepsy aged 5–12 years at Philippine Children's Medical Center using PedsQL Tagalog version.**Method:** This is a cross sectional study. Health related quality of life was measured using PedsQL generic score questionnaire.**Results:** A total of 117 children with epilepsy aged 5–12 years old and their caregiver were evaluated. Total overall mean PedsQL was 70.44 while for parents was 67.66. Physical functioning has the highest score while school functioning has the lowest mean score. The means scores are comparable with that of patients with chronic illness.**Conclusion:** Almost 50% of children with epilepsy had poor quality of life. There was good correlation between child self report and parent proxy report. Predictors to a poor quality of life were male sex, on Pheno-barbital and uncontrolled seizures.

P282

**PSYCHIATRIC MORBIDITY AND BURDEN OF CARE AMONG CARERS OF CHILDREN WITH SEIZURE DISORDERS***Babalola EO<sup>1</sup>, Ogunwale A<sup>1</sup>*<sup>1</sup>*Neuropsychiatric Hospital, Aro, Psychiatry, Abeokuta, Nigeria***Purpose:** The aim of this study was to assess the prevalence and correlates of psychiatric morbidity and burden of care among carers of children with seizure disorders attending the Child and Adolescent Clinic of the Neuropsychiatric Hospital, Aro Abeokuta.**Method:** A sociodemographic questionnaire was administered to 200 caregivers attending the clinic between November 2011 and February 2012. The Zarit Burden Interview was used to assess burden of care, while Structured Clinical Interview for DSM IV axis I Diagnosis was used for diagnosis of Generalised Anxiety Disorder and Major Depression.**Results:** Of the 200 caregivers, one hundred and forty four (72%) were females, with mothers of patients accounting for 66%. The prevalence of psychiatric morbidity was 50.5%. Among the carers, twenty percent reported mild to moderate burden while 40.5% reported severe burden. there was significant relationship between burden of care and psychiatric morbidity ( $\chi^2 = 1.32$ ,  $df = 2$ ,  $p = 0.001$ ). The sociodemographic characteristics of carers associated with psychiatric morbidity included older age, being employed, longer duration of care, and being patients mother. Patients clinical variables associated with carers' psychiatric morbidity included younger age of seizure onset, longer duration of illness.**Conclusion:** Carers of children with seizure disorders experience immense burden. Prevalence of psychiatric morbidity is high among these carers and is related to their sociodemographic characteristics. These findings suggest wholistic approach to the detection of these disorders and developing adequate and appropriate intervention. Formation of support groups and provision of psychological intervention by healthcare team can go a long way in ameliorating these challenges.

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**A SELECTIVE MAGNESIUM TRANSPORTER-NIPA2 PLAYS A VITAL ROLE IN THE PATHOGENESIS OF CHILDHOOD ABSENCE EPILEPSY***Xie H<sup>1,2</sup>, Zhang Y<sup>1</sup>, Zhang P<sup>1</sup>, Wang J<sup>1</sup>, Wu Y<sup>1</sup>, Wu X<sup>1</sup>, Netoff T<sup>2</sup>, Jiang Y<sup>1</sup>*<sup>1</sup>*Peking University Health Science Center, Peking University First Hospital, Beijing, China, <sup>2</sup>University of Minnesota, Minneapolis, MN, USA***Purpose:** NIPA2 is a very selective magnesium transporter. Three NIPA2 mutations were first identified recently from patients with Childhood Absence Epilepsy (CAE), including 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). We attempt to elucidate how these mutations cause CAE through functional studies of the mutations.**Method:** Immunofluorescence, Inductively Coupled Plasma Mass Spectrometry Optical Emission Spectrometry (ICP-OES), MTT metabolic rate detection and computational model were applied in our functional studies.**Results:** We found NIPA2 (wild-type) was localized to the cell periphery, whereas the three mutations were not effectively trafficked to the cell membrane when we transfected the wild-type and mutant NIPA2 in cultured neurons. Further, decreases of intracellular magnesium in the neurons transfected by mutant NIPA2 were found, but the mutants did not affect the survival of neurons. We also built a computational model to imitate effects of mutations, and observed that neurons with lower intracellular magnesium became more excitable by reducing the activation of BK channels.**Conclusion:** That the mutations of NIPA2 make NIPA2 proteins trapped in the cytoplasm hinders magnesium influx. Lower intracellular magnesium may reduce the activation of BK channels which is very important for the termination of action potential, and eventually may make neurons more excitable.

P284

**NEUROPEPTIDE Y (NPY), BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF), INTERLEUKIN-6 (IL-6) IN PLASMA AND CEREBROSPINAL FLUID (CSF) OF CHILDREN WITH CONVULSIVE DISEASES***Guo XY<sup>1</sup>, Jiao FY<sup>1</sup>, Wang X<sup>1</sup>, Gao Y<sup>1</sup>, Yan XH<sup>1</sup>*<sup>1</sup>*Shaanxi Province People's Hospital, Xi'an, China***Purpose:** In order to study the levels and relationship of neuropeptide Y (NPY), Brain-derived neurotrophic factor (BDNF), Interleukin-6 (IL-6) in plasma and cerebrospinal fluid (CSF) in children convulsion.**Method:** Seventy-four children with convulsive diseases were studied as following: obtaining the samples of plasma in the 1st and 7th day after being in hospital, and the samples of CSF in the 1st after being in hospital. We investigated the changes of NPY, BDNF, IL-6 in plasma and CSF with radioimmunoassay (RIA).**Results:** In children with convulsive diseases (febrile seizure, epilepsy) NPY, IL-6 in plasma and CSF were increased, but BDNF decreased. NPY, IL-6, BDNF were higher in the seventh day than in the first day in plasma and CSF. NPY, BDNF in different types of febrile seizures and epileptic seizures were no difference, but IL-6 have differences. The levels of NPY, IL-6 in plasma and CSF correlated to the times of convulsion, but BDNF had no correlation to the times of convulsion (4) NPY, BDNF, IL-6 In plasma were positively correlation to those in CSF respectively ( $p < 0.05$ ); In plasma and CSF NPY had significantly positive correlation to IL-6 ( $\gamma = 0.671, 0.657, p < 0.01$ ), and negatively correlation to BDNF ( $\gamma = 0.051, 0.269, p < 0.01$ ); BDNF was negatively correlation to IL-6 ( $\gamma = 0.226, 0.162, p < 0.01$ ).**Conclusion:** NPY, IL-6 in plasma and CSF are elevated in children with convulsive diseases and have correlation to the times of convulsion, changing in the different course of convulsion. There are positive correlation in NPY, BDNF, IL-6 between plasma and CSF. The levels of those in plasma could indirectly reflect the levels of those in CSF. In

plasma and CSF NPY had significantly positive correlation to IL-6 and negatively correlation to BDNF; BDNF was negatively correlation to IL-6.

#### P285

### THE KETOGENIC DIET: A REVIEW OF THE EXPERIENCE AT KING FAHAD MEDICAL CITY, RIYADH

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**Purpose:** Few centers in the Middle East offer ketogenic diet as an option for epilepsy treatment. Anecdotal data that ratio of the diet needed to reach the state of ketosis might differ in different races. This lead to thinking that there might be racial differences as to response to the diet.

We tried to evaluate this issue as well as the effect of the diet on seizure control, alertness, ambulation and continuation of antiepileptic drugs (AED) in our patients who were on the diet. We aimed to document any differences between our patients in Saudi Arabia and those reported internationally.

**Method:** We conducted a retrospective analysis of pediatric epilepsy patients on ketogenic diet in King Fahad Medical City since November 2008. Thirty patients were included initially. Ages ranged from 10 months to 11 years of different etiologies for intractable epilepsy. Follow up was at least for 6 months and longer.

**Results:** Twenty four patients continued on the diet, 6 discontinued (3 no improvement, 1 had persistent hypokalemia, 1 developed lipoid pneumonia and 1 for social reasons). Of the 24 patients: 8 (33%) became seizure free, Six (25%) had 90% improvement, 6 (25%) had more than 50% improvement and 4 (16%) had no clear improvement in seizures.

In 9 out of 24 patients (37%) family reported better ambulation after the diet. And in 16/24 (66%) showed better alertness and became calmer on the diet. The dose and number of AEDs per patient were decreased, and two patients became off medications. Our patients reached 3:1 ratio (except two patients on 4:1) and showed ketosis.

**Conclusion:** Ketogenic diet is a therapeutic alternative for many children. Our results are similar to other international experiences. Community and physicians should be aware and educated about the ketogenic diet.

#### P286

### FEBRILE CONVULSIONS: RESULTS OF THE CLINICAL AND EPIDEMIOLOGICAL STUDY DURING A 5 YEAR PERIOD AT PAEDIATRIC HOSPITAL "CENTRO HABANA", HAVANA, CUBA

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**Purpose:** Febrile convulsions (FC) constitute the most common problem in the practice of paediatric neurological practice, from three to five children of 100 suffer FC; more than 60% are simple or typical. Our objective is to describe the clinical and epidemiological characteristics of febrile convulsions in a study during a 5 year period.

**Method:** An observative, prospective and descriptive study of 327 children, who were attended by the services of the CHPH-urgency, was done, following neuropaediatrics consultation during 5 years. All children with at least one febrile convulsion were selected excluding patients with SNC infections or similar. The age at which occurred the first FC of a patient was correlated with the clinical characteristics, the diagnostic when the patient leaves the hospital, and recurrent risk factors. The patients were classified as simple, complex and recurrent. Their evolution was evaluated during a 5 year period as well as the use of antiepileptic drugs (AED).

**Results:** Sixty-four percent of children studied has had a simple FC, 15% had complexes and 21% recurrent. There was no difference related to sex, the most frequent age of start were between 1 and 4 years old (69.9%). Acute respiratory infection was the most frequent etiology related with the FC (72.8%). The most frequent risks factors related with FC were the family antecedent of FC (37.8%) and the initial age before the 1st year old (21.7%). The most significant risk factor of recurrent FC was family antecedent of epilepsy (15.6%). 31.8% of the children who received treatment with AED presented convulsions after 5 years of age.

**Conclusion:** Our study confirms the relation between family antecedents of epilepsy and recurrent febrile convulsions in children.

#### P287

### COGNITIVE BEHAVIORAL THERAPY IMPROVES COGNITION AND REDUCES AMOUNT OF SEIZURES IN CHILDREN

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**Purpose:** Epilepsy is a medical diagnostic entity that is often associated with anxiety and depression; which in return are often related to a higher number of seizures. This study investigated the neuropsychological/cognitive and health-related benefits following cognitive behavioral therapy (CBT) in a group of children.

**Method:** Twenty-one children (ages, 8–12) diagnosed with epilepsy (a homogeneous group with temporal lobe epilepsy with simple partial seizures) underwent CBT (8 weeks). Children were medicated (no changes during treatment) and had on average 5.4 recorded seizures per month. Parent/teacher evaluations (CBCL) were used to assess their anxiety and mood every other week and a neuropsychological evaluation was administered pre-post treatment. A control group of 19 matched children did not receive CBT during the same period.

**Results:** The children who underwent CBT experienced 3.2 fewer seizures ( $p < 0.01$ ) than their peers and had significantly lower CBCL scores on anxiety, withdrawal, and depression ( $p < 0.01$ ) and better neuropsychological functioning (memory, attention, and executive functioning;  $p < 0.05$ ).

**Conclusions:** Overall, CBT appears to significantly benefit children medically, psychologically, and neuropsychologically-cognitively.

#### P288

### THE DIAGNOSIS AND TREATMENT OF EPILEPSY AND NARCOLEPSY COMORBIDITY

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**Purpose:** We report two cases with narcolepsy and epilepsy co-existence. By analyzing of the We report two cases with narcolepsy and epilepsy co-existence. By analyzing of the clinical diagnosis and treatment process, we want to raise awareness of such cases.

**Method:** The clinical manifestation of two cases were observed, and video-electroencephalogram (VEEG), multiple sleep latency test (MSLT) were performed. HLA DR<sub>2</sub>, HLA DQB1\*0602 and hypocretin level in cerebrospinal fluid were examined.

**Results:** The onset disease of case one was epilepsy with myoclonic seizure. Because the manifestation of seizure showed head shaking to the left, the patient had been misdiagnosed Tic disorder and then partial seizures, which led to inappropriate treatment with oxcarbazepine and seizures aggravated. Epilepsy was diagnosed when VEEG monitored the seizures. After half a year, the symptoms of narcolepsy appeared and cataplexy was the first symptom. Narcolepsy was determined by clinical manifestation, result of MSLT, positive HLA DR<sub>2</sub> and HLA DQB1\*0602, and the decreased hypocretin level. Valproate was given and seizure was controlled completely, but the symptoms of narcolepsy were aggravated. Combination of valproate, methylphenidate and clomipramine treatment improved the symptoms of both narcolepsy and epilepsy. The onset disease of case two was narcolepsy, which was determined by clinical and various detections. The treatment was ineffective because of bad compliance and further withdrawal. After 2 years, complex partial seizures occurred and temporal epilepsy was diagnosed according to the clinical and VEEG. Oxcarbazepine was used and seizures were free, but the symptoms of narcolepsy were still obvious because of drugs for narcolepsy refused by parents.

**Conclusion:** Narcolepsy and epilepsy should not only be identified, but also need to pay attention to the rare comorbid of the two diseases with onset in succession in same patient.

## P289

### POST-CONCUSSION CONVULSIONS AND EPILEPSY

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**Purpose:** To present children admitted to the hospital due to loss of consciousness and convulsions related to sports. Sports commonly leading to concussions include contact martial arts sports, football, soccer and others. Main post-concussive symptoms are headache, followed by convulsions, dizziness, vomiting, lack of motor coordination, cognitive and emotional problems. Repeated concussions can lead to persistent neurological problems.

**Method:** Retrospective data analysis of patients with symptoms related to loss of consciousness and suspected epilepsy, playing different contact sports treated at our Neuropediatric Department during 16 months was done.

**Results:** Fifty four children (mean age 12.5 years) playing different contact sports were admitted to our Department. Epilepsy was suspected in 8 urgently admitted children (3 from playground): 3 had epileptic fits, 3 loss of consciousness, 2 confusion with unilateral cramps; after an outpatient visit 2 came with cramps and 1 with tremor. All children had on average training during 2–7 years, 2–3 times a week, and nearly each weekend. Three children had the diagnosis of epilepsy followed by antiepileptic treatment with a good control of seizures.

**Conclusion:** Concussions cause different neurological symptoms and convulsions if rest is not long enough to allow the brain to fully heal afterwards. Repeated concussions may lead to epilepsy and chronic encephalopathy. A neuropediatrician must monitor children involved in contact

sports, perform diagnostic procedures according to medical history and clinical presentation, advise a child to avoid the activities that may put them at risk for future head injuries and to discontinue contact sports if necessary.

## P290

### EPILEPSIES OF CHILD AND ADOLESCENT

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**Objective:** Epilepsy is a public health problem in Senegal, with a prevalence of 8.3 to 14/1000. It mainly affects children. The Objective of this work is to study the biographical aspects, phenotypic and evolutionary of epilepsy in a cohort of children in Senegal.

**Patients and methods:** This is a retrospective chart review of children with epilepsy followed up regularly at Fann University Hospital and Children's Hospital Albert Royer, July 2003 to December 2010. Inclusion criteria were: epilepsy aged under 16 years, regularly monitored for at least 3 years, with appropriate treatment, effective dose, with good adherence.

**Results:** We collected 522 children, aged 3 months to 16 years, with a sex ratio of 1.7 in favor of boys. The epilepsy was idiopathic in 57% of children and non-idiopathic in 43% of patients. Etiological factors were dominated by parental consanguinity, abnormal pregnancy and childbirth, infections of the central nervous system. In the group of idiopathic epilepsies not, the signs associated with epilepsy were language disorders (15.70%), behavior (15%) and motor deficits (10.32%). 22.41% of school children had learning difficulties sometimes leading to repetition or school exclusion.

**Conclusion:** The fight against epilepsy in Senegal implies an effective prevention policy which necessarily improving the socio-health and the fight against infections. This is the challenge of the Senegalese league against epilepsy.

## P291

### THE KETOGENIC DIET IS EFFECTIVE FOR REFRACTORY EPILEPSY DUE TO ACQUIRED STRUCTURAL EPILEPTIC ENCEPHALOPATHY

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**Purpose:** Patients with epileptic encephalopathy due to an acquired structural lesion often have refractory seizures that are not amenable to surgery. The ketogenic diet (KD) is effective for generalized epileptic encephalopathies. The purpose of this study was to report a series of nine patients with intractable epilepsy due to acquired structural epileptic encephalopathy that responded to the KD.

**Method:** Nine patients were recruited from the KD clinics at Austin Health, Melbourne, Australia and Great Ormond Street Hospital for

## Abstracts

Children, London, UK. The KD was initiated using a modified Johns Hopkins protocol. A fat to carbohydrate and protein ratio of 3:1 to 4.4:1 was used to achieve the appropriate level of ketosis. Urinary ketones were monitored twice daily (target: 8 mm in the morning and 16 mm at night). The primary outcome was the percentage change in seizure frequency at 1, 3, 6 months and 1 and 2 years compared to baseline. A responder was defined as a patient who achieved >50% reduction in seizure frequency.

**Results:** Median seizure onset ranged from 1 month to 4 years. Patients had multiple seizure types with frequencies ranging from 5 to innumerable seizures per day. At 3 months following diet initiation, 7/9 (78%) were responders and all patients showed improvement. At 6 months, 6/7 (86%) patients on the diet were responders (3 seizure-free; 2 with >94% reduction). After 1 year, 6/6 patients on the diet were responders (3 seizure-free; 2 with >90% reduction). After 2 years, 5/5 patients on the diet were responders (3 seizure free; 2 with >70% reduction). Subjective improvements in cognition were documented even with minimal effect on seizure frequency.

**Conclusion:** The KD is effective in patients with acquired epileptic encephalopathy. It should be considered early in patient management, as it improves seizure control and potentially developmental outcome.

## P292

### RISK FOR ANTIEPILEPTIC DRUG WITHDRAWAL IN CHILDREN WITH CEREBRAL PALSY AND FOCAL SYMPTOMATIC EPILEPSY

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**Purpose:** Purpose of this study was to find risk factors for antiepileptic drug withdrawal in children with epilepsy and cerebral palsy.

**Method:** One hundred and thirty-eight children with epilepsy and cerebral palsy (CP), followed in Institute for child and youth health care of Vojvodina from 01.01.1993 to 01.01.2012 for median period of 7 years.

**Results:** Seizure control has been achieved in 42 children, using one antiepileptic drug (AED) in 28.57%, using two AED in 38.09% and using three or more AED in 31.11% children. Seizure relaps after AED withdrawal appear in 25% children on one or two AED, 42.86% on three or more AED at start of AED withdrawal. Focal symptomatic epilepsy was diagnosed in 76 (55.07%) of those children.

**Conclusion:** AED polytherapy necessary for seizure control, with relative risk 1.39, and AED polytherapy at the time of beginning AED withdrawal with relative risk 1.69 are prognostic factors for seizure reappearances in our group. The age of onset of seizures, seizure type, time, time necessary for reaching seizure control, neonatal seizures, febrile seizures and status epilepticus, mental retardation, MRI CNS pathology, and epileptiform EEG discharges present at the time of AED withdrawal starting did not have prognostic value for

seizure relapses in children with CP and epilepsy after AED withdrawal.

We perform discontinuation of AED in children with epilepsy and CP, on monotherapy with seizure remission periods of 3 or more years.

## P293

### SUDDEN UNEXPECTED DEATH IN EPILEPSY INFORMATION PROVISION TO PARENTS OF CHILDREN WITH EPILEPSY: A SERVICE EVALUATION

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**Purpose:** NICE recommends that parents of children with epilepsy are informed about the risk of Sudden Unexpected Death in Epilepsy (SUDEP). This service evaluation was performed to assess SUDEP information-giving by healthcare professionals to parents of children with epilepsy.

**Method:** Fifty families of children with epilepsy were identified by attending follow-up paediatric neurology appointments at three hospitals in South-East Wales. A questionnaire was designed and used to interview participants about their awareness of SUDEP and from where they had sourced this information. Results were analysed using PASW Statistics 18.0.

**Results:** Fifty-two percent of participants were aware of SUDEP. 16% of participants had been informed of SUDEP by a healthcare professional. 70% of parents aware of SUDEP had used alternative sources. The commonest alternative source used was the internet. Participants regarding their child's epilepsy as poorly controlled had increased SUDEP awareness ( $p < 0.05$ ). Parents of children with nocturnal seizures aware of the risk of SUDEP were more likely to supervise their children at night than those unaware of SUDEP ( $p < 0.05$ ).

**Conclusion:** Improvements are needed in the provision of SUDEP information to parents of children with epilepsy. Awareness is shown to influence night-time supervision for nocturnal seizure detection, which could reduce SUDEP risk. Parents should receive reliable and accurate information by a healthcare professional, tailored to their child in a sensitive manner. This should reduce SUDEP risk, provide reassurance in cases where there is minimal risk and reduce the distress and uncertainty of SUDEP experienced by parents of children with epilepsy.

## P294

### CHARACTERISTICS OF HEADACHE IN CHILDREN WITH EPILEPSY

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**Purpose:** Epilepsy and headache are paroxysmal disorders. The association of headache with seizures is well known to neurologists but poorly understood. The purpose of this prospective study was to evaluate the type and the frequency of seizure-associated headache in children with epilepsy.

**Methods:** Patients with focal and generalized active seizures and on treatment at the time of administration were included. Patients with progressive brain disease or recent brain injury were excluded.

Patients were prospectively interviewed as to whether or not they suffer from headaches associated with seizures. The data obtained for each patient included seizure type, seizure frequency, and number of antiepileptic drugs taken. Seizure-associated headache was defined as a headache beginning within an hour before or after the seizure.

**Results:** Of 98 patients (43 males and 55 females; age 5–18 years), 34 (34.7%) patients (10 males and 24 females; mean age  $12.4 \pm 3.3$  year) complained about seizure-associated headache. The headache occurred preictally in 10 of 34 patients with seizure-associated headache, postictally in 28 of 34 patients, and both pre- and postictally in 4 of 34 patients. In 34 patients with seizure-associated headache, seven patients (20.6%) had migraine-like headache. Others (79.4%) had tension-type headache. Headache was present in 31/74 (41.9%) with partial vs. 3/24 (12.5%) with generalized seizures showing a statistically significant difference ( $p = 0.012$ ). Comparing the frequency of seizure attack on the basis of headache presence and non-presence group, there was 4.1 and 0.7 times during 1 year, respectively. 58.8% of patients complained about headache at frontal region. The location of headache was not always in agreement with electroencephalogram foci.

**Conclusions:** Headache has been encountered more frequently in patients with partial epilepsy and frequent seizures.

## P295

### CHARACTERISTICS OF EPILEPSY BEFORE FIRST YEAR OF LIFE IN PEDIATRIC HOSPITAL OF CENTRO HABANA FROM 2004 TO 2009

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**Purpose:** Epilepsy of early presentation has a special relevance by its association with poor prognosis related with cause.

**Method:** A descriptive study was carried out of epilepsy presented before first year of life, with first afebrile crisis and no acute symptomatic. The sample included cases assisted in Neuropediatric Service of Pediatric University Hospital of Centro Habana from January 1, 2004 to December 31, 2009. The patients were compared in the following categories: idiopathic, symptomatic, and probably symptomatic.

**Results:** Forty-one patients were included: 23 with idiopathic epilepsy, 17 with symptomatic epilepsy and 1 with probably symptomatic. In children with idiopathic epilepsy 14 have family history of epilepsy. In symptomatic epilepsy were reported 29 prenatal antecedents. Twenty patients have more than one prenatal and familiar antecedent. The more frequent cause was included in prenatal origin (15) and perinatal (10), combined in one patient with more than one origin. According electroencephalographic characteristic: 12 are generalized, 26 without generalization, and 3 with hypsarrhythmia and West syndrome. In relation with the psychomotor development normality was detected in 22 patients, 8 have mild retardation and 11 moderate to severe retardation.

**Conclusion:** This study is compatible with the existence of benign epilepsies and good prognosis before first year.

**Key words:** Infantile development, Epilepsy, Generalized epilepsy, Mioclonic epilepsy, Infantile spasms, Mental retardation.

## P296

### AUDIT ON USE OF EMERGENCY SERVICE BY CHILDREN WITH EPILEPSY

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**Background:** Unnecessary admissions to emergency room are a waste of resources. Furthermore, the patients realization that convulsion resulted in having to rush for help or end up in hospital will certainly heighten self awareness of their epilepsy.

**Objectives:** To investigate the extent to which known epilepsy patients use emergency services and attend emergency room with epileptic attack and how much of it is of a real benefit to the patient.

**Methods:** Children attended emergency room for seizures related to their diagnosis of epilepsy for a period of 6 months were included; those with febrile and undiagnosed afebrile seizure were excluded. Children were identified by searching the hospital database. Clinical notes were retrieved and scanned for information regarding clinical data using a pre-prepared questionnaire.

**Results:** The selected records were studied against a benchmark standard. Eight (27%) of the attendances were deemed unnecessary of which seven (87%) used ambulance as a mode of transport to arrive to hospital. Only 33% have an emergency care plan in place and out of those only 62% followed the plan. More than 50% of children arrived in full awake status and a third in ictal or post-ictal phase.

**Conclusion:** Unnecessary uses of emergency service by patients were widely acknowledged. Factors such as lack of support and education to children and their families were evident in our group. Provider should be aware of inefficient use of resources and the potential cost-savings while aiming to deliver optimal care to their clients.

## P297

### PARADOXICAL COEXISTENCE: IDIOPATHIC EPILEPSY WITH BOTH FOCAL AND GENERALIZED SEIZURES

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**Purpose:** Investigation of the spectrum of idiopathic epilepsies (IEs) in our Institute.

**Method:** The study of 407 patients with established diagnosis of idiopathic epilepsies, with age of seizure onset from the first days of life till 18 years.

**Results:** Among 407 patients, IGE was diagnosed in 49.8% cases and IFE in 42.3% cases. We revealed the separate group of 32 patients (7.9% of all IEs) with both focal and generalized seizures (IEFGS), including 14 males and 18 females. IEFGS was characterized by onset in the childhood (6 months–11 years, med. -5.1 years). It presents both generalized seizures, caused by the phenomenon of secondary bilateral synchronization and focal motor seizures on awakening. EEG shows combination of generalized spike-wave discharges with «rolandic» activity. This group of patients has the favorable prognosis for seizure free, and the normal cognitive functions. At the moment of investigation, remission was achieved in IFE – 95.9%, IGE – 87.7% and IEFGS – 75.0%.

**Conclusion:** The IEs is not a homogeneous group. In our opinion, IEFGS is an Idiopathic focal epilepsy with both focal and generalized seizures, caused by SBS. The pathogenesis factor might be «hereditary impairment of brain maturation», which is genetically determined. The similar coexistence was described by Beaumanoir & Nachory under the name «Benign Frontal Lobe Epilepsy in Childhood». The main result of our investigation – that this coexistence belongs to IEs, it has a benign course for both seizures and cognition.

## P298

## FEBRILE SEIZURES AS A PREDICTOR OF EPILEPSY

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## P299

## LONG-TERM DEVELOPMENTAL OUTCOME AFTER EARLY HEMISPHEROTOMY FOR HEMIMEGALENCEPHALY IN INFANTS WITH EPILEPTIC ENCEPHALOPATHY

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## P300

## POTENTIAL RISK FACTORS OF EPILEPSY-RELATED HEADACHE IN CHILDREN

Levitina E<sup>1</sup>, Rakhmanina O<sup>1</sup><sup>1</sup>Tyumen Medical Academy, Tyumen, Russia**Purpose:** To study types of headache and possible causes of its emergence in children with epilepsy.**Method:** There's been conducted comparative study involving 46 children aged from 6 to 18 y.o. with proven diagnosis of epilepsy. The primary group of patients is comprised of 23 children suffering from headache (12 boys, 11 girls aged  $13.4 \pm 3.6$  years old), group of comparison – 23 patients without headache (14 boys, 9 girls,  $13.1 \pm 3.5$ ).**Results:** Children from primary group suffered from the following types of headache: 66% – tension type headache, 22% – migraine, 12% – secondary headaches (intracranial processes-related headaches; chronic posttraumatic headache due to moderate or major head trauma; headaches related to secondary intracranial hypertension due to hydrocephalus). There's been revealed no reliable difference at the onset age and epilepsy experience between children with and w/o headache. Children with headaches appeared to have focal types of epilepsy more frequently – 91%. Children w/o headaches appeared to suffer more frequently from idiopathic generalized type of epilepsy (40%). 96% of children with headache had underlying condition while in the group of comparison 35% (mainly diseases of vegetal origin: arterial hypotonia, faintness, gastrointestinal disorders, neuroendocrine disorders). Analyses of relatives' illness rate indicated higher level of hereditary load on headache – 48% and 4% in the group of comparison. It is considered that headache in children with epilepsy is associated with adverse effects of antiepileptic drugs. There was revealed no reliable difference in mono/polytherapy, spectrum and dosage of antiepileptic drugs.**Conclusion:** As well as in population, in children with epilepsy primary forms of headache (tension type headache and migraine) are predominant. There've been revealed some factors assisting in headache progression in children with epilepsy (focal types of epilepsy, presence of underlying condition of vegetal origin, hereditary factor).

## P301

## TREATMENT OF CONTINUOUS SPIKES-WAVES DURING SLOW SLEEP IN BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES BY LEVETIRACETAM IN COMBINATION WITH SHORT CLONAZEPAM

Su T<sup>1</sup>, Xu S<sup>1</sup><sup>1</sup>Department of Pediatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China**Purpose:** To assess the efficacy of levetiracetam (LEV) in combination with short clonazepam (CZP) on the electroencephalogram (EEG) and clinical status of continuous spikes-waves during slow sleep (CSWS) in children with benign childhood epilepsy with centrotemporal spikes (BECTT).

**Method:** Nine boys and six girls diagnosed with BECCT with CSWS were enrolled and received LEV 10–20 mg/kg/day in combination with 2 months' short CZP treatment (0.02–0.03 mg/kg/day in the first month, qn; then 0.02–0.03 mg/kg/day in the second month, qod). All patients were prospectively followed for at least 6 months.

**Results:** Five children were only given LEV when diagnosed with CSWS in the early stage, but didn't have seizure free while EEG displayed no improvement, then received LEV in combination with CZP. Other 10 children received such combined treatment programme above once CSWS diagnosed. All children demonstrated good EEG response to LEV in combination with short CZP and seizure free. EEG was normal or had rare unilateral rolandic spike at 1 month and 6 month time-point. Only one boy (11 years old) underwent a relapse of CSWS pattern 1 month later after discontinuation of CZP, but EEG showed good 6 months later after repeated therapy.

**Conclusion:** LEV in combination with short CZP is effective in treating children with CSWS syndrome in children with BECCT.

### P302

#### IMPACT OF FAMILY AND PARENTAL PERCEPTION OF CHILDHOOD EPILEPSY AT FANN TEACHING HOSPITAL, DAKAR, SENEGAL

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**Purpose:** Epilepsy is a real public health problem. Patients living with epilepsy suffer from psychological and sociocultural problems which are obstacles to their development and social integration. Our objective was to assess the impact of epilepsy on quality of life of parents and their perception of the disease.

**Method:** During 3 months, 58 children (2–16 years) with epilepsy were recruited, and their parents were interviewed, the parent interviewed lived with the patient for at least 1 year. The presence of major changes in life during the previous 3 months on the social or economic conditions of the family (separation, parental unemployment), significant comorbidities and mental retardation were exclusion criteria.

**Results:** Epilepsy has an impact on the health of mothers, 74% of mothers had sleep disorders, 29% had headache. More than half of the mothers had seen a significant impact on their work, for 88% of mothers, the family economy was affected by the disease. While 23% of parents believe that their child's epilepsy brought them together, 61% believe it has not led to conflicts in their marriage, and 16% disagreed. According to 6.8% of mothers, their child's epilepsy removed any desire to conceive again.

**Conclusion:** Epilepsy is a neurological problem important in developing countries and is associated with significant psychosocial maladjustment in both, affected children and family.

### P303

#### PATTERN OF EEG IN NEONATAL SEIZURES (0–28 DAYS) AND ITS RELATION WITH NEURODEVELOPMENT AT 6 MONTH OF AGE IN FULL TERM NEONATES

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**Purpose:** EEG is bedside tool to document seizure disorder. The study was aimed to co-relate EEG changes with neurodevelopmental outcome, that will help to understand the prognostic value of EEG in newborns in regards to its neurodevelopmental outcome, hence to initiate early intervention therapy to minimize disability.

**Objective:** To Study EEG changes in neonatal seizures within 7 days of episode and to co-relate these changes with neurodevelopment outcome at 6 month of age.

**Method:** Total number of 28 cases of neonatal seizures were studied, sample size calculated by temporal association. Only full term neonates (37–42 weeks) with documented seizure disorder were included in the study. HIE I cases, babies of mother on anti-epileptics, pre term neonates (<37 weeks), full term neonates (37–42 weeks) with undocumented seizure disorder were excluded. The neurodevelopment examination was performed periodically to assess the progress of encephalopathy. Neurodevelopment assessment was done by the DDST II scale.

#### Results:

- 1 In 23 out of 28 EEG, generalized seizure disorder in form of generalized sharp waves was observed. 5 were normal.
- 2 No developmental delay on DDST at 4 weeks in 16 cases was observed.
- 3 Six died due to other medical illness at mean age of 11 days.
- 4 Six cases to be follow up.
- 5 Future developmental follow up 3 month and 6 month with not only co relate with EEG pattern but also reveal sensitivity and specificity of DDST at 4 weeks of age.

### P304

#### PSYCHOLOGICAL CHARACTERISTICS OF PEDIATRIC EPILEPSY WITH AUTISTIC REGRESSION

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**Purpose:** To describe demographic, epilepsy-related clinical, and psychological characteristics in children with epilepsy and autistic regression.

**Method:** Patients (1–16 years old) were identified from hospital records on the basis of having both epilepsy and autism diagnoses. Neurocognitive functions (development, intelligence, memory, general adaptive function, and attention) and psychological functions (emotional/behavioral problem, mother's depression, parenting stress, and social ability) were assessed with standardized measures. Epilepsy-related variables examined included age of onset epilepsy, etiology, seizure type, epilepsy classification, seizure frequency, EEG & MRI features, medications.

**Results:** Twenty-two children (13 boys, 9 girls), average age at onset 3.19 years (SD = 3.5 years), age at evaluation = 8.45 years (SD 4.6 years), with epilepsy and ASD were investigated. Five cases started with infantile spasm, later evolved to Lennox-Gastaut syndrome (LGS) in 3, temporal lobe epilepsy in one case. Fourteen cases were symptomatic focal epilepsy (7 frontal, 4 temporal, and 3 parietal), 2 cases of LGS, and one case of Dravet syndrome. Significant developmental delays or cognitive impairments were present in 16/22 (73%). Internalizing and externalizing behavioral problems were significantly elevated compared to test standardization values. Social and school competence were significantly depressed. More than half of caregivers, showed significantly increased level of depression and parenting stress.

**Conclusion:** Children with epilepsy and autism have especially high levels of intellectual or developmental disability. Future steps to understand the relationship between autism and epilepsy will need to incorporate information about the severity of autistic features, epilepsy symptoms, and intellectual disability.

## P305

### VAGUS NERVE STIMULATION OUTCOME IN CHILDREN WITH EPILEPSY: EXPERIENCE AT KING FAHD SPECIALIST HOSPITAL-DAMMAM, SAUDI ARABIA

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**Purpose:** We discuss the effectiveness, tolerability, and safety of vagus nerve stimulation (VNS) as adjunctive therapy in 12 pediatric patients with refractory epilepsies.

**Method:** A retrospective review of the records of pediatric patients (age <16 years) who had undergone primary VNS system implantation between 2010 and 2012. Considered data included demographics, epilepsy type (partial vs generalized), seizure frequency, seizure duration, postictal period duration, quality of life, and antiepileptic medication use.

**Results:** Twelve patients (58% female) were followed up for a mean of 29 months after VNS implantation. Fifty-eight percent of patients had partial epilepsy and 42% had generalized epilepsy. After VNS system implantation, seizure frequency was reduced in 66% of patients, seizure duration in 50%, postictal period in 44%, and antiepileptic medication use in 16.6%. There was no significant difference in age, sex, or duration of follow-up according to epilepsy type. Neither was there any significant difference in seizure frequency reduction, seizure duration, postictal period, medication use, overall clinical improvement, or improvement in quality of life.

**Conclusion:** Vagus nerve stimulation reduced both seizure frequency and antiepileptic medication use in the majority of pediatric patients regardless of sex, age, or epilepsy type. Vagus nerve stimulation also reduced seizure duration and postictal period, and quality of life in approximately half of the pediatric patients.

## P306

### EFFICACY OF VNS THERAPY IN CHILDREN WITH REFRACTORY EPILEPSIES ASSOCIATED WITH EPILEPTIC SPASMS

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**Purpose:** To evaluate the clinical efficacy of vagus nerve stimulation (VNS) in children with refractory epilepsies associated with epileptic spasms.

**Methods:** Twelve (four boys, eight girls) children aged between 4 and 12 years with drug-resistant epilepsies associated with epileptic spasms were prospectively followed for 6–18 months since VNS-therapy initiation. Epilepsy was symptomatic in all but one patient: cortical malformations – 7, hypoxic-ischaemic brain injury – 3, encephalitis – 1. In one patient the epilepsy aetiology was unknown. The majority of patients (11/12) had epileptic spasms associated with tonic seizures, two of them had also focal and one child – generalized tonic-clonic seizures. One patient had epileptic spasms as the only seizure type. Antiepileptic drug treatment has been unchanged during minimum first 6 months (range 6–12 months) since VNS start. The efficacy and tolerability of VNS-therapy were evaluated after 3, 6, 12 and 18 months after treatment initiation.

**Results:** The initial mean spasm frequency was 45 per day (range 15–80). After 3 months since the initiation of VNS-therapy it decreased to 24 spasms per day (range 10–60), after 6 months – 15 (range 5–60), and after 12 months – 10 spasms per day (range 5–30). Three children were followed for 18 months, and in two of them the significant spasm reduction was observed – from 60–70 to 10–15 spasms per day. Four out of 11 patients had a significant reduction (>75%) of tonic seizures after start of VNS-treatment, three – decrease for 50%, and in four children tonic sei-

zure frequency was unchanged. No serious side effects have been observed.

**Conclusion:** VNS-therapy can be an additional therapeutic option for children with drug-resistant epilepsies associated with epileptic spasms.

## P307

### VERY PRETERM CHILDREN AND WEST SYNDROME

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**Purpose:** To compare the frequency of occurrence of West syndrome among children with neurological problems, who was born very preterm or with 1–2 degree of prematurity.

**Method:** We conducted retrospective and prospective study of 156 premature patients receiving inpatient care at the children's hospital № 8 Kazan relatively various neurological diseases. We used a number of children with West syndrome among the studied preterm children as an unfavorable outcome measure. For outcome measures we calculated Risk Ratio (with Review Manager 5.2).

**Results:** The first group included 100 patients with a birth weight 1500 g or less (with 3–4 degree of prematurity). The mean gestational age at birth of children was 28.9 weeks (26–32 weeks). The proportion of boys and girls in this group was 1.15:1. The proportion of children with extremely low birth weight (<1,000 g) at birth in the first study group was 20%. The control group included 56 children with 1–2 degree of prematurity. The mean gestational age – 34.9 weeks (32–37 weeks). Age of children in the groups at the time of analysis was similar, varying from 2 to 12 years. At the age of 3 months to 2 years some patients had West syndrome; in the first group – 18% (18/100) of cases; in the comparison group – 5.4% (3/56). Relative risk (RR) was as follows: 3.36 [1.03; 10.91],  $p = 0.04$  (unfavorable outcome – the number of children with West syndrome).

**Conclusion:** In our study West syndrome was more common for the very preterm children with neurological problems than for children with 1–2 degree of prematurity.

## P308

### RESULTS OF 1-YEAR FOLLOW-UP IN FAR-EAST ASIA CATASTROPHIC EPILEPSY (FACE) STUDY

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**Purpose:** Catastrophic epilepsy is an urgent issue to be resolved. To investigate etiology, clinical features, treatment modalities and prognosis of seizure and development in catastrophic epilepsy children, and to clarify the prognostic factors, we initiated a multicountry study, the Far-East Asia Catastrophic Epilepsy (FACE) study.

**Method:** The study was designed as the retrospective cohort study using data of catastrophic epilepsy patients <6 years old admitted in hospitals from April 2009 to March 2010. Seizure and developmental outcomes were observed as main outcome measurements.

**Results:** In the study, 317 patients were recruited from four countries, 258 were followed-up for 1 year, and 59 dropped out because of lack of follow-up and data missing. Thirty underwent resective surgery, 34 underwent only palliative surgery, and 194 were not carried out any surgery. Multiple logistic analysis indicated that the younger seizure onset (odds ratio: 1.047, 1.012–1.083) and the resective surgery (odds ratio: 6.394, 1.443–28.340) were positive prognostic factors for good seizure outcome. Patients who obtained seizure-freedom were more in resection surgery (60%) compared with palliative surgery patients (27%) and patients without any surgery (16%) ( $p < 0.05$ ). DQ of resective surgery patients did not show difference between DQs on admission ( $60.1 \pm 6.3$ ) and on follow-up ( $58.8 \pm 4.9$ ) ( $p = 0.711$ ), whereas DQ of palliative surgery patients (admission:  $47.7 \pm 6.9$ , follow-up:  $41.0 \pm 5.1$ ;  $p = 0.039$ ) and no surgery patients (admission:  $44.4 \pm 2.6$ , follow-up:  $37.6 \pm 2.3$ ;  $p < 0.001$ ) declined significantly.

**Conclusion:** The results suggest that resection surgery may improve seizure outcome and development of children with catastrophic epilepsy.

### P309

#### INJURIES IN CHILDREN WITH EPILEPSY: A HOSPITAL BASED PROSPECTIVE STUDY

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**Purpose:** To study the magnitude and pattern of injuries in children with epilepsy in comparison with normal children.

**Method:** This was a hospital based prospective case control study. Children aged 2–16 years with a diagnosis of epilepsy and on treatment with anti-epileptics for minimum duration of 1 month were studied and compared with controls (siblings of children with epilepsy). A semi-structured questionnaire was used to collect details about epilepsy and type and frequency of injuries sustained. Cases and controls were followed up for 6 months for occurrence of injuries.

**Results:** Four hundred and forty children including 208 cases and 212 controls were analyzed. Twenty-one cases (10.1%) and 10 controls (4.7%) had sustained injuries (p-value 0.03). Nine out of 21 cases (4.32%) were seizure related. After excluding seizure related injuries, risk was insignificant (p-value 0.6). Out of all the seizure types, seizure related injuries were more commonly seen with generalized tonic-clonic seizures. Amongst children with epilepsy (CWE), 50% had sustained soft tissue injuries, 34.6% had abrasions and 11.5% had fractures while amongst controls, 40% had abrasions, 30% had soft tissue injuries and 20% had burns. In CWE, most injuries occurred during activities of

personal care at home whereas in controls, injuries were sustained mostly at street during playing.

**Conclusion:** In our study, the frequency of injuries in children with epilepsy was found to be significantly greater. However only nine out of 21 cases who had an injury had seizure related injuries. After excluding seizure related injuries, risk was not significantly greater in cases.

### P310

#### LONG-TERM COURSE OF DRAVET SYNDROME: A STUDY FROM AN EPILEPSY CENTER IN JAPAN

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**Purpose:** This study attempted to clarify the long-term course of Dravet syndrome (DS).

**Methods:** Ninety-one patients (47 males and 44 females) diagnosed as DS were studied. The long-term outcomes of clinical seizures, neuropsychological findings, and social situation were analyzed. The follow-up period ranged from 10 to 34 years and 5 months (median 18 years and 5 months).

**Results:** At the last follow-up, 86 patients (94.5%) continued to have generalized tonic-clonic seizures (GTCS), while status epilepticus and unilateral seizures were not observed; and myoclonic seizure, atypical absence, and photosensitive seizures were resolved in most patients. Five patients achieved seizure remission (seizure free 5 years or longer). Intellectual disability of various severities was found in all patients (severe in 61, moderate in 27, and mild in 3). Patients who achieved seizure control had milder intellectual disability, and higher GTCS frequency correlated with severer intellectual disability ( $p < 0.01$ ). The presence of occipital alpha rhythm in the basic activity was associated with milder intellectual disability ( $p < 0.01$ ). Three patients died. All patients had persistent GTCS, and seizure frequency didn't change before death. Mutations of the SC1NA gene were detected at a high frequency (46/49). Seizure remission was found in patients with missense mutations.

**Conclusion:** The present study reconfirms that the long-term seizure and intellectual outcomes of DS are extremely poor. Use of effective new drugs and further development of novel therapies are expected to improve the long-term outcomes of DS.

### P311

#### PREDICTORS OF RECORDING A SPELL OF INTEREST DURING PROLONGED INPATIENT VIDEO ELECTROENCEPHALOGRAPH MONITORING (IVEEG) IN CHILDREN

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**Purpose:** Prolonged iVEEG is the gold standard to differentiate non-epileptic spells from seizures. However, inpatient monitoring is expensive and disruptive to patients and families, and it may be low-yield if events are not captured. To aid clinical decisions regarding pursuit of iVEEG, we sought to identify factors predictive of recording a spell.

**Method:** Retrospective chart review of all children undergoing iVEEG for spell classification at Mayo Clinic, Rochester between September 2009 and October 2012. In patients admitted more than once during the

study period, only the first admission was considered. Data were extracted from the medical record, and predictors of recording a spell were determined.

**Results:** Two hundred and thirteen children (median age 7 year, 54% male) were monitored. Most (74%) had a single spell type. Median duration of monitoring was 24.8 h (interquartile range [IQR]: 22.4–48.5). A spell of interest was captured in 66.2%, with median latency to first spell of 4.03 h (IQR 1.33–17.06). Predictors of spell capture included higher lifetime number of spells ( $p < 0.001$ ), greater spell frequency ( $p < 0.001$ ), shorter time since most recent spell ( $p < 0.001$ ), developmental delay ( $p = 0.001$ ), sleep deprivation ( $p = 0.04$ ), and antiepileptic drug withdrawal ( $p = 0.04$ ). Spells were recorded in 72% with spell frequency of at least thrice weekly, 43% with frequency  $< 3$ /week to monthly, and only 26% with frequency less than monthly. Neither gender, age, previous diagnosis of epilepsy antiepileptic drug use, use of other provocative measures (photic stimulation, hyperventilation, exercise), or interictal discharge on prior EEG predicted spell capture.

**Conclusion:** Spells that occur at least thrice weekly are more likely to occur during iVEEG than those that occur less frequently. Sleep deprivation and antiepileptic drug withdrawal increase the likelihood of recording a spell.

### P312

#### POPULATION-BASED STUDY ON PREVALENCE, SYNDROMES, SEVERITY AND CONSEQUENCES OF PEDIATRIC EPILEPSY IN CUBA

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**Purpose:** Population studies of pediatric epilepsy are scarce. To determine the prevalence, types, severity and consequences of epilepsy in Cuban pediatric population.

**Method:** By antiepileptic drug use in pediatric populations from Plaza, Cojimar and Chambas municipality, were identified all the possible pediatric cases with epilepsy that were evaluated to confirm the diagnosis. It was defined the point prevalence, distribution of syndromes and severity of childhood epilepsy. The Impact of Pediatric Epilepsy Scale (IPES) was validated and applied to the cases detected.

**Results:** The prevalence of pediatric epilepsy from Plaza, Cojimar and Chambas municipality was 3.1, 4.1 and 4.0 per 1000 respectively. Focal epilepsies were predominant in the three populations studied (77% in Plaza, 88% in Cojimar and 80% in Chambas). Most (73%) had good seizure control and those with worse seizure control were more likely to have behavior disorders, a defined etiology and focal epilepsy. The IPES showed good validity, two factors accounted for 72% of the variance of the scale, and differentiated well between different groups. Internal consistency (Cronbach's  $\alpha$  0.96) and test-retest reliability (ICC 0.979) were excellent. The IPES applied at the population level showed less impact of the disease in patients with idiopathic epilepsies.

**Conclusion:** The low prevalence of pediatric epilepsy and its acceptable impact on the child and on family may reflect adequate pediatric epilepsy prevention and care in Cuba.

### P313

#### MIGRATORY FOCAL EPILEPSY OF INFANCY, CASE REPORT

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**Purpose:** To present the main features of this disease and make a case report.

**Method:** Observation.

**Results:** Case report: An 8-month-old male patient, presented with refractory focal seizures. He was the second child born to a non-consanguineous couple. His perinatal period was uneventful. He started having generalized clonic seizures at the age of one and a half month; although treated with valproic acid, he presented one seizure weekly. At 6 months old, he presented complex partial seizures lasted 10 s with eye deviation and pallor, with initial frequency of six times per day but it increased over the next days; adding sialorrhea, inconsolable crying and irritability. The focal seizures became migratory, with clinical and electroencephalographic correlation. He was treated with multiple antiepileptic drugs (levetiracetam, valproic acid, pregabalin, clonazepam, vigabatrin and potassium bromide) without success. The patient presented status epilepticus, and was put under barbiturate-induced coma. He got a ventilator-associated pneumonia, and finally died of metabolic acidosis secondary to status epilepticus.

**Conclusion:** The migratory focal epilepsy of infancy is a rare encephalopathy with a poor prognosis, so efforts should be focus to early diagnosis, appropriate combination of antiepileptic and supportive care.

### P314

#### PHENOTYPIC SPECTRUM OF SPTANI ENCEPHALOPATHY

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**Purpose:** We previously reported that in-frame *SPTANI* mutations could cause West syndrome with severe cerebral hypomyelination and reduced white matter as a new clinical condition. We aimed to delineate the clinical and neuroradiological spectrum of patients with *SPTANI* aberration.

**Method:** Five patients with a *SPTANI* in-frame mutation and two patients with chromosomal 9q33.3-q34.11 microdeletion involving *STXBPI* and *SPTANI* were ascertained. Clinical histories, neurological examinations, and neurophysiological and neuroradiological data were obtained.

**Results:** Four out of five patients with *SPTANI* in-frame mutation presented intractable infantile spasms with hypsarrhythmia, lack of visual attention, spastic quadriplegia, and diffusely reduced white matter and brainstem volumes with hypomyelination on MRI. Among them, coloboma-like optic discs were observed in one patient. One

patient with *SPTANI* in-frame mutation presented generalized epilepsy and pontocerebellar atrophy, but without infantile spasms. Two patients with microdeletion presented Ohtahara syndrome with suppression-burst EEG pattern and mild hypomyelination, and thin corpus callosum in one patient, which are consistent with phenotype of *STXBPI* mutation.

**Conclusion:** Four out of five patients with in-frame *SPTANI* mutation presented distinct phenotype of West syndrome with severe hypomyelination and atrophy of infratentorial structures, suggesting *SPTANI* encephalopathy. More severe phenotype than those of patients with *SPTANI* deletion indicates the dominant negative effects of the mutations. Mild phenotype in one patient indicates the phenotypic variation of *SPTANI* mutation. Functional analysis suggested that severity of phenotypes caused by *SPTANI* mutation may be correlated with degree of aggregation of  $\alpha/\beta$  spectrin heterodimer.

### P315

#### THE COGNITIVE CHARACTERISTICS IN CHILDHOOD ABSENCE EPILEPSY: POOR FRONTAL LOBE PROFILE

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**Purpose:** To clarify the characteristics of cognitive impairments in CAE (childhood absence epilepsy), we designed a neurocognitive test battery to investigate the cognitive function of frontal and parietal as well as temporal lobe.

**Method:** Cognitive function of 46 children with CAE in different therapy stages were measured using a computerized neuropsychological test battery including nine items. Their scores across the neuropsychological measures were compared with healthy control from the general population matched for age, sex.

**Results:** Children with CAE showed poorer performance in frontal lobe of Raven's progressive matrices (4.07 vs.5.0,  $p < 0.01$ ) and visual tracing test (3.93 vs.5.0,  $p < 0.01$ ). On the other hand, no differences were found between the two groups on measures of the function of parietal (i.e., simple subtraction, number comparison, Three-dimension mental rotation) and temporal lobes (i.e., word-rhyming, word semantics, verbal working memory and paired associative learning test),  $p > 0.05$ . Raven's progressive matrices and visual tracing performances were not related to the onset age before 5 years old, seizure control and monotherapy on valproic acid or combination with clonazepam,  $p > 0.05$ .

**Conclusion:** Children with CAE profile impairment in progressive matrices and visual tracing tests which stands for frontal function, nevertheless, CAE children perform as the same as healthy control in calculation, visual space, Chinese language and memory function. Whether the psycho-cognitive study should provide evidence that parietal and temporal lobe is a default area in absence epilepsy needs further study.

### P316

#### EARLY CLINICAL FEATURES AND DIAGNOSIS OF DRAVET SYNDROME IN 138 CHINESE PATIENTS WITH SCN1A MUTATIONS

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**Purpose:** Dravet syndrome (DS) is a severe epileptic encephalopathy. Although the seizure onset of DS usually occurs within the first year of life, DS is often misdiagnosed due to its atypical clinical manifestations. The aims of this study were to summarize the early clinical characteristics of DS and their relevant factors before the age of one.

**Method:** The clinical data and peripheral blood DNA of DS patients and their parents were collected. The features of seizures in 138 patients with SCN1A gene mutation were analyzed before the age of one.

**Results:** All 138 patients were followed up at the age from 18 months to 17 years and 5 months. Epilepsy started at a median age of 5.25 months. In addition 99 patients (71.7%) experienced seizures with duration more than 15 min. Two or more seizures induced by fever within 24-h were observed in 93 patients (67.4%). Also, 80.4% (111/138) of patients had hemi-clonic and (or) focal seizures. Seizures had been triggered by fever of low degree in 62.3% (86/138) patients before the first year of life. Vaccine-related seizures were observed in 48 patients (34.8%).

**Conclusion:** The seizure onset age in DS patients was earlier than those in common febrile seizures. When a baby exhibits two or more features of complex febrile seizures a diagnosis of DS should be considered, and SCN1A gene mutation screening should be performed as early as possible. Early diagnosis of DS will help clinicians more effectively prescribe antiepileptic drugs for stronger prognosis.

### P317

#### PREVALENCE OF GENETIC POLYMORPHISMS OF UGT1A6 AND THEIR ASSOCIATION WITH SERUM VALPROATE LEVELS IN NORTH INDIAN CHILDREN WITH EPILEPSY ON VALPROATE MONOTHERAPY

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**Purpose:** There is marked inter-individual variability in the pharmacokinetics and pharmacodynamics of valproate. Polymorphisms in UGT1A6, one of the major enzymes involved in the hepatic glucuronidation of valproate, may partly explain this. This study aimed to assess the association between the genetic polymorphisms of UGT1A6 in Indian children with epilepsy and the pharmacokinetics of valproate.

**Method:** This cross-sectional study was carried out in the Department of Pediatrics, AIIMS, New Delhi, between March 2011 and July 2012. Children aged 3–12 years of North Indian Origin diagnosed as epilepsy on valproate monotherapy for at least 1 month were enrolled. They underwent a detailed clinical examination as per a pre-designed proforma. The UGT1A6 polymorphisms were detected by PCR-restriction fragment length polymorphism. Random samples were checked by genetic sequencing. The steady state plasma concentrations of valproate were measured by High Performance Liquid Chromatography (HPLC) and associated with UGT1A6 polymorphisms.

**Results:** The most common etiological causes of epilepsy were neurocysticercosis (37.5%) and cerebral palsy (30%). The mean age at seizure onset was  $5.6 \pm 3.4$  years. The mean dose of valproate was  $21.8 \pm 9.1$  mg/kg/day. The prevalence of UGT1A6 T19G was as follows: TT (45%), TG (38.8%) and GG (16.3%); that of UGT1A6 A541G was: AA (48.8%), AG (38.8%) and GG (12.5%); and that of UGT1A6 A552C were: AA (43.8%), AC (40%) and CC (16.3%). There was no significant association between valproate doses or standardized serum valproate concentration and the various UGT1A6 genotypes.

**Conclusion:** Although no significant association was found between valproate doses or standardized serum valproate concentration and the various UGT1A6 genotypes, larger studies, studies in different ethnic backgrounds and meta-analyses of current data will help clarify the functional impact of UGT1A6 polymorphisms.

### P318

#### LONG TERM OUTCOME OF CHILDREN WITH WEST SYNDROME: RETROSPECTIVE ANALYSIS OF 135 CHILDREN TREATED AT A TERTIARY CARE CENTRE

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**Purpose:** West syndrome is an age-related epileptic encephalopathy which manifests after 4–6 months of age. Its etiology is heterogeneous and course variable. This study was undertaken to describe the clinical characteristics, treatment received and the long term outcome of children with West syndrome in a developing country.

**Method:** The case records of 135 children with west syndrome enrolled in Pediatric Neurology Clinic at a tertiary care and referral centre in north India, from January 2009 to December 2012, were reviewed retrospectively.

**Results:** The mean age at presentation was 26.6 months (SD: 14.1 months) with 72% males. The mean age of onset of spasms was 5.5 months (SD: 4 months). The semiology of spasms was flexor (74.3%), extensor (13.2%) and mixed (12.5%). 81.5% patients were symptomatic West syndrome. Etiology could not be found in rest of the children. The underlying etiologies included hypoxic ischemic sequelae (56.3%), CNS infections (10.4%), cerebral malformations (4.5%), Tuberos sclerosis (3.7%) and others. 80% children received hormonal therapy. 55.6% patients showed resolution of spasms, 13.3% children evolved to Lennox-Gastaut syndrome, 11.1% showed relapse of spasms after stopping hormonal therapy and 8.9% patients had persistent spasms at last follow up. 44% children with Lennox-Gastaut syndrome had hypoxic ischemic sequelae and 10.5% children with hypoxic ischemic sequelae developed Lennox-Gastaut syndrome.

**Conclusion:** West syndrome is common epileptic encephalopathy. Hypoxic ischemic sequelae and CNS infections are the major causes in a developing country. Half of these patients show resolution of spasms with appropriate therapy. A fraction of these children progress to Lennox-Gastaut syndrome. Early identification, aggressive management and good supportive care are critical for favourable neurodevelopmental outcome.

### P319

#### MEDICAL AND SOCIAL CARE FOR CHILDREN WITH EPILEPSY IN YAKUTIA

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**Purpose:** Evaluate provided medical and social care for children with epilepsy in Yakutia.

**Method:** We used clinical, epidemiological and statistical methods. Children from 0 to 18 years of age with a diagnosis of epilepsy were examined, living in the Republic of Sakha (Yakutia).

**Results:** According to the research of epidemiology of epilepsy of children in Yakutia, the prevalence of the disease was 4.9–5.2 per 1,000 of child population. Disability was established by 33.8% of children with

epilepsy. The highest incidence of epilepsy among the child population of the Republic was identified in the industrial regions: Nyurba, Ust-Maisky, Neryungri and in the capital of the Republic – the city of Yakutsk. Since 2004 there are the republic office of epileptologist in Yakutsk. In 2009 in Yakutsk was opened the office of the city of child epileptologist, performed video-EEG monitoring, that has allowed to improve not only diagnose, but also the treatment of epilepsy in children. There are 351 child with epilepsy in total in Yakutsk according of registered data of epileptologist. Since 2004 there is “School epilepsy” for parents and children with epilepsy. The School aims to provide educational and psychological assistance to families with children suffering from epilepsy. The treatment is carried out modern: in the first place – valproate, on the second – carbamazepine, on the third – lamotrigine and others. In the Republic of disabled children are provided with anticonvulsants free of charge, and in the city of Yakutsk all children consisting on the account of a neurologist receive free anticonvulsants.

**Conclusion:** Organization of integrated health care allowed to form a coherent strategy for patients with epilepsy in Yakutia.

### P320

#### EPILEPSY IN THE CROATIAN GIRL WITH RETT SYNDROME AND NOVEL MUTATION IN EXON 4 – 25BP DELETION (C.881\_905DEL25, NM\_004992.3) OF MECP2 GENE

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**Purpose:** To present the genetic and clinical features of a girl with Rett syndrome, particular in regards to epilepsy. Rett syndrome is pervasive developmental disorder caused by mutations in the X-linked methyl-CpG-binding protein2 (MECP2) in the majority of cases. It is predominantly found in females with normal development prior to an onset of symptoms, usually between 7 and 18 months of age. Epilepsy is considered as a major problem for these patients.

**Methods:** Retrospective review of data, electroencephalography and treatment was done in a 19 years old girl, previously diagnosed with a MECP2 mutation.

**Results:** The girl was born in a healthy family as the 4th child, after an uneventful pregnancy, delivery and perinatal period. Growth and psychomotor development were normal, except for delayed speech. First absence seizure occurred at the age of 3 years during a bath. The EEG showed focal discharges and therapy with CBZ was started. After frequent absences EEG showed generalised discharges and VPA was added. At the age of 3.5 years autistic behaviour was observed followed by rapid mental deterioration, loss of speech and motor skills, with periods of hyperventilation and fear. Occasionally „hand-washing” movements appeared. After exclusion of a wide spectrum of neuro-metabolic diseases, genetic analysis revealed a mutation on exon 4 – 25 bp deletion (c.881-905del25) of the MECP2 gene, at the age of 5 years. Till now multiple epileptic seizure types occurred daily, refractory to all anti-epileptic polytherapy with normal videoEEG background. She is able to walk slowly on wide based gait, she is atactic and spastic.

**Conclusion:** In this girl onset of symptoms began much later than in typical cases of Rett syndrome, epilepsy has a daily frequency and a drug resistance. Unexpectedly she is able to walk at the age of 19 years. There might be genotype-phenotype correlation.

### P321

#### TWO CASES OF HYPOMELANOSIS OF ITO AND EPILEPSY

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**Purpose:** To understand hypomelanosis of Ito and the pathogenesis of HI phenotype.

**Method:** Detailed presentations of clinical manifestations and diagnostic procedures of two recent cases of HI with epileptic seizures in children.

**Results:** Manifestations of HI are heterogeneous, it is necessary to differentiate HI with epileptic seizures from similar neurocutaneous syndromes.

**Conclusion:** Hypomelanosis of Ito, also known as the lack of incontinentia pigmenti achromians, is mainly with skin and nervous system symptoms and may be associated with many side symptoms such as head and facial dysplasia, congenital malformation of heart and reproductive systems, etc. Because it is related to multiple systems and organs it is now considered a multi-system involved skin disease. Ito (Ito's) first reported this disease in 1951 and he considered it might be due to autosomal dominant inheritance. Now people are inclined to think that the possible pathogenesis of the disease is mutations caused by the X chromosome inactivation or activation that caused abnormal transition of mesoderm and ectoderm precursors during embryonic development, and as a result, leading to skin section line development disorder, neuronal migration disorder, neurodysplasia, and forming multi-system abnormalities. At present the available epidemiological data for such kind of neurocutaneous syndrome disease is very limited. Two cases were identified in Changsha, China and is reported here. At first the whole process of diagnosis and treatments for the patient will be described in detail. Then, discussions are presented on how to identify Hypomelanosis of Ito from another two similar neurocutaneous syndromes: incontinentia pigmenti and tuberous sclerosis. The last part of this paper is recommendations on general procedures of diagnosis and treatments for this disease.

### P322

#### ADJUNCTIVE LACOSAMIDE EFFICIENCY AND TOLERABILITY IN PEDIATRICS IN FRANCE

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**Purpose:** Lacosamide is a new antiepileptic drug (AED) prescribed in association for the treatment of partial seizures in adult patients. This study evaluates the efficiency and tolerance of lacosamide as add-on therapy for refractory partial seizures in children aged 3–15 years based on our single-center pediatric experience.

**Method:** Descriptive, retrospective study. Twelve patients were identified (mean age 12 years). Patients had previously received a median of 3.1 AED for 7 years. All parents gave informed consent. Lacosamide was administered orally and prescribed in addition to the baseline AED (median of 2.1 AED in addition to lacosamide at inclusion) without constraint concerning dose increments, associated treatments, nor final drug dose. Parents held crisis diaries. Patients were regularly evaluated by a neuropediatrician. Efficacy variables included response ratio and percentage change in the frequency of all partial seizures from baseline to a minimum of 4 months of stable lacosamide treatment. Adverse reactions were assessed. Follow-up was documented for a mean of 48 weeks.

**Results:** No severe adverse drug reactions were observed. The median initiation dose was 2.85 mg/kg/day. Progressive increments led to a final median dose of 5.49 mg/kg/day (min 3.2; max 7.69). Seven patients (58.3%) responded to therapy (average seizure reduction of more than 50%), four patients (33.3%) showed a partial response (10–50% reduction), and one patient showed no change. The total mean number of monthly seizures was diminished by 35%. The mean seizure free interval went from 11 to 35 days. Treatment was interrupted in three patients due to lack of efficiency.

**Conclusion:** This study of 12 children suggests that oral administration of adjunctive lacosamide is well tolerated and effective in children and adolescents. Lacosamide may contribute to maximizing seizure control in pediatric patients presenting partial seizures without added adverse reactions.

### P323

#### MONITORING OF CONTENTS AND COMPARISON OF LEVELS OF HORMONES IN CHILDREN WITH EPILEPSY AND CONTROL GROUP

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Pathogenesis of epilepsy is complex and insufficiently studied, particularly the role of hormones in epileptogenesis in children. Screened 50 girls and 39 boys with epilepsy, and also 47 girls and 57 boys of control group of 8–17 years for research of the content in blood thyrotropic hormone (TTG), antibodies to thyroglobulin (a/b to TG), triiodothyronine (T3), thyroxine (T4), cortisol (C) and parathyroid hormone (PTH). It is established that there are two age groups in which ( $p \geq 0.90$ ) the content of TTG and C in boys with epilepsy, C in girls with epilepsy, in boys of control group – T3, T4, C, in girls of control group – T3, T4, C and PTH significantly differs. The content of PHT in blood of girls with epilepsy significantly differs in three age groups. Was found significant difference in content of all hormones in blood of boys with epilepsy and boys of control group, of girls with epilepsy and girls of control group, and also in content of C at boys and girls with epilepsy, and T3, T4, PHT at boys and girls of control group.

**Conclusions:** It is necessary to carry out research of the hormonal status and consultation by the endocrinologist to all children with epilepsy.

### P324

#### RESULTS OF RESEARCH OF CYP2C9 AND CYP2D6 GENE POLYMORPHISM IN CHILDREN WITH EPILEPSY

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It is proved that genetic polymorphism is a basis of individual sensitivity to medicines, and the important role of CYP2C9 and CYP2C19 gene polymorphism is established in a metabolism of antiepileptic drugs. Detoxication genes CYP2C9 and P450 system CYP2C19 were studied at 86 children with severe forms of epilepsy, among which 46 (53.49%) boys and 40 (46.51%) girls at the age from 3 months till 17 years. As a result of complex survey of children was found that 26 (30.23%) children had symptomatic generalized form of epilepsy, 9 (10.47%) children – epileptic encephalopathy (West and Lennox-Gasto syndromes), 47 (54.65%) children – symptomatic focal epilepsy (with secondary generalization and without it) and 4 (4.65%) children – idiopathic forms of epilepsy (generalized and focal). Screening revealed that 36 children had resistant to treatment epilepsy forms, those children who hadn't resistant forms of the epilepsy were accompanied complications from antiepileptic therapy, and 43 (50%) children had polymorphic detoxication genes CYP2C9 and CYP2C19 of system P450. Research found that the average daily dose of valproic acid at all children with polymorphic genes exceeded one at children who didn't have polymorphic genes.

**Conclusions:** Fifty percent of children with severe forms of epilepsy had CYP2C9 and CYP2C19 gene polymorphism, and in 41.86% rare genotypes were found in children with resistant to treatment form of disease. Therefore, treatment of such children should be based on the results of genetic research, which determines the presence or absence of polymorphic genes of P450 detoxication system.

## P325

### SEIZURE OUTCOMES IN PEDIATRIC PATIENTS AFTER A NON-FUNCTIONAL VAGAL NERVE STIMULATOR DEVICE

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**Purpose:** Vagal nerve stimulation (VNS) is an effective surgical procedure for patients with intractable epilepsy who are not candidates for resective surgery. Seizure reduction can be achieved in up to 40% of patients, however the device has a variable life span due to the differences in the settings utilized for certain cases. We wanted to follow on variables of seizure frequency after a non-functional device (NF).

**Method:** A population of four patients ages 15–21 was analyzed; the original procedure was done for intractable epilepsy in all of them. The device was NF for more than 2 years in one case and in three cases was NF for 1 year or more. In all the cases there were recurrent events with the usual pre-operative seizure semiology.

**Results:** All were refractory patients, one case with double cortex syndrome, two cases with focal cortical dysplasia in eloquent areas, one case with severe encephalomalacia. The length of time with a functioning device (FD) was variable; the shortest time being about 4 years, the longest was close to 6 years. The overall mean seizure reduction for all patients was 25–35% FD. The patients have an overall mean increase in seizures of 5–10% after the VNS device became NF.

The parents did not want to change or remove the stimulator in all cases after becoming NF.

**Conclusion:** The battery duration of the device has significant variability with short duration in those cases with higher settings and therefore significantly reduced than the expected battery lifespan at implantation. There is still a significant reduction in the seizure frequency, as compared to the pre-surgical status, even when having a NF stimulator, in patients with intractable epilepsy. It is unclear if local structural changes in the vagal nerve contribute to this finding.

## P326

### THE CHARACTERISTICS OF EPILEPTIC SEIZURES IN CHILDREN WITH PERINATAL POST-HEMORRHAGIC PORENCEPHALY OR POST-HEMORRHAGIC HYDROCEPHALUS

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**Purpose:** The aim of this study is to elucidate the characteristics of epileptic seizures in children with perinatal post-hemorrhagic porencephaly (PHP) or post-hemorrhagic hydrocephalus (PHH).

**Method:** The inclusion criteria are (1) subjects with neuroimaging findings consistent with PHP or PHH, (2) followed in our institutes by 2012, and (3) occurred seizures during the follow-up period. We reviewed subjects' charts to investigate their clinical data.

**Results:** Twenty-four subjects were included. The mean follow-up period was 111 ± 66 (SD) months (13–275 months). Spasms occurred in 8

(33%), partial seizures (PS) in 22 (92%), and both in 6 (25%). The mean onset of spasms was 10 ± 5 months (6–22 months), and that of PS was 43 ± 29 months (12–114 months). The frequency of PS was daily in 2, weekly in 3, monthly in 2, yearly or less in 15. The average duration of the longest PS was 37 ± 28 min (<1 to 80 min). Thirteen subjects (59% of patients with PS) had status epilepticus (SE). Eleven subjects (50% of patients with PS) had fever-induced seizures. Interictal electroencephalograms revealed no paroxysmal discharges (PD) in 4, monofocal PD in 3, bilateral focal PD in 4, multifocal PD in 9, and diffuse PD in 1. PD was identified in frontal area in 12 cases, central in 14, parietal in 12, occipital in 12, and temporal in 12.

**Conclusion:** Children with PHP/PHH can develop spasms and/or partial seizures. Patients with PS tend to develop SE and fever-induced seizures.

## P327

### BIOCHEMICAL ABNORMALITIES IN NEONATAL SEIZURES

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**Purpose:** Biochemical abnormality occurs frequently in neonatal seizures either as an underlying cause or as an associated abnormality. Prompt recognition of these abnormalities and early therapy are important in neonatal seizure control. We aimed to determine the frequency of biochemical abnormalities in neonates with clinical seizures in a university teaching hospital.

**Method:** In this prospective study, blood glucose, serum sodium, calcium, magnesium and indication based serum lactate and/or ammonia along with metabolic screen parameters were determined. Clinical data, risk factors, CBC and sepsis screen in all, and CSF analysis, blood culture, EEG and neuroimaging on indications were obtained. Standard definitions were used to identify biochemical abnormalities. Biochemical abnormality was considered isolated when known risk factors were absent.

**Results:** Of 672 NICU admissions, 80 (11.9%) neonates had seizures; 73 (91.2%) term, 48 (60%) male and 27 (33.7%) weighing <2500 g. HIE (26.3%) and sepsis (35.1%) were the predominant etiology. Biochemical abnormality was identified in 57.5% (46/80). Hypoglycemia was the commonest abnormality (47.8%) followed by hypocalcaemia (21.7%), hypomagnesaemia (13.1%) and hyponatremia (13.1%). Other metabolic abnormalities, multiple abnormalities and isolated biochemical abnormalities were identified respectively in 15.2%, 10.5% and 23.7%. Hypoglycemia constituted 52% in isolated abnormality. Biochemical abnormalities were found in 42.9% of HIE associated seizures and 46.4% of sepsis associated seizures. Neonates with isolated biochemical abnormalities had shorter hospital stay and less mortality. About 30% neonates with isolated hypoglycemia and 85% with other metabolic abnormalities required anticonvulsants at discharge.

**Conclusion:** Low levels of blood glucose and divalent cations are the most frequent biochemical abnormalities in neonatal seizures including those associated with HIE and sepsis.

## Poster Session: Psychiatry Monday, 24 June 2013

## P328

### PSYCHOGENIC NONEPILEPTIC SEIZURES IN MEN: COMPARISON OF CLINICAL AND PSYCHOSOCIAL FEATURES AMONG AFRO-AMERICAN AND CAUCASIAN PATIENTS

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**Purpose:** PNES represent an alternative diagnosis for refractory epilepsy (frequency between 10 and 40%). Reports of PNES in males are scarce, especially among African-American males (AAM). We compared demographic, clinical and psychosocial features of PNES in AAM and Caucasian males (CM).

**Method:** We retrospectively reviewed 3359 charts of all patients admitted to UMC epilepsy monitoring unit (between 2001 and 2011). Demographic, clinical and psychosocial characteristics were evaluated for AAMs and CMs. Separate independent-samples Mann Whitney U-tests were conducted comparing the distribution of several seizure variables between AAM and CM.

**Results:** Out of 282 with the diagnosis of PNES, 54 (19%) were males (16 AAMs, 19–55 years; 31 CMs, 18–58 years). Seven patients were excluded. Patient characteristics were as follows: (1) PNES for a duration of 1–5 years (50% AAMs; 45.2% CMs); (2) taking 1–3 AEDs (93% AAMs; 77% CMs); (3) daily/weekly seizures (62.5% AAMs; 77% CMs); (4) head injury history (56% AAMs; 19% CMs); (5) depression/anxiety (50% AAMs; 64.5% CMs); (6) alcohol/substance abuse (19% AAMs; 6.5% CMs); (7) disability benefits (75% AAMs; 55% CMs); (8) employment (6.25% AAMs; 22.6% CMs). Nineteen percent in both groups were without disability benefits or employment. Seizure frequency was higher in AAMs (mean = 2.25) than CMs (mean 1.77). Hyper-motor activity was the most frequent clinical manifestation for both groups (93% for AAMs, 70% for CMs). Limb/unresponsiveness occurred significantly more in CMs (38.7%) than in AAMs (6.25%). Clinical manifestations lasted >5 min in both groups. Spells were recorded within 24 h of admission in 62.5% of AAMs and 71% of CMs.

**Conclusion:** Few significant group differences suggest that PNES in males does not vary as a function of ethnicity. Differences such as more frequent clinical manifestations of limb/unresponsiveness in CMs and higher incidence of head injury report, alcohol/substance abuse and disability benefit in AAMs may provide insight into causative/associative factors of PNES.

### P329 SERVICE REVIEW OF THE JOINT EPILEPSY AND LEARNING DISABILITY CLINIC IN THE SOUTH EASTERN HEALTH AND SOCIAL CARE TRUST, NORTHERN IRELAND

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**Purpose:** There is currently a joint epilepsy and learning disability clinic for the South Eastern Health and Social Care Trust that began in October 2006. The clinic is for patients who would otherwise have to attend an epilepsy and psychiatric learning disability appointment separately. This is currently the only clinic of its type in Northern Ireland. The purpose is to review and assess service evaluation and to provide information for future comparison with similar services.

**Method:** There were forty-eight patients who attended the joint clinic during the period of October 2006, when the clinic first began and December 2011. Chart reviews for these patients were completed to gather demographic information including age, sex, co-morbidity and severity of learning disability. To evaluate the service the number of appointments attended and missed, reasons for referral, outcome from attendance at the clinic such as changes in seizure frequency and duration.

**Results:** The majority of patients attended one appointment (52%) and missed no appointments (90%). The most common reason for referral

was due to increase in seizure frequency (32%) and the most common intervention was change in medications (61%). The majority showed improvement in seizure frequency (68%) with a significant number having improvement in seizure duration (33%).

**Conclusion:** From the results, it shows there is an obvious benefit from having a joint epilepsy and learning disability clinic with a significant proportion that either showed an improvement in seizure frequency or seizure duration with 14.3% who had no further seizure. Since the clinic began in 2005, there has been 10 missed appointments suggesting that the clinics meets the majority of patient's expectations while not compromising on patient's experience.

### P330 MOOD AND ANXIETY DISORDERS IN MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** We aimed to evaluate some psychiatric disorders (PD), such as mood (MD) and anxiety disorders (AD) in mesial temporal lobe epilepsy (MTLE) and to correlate these data with clinical and demographic characteristics.

**Methods:** We evaluated 104 patients with MTLE from 02/2010 to 07/2011 with the Structured Clinical Interview for DSM-IV – Axis I (SCID-I), the Inventory of State and Trait Anxiety (STAI I-II) and the Beck Depression Inventory (BDI).

**Results:** MD were identified in 34 (32.70%) patients, of whom 06 (5.77%) also had AD. Among these patients, 47.06% didn't have a prior diagnosis of these comorbidities. The group with PD presented higher monthly frequency of seizures ( $p = 0.004$ ). We subdivided the group of patients with psychiatric comorbidities into two groups: one with MD (28 subjects) and the other with both MD and AD (MAD, six subjects). The subgroup MAD presented highest monthly frequency of seizures ( $p = 0.029$ ) than MD subgroup. We observed a trend toward a higher incidence of PD ( $p = 0.052$ ) and higher scores on the BDI ( $p = 0.029$ ) in women. Suicidal ideation was significantly higher ( $p < 0.0001$ ) in patients with PD. Higher BDI scores were related to patients who did not have a professional occupation ( $p = 0.046$ ).

**Conclusions:** The association between epilepsy and PD is still underdiagnosed and may negatively influence the clinical treatment of epilepsy. More attention should be directed towards the detection of subtle symptoms in order to provide specific treatment when necessary.

**Keywords:** Epilepsy, mood, anxiety. Financial support: CNPq and FAPESP (2011-21818-6)

### P331 THE MULTI-DISCIPLINARY TEAM MEETING ACHIEVES FAVORABLE OUTCOME OF PSYCHOGENIC NON-EPILEPTIC SEIZURE

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**Purpose:** The prevalence of psychogenic non-epileptic seizures (PNES) among patients admitted to epilepsy centers is estimated to be approximately 20%. Despite high percentage of patients with PNES, an effective therapy has not been established, although supportive psychotherapy and cognitive behavioral therapy are recommended.

**Method:** We have developed a care management system for patients with severe mental disability, Care Program Approach in Japan (CPA-J), and applied it for those with PNES. Three cases with positive outcomes are presented in this study. Using CPA-J framework, the patients with PNES worked on strength assessment and individual care plans with the help of our interdisciplinary team. Stress control guidance and employment preparation training were provided, and meeting with community support providers were held during the hospitalization to prepare for discharge. In addition, psychological education was given to their family as a part of the program. Through these interventions, all three patients became free from PNES and anxiety symptoms were ameliorated.

**Results:** After discharge, they continued to work part-time or to receive job training at employment support centers. All three of them showed no psychogenic seizures for over 1 year after discharge. The patient's own management of the stressors and possible causes of psychogenic seizures, the family support, and the establishment of a reassuring support system all contributed to a complete control of psychogenic seizures, which allowed them more stable living after discharge.

**Conclusion:** The present results suggest that utilization of the CPA-J framework to provide coordinated comprehensive support is effective for the patients with PNES.

### P332

#### A STUDY ON PERSONALITY TRAIT OF JAPANESE PATIENTS WITH EPILEPSY USING THE NEO-PI-R

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**Purpose:** The NEO-PI-R is a widely used self-completed questionnaire method for character research that evaluates the five main factors of character: neuroticism (N), extraversion (E), openness (O), agreeableness (A), and conscientiousness (C) and each of their sub-classes. We assessed the subjective character traits of the patients with epilepsy using the NEO-PI-R.

**Method:** Seventy-seven outpatients (female: n = 43, male: n = 34; age 35.7 ± 10 years; seizure frequency 23.6 ± 75.9/year; TLE: n = 28, FLE: n = 27, IGE: n = 21, unknown: n = 1) completed the NEO-PI-R (Japanese version). We confirmed that they had jobs or were well adjusted domestically, and they had not been diagnosed with psychiatric illness. The five main factors and their sub-classes for each patient were scored with T-score normalized by gender and the age group in the general population. T-scores >55 and <45 were designated "high" and "low", respectively.

**Results:** Of the five main factors, only N was "high" (average ± SD: 55.8 ± 11.2). Among sub-classes of N, anxiety (N1: 56.6 ± 10.1), depression (N3: 55.7 ± 11.2) and vulnerability (N6: 55.7 ± 11.2) were "high." Although the C factor was in the lower limit of the normal range (45.9 ± 9.50), we also found a "low" score in one sub-class of C competence (C6: 44.7 ± 10.4). The scores of the five main factors had no clear correlation with epilepsy subtypes (TLE, FLE, and IGE), seizure frequency or schooling history.

**Conclusion:** Our results suggest that the patients with epilepsy generally tend to consider themselves as anxious, depressive and vulnerable and to have low self-esteem.

### P333

#### CO-EXISTING PSYCHOGENIC NON-EPILEPTIC SEIZURES AND EPILEPTIC SEIZURES IN AN EPILEPSY MONITORING NIT POPULATION: INCIDENCE AND RELEVANCE

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**Purpose:** It is well described that psychogenic non-epileptic seizures (PNES) and epileptic seizures (ES) may co-exist in the same patient, but how to best define this co-existence and its incidence are debated and remain to be established.

**Method:** We reviewed all epilepsy monitoring patients at the University of Maryland Medical Center over a recent 18 month period to assess the incidence of both PNES and ES co-existing in the same patient as documented by capturing both PNES and ES during the same admission. Patients who had more than one admission were counted only once. Patients who were characterized in our database as having both PNES and ES were identified and those cases were reviewed.

**Results:** Of our 256 total epilepsy monitoring patients, 167 (65%) were female, and the mean age was 41 years (range 16–88, standard deviation 14.7). Of the total patients, 70 (27%) had documented PNES during their admission, and 11 (15.7%) of these PNES patients had co-existing epileptic seizures determined by video EEG during that same admission. In some cases diagnosed as PNES, the possibility of embellished epileptic auras were a concern.

**Conclusion:** The percentage of co-existing PNES and ES captured on video EEG monitoring in our patients (15.7% of all PNES patients) was higher than expected, and may relate in part to more aggressive seizure medication tapers to provoke events, thereby unmasking more epileptic seizures in our patients. In addition, embellished auras mimicking PNES remain difficult to distinguish from PNES in a small number of cases. Still, the incidence of co-existing PNES and ES in such a high percentage of patients is notable and suggests that caution is warranted when considering aggressively tapering medication in some patients with PNES.

### P334

#### THE NEUROLOGICAL DISEASE AND DEPRESSION STUDY (NEEDS): CHALLENGES IN EPILEPSY

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**Purpose:** The Neurological Disease and Depression Study is a multi-disciplinary team grant addressing the burden, course and impact of depressive disorders in neurological conditions, including epilepsy. The processes and outcomes of recruiting epilepsy patients in a large urban city are discussed here.

**Method:** Consecutive English-speaking patients seen in a tertiary care outpatient epilepsy clinic in a large city were screened (exclusion: moderate or severe developmental delay, dementia, aphasia or hearing impairment). Eligible participants were first presented with a preliminary consent form by clinic staff not involved in the NEEDS project; if agreeable, they were approached by study staff. A questionnaire addressing demographics, depression, quality-of-life, epilepsy severity and adverse event profile was completed by participants in the waiting room before their appointment. Participants were booked for a psychiatric Structured Clinical Interview for DSM-IV (SCID) within two



weeks of their appointment. All recruitment processes (including SCID scheduling) and data were managed through secure custom online programs.

**Results:** Of the 333 eligible, screened patients, presented with the full consent, 300 (90%) had epilepsy, of those 268 agreed to participate (89%). Of those with epilepsy, 196 (66%) completed the SCID.

**Conclusion:** Recruitment to such a study is challenging since data collection needs to occur in a busy clinical setting with intense time pressures as well as concerns about privacy and confidentiality. An good response rate for the SCID interviews was achieved indicating its acceptability in this population. The use of online database managers for scheduling and data management has facilitated study processes considerably.

### P335

#### DEPRESSIVE SYMPTOMS IN PATIENTS WITH EPILEPSY: ANALYSIS OF SELF RATING AND PHYSICIAN'S ASSESSMENT

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**Purpose:** Depression has significant negative consequences on the quality of life of patients with epilepsy (PWE). This study assessed the prevalence of depressive symptoms among PWE and the impact of seizure variables on their depression scores.

**Method:** A case-control study of randomly selected patients with epilepsy attending a tertiary hospital in metropolitan Nigeria. A total of 152 randomly selected subjects used the Beck's depression Inventory (BDI) for quantitative assessment of depression while the Hamilton Rating Scale for Depression (HRSD) was used by the authors. The Student t test assessed statistical significance of differences in the BDI and HRSD scores while the scores were correlated with the Pearson's correlation coefficient. Logistic regression analysis and chi-square for trend assessed the impact of seizure variables on the scores. The level of significance was taken as  $p < 0.05$ .

**Results:** The prevalence of depressive symptoms was 42.11% and 44.74% using the HRSD and BDI respectively with significant differences in the scores of the patients and controls on both scales ( $p < 0.001$ ). The PWE scores on both scales yielded a correlation coefficient of 0.8 indicating their utility in detecting depressive symptoms. Seizure control was the most potent predictor of depression (HRSD:  $p = 0.004$ ; BDI:  $p = 0.001$ ).

**Conclusion:** Depressive symptoms are common in epilepsy. Early detection and prompt management are recommended. Good seizure control with an appropriate antiepileptic drug, among other interventional measures, may contribute to prevention of depression in epilepsy.

### P336

#### PSYCHIATRIC DISORDERS IN PATIENTS WHO UNDERWENT VIDEO EEG

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**Purpose:** Drug Resistant Epilepsy (DRE) and Psychogenic Non Epileptic Seizures (PNES) present high comorbidity with psychiatric disorders.

The aims of this study were to analyze psychiatric diagnoses, and compare the psychiatric profile and trauma history, between DRE and PNES group of patients who underwent Video EEG at Epilepsy Center of Ramos Mejia Hospital. We included patients aged 18–65 years, with pure PNES and compared with patients with DRE, both groups diagnosed by Video EEG. All patients underwent psychiatric interviews using DSM IV criteria. Variables analyzed and compared between the two groups: Age, gender, current psychotropic medication, psychiatric diagnoses, trauma history and global assessment of functioning.

Student's t test was performed to compare the quantitative variables and chi square test or Fisher's exact test to compare qualitative variables. SPSS for Windows was used for statistical analysis. A p value of at least 0.05 was considered significant.

**Results:** Eighty-four patients were evaluated, 49 DRE (42% men 58% women) and 35 PNES (20% men 80% women). Axis I psychiatric diagnoses were found in 33 DRE (67%) and 33 PNES (94%) ( $p < 0.05$ ), with significant differences in anxiety disorders ( $n = 14$ , 40%) ( $p < 0.05$ ) and PTSD ( $n = 8$ , 22%) ( $p < 0.05$ ) for the PNES and more psychosis in DRE ( $n = 10$ , 20%) ( $p < 0.05$ ). PNES presented more axis II diagnoses ( $n = 25$ , 71%) than DRE ( $n = 27$ , 55%) ( $p < 0.05$ ) being cluster B disorders the most diagnosed ( $n = 15$ , 42.85%) ( $p < 0.05$ ). Trauma was reported by 17 PNES (48.5%) and 12 DRE (24.5%) ( $p < 0.05$ ).

**Conclusions:** Both groups of patients present a different psychiatric profile: PNES patients are mostly women, with more axis I disorders (specially PTSD and other anxiety disorders) axis II cluster B disorders and report more history of psychic trauma than DRE patients, while DRE have similar depression rates and more psychosis than PNES patients.

### P337

#### 'MODIFIED SEMIOLOGICAL CLASSIFICATION' AND OUTCOME OF PSYCHOGENIC NON-EPILEPTIC SEIZURES (PNES) IN ADULTS

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**Purpose:** To analyze the phenotype, outcome and propose a modified semiological classification in adults with PNES.

**Methods:** This retrospective analysis included 82 patients (M: F = 38:44; age:  $33.4 \pm 12.0$  years) of PNES based on video-EEG from August 2005–August 2012. The semiological characteristics like limb/body movements, emotional manifestations, "aura", consciousness, psychiatric diagnosis, follow up, outcomes etc were recorded. We classified the patients as per available classifications. We propose a modified new classification based on this study.

**Results:** The age at onset and diagnosis of PNES was  $21.8 \pm 14.1$  and  $29.3 \pm 12.7$  years respectively. A total of 369 attacks were recorded. Forty seven (57.3%) patients were incorrectly diagnosed to have true seizures and received AEDs, 15 (18.3%) patients as PNES while 20 (24.4%) patients had both PNES and true seizures. About 40–66% patients couldn't be classified into existing classifications. A modified classification is proposed: abnormal generalized motor: 23 (28%), abnormal partial motor: 18 (22%), affective/emotional behaviour phenomena: 4 (4.9%), dialeptic: 5 (6.1%), non-epileptic aura: 5 (6.1%) and mixed: 27 (32.9%). The mean follow up duration in 63/82 (76.8%) patients was  $0.9 \pm 1.7$  years. The PNES attacks were controlled in 23/63 (36.5%) patients. Seizures were uncontrolled in 9/16 patients (56.2%) with coexistent true seizures with follow up. The diagnoses in

63 patients with follow up were: dissociative disorder- 31 (49.2%), depression- 5 (7.9%), psychogenic movement disorder- 3 (4.8%), psychosis- 3 (4.8%), anxiety- 2 (3.2%), OCD- 2 (3.2%), no definitive diagnosis- 17 (26.9%).

**Conclusion:** Incorrect diagnosis of PNES leads to unnecessary AED usage, costs and its side-effects. PNES attacks were controlled in 1/3rd of patients. A modified systematic classification of PNES is proposed for better characterization of PNES.

### P338

#### PSYCHOPATHOLOGY IN ADULTS WITH INTELLECTUAL DISABILITIES WITH OR WITHOUT EPILEPSY: A CASE CONTROL STUDY

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**Purpose:** Epilepsy-related factors may increase the risk of developing psychopathology in adults with intellectual disabilities (ID). We examined the patterns of problem behaviours and psychiatric disorders among adults with ID and epilepsy.

**Method:** We recruited 25 adults with ID and epilepsy (14 males) and a control group of 25 adults with ID alone (13 males) matched for age and ID level. The mean age of the overall sample was 41 years (SD = 17). Their carers were interviewed using the Modified Overt Aggression Scale (MOAS) (which provided a total score for aggression but also separate scores for verbal aggression, and physical aggression against people, objects and self respectively), and mini PAS-ADD Interview to assess co-morbid psychiatric disorders.

**Results:** A significantly higher proportion of adults with ID and epilepsy, compared with adults with ID alone manifested aggression against people and objects. Although there was no significant difference between the two groups in the proportion of adults meeting mini PAS-ADD Interview threshold scores for the presence of at least one psychiatric disorder, the group without epilepsy (24%) was significantly more depressed compared with the epilepsy group (4%). The results also showed that higher seizure frequency was associated with aggression against people and total MOAS aggression scores.

**Conclusion:** This study supports previous research (Deb & Hunter, 1991, *BJP*, 159, 822–30) that the overall rates of psychopathology and patterns of aggressive behaviours or psychiatric disorders are similar among adults with ID with or without epilepsy, although frequent seizures increases the risk for aggression against people.

### P339

#### VALIDATION OF A GERMAN VERSION OF THE NEUROLOGICAL DISORDERS DEPRESSION INVENTORY FOR EPILEPSY (NDDI-E)

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**Purpose:** The Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) (Gilliam F et al. *Lancet Neurology* 2006; 5:399–455) is a six-item screening instrument for major depression in people with epilepsy. The aim of this study was to validate the German version of the NDDI-E.

**Method:** The NDDI-E was translated into German, translated back into English and approved by the group that had developed the instrument. One hundred and forty-four in-patients (52.8% female, mean age

34.1 years, 68.1% focal epilepsies) of Bethel Epilepsy Centre were examined using the NDDI-E, Beck Depression Inventory II (BDI II), symptom check-list SCL-90-R, and Mini International Neuropsychiatric Interview Plus (MINI Plus).

**Results:** Twenty-five (17.4%) out of the 144 patients had depression according to MINI Plus. Internal consistency reliability (Cronbach's Alpha) of the NDDI-E was 0.83; explorative and confirmative factor analyses indicated unidimensionality. NDDI-E was significantly correlated with BDI II ( $r = 0.77$ ) and the depressiveness subscale of the SCL-90-R ( $r = 0.75$ ). The AUC of Receiver Operating Curve of the NDDI-E with MINI Plus-defined current major depression was 0.85 (95% CI: 0.77–0.94). An NDDI-E score of >15 had a sensitivity of 0.68, a specificity of 0.82, a negative predictive value (NPV) of 0.82 and positive predictive value (PPV) of 0.45; a score of >16 had the same sensitivity, but a specificity of 0.90, a NPV = 0.93 and PPV = 0.59.

**Conclusion:** The German version of the NDDI-E is a valid and reliable screening instrument for the detection of depression in epilepsy patients. A cut-off score of >16 might be more suitable than one of >15 as used in the original version.

### P340

#### A STUDY ON PSYCHOGENIC NONEPILEPTIC SEIZURES: CLASSIFICATION AND CULTURAL VARIABILITY IN SOUTH INDIAN POPULATION

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**Purpose:** Psychogenic nonepileptic seizures (PNES) is a common problem encountered by neurologists whose prevalence is estimated to be 2–33 per 100,000 when compared to prevalence of 4–6 per 1,000 in epilepsy. Pattern recognition of events from video-EEG findings is the cornerstone for diagnosis and treatment. Lack of a classification system of PNES makes it difficult to understand across various studies due to lack of homogeneity as well as understanding of the long-term prognosis of different subgroups. To study semiology of PNES observed by video-electroencephalography (vEEG) monitoring and classify the typical patterns observed and to see any cultural differences in manifestation.

**Method:** vEEG records of 90 consecutive patients from activation clinic were reviewed retrospectively to identify those who had suspected PNES with or without a background of epilepsy. The behavioural patterns observed were classified into six groups like rhythmic minor motor, complex motor, non epileptic auras, mixed PNES, atonic, hypermotor according to the predominant motor manifestation.

**Results:** Of these, most common type of PNES being minor motor (45.7%), and least common being hyper motor PNES (5.1%). In a given patient, all the seizures belonged to a single type in 81% of cases and in 2% of patients PNES is diagnosed mistakenly. Most of the cases got their seizures on provocation with tuning fork.

**Conclusion:** Nonmotor seizures are more common in south Indian population when compared to other studies where rhythmic motor seizures are more common. vEEG is important to differentiate PNES from true epilepsy. Activation with tuning fork with suggestion is important to diagnose when compared to PS & HV in South Indian Population.

### P341

#### PSYCHOSIS OR EPILEPSY? PROLONGED EVENTS DO NOT ALWAYS INDICATE PSYCHOSIS AND SHOULD PROMPT, UNDER CERTAIN CONDITIONS, FURTHER INVESTIGATION

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**Purpose:** To underpin the importance of Video-EEG recordings in patients with psychotic symptoms suspected of partial seizures of prolonged duration.

**Case:** A 16 year old girl with a 2-year history of panic attacks was referred as having developed psychotic symptoms over the last 16 months: 1. auditory hallucinations “birds calling my name” mostly during daytime 2. a sense of “a bad girl stabbing my back with a knife” during nighttime. The duration of her symptoms was usually more than 2–3 min and up to 30 min. During episodes she retained consciousness. Increased dosages of antipsychotic drugs had no effect. MRI was normal. A routine and later a sleep deprived EEG revealed intermittent polymorphic theta slowing over the left temporal region. Clobazam was added for her night-time symptoms and a slight improvement was noted. A video-EEG revealed very frequent spikes and slowing over the left temporal region. Antipsychotics were withdrawn and Carbamazepine was commenced at 400 mg daily; she then became free of hallucinations.

**Conclusion:** Differentiating PA and/or psychotic symptoms from epileptic attacks is not always easy. In this case, the duration of the events exceeded that seen in partial epilepsy; however prolonged seizures or even status could explain such events. Psychotic symptoms atypical of functional psychosis and a lack of response to antipsychotic drugs should alert us to the possibility of partial seizures. In the event of non-specific findings indicative of epilepsy, in routine EEG recordings, video-EEG is the gold standard.

### P342 PREVALENCE OF COEXISTING EPILEPSY AND PSYCHOGENIC NONEPILEPTIC SEIZURES

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**Purpose:** To estimate the prevalence of epilepsy in patients with psychogenic nonepileptic seizure (PNES).

**Background:** Up to one third of patients referred to epilepsy monitoring units are diagnosed with PNES. Depending on the criteria used, the proportion of patients with PNES who also have evidence of epilepsy has been reported to be 8–60%. Patients with only PNES do not require antiepileptic drugs (AEDs), although many are receiving AEDs at the time of referral for diagnostic monitoring.

**Methods:** We reviewed all adult admissions to the EMU at Neurology dept during 1 year. Patients with PNES fulfilled the following criteria: at least one typical attack with impairment of consciousness was recorded; Normal EEG prior to, during, or after a clinical event; no clinical suggestion that attacks were due to other neurological or physiological disorders. Patients with PNES and definite or possible epilepsy met the following criteria: epileptic seizures and/or interictal epileptiform discharges were recorded in addition to PNES. The use of AEDs at the time of referral was documented.

**Results:** Four hundred and nine patients were monitored; 112 (27%) had PNES. The mean age of patients with PNES was 35 years (range 18–67), and 80 (71%) were women. PNES patients were monitored for 1–11 days. 68 (61%) were on AEDs at the time of referral. Of the 112 patients with PNES, 12 (11%) had evidence of epilepsy. Eight of these had unilateral focal spikes and one had rare bioccipital spikes. Three patients had recorded epileptic seizures, interictal epileptiform discharges and PNES.

**Conclusions:** Only 11% of patients with PNES had evidence of coexisting epilepsy. The low prevalence of epilepsy in patients with PNES indicates that most of them can be withdrawn from AEDs and offered treatment for their underlying psychiatric disorder. Use of video-EEG monitoring is critical if PNES are to be detected early.

### P343

#### INFLUENCE OF PSYCHIATRIC COMORBIDITY ON TEMPORAL LOBE EPILEPSY SURGERY OUTCOME

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**Purpose:** Psychiatric diseases are more common in patients with epilepsy both prior and after epilepsy surgery comparing to general population. Evidences of the influence of psychiatric diseases on postoperative prognosis are emerging.

**Method:** During the 3 years period, 47 patients (24 men, 23 women, mean age: 36 ± 10 years) underwent right (20) or left (27) anterior temporal lobe resection with amygdalohippocampectomy due to refractory temporal lobe epilepsy. Psychiatric examination was performed before and after surgery in all patients and appropriate diagnosis was made if the required criteria were met.

**Results:** Patients were followed for 6–48 months after surgery (median follow-up 14 months). In 41/47 (87%) patients, the surgery was successful (Engel score Ia). In 10/47 (21%), criteria for psychiatric illness were fulfilled before surgery (anxiety: 1, depression: 4, impulsiveness: 4, psychoses: 1), and were still present after surgery in 7/47 (15%) patients (anxiety: 1, depression: 2, impulsivity: 3, psychosis 1). In 6/47 (12.7%) patients, acute postictal psychosis occurred after a series of seizures during video-EEG monitoring, and 4/6 (66%) had a psychiatric disorder after surgery (de novo in 2). De novo psychiatric diagnosis was made in 9/47 (19%) patients (anxiety: 3, depression: 3, psychosis: 3) after surgery. Psychiatric disorders were observed in 4/6 (66.6%) patients who failed surgery and in 15/41 (34%) patients (p = 0.16) rendered seizure-free after surgery.

**Conclusion:** Our results suggest that the psychiatric illness is frequent in refractory temporal lobe epilepsy and probably could negatively affect prognosis in respect to seizure remission.

### P344

#### PREVALENCE OF ANXIETY AND DEPRESSION DISORDERS IN PERSONS WITH EPILEPSY IN A UNIVERSITY HOSPITAL

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**Purpose:** To determine the prevalence of depression and anxiety in persons with epilepsy (PWE) in a Mexican population.

**Method:** Observational, descriptive and transversal study of 54 adult patients during the May-July 2012 period, using Hamilton Anxiety Scale

and Montgomery-Asberg Depression Scale (MADRS). Statistical analysis using T of student and Spearman's correlation coefficient.

**Results:** Average age  $35 \pm 14$  years, 50% women, 58% singles, 67% education below high school level, 40% economically active, 85% without previous psychiatric diagnosis, age of onset of epilepsy  $23 \pm 16$ , 60% had partial onset seizures, 58% had complex partial onset seizures, time evolution  $15 \pm 16$  years, 55% cryptogenic etiology. Out of the total, 41% had some degree of anxiety -predominantly moderate/severe-, 14% depression -predominantly mild-, they coexist in 29%. At older ages, the MADRS score was higher ( $p < 0.01$ ). Likewise, we found a correlation directly proportional between the Hamilton score and MADRS ( $p < 0.01$ ). There were no significant differences based on education, age of onset, time evolution, type or frequency of crises. The results suggest a correlation between time evolution and MADRS score, however, it did not reach statistical significance.

**Conclusion:** This study shows the high prevalence of anxiety and depression disorders on PWE in a Mexican population and proves the low diagnostic and treatment in them. This is one of the first studies in our country to report the statistics of these comorbidities and coincides with the literature. These results emphasize the needed to improve identification and management of depression and anxiety in PWE.

#### P345

##### THE RISK FACTOR OF SKIN RASH ASSOCIATED WITH LAMOTRIGINE MONOTHERAPY IN NEWLY DIAGNOSED EPILEPSY

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**Purpose:** The skin rash associated with lamotrigine (LTG) is the leading cause of withdrawal in patients with epilepsy. We studied the risk factors developing skin rash related to LTG in patients with newly diagnosed epilepsy.

**Method:** We consecutively enrolled patients who were first diagnosed epilepsy in our clinic. We administered them LTG as a monotherapy. LTG administration started as 25 mg qd, and increased 25 mg in an every week. The target dose was 100 mg/day. We observed skin rash during the initial 3 months. We investigated risk factors developing skin rash related to LTG among demographic, clinical, and psychiatric variables.

**Results:** Totally, 52 patients were eligible to the study. Among them, nine patients (17.3%) developed skin rash within a month of observation. Daily dosages of LTG eliciting skin rash were ranged from 25 mg to 100 mg. Fourteen patients (26.9%) exhibited affective symptoms. The risk factor associated with LTG-induced skin rash was affective symptoms (OR = 9.242, 95% CI: 1.097–77.877,  $p < 0.041$ ).

**Conclusion:** Depression or anxiety symptoms may be a predictor of LTG-induced skin rash.

## Poster Session: Social Issues/Nursing Monday, 24 June 2013

#### P346

##### FACTORS INFLUENCING QUALITY OF LIFE IN 160 SUBJECTS WITH EPILEPSY AND THEIR CAREGIVERS

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**Purpose:** To assess the subjective quality of life (QOL) of People with Epilepsy (PWE) and their caregivers, using the QOLIE-31 and SF36 Instruments, and study the predictors of QOL. Study of quality of life in both groups may help in improving epilepsy care.

**Method:** This analysis was conducted at G. B. Pant Hospital, using a cross sectional design. Total 160 Subjects with epilepsy (all types) of at least 1 year duration and their care givers, age range 18–60 years were included. Detailed history and demographic characteristics, including type of seizures, treatment history, and socioeconomic status were recorded in a structured Proforma. Assessment was done by using adapted version of QOLIE 31 (Quality of Life in Epilepsy Subjects 31) for epilepsy subjects and SF 36 (Short Form Health Survey 36 version 2) for their care givers.

**Results:** In this study there was male preponderance and subjects (78.75%) were young (age <30 years) and of lower middle and lower class (56.87%). Generalized seizure (65.63%) was the most common type of and majority of subjects (74.37%) had epilepsy of less than 10 year duration. Low education and socioeconomic status, earlier age of onset, higher frequency of seizures, more duration of epilepsy and less time passed since last episode of seizure and polytherapy were predictors of lower quality of life in subjects and care givers. QOL was found to be low if care givers was female (mother or wife) of subjects.

**Conclusion:** Persons with epilepsy as well as their caregivers have poor quality of life which may be related to disease per se, drug therapy, and variety of social factors. Their proper assessment and relevant management should be included in the holistic epilepsy care.

#### P347

##### ATTITUDE TOWARD EPILEPSY AFTER MEDIA COVERAGE OF CAR ACCIDENTS RELATED TO PERSONS WITH EPILEPSY IN JAPAN

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**Purpose:** In order to clarify the effect of media coverage on car accidents by persons with epilepsy, we compared the familiarity with and attitude toward epilepsy among non-medical students before and after the accidents.

**Method:** We have annually conducted a questionnaire survey on attitude toward epilepsy since 2008. We divided students into two groups: Pre-accidents era, years 2008–2010, and post-accident era, years 2011–2012.

**Results:** The rate of students who have read or heard about epilepsy was significantly higher during the post-accident era. Students during post-accident era answered more frequently that they do not oppose their kids to playing or attending school with children with epilepsy, think that people with epilepsy should be hired in the same way as other people, and do not oppose their kids to marrying with a person with epilepsy.

**Conclusion:** Media coverage of car accidents related to persons with epilepsy positively affected familiarity with and attitude toward epilepsy.

#### P348

##### YOUTH LIVING WITH EPILEPSY SPEAK OUT!

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**Purpose:** Epilepsy Associations in Africa have inadequate representation of Young educated persons with epilepsy within their organizational structures both in regard to activities and political influence, resulting into knowledge gaps on youth priorities in strategies for each of the organizations.

**Method:** Creation of awareness on epilepsy care and management and the special needs to be considered when teaching students with epilepsy among secondary schools also falls within the mandate of Epilepsy Associations in Africa as a high priority area, as ignorance about epilepsy causes stigma hence discrimination of children and young people with epilepsy which becomes a barrier to their ability to learn.

**Results:** This will in return enable various Epilepsy Associations dispel myths about epilepsy in the selected schools and as a result help provide an enabling learning environment for young learners with epilepsy, provide youth accommodative organizational structures within the given organizations. The stated purpose of Youth with epilepsy, speak up is to mobilize and support Young Persons with Epilepsy (YPWE) attending secondary schools expected gain three-fold outcomes: YPWE will learn how to manage epilepsy and improve their opportunities through knowledge on leadership and development, complete secondary education; the targeted secondary schools will become more inclusive to young people with epilepsy and will stand out as model schools in this regard; and Epilepsy Associations' will become more attractive to YPWE.

**Conclusion:** This paper examines the governance effect and impact of epilepsy associations mobilizing youth with epilepsy in secondary schools into Epilepsy Associations.

### P349

#### PERCEPTION ABOUT JOB TRAINING FOR PEOPLE WITH EPILEPSY AND SEVERE COGNITIVE IMPAIRMENT IN THE COLOMBIAN FOUNDATION CENTER FOR EPILEPSY AND NEUROLOGICAL DISEASES (FIRE)

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**Purpose:** To understand the perception about job training for people with epilepsy and severe cognitive impairment in the Colombian Foundation Center for Epilepsy and Neurological Diseases.

**Method:** Particular ethnographic study, qualitative approach in a population of 15 children operated on because of Epilepsy, Parents and FIRE Rehabilitation Team.

**Results:** The favorite activities of the Program are: physical activities, and those of labor inclusion pertaining individual capacities to achieve work. For parents it is valuable because their children learn how to perform important work functions. It allows the rehabilitation team to acquire responsibilities such as commitment, friendship; making the achievement of the particular goals easier, the child feels appreciated which prompts a positive attitude making a better life quality.

**Conclusion:** The family is fundamental for the accomplishment of the goals, preparation and attention; it promotes trust for a major involvement of the children. It is necessary to develop integral programs for the achievement of skills of children operated on because of Epilepsy also for those with cognitive and motion limitations where they can get some work capacity, in response to their needs, their own limitations and their tastes, having them be part of the productivity process.

FIRE Cartagena, uses the possible means to reduce the impact of these limitations in productivity, noting that rehabilitation belongs to a multi-disciplinary team, a group of professionals in various fields that cooperate with a common goal which is the individual welfare.

### P350

#### ANALYSIS ON THE DISABILITY DUE TO EPILEPSY AND ITS ECONOMIC BURDEN IN CHINA

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This study aimed to estimate the disease economic burden of the disabled due to epilepsy in China with the data from the Second National Sample Survey on Disability in 2006 and the household income and expenditure data from the Annual Disability Monitoring, as well as the data from the supplemental survey to the inpatients with epilepsy and their doctors. The results indicated: (1) The morbidity varied in different population. The morbidity of the rural residents, the male, the youth and middle-aged was higher, while the morbidity was even higher in the population with lower income. The category of disability due to epilepsy was mainly mental or speech disability and the severe degree were also higher than the average. (2) The household economic status of the epilepsy families was poorer than the others. The annual per capita household income was 2295.99 ± 2151.84 yuan RMB, which was less than half of the income of the families without disability. (3) The average length-of-stay (LOS) of the epilepsy inpatients was 26.4 ± 17.36 days. The LOS of 36% inpatients was between 1–2 months and 5% was more than 2 months. (4) The average expenditure of epilepsy inpatients was 78333.79 ± 73748.27 yuan RMB and 34% of them is more than 100 thousands yuan RMB. (5) The average annual disease economic burden of the epilepsy was about 7263 yuan RMB (906 USD) in 2006, which was a little higher than that in other developing countries. Among the disease burden, 17.58% was direct and 82.42% was indirect. (6) The estimated national total economic burden of the disabled with epilepsy was 5.67 billion yuan RMB (0.71 billion USD) in 2006, and the burden would reach 67.67 billion yuan RMB (8.44 billion USD) if we used the cost from epilepsy inpatients as the direct burden, which was even higher than the former.

### P351

#### CONFRONTING STIGMA OF EPILEPSY IN ACCRA, GHANA

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**Purpose:** Stigma associated with chronic diseases is one of the greatest challenges to the treatment of the disease. In this study, the aim is to describe stigma perceived by patients attending the epilepsy clinic at the Korle Bu Teaching Hospital and the Accra Psychiatry Hospital in Ghana, and to compare the perception of stigma among patients with epilepsy and a comparison condition, HIV.

**Method:** This study is being conducted at the Korle Bu Teaching Hospital and the Accra psychiatric hospital. Epilepsy patients have been recruited from these two locations; so far 200 subjects have been recruited. The Kilifi stigma scale was validated and used to obtain perception of stigma in subjects through a face to face interview at the clinics as the dependent variable. Demographic information such as age, gender and socioeconomic status, information on disease process such as frequency of seizures, onset of disease were obtained during the face to face interview as independent variables. Preliminary analysis using descriptive, multilevel linear regression and comparative analysis has been done on data with SPSS 16 statistical programme per statistical significance at 0.05

**Results:** Preliminary results suggest a high perception of stigma of epilepsy in Accra which is influenced by the clinic location and age of patient.

**Conclusion:** Perceived stigma not only affects quality of life of the affected person, but may impact negatively on medication adherence among people with epilepsy and family members. Understanding of the complexity of the perception of stigma in epilepsy will help stakeholders to design targeted intervention programs to help combat epilepsy in Ghana:

### P352

#### A QUALITATIVE INVESTIGATION OF CARER BELIEFS CONCERNING SEIZURE PRECIPITANTS IN ADULTS WITH INTELLECTUAL DISABILITY AND EPILEPSY

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**Purpose:** In clinical practice, carers of individuals with intellectual disabilities (ID) and epilepsy often report precipitants for the seizures experienced by the person they support. However, little is known about what carers mean by these reports and the consequences of these beliefs for the support of the person with epilepsy.

**Method:** Twenty-three individual semi-structured interviews were undertaken with paid support workers, key workers, and managers of group homes for people with intellectual disabilities. Individuals were invited for interview if they thought there might be a seizure precipitant for somebody with epilepsy and ID they currently support. The interviews were analysed using thematic analysis.

#### Results:

1. A number of themes were identified concerning
2. How carers of adults with epilepsy and ID define seizure precipitants,
3. How carers who report seizure precipitants come to hold these beliefs, and
4. How these beliefs impact on the carer and their support of the person.

**Conclusion:** These results will assist clinicians in communicating with carers who believe there may be seizure precipitants for the people they support. They may also inform future research into educational interventions for carers regarding how to manage events they believe to be seizure precipitants in a way that best serves the interests of the people they support and how they might communicate their beliefs to clinicians.

This research was funded by an Epilepsy Action studentship and approved by the Cambridge East NHS Research Ethics Committee.

### P353

#### “REARRANGING THE FRONT DOOR” IMPROVING PATHWAYS FOR SUSPECTED FIRST SEIZURE PATIENTS

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**Purpose:** Suspected first seizures presenting in Emergency Units can be difficult to triage. As a result a range of clinicians from psychiatrists' to cardiologists to neurologists can become involved in their care. Misdiagnosis of this group is common and can be fatal. NICE guidelines 2012 recommend review by a specialist within 2 weeks but within our service this only occurred 35% of cases. Improvements to services within existing resources were needed.

**Method:** We established a steering group involving patient representatives and professionals to identify ways in which realistic improvements could be achieved. A new service utilising the skill and experiences of the epilepsy specialist nurses was incorporated. They began assessing patients in the emergency unit at their initial presentation. Weekly meet-

ings with cardiology were formed to allow rapid triage into either cardiology or neurology. This led to swift assessment with the opportunity to talk to patients about what had happened, and discuss lifestyle issues (particularly driving and bathing) at the front door.

**Results:** Since implementing the average number of patients reviewed within 2 weeks has nearly doubled. By cutting out unnecessarily waits time to diagnosis has changed from an average of 111 days to 30 days and patient stories have shown us that patients and families value the new service.

**Conclusion:** Involving a full range of partners both internal and external to evaluate existing services can lead to surprising options. Links with other departments developed during the process now allow for a smooth transition for patients between specialities when required.

### P354

#### RELIGIOUS AND CULTURAL BELIEFS IN THE CAUSES AND TREATMENT OF EPILEPSY AMONG PATIENTS WITH EPILEPSY IN SAUDI ARABIA

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**Purpose:** This study was conducted to discover the beliefs of patients with epilepsy (PWE) from Saudi Arabia (SA) regarding the cause of epilepsy and treatment methods.

**Methods:** Hundred and ten PWE, (61) male and (49) female, age (18–60) years old, all from Saudi Arabia were asked to answer a questionnaire in Arabic listing different causes and treatment methods. Ethical approval was obtained from ethical committee in Prince Sultan Military Medical City in Riyadh.

**Results:** Descriptive analysis was used to analyse the results which showed that most of PWE in Saudi Arabia believe that epilepsy is a condition that is caused by multifactorial reasons. They also believe that epilepsy could be treated by different treatment methods which may include medical and religious treatments at the same time. Almost 74% of PWE in SA believe that epilepsy is an illness and caused by organic reasons, (83%) of patients believe that epilepsy is a test from God, (62%) believe in envy as a cause, (35.5%) believe that epilepsy is caused by Jinn (spirits) and only (10%) of the same sample believed epilepsy to be caused by other factors. In regards to treatment, (72.7–90%) of the patients rely on different religious methods such as rehearsing the holy Quran and faith healing. At the same time almost 81% of PWE believe in taking AEDs even if they use other treatment methods.

**Conclusion:** The majority of PWE in our sample believe that epilepsy is a medical condition that needs to be treated by medication. Additionally, they also believe that epilepsy is a result of God's will and have beliefs about the religious factors of the cause and treatment of epilepsy.

### P355

#### WHICH FACTORS HAVE THE GREATEST EFFECT ON QUALITY OF LIFE AMONG PATIENTS WITH EPILEPSY IN SAUDI ARABIA?

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**Purpose:** This study was conducted to compare different factors such as (age of onset, seizure type, seizure frequency, seizure severity, number of AEDs, mental and physical side effects of AEDs, depression, anxiety, and feeling of stigma) on the overall quality of life (OQOL) of patients with epilepsy (PWE) in Saudi Arabia (SA).

**Methods:** The quality of life (QOL) of 110 PWE, (61) male and (49) female, age (18–60) years old, all from Saudi Arabia was investigated using translated scales to Arabic such as, The National Hospital Seizure Severity Scale (NHS3) and The Liverpool Adverse Drug Events Profile (LAEP). Some of those scales were administered by the health professional and some were self-completed. Ethical approval was obtained from ethical committee in Prince Sultan Military Medical City in Riyadh.

**Results:** Linear regression analysis was used and the results showed that the most significant factors which affect the OQOL was, mental side effects of AEDs, depression and anxiety symptoms and feeling of stigma. However, splitting the outcome analysis by the seizure type showed that patients who suffered from Tonic-clonic seizure showed more significant effect of mental side effects of AEDs, depression, anxiety, and to some extent stigma on OQOL. Patients with partial seizure showed only negative effect of depression on OQOL, while patients with other types have no significant relation with OQOL.

**Conclusion:** Overall QOL of PWE in SA get worse with different factors such as the AEDs mental side effects, depressive and anxiety symptoms and feeling of stigma. Patients with Tonic-clonic seizure showed more depressive and anxiety symptoms, worse mental side effects of AEDs and to some extent more stigmas.

### P356

#### A COMPARISON OF QUALITY OF LIFE BETWEEN PATIENTS WITH EPILEPSY, PATIENTS WITH MULTIPLE SCLEROSIS, AND HEALTHY CONTROLS FROM SAUDI ARABIA

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**Purpose:** This study was conducted to compare the quality of life (QOL) between patients with epilepsy (PWE), patients with multiple sclerosis (MS), and healthy controls (HC).

**Methods:** Three groups completed the RAND 36 (aka SF-36) Arabic version. 110 PWE, (61) male and (49) female, age (18–60) years old. 114 MS, (35) male and (79) female, age (18–55) years old, mixture of MS patients were included as long as they don't have significant motor disability. 136 HC, (58) male and (78) female, age (18–60) years old, all healthy controls were the patients relatives who were healthy.

**Results:** Kruskal-Wallis Test was used to compare the QOL subscales of the RAND 36. Results showed that PWE were significantly worse than MS patients and HC on the following subscales means; Physical function: PWE (72.22 ± 24.84), MS (73.16 ± 20.63), HC (92.28 ± 7.42), Role limitation due to physical health: PWE (58.48 ± 41.87), MS (72.59 ± 33.09), HC (96.69 ± 9.03), Role limitation due to emotional problems PWE (58.27 ± 43.35), MS (69.88 ± 40.64), HC (94.85 ± 13.38), Emotional wellbeing: PWE (55.55 ± 26.75), MS (60.54 ± 25.78), HC (78.1 ± 14.19), Social function: PWE (68.59 ± 33.36), MS (74.67 ± 29.36), HC (94.72 ± 10.36). MS patients scored worse than PWE in the following subscales; Pain PWE (76.95 ± 30.22), MS (69.78 ± 25.78), HC (90.29 ± 14.82), Energy fatigue, PWE (57.61 ± 24.45), MS (53.81 ± 23.07), HC (75.46 ± 14.31), General health PWE (60.11 ± 24.68), MS (59.25 ± 21.35), HC (87.68 ± 10.18).

**Conclusion:** PWE from Saudi population showed worse QOL in most of the RAND 36 subscales, in comparison to MS and HC. However, MS patients scored worse on pain, energy fatigue and general health subscales in comparison to PWE and HC.

### P357

#### FELT AND ENACTED STIGMA IN PARENTS WITH EPILEPTIC CHILDREN

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**Purpose:** Epilepsy may have a negative psychosocial impact on all family members, especially on parents of epileptic child. Stigma is a prototype of such an impact and it may affect their interpersonal relationship or coping ability. The present study aimed to evaluate the degree of felt and enacted stigma in parents of epileptic children, and analyze the relationship between the general and clinical factors and their social stigma.

**Method:** Participants were 60 parents whose child was diagnosed and had been treated as epilepsy at pediatric epilepsy clinics in Dongguk University Ilsan Hospital. The parental social stigma scales were developed by modifying Jacoby's stigma scales. Data were analyzed using Oneway ANOVA, multiple range test, multiple regression.

**Results:** The results of analysis showed that 21.7% of parents have social stigma. The felt stigma and the enacted stigma was found in 18.3% and 13.3% of parents, respectively. Oneway ANOVA showed the significant differences of the parental social stigma level according to the parental academic background, the frequency of the seizure, the number of anti-epileptic drugs, and the combined disabilities. Multiple regression showed that the age of epileptic child, the seizure frequency, and the existence of combined disabilities are the factors which influence significantly on enacted stigma where as the seizure frequency and the number of anti-epileptic drugs are the factors influencing on felt stigma.

**Conclusion:** These results suggest that the parents caring for older epileptic child may have more enacted stigma and those caring for the epilepsy-plus child may have both more felt and enacted stigma. These findings may help healthcare providers prepare the epilepsy family programs relieving their stigma.

### P358

#### RAISING AWARENESS ABOUT EPILEPSY THROUGH FORUM THEATRE IN UGANDA

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**Purpose:** Forum Theatre was identified by Epilepsy Support Association Uganda (ESAU) as a tool of providing accurate information on epilepsy. This tool was used in Uganda to sensitize young professionals and community members on epilepsy in order to enhance a better understanding of epilepsy so that they can provide adequate support to people with epilepsy.

**Method:** Forum Theatre is an interactive form of theatre that encourages audience interaction and explores different options for dealing with a problem or issue and it is often used by socially excluded and disempowered groups.

**Result:** In the year 2010–2012 Epilepsy Support Association Uganda implemented a forum theatre project and the Organization was able to reach a total of 20,739 people through the performances. Out of this total number reached 10,273 were males while 10,466 were females. From this strategy alone ESAU managed to reach more people than it had expected. As a result of this achievement, ESAU was able to secure another funding to implement a 2 year project in the four districts where ESAU intends to form 12 Psycho social support groups for people living epilepsy. This project is targeting 70 performances in 50 communities and 20 institutions. ie 1,000 People with Epilepsy, 10,000 parents of people with epilepsy, 6,000 community members from 50 communities, 4000 professionals &, 50 district leaders reached with epilepsy information through forum theatre and 50% incorporate epilepsy issues in their planning and ESAU also intends to established partnerships with the nodding syndrome task force

**Conclusions:** Forum Theater has been proven to be the best strategy in raising awareness in both institutions and communities since it encourages massive participation of the audience and ESAU would like to share this idea with other delegates during the forth coming 30 International Epilepsy Conference in Montreal.

### P359

#### PERCEPTION OF EPILEPSY AMONG NIGERIAN PRIMARY SCHOOL PUPILS

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**Purpose:** It is estimated that 80% of people suffering from epilepsy around the world, reside in developing world such as Africa and it remains a stigmatized condition. Reducing the stigma of epilepsy is paramount to reducing its impact and so improving quality of life. Unfortunately, there have been no studies conducted to explore the perception of epilepsy among Nigerian children. We therefore carried out a survey on the knowledge and attitude of epilepsy among primary school students aged 9–12 years.

**Methods:** We used a questionnaire to determine if the children knew what epilepsy is, and if they did not know, what did they think epilepsy is. Fifty children (35 boys and 15 girls) with mean age 11 years; from a sixth grade of a primary school in northeast Nigeria completed the questionnaire individually at the same time in the classroom. All of them were from a sixth grade class of a public elementary school in Yola, northeast Nigeria. This school was chosen because it is typical of the public schools in this city. The students were, on average, from lower-middle socioeconomic status families and attended school for 5 h each day. We chose the sixth grade because it comprises the eldest children capable of expressing themselves adequately in writing and reflecting social perceptions. The process took about 15 min.

**Results:** Only 5 (10%) children said they knew what epilepsy is; which 3 perceived as a disease of evil spirit and 2 thought as disease which is contagious and without a cure. Seventy percent would not like to associate with a peer with epilepsy.

**Conclusion:** The perception about epilepsy was poor with antecedent negative consequences. There is a need for educational programs in elementary schools which must be adapted to the specific cultural nuances of the localities.

### P360

#### IMPACT OF KNOWLEDGE OF EPILEPSY ON ITS STIGMA IN JAPAN

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**Purpose:** Epilepsy is associated with a significant burden of social stigma, which has a negative effect on the management of people with

epilepsy (PWE). This study aimed to assess knowledge of and attitudes toward PWE among the Japanese population.

**Method:** A set of questions was selected from questionnaires identified in the literature. In all, 360 people (180 female, aged 20–78 years) completed the 95 questions on a Web site.

**Results:** Of the participants, 93% had heard or read about epilepsy; the rate was higher among elderly participants. Although most people thought epilepsy was neither a contagious disease nor a mystical phenomenon, only 32% of participants answered that epilepsy was a neurological disease; 55% answered that epilepsy was treatable by medicine. Among the participants, 26% answered that epilepsy was a genetic disease. More elderly than younger participants and more females than males answered that epilepsy was a curable disease. The stigma scores for general opinions regarding PWE were more negative than with personal opinions. Negative attitudes about marrying PWE were stronger among elderly than younger participants. The attitude to marrying PWE did not correlate with the participants' belief in epilepsy being curable, though it strongly correlated with the participants' belief in epilepsy as a genetic disease.

**Conclusion:** It was found that the level of stigma differs according to sociocultural factors, such as age and gender. Education may help to improve attitudes to PWE.

### P361

#### THE FACTORS EFFECTING QUALITY OF LIFE IN EPILEPTIC PATIENTS

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**Aim:** Cessation of seizures that is the main goal of the epileptic treatment effects quality of life (QOL) as positively. This study aims to examine the other factors effecting QOL in addition to seizure frequency.

**Methods:** Ninety eight patients (43 male, mean age 34.8 ± 10.1 years) 59 of whom underwent epileptic surgery were included in the study. The affective state and quality of life of the patients were assessed using The Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and Quality of Life in Epilepsy Inventory-31 (QOLIE-31). We examined predictors of QOLIE-31 scores among various demographic and clinical factors.

**Result:** The mean onset age of seizures was 14.3 ± 11.4 (range 0–47) years and the mean duration of the disease 20.0 ± 10.1 (range 2–47) years. 42% of the patients were seizure free at least for 1 year. 28% of the patients had psychiatric comorbidity. We detected anxiety in 32% of the patients and depression in 34%. The mean score of QOLIE-31 was 58.4 ± 27.2 (range 6–100). There was positive correlation between QOL and epileptic surgery, employment, seizure freedom whereas a negative correlation was found with antiepileptic drug usage, anxiety, and depression. Thirty-five patients without seizure and affective symptoms had the best score of QOLIE-31.

**Conclusion:** Our findings suggest that presence of the affective symptoms affects QOL as independently from seizure frequency. Therefore, consideration and treatment of the affective symptoms are important in rising QOL of epileptic patients.

### P362

#### PARENT INFORMATION BEFORE INITIATION OF VNS-THERAPY: QUALITY ANALYSIS

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**Purpose:** To evaluate the quality of information on VNS-therapy given to the parents of children with drug resistant epilepsy.

**Method:** Twenty children (10 boys, 10 girls; aged 3–12 years) with drug resistant epilepsies being on VNS-treatment were included. Their parents participated in the anonymous survey on the quality of information given by medical professionals prior to VNS-therapy initiation. The questionnaire included five questions:

- 1 Was the information sufficient;
- 2 Did it help to fulfil your expectations about VNS-therapy;
- 3 How do you assess given information materials;
- 4 Are there missing points in the information you got;
- 5 Based on your current knowledge, would you still say “yes” to VNS-treatment.

The answers were scored from 1 to 5 (poor, fair, satisfactory, good, very good respectively).

**Results:** The quality of the given information as well as the information materials were highly rated by all parents (4 – good, 16 – very good). None of the families reported about the missing points in the given information. All parents answered “yes” to the fifth question. Twelve from 20 families expected more from VNS-therapy. However, it was due to their personal hopes but not insufficient quality of information. More than half of the parents mentioned that it would be helpful for them before start of VNS-therapy to get in contact with the other families who had experience with this treatment.

**Conclusion:** Measurements of quality care can provide better management of this difficult patient category.

### P363

#### SURVEY OF INFORMATION AND PSYCHOSOCIAL SUPPORT NEEDS OF PARENTS OF A CHILD WITH EPILEPSY

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**Purpose:** The aim of this study was to assess the need for information and psychosocial support of parents of children with epilepsy, including those with uncontrolled epilepsy and with mental retardation.

**Method:** A structured questionnaire using a Likert scale was sent to 408 parents of children with epilepsy between age 2 and 12 years treated at our epilepsy centre.

**Results:** A total of 174 parents (42.6%) took part. The need for information concerning epilepsy was higher (94%) than the need for psychosocial support (48%). Especially, parents required information on the evolution and prognosis of epilepsy (76%), on learning problems related to epilepsy (71%), and on the specific type of epilepsy of their child (66%). Also, information on behavioural problems related to epilepsy, possible consequences of epilepsy (death, cognitive decline, brain damage), anti-epileptic drugs (side effects, interactions, anticipated effect), and possibilities of special support at school were frequently needed (53–63%). There were two factors with a significant predictive value: the use of more anti-epileptic drugs leads to a higher need for information and psychosocial support, and previous consultations with the nurse practitioner leads to a lower of the need for information and psychosocial support.

**Conclusion:** A substantial number of parents have unmet information needs, and psychosocial support needs. The needs mentioned above could offer a guideline when giving information. Consultations with the nurse practitioner can contribute to a lower need for information, and guidance of parents.

### P364

#### ANALYSIS OF IMPLEMENTATION OF US CONSENSUS STANDARDS FOR LICENSURE OF DRIVERS WITH EPILEPSY IN MARYLAND

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**Purpose:** Driving restrictions for applicants with epilepsy vary by state and country, with decisions based on seizure-free periods, Medical Advisory Board (MAB) or treating physician opinion. US consensus guidelines propose general standards for US states, although individual state rules vary widely. Here we assess longitudinal decision-making in Maryland where the MAB adopted the US consensus guidelines.

**Method:** Data was collected on the initial and follow-up applications of 303 Maryland drivers reporting seizures who were first reviewed by the MAB between the years of 2003–2005.

**Results:** Twenty-seven percent of applicants were denied at initial review; 73% were approved (22% exempted from further review). Seizure-free intervals differed markedly for denials—median 97 days (IQR 54, 143); applicants approved with MAB monitoring—median 395 days (IQR: 202, 785) and those approved and exempted—median 1759 days (IQR: 946, 3462).

Treating physicians estimated prognosis more favorably than the MAB. Physicians reported 89.1% of their “denied” patients were controlled (despite a median seizure free interval of 104 days). AED non-compliance was cited only in two cases.

The strongest factor associated with MAB driving approval was longer seizure free interval ( $p < 2e-16$ ). Factors associated with unfavorable decisions were: substance abuse ( $p = 0.00013$ ,  $\chi^2 = 17.9$ ), police referral ( $p = 0.00451$ ,  $\chi^2 = 10.8$ ), and treating physician concerns ( $p = 0.00426$ ,  $\chi^2 = 10.9$ ).

**Conclusion:** Individualized assessments by Maryland MAB utilizing US consensus guidelines for licensure of drivers with epilepsy resulted in applicants with long seizure-free intervals being approved to drive, with other considerations much less important. Treating physicians tend to have more optimistic assessments of seizure prognosis than the MAB.

### P365

#### THE IMPACT OF EPILEPSY ON CANADIANS: REGIONAL RESULTS FROM A CANADA-WIDE SURVEY

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**Purpose:** To explore regional variations in the lived experience of Canadians with epilepsy.

**Method:** A nationwide survey, in English and French, was administered to adults ( $\geq 18$  years) with diagnosed epilepsy. Responses to questions on epilepsy management, activities of daily living, access to healthcare and support services were analysed by region: Western Provinces, Ontario, Québec and Atlantic Provinces.

**Results:** Six hundred and fifty-seven volunteers responded to the survey with a regional breakdown of 22% Western, 42% Ontario, 29% Québec, and 8% Atlantic. Respondents from the Western provinces and Ontario were more likely to use multiple coping strategies to manage their epilepsy and pay out-of-pocket for medication than Québec respondents. 69.8% of Québec respondents said government disability programs were unavailable to them. Western respondents were less likely to use the services of a community epilepsy organization, and less likely to indicate that they are (or were) surgical candidates. 45% of Québec respondents (vs. 33% elsewhere) received an epilepsy diagnosis in  $\leq 6$  months. In the Atlantic and Western Provinces a greater number of respondents (vs. Québec) had a time to diagnosis of 1–5 years. There were some respondents from all regions with a time to diagnosis beyond 5 years. 28.8% of Atlantic respondents lived in small towns which was higher than other regions. Atlantic and Ontario respondents were more likely to drive >100 km to see a specialist. Across all regions the full-time employment rate ( $X = 31.9\%$ ) was well below the national average. Fewer Ontario respondents were employed full-time (27.5%) vs. respondents from Québec (38%).

**Conclusion:** This survey reveals regional variations in access to health care, seizure management, employment, and support services for Canadians living with epilepsy. Development of national guidelines for the optimal management of persons with epilepsy could help prevent disparities in care.

UCB-Funded.

### P366

#### GENERAL KNOWLEDGE AND ATTITUDES TOWARD EPILEPSY AMONG PRIMARY AND SECONDARY LEVEL TEACHERS IN MACEDONIA

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**Purpose:** To determinate the general knowledge regarding epilepsy, recognition and management of seizures in pupils, attitudes toward epilepsy and the influence by the degree of knowledge to it.

**Method:** Self administered questionnaire was answered by 220 teachers, with different lever of education: university 188 (85.4%), academy 32 (14.6%) and different working experience 41 up to 5 years, 76 (5–15 years), 38 (15–25) and 65 (more than 25 years).

**Results:** All of the teachers had heard about epilepsy. 121 (55%) have had pupil with epilepsy (longer working experience) and 66 (30%) have been eyewitness of seizure. Mostly information's are from Internet (younger) TV and family/friends. 100% knows that epilepsy is not contagious. Ethology: 85% epilepsy is brain disorder, 34% psychiatric disorder, only one accept it as "good punishment" (multiple choice question). 28 (12.7%) answered that death can occurred frequently during the seizure. Elements of GTCS were recognized almost by all of them, but only two of them recognized description of absence seizure. Seventy five percents think that seizures could be controlled, 88.2% elect medications as treatment (9 in combination with psychotherapy, one medication and diet, one medications and operation). Fifty eight percents judge themselves as educated what to do if seizure occur, but unfortunately only 33 (15.1%) answered correctly. Almost 85% chose pulling the tongue and putting the object between the teeth as first aid. Thirty (13.6%)-pupils with epilepsy have to be educated in special schools, mostly from the teacher group with longer working experience (attitudes). Twenty one (9.5%) have objections if they have pupil with epilepsy in the class (stigma). More than 37% have different criteria during the evaluation.

**Conclusion:** Negative attitude and bias towards epilepsy is still present, especial in the group with longer working experience. All of the teachers

have heard about epilepsy, but their awareness unfortunately does not equate with the acceptance and understanding of epilepsy.

### P367

#### QUALITY OF LIFE, RESTRICTIONS AND STIGMA OF ADULT OUTPATIENTS WITH EPILEPSY TREATED BY NEUROLOGISTS IN GERMANY (EPIDEG STUDY REVISITED)

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**Purpose:** A cross-sectional study (EPIDEG 2011) was carried out in Germany to investigate the quality of life and related aspects in outpatients treated by neurologist in own practice. Furthermore, the current results were compared with a previous survey in 1995.

**Method:** In total, 72 neurologists participated in this study and handed out (consecutively) a short questionnaire to their patients with epilepsy. The questionnaire included subscales/items from the QOLIE-31 and PESOS questionnaire. 648 patients (53% female) aged between 16 and 87 years responded anonymously.

**Results:** Patients were characterized by a long duration of epilepsy (mean  $\pm$  SD: 19  $\pm$  16 years) and 98.4% were treated with antiepileptic drugs (AED). Most patients reported no (41.2%) or only mild adverse effects (38.1%), about 21% reported moderate or severe adverse effects. 55.3% were seizure-free for more than 1 year, whereas 14.4% had had one or more seizures per month. However, 77.5% reported at least slight restrictions due to epilepsy; most often in mental health (61.3%; 'strong': 18.6%), but strongest in driving (42.5%; 'strong': 31.4%). Patient ratings of overall quality of life and health [range: 0–10] were 6.7  $\pm$  2.2 and 6.6  $\pm$  2.2, respectively; both were significantly affected by seizure frequency, patient rated efficacy and tolerability of AED, employment and co-morbidity. The rate of employment (60%) was lower than in the general population (76%).

**Conclusion:** Compared to our survey in 1995, the rate of seizure-free patients as well as of employed patients was higher, while the rate patients who felt stigmatized was lower. In contrast, patient-reported restrictions due to epilepsy did not change significantly.

### P368

#### DRIVING LICENCE AND EPILEPSY IN MOROCCO

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**Purpose:** The number of traffic accidents is frequent in epileptic patients. In occidental countries, patients with epilepsy have been absolutely banned from driving since recently. In Morocco, the driving licence regulation has recently been actualized in 2011.

**Method:** Authors analyzed retrospectively 70,240 driving licence's form in medical driving licence department in Marrakech, during 4 years (2000–2003), and studied all rejected requests for neurological reasons, especially for epilepsy.

**Results:** Among 70,240 candidates, 216 were inapt to drive (0, 3%). In these inapt candidates, 66% had visual disorders and 34% had neurological problems. Among these neurological reasons, 97% had motor problems, and epilepsy was the reason in only one case (1.5%).

The driving licence form includes only a visual acuity, without any neurological examination or investigation. That is why a committee of the Moroccan league against epilepsy proposed for driving licence candi-

dates to fill an honour declaration certifying the absence of any neurological disorders such seizures, absences, jerks....; than, a neurological examination will be realized by general practitioner, and eventually by neurologist if needed.

This study pointed out the very few number of epileptic patients investigated for being epileptic, and if they are very few are checked for that to be excluded for having their driving licence, at least if they are not well treated and their seizures uncontrolled.

The driving licence legislation which was recently actualized is not enough and a many factors should be fulfilled (related to epileptic patients, all authorities involved in the driving licence process, and finally all physicians involved in health care centres in charge of medical certificates).

**Conclusion:** Finally the good application of driving licence regulation will either protect the right of stabilized epileptic patients by having their driving licence, than every citizen exposed to an accident where epileptic patients are involved.

### P369

#### FACTORS ASSOCIATED WITH PERCEIVED STIGMA OF EPILEPSY: FIRST STUDY OF EPILEPSY STIGMA IN CROATIA

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**Purpose:** Epilepsy is a condition highly associated with feelings of stigma. Aim of this study was to determine factors contributing to feelings of stigma in outpatients with chronic epilepsy in Croatia.

**Method:** Adult outpatients with epilepsy during their regular visits to hospital-based epilepsy services in Croatia self-completed an anonymous questionnaire addressing demographic data and clinical features of their epilepsy, together with the revised version of the Epilepsy Stigma Scale (rESS), translated into Croatian. Groups of patients reporting no stigma, mild to moderate stigma and severe stigma were compared using  $\chi^2$  test to find differences in clinical and demographical characteristics. Multiple regression analysis was also performed.

**Results:** Analysis was performed on 298 subjects. Fifty-three percent reported feeling stigmatized, with 45% mild to moderately and 8% highly. Feelings of stigma were associated with younger age ( $p = 0.040$ ), younger age at epilepsy onset ( $p = 0.017$ ), greater number of seizures ( $p = 0.003$ ), grand-mal seizures ( $p = 0.029$ ), and not being seizure free during the former 6 months ( $p = 0.018$ ). The most important factor determining score on the rESS was number of seizures so far ( $p < 0.001$ , adjusted  $R^2 = 0.057$ , Beta = 0.246). Croatian translation of rESS proved to have good internal consistency (Cronbach's alpha = 0.887).

**Conclusion:** A relatively large proportion of people with epilepsy in Croatia still experience stigma, similarly to other European countries. Although seizure control is very important, there are many other factors contributing to feelings of stigma, and those should be properly addressed when planning multidisciplinary interventions in order to reduce social stigma of epilepsy.

## Poster Session: Status Epilepticus Monday, 24 June 2013

### P370

#### THREE CASES OF NONCONVULSIVE STATUS EPILEPTICUS INDUCED BY NEWER ANTIDEPRESSANTS USED AT THERAPEUTIC DOSES

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**Introduction:** Classic antidepressants have been known to induce convulsive seizures and non-convulsive status epilepticus (NCSE). On the other hand, many reports have emphasized the safety of new antidepressants such as selective serotonin reuptake inhibitor (SSRI), serotonin and norepinephrine reuptake inhibitor (SNRI) and noradrenergic and specific serotonergic antidepressant (NaSSA). However, we encountered three cases of NCSE in elderly patients, which was induced by the use of newer antidepressants at therapeutic doses. We therefore reviewed the safety of antidepressants use in the elderly, with respect to NCSE.

**Case Presentation:** Case 1: A 73-year-old man had a history of sudden onset of catatonic clinical symptoms while taking amitriptyline 100 mg at age 69, and while taking sertraline 50 mg + mirtazapine 30 mg at age 73. EEG conducted at our center showed generalized slow wave with intermittent spike-slow wave complex. Intravenous injection of antiepileptic drug (AED) improved EEG findings and clinical symptoms. The above-mentioned antidepressants were tapered and discontinued. Then AED was discontinued, and there has been no relapse. Case 2: A 76-year-old man had onset of temporal lobe epilepsy at age 73. Depressive symptoms became severe at age 76. During titration of lamotrigine (LTG), depression deteriorated and suicidal ideation also increased. Therefore, sertraline was started. After titrating to 50 mg, impaired consciousness appeared. Intermittent spike-slow wave complex was found on EEG. Tapering and discontinuation of the antidepressant improved consciousness. Case 3: A 76-year-old man developed impaired consciousness after starting treatment with paroxetine 20 mg. On EEG, generalized slow spike-slow wave complex was observed consistent with impaired consciousness. Discontinuation of paroxetine resolved impaired consciousness and EEG abnormality.

**Conclusion:** Like classic antidepressants, newer antidepressants also may cause NCSE in the elderly, even when used at therapeutic doses. Caution has to be exercised when using newer antidepressants in patients who may have low drug tolerability.

### P371

#### DIFFUSION WEIGHTED MRI IN PATIENTS WITH NCSE: PREDICTOR OF SEVERITY OF SE AND ITS PROGNOSIS?

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**Purpose:** Changes in diffusion weighted image (DWI) are not infrequent findings in NCSE. This study aimed to determine which factors contribute to the change of signal intensity of DWI in patients with NCSE and its correlation to the prognosis.

**Method:** Between Jan. 2007 and Dec. 2011, 173 patients were diagnosed as NCSE at Chungnam National University hospital. Brain MRI was taken during the ictal period. All the MRIs were evaluated by two different neurologists. Patients with acute or progressive brain lesion were excluded. To assess contributing factors for signal change, we divided patients into two groups; high signal intensity group (HSI) and iso-signal group (ISO). The differences of demographic features, SE duration before/after treatment, time of brain imaging, EEG and MRI correlation, and prognosis between two groups were compared.

## Abstracts

**Results:** One hundred and seventy-three patients were diagnosed as NCSE by EEG monitoring during this period. After excluding patients who could not take brain MRI immediately, 48 patients were included in this study. Twenty five patients were categorized as HSI. Timing of brain imaging from detection of SE was delayed in HSI group ( $46.1 \pm 10.5$  vs.  $9.1 \pm 2.6$  h,  $p < 0.05$ ). SE duration before treatment was also prolonged in HSI group ( $34.2 \pm 10.5$  vs.  $11.8 \pm 3.1$  h,  $p < 0.05$ ). PLEDs or PLEDs plus were common in HSI group (88.0% vs. 34.8%,  $p < 0.05$ ). MRI correlation was consistent with the ictal EEG in 18 patients. Prognosis was poor in HSI group compared with ISO group (54.2% vs. 21.7%,  $p < 0.05$ ).

**Conclusion:** High signal intensity on DWI in NCSE is common findings and reflects the duration and severity of SE. These findings suggests that the high signal intensity is shown after sufficient duration of SE and also related to the poor prognosis. We suggest that high signal intensity in DWI reflects the severity of SE and in this cases, aggressive treatment should be considered.

## P372

### STATUS EPILEPTICUS IN PATIENTS WITH BRAIN TUMORS: FINDINGS OF A TERTIARY REFERRAL CENTER IN TURKEY

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**Purpose:** Cancer often affects the nervous system and may result in significant morbidity and mortality. Seizures are common manifestations of primary or metastatic central nervous system tumors and mostly focal depending on the location and the pathology of the lesion. The aim of this study were first to assess the type of Status epilepticus (SE) in patients with brain tumors and second to determine the effects of primary and metastatic brain tumors and the type of SE on the response to treatment and mortality.

**Method:** We retrospectively analyzed episodes over a period of 8 years. A total of 290 patients had 303 episodes. Recurrent episodes (a total of 13) were excluded from further analysis in order to avoid confounding in prognostic data.

**Results:** Among these 39 (19 female, 20 male;  $58 \pm 19.4$ ) cases (13.5%) brain tumor with SE were identified and evaluated. Seventeen (43.6%) of them have a history of seizure. Convulsive SE is the most frequent presenting SE type, whereas NCSE is the most refractory type of SE in our study group. SE associated with primary brain tumors are seen (59%) more than the metastatic ones and they are more refractory, too (53.3%). Fifteen percent of patients' were died, but refractoriness is not found a predictor of death.

**Conclusion:** As a conclusion CSE type seemed to be most frequent SE type and NCSE appeared the most refractory SE type associated with brain tumors. In terms of type, primary brain tumors are more frequent than metastatic ones in our study group.

## P373

### AUTOIMMUNE ENCEPHALOPATHY AND REFRACTORY SEIZURE WITH THE PRESENCE OF TWO SURFACE NEURONAL AUTOANTIBODIES

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**Purpose:** To report an interesting case of autoimmune mediated encephalopathy and refractory seizures caused by autoantibodies to voltage-

gated potassium channels (VGKC) and voltage-gated calcium channels (VGCC) (P/Q-type) and the response to immunotherapy.

**Method:** Case Report.

**Results:** After treatment with IV steroids and IVIG, our patient had significant clinical improvement in terms of seizure control.

**Conclusion:** An extremely rare case of autoimmune encephalopathy and seizure associated with the presence of two surface neuronal autoantibodies. This report highlights the importance of early diagnosing autoimmune epilepsy and prompt immune therapy and its impact on outcome.

## P374

### COMMON REFERENCE-BASED INDIRECT COMPARISON META-ANALYSIS OF INTRAVENOUS VALPROATE VS. INTRAVENOUS PHENOBARBITONE IN GENERALIZED CONVULSIVE STATUS EPILEPTICUS

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**Purpose:** To perform a meta-analysis of intravenous valproate (IV VPA) compared with intravenous phenobarbitone (IV PB) in the treatment of established generalized convulsive status epilepticus (GCSE) in patients of any age, indirectly estimating its efficacy and safety compared with IV PB in a common-reference based indirect comparison meta-analysis (CRBMA). To indirectly estimate the efficacy and safety of IV VPA compared with IV PB in a CRBMA to evaluate whether such a method may be considered a reliable tool whose results are consistent with direct head-to-head RCTs.

**Method:** Randomized controlled trials of IV VPA and IV PB vs. IV PHT for GCSE were systematically searched. A random effects model was used to estimate Mantel-Haenszel odds ratios for efficacy and safety measures vs. IV PHT. Adjusted indirect comparisons were then made between VPA and PB using the meta-analysis results.

**Results:** The CRBMA showed that, compared with PB, VPA has no statistically significant difference either in seizure cessation after drug administration (OR 1.12, 95% CI 0.74–1.68) or in occurrence of adverse effects (OR 0.19, 95% CI 0.12–0.28). Results of CRBMA are only partially consistent with results of a recently published head-to-head comparison which found a statistically significant higher occurrence of adverse effects in patients allocated to IV PB.

**Conclusion:** There is no enough evidence for a superiority of IV VPA over IV PB for the treatment of GCSE in terms of efficacy. Some data derived from direct comparisons suggest that VPA have a better safety profile than PB. CRBMA is not a substitute for comparative clinical trials. Nevertheless, in the absence of such studies, the adjusted indirect method provides some evidence of the relative efficacy and safety of competing AEDs.

## P375

### CHARACTERIZATION OF SEIZURES INDUCED BY ALERTING STIMULI IN PATIENTS WITH NONCONVULSIVE STATUS EPILEPTICUS

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**Purpose:** To describe the etiology, clinical features, morphology and localization of stimulus induced electrographical or electroclinical seizures (SI-seizures) in patients with nonconvulsive status epilepticus (NCSE).

**Method:** We retrospectively reviewed all consecutive prolonged or continuous EEG monitoring done between June 2009–November 2012. We selected all stuporous or comatose patients with electroclinical or electrographical findings consistent with NCSE having also unequivocal SI-seizures during tactile, photic, auditory and/or noxious stimulation. We reviewed demography, etiology, and the clinical features associated with spontaneous and SI-seizures. EEG patterns were analyzed with regard to morphology and location of ictal discharges. A comparison of EEG findings was done between spontaneous and SI-seizures.

**Results:** Forty-seven patients were selected, 27 male; mean age: 58.2 years old (range 17–91). Most frequent etiologies were intracranial haemorrhage (12 patients), severe head trauma (10 patients), and brain infarct (nine patients). Most frequent EEG pattern in SI-seizures was focal, rhythmic, and evolving activity, 38.1% of them having also intermixed repetitive sharp waves. 19.1% of patients had clinical changes during SI-seizures, 66.7% of them with semiological features similar to spontaneous events. Correlation of location and morphology of ictal discharges between spontaneous and SI-seizures was good.

**Conclusion:** SI-seizures in patients with NCSE can occur in different brain diseases. More frequently the EEG pattern is characterized by focal, rhythmic, and evolving discharges, and sometimes they are associated to clinical changes. SI-seizures have good electrographical correlation with spontaneous seizures. They could represent reflex events and they are probably under-diagnosed if stimulus protocols are not consistently applied in patients with NCSE.

### P376

#### TREATMENT AND VIDEO-EEG MONITORING IN CHILDREN WITH NONCONVULSIVE STATUS EPILEPTICUS

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**Purpose:** To explore the clinical feature and VEEG monitoring of NCSE in children.

**Method:** Data on demographics, etiology, VEEG manifestation, response to clonazepam therapy and outcomes were analyzed.

**Results:** Nine male and eight female of 17 patients with NCSE ranged from 11-month to 11.4-year old. The clinical attacks lasted a variable time from 4 h to 3 months. Each patient had a prolonged change of consciousness, accompanied by psychological or behavioral changes. Definite medical causes were identified in 65% of the patients. Secondary epilepsy was the dominating cause. The characteristics of ictal VEEG in NCSE generally included slow activity and focal or generalized  $\delta$  or  $\theta$  activity. After clonazepam treatment, the conditions of 12 patients were under complete control, five had improvement. The time needed to control NCSE varied from 15 min to 1 week. The prognosis of CNS infection sequelae patients, metabolism disorders and brain structural damage was poor.

**Conclusion:** NCSE may present with confusion, behavioral disturbances and psychiatric conditions. The diagnosis can be made by the ictal and interictal VEEG monitoring. It is necessary to make the diagnosis and control the seizures as quickly as possible. Clonazepam is useful in NCSE.

### P377

#### CLONIC MOVEMENTS OF THE ABDOMINAL MUSCLES DURING STATUS EPILEPTICUS

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**Introduction:** The trunkal muscles are seldom involved in epileptic seizures. A few case reports in the literature have described abdominal muscles myoclonus during *epilepsia partialis continua*. The anatomical origin of this phenomena is still debated as most reports fail to detect epileptic activity in relation to the muscles twitches.

We describe the clinical and ictal electrophysiological features, with video support, of persistent clonic twitches of the abdominal musculature as a rare manifestation of status epilepticus.

**Case report:** A 78-year-old woman was hospitalized with the diagnosis of decompensated chronic renal failure and metabolic acidosis. She had a history of metastatic gastrointestinal adenocarcinoma.

During hospitalization the patient developed persistent spontaneous contractions of abdominal muscles, with a rhythmic quality, more intense on the right side. She was stuporous and the EEG showed continuous periodic epileptiform discharges at 1 Hz with a centro-parietal topography, synchronous with myoclonus registered on surface EMG. The movements persisted despite treatment with benzodiazepines and valproic acid. Computed tomography scan of the brain didn't reveal any lesion. Unfortunately the patient died before a magnetic resonance of the brain has been performed.

**Conclusion:** Isolated clonic twitches of the abdominal musculature are a rare motor manifestation of status epilepticus, taking into account the small representation of this area on the classical cortical homunculus. The topography of the epileptiform discharges is consistent with a ictal focus involving the parasagittal sensorimotor Cortex.

We underline the importance of recognizing this condition and the essential role of neurophysiologic evaluation.

### P378

#### ACUTE PORPHYRIA PRESENTING AS EPILEPSIA PARTIALIS CONTINUA: A REPORT OF TWO CASES

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**Purpose:** The porphyrias are a defect in the biosynthesis of haem which can be associated with different neurologic symptoms during acute attacks such as peripheral neuropathy, mental disturbance and seizures. So far, there have only been a few case reports of status epilepticus, none of which were of *epilepsia partialis continua* (EPC). We present here two cases of hereditary coproporphyrin manifesting EPC as part of clinical presentation.

**Method:** Case series. The patients' medical charts, EEG and imaging studies were carefully reviewed.

**Results:** Case 1 is a 30-year-old male who came to the emergency room for a convulsive status epilepticus. Case 2 is a 49-year-old male who first presented a tonic-clonic seizure. Both evolved to EPC over the next days. EPC persisted despite several antiepileptic drugs trials. Diagnosis of hereditary coproporphyrin was confirmed by high level of urine, fecal and serum porphyrins in both and by genetic testing in one. The first patient died a month and half after admission from brain oedema. Over the last 3 years, the second patient has continued to present non-disabling EPC and has had four tonic-clonic seizures associated with alcohol consumption.

**Conclusion:** Acute porphyrias should be included in the differential diagnosis of new onset status epilepticus, including *epilepsia partialis*

continua. Their recognition is important as it modifies significantly patient management, since many anticonvulsants are porphyrogenic.

### P379

#### INTERACTION OF CRF<sub>1</sub> AND 5-HT<sub>2A/2C</sub> RECEPTORS IN EXPERIMENTAL EPILEPSY

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Epilepsy is a common neurological disorder characterized by seizures. Corticotropin Releasing Factor (CRF) is a neurotransmitter that is implicated during stress. Another neurotransmitter that may be implicated in stress conditions is serotonin. Recently, it was shown that these two neurotransmitter systems interacted in prefrontal cortex of mice to produce anxiety. Anxiety, stress and epilepsy are often co-existing. There have been no reports how these two systems interact in piriform cortex (PC), one of the most seizurogenic regions of the brain. We hypothesize that the interaction between CRF<sub>1</sub>/5-HT<sub>2a/2c</sub> receptors may decrease neuronal activity in a control brain. These actions will be reversed in epileptic brain in a manner that may increase excitability and therefore tend to increase seizure generation. The PC has high expression of both CRF and 5HT<sub>2a/2c</sub> receptors. Neuronal activity was measured using "Voltage Sensitive Dye Imaging technique in coronal brain slices. A typical response to a stimulus >20 Hz consisted of the down regulation of layer-III activity and a concomitant increase in layer-II excitation. It suggests that excitation of the PC is facilitated by disinhibition of the layer-III inhibitory neurons. We observed that CRF (100 nM) reduced the disinhibition of layer-III while reducing neuronal excitation in layer-II. This response was antagonized by the CRFR<sub>1</sub> antagonist antalarmin (IC<sub>50</sub>.100 nM). The 5-HT<sub>2a/2c</sub> selective agonist DOI alone had no significant effect. However, following CRF, DOI was able to further suppress the excitation and the disinhibition. In kindred brain the receptor interaction produced quite opposite effects. These results show that CRF and 5-HT systems interact differently in a normal and epileptic brain to alter the PC neuronal activity.

### P380

#### CHRONIC STATINS INTAKE IS RELATED TO BETTER OUTCOME AFTER STATUS EPILEPTICUS

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**Purpose:** Statins display anti-inflammatory and antiepileptogenic properties in animal models, and may reduce epilepsy risk in elderly humans, but studies in patients with status epilepticus (SE) have not been undertaken. We investigated if statins influence the clinical outcome in patients with SE.

**Method:** This cohort study is based on a prospective registry including adults with an incident SE treated in our tertiary care center between April 2006 and September 2012. SE outcome was categorized at hospital discharge into "return to baseline", "new handicap", and "mortality". The role of potential predictors, including regular statins treatment upon admission (assessed through charts review), was evaluated using uni- and multivariable analyses.

**Results:** We identified 427 patients; in 413 data regarding statin treatment was available. Mean age was 60.9 (±17.8) years; 201 (49%) were women; 211 (51%) had a potentially fatal SE etiology; and 191 (46%)

experienced generalized-convulsive or subtle SE. Statins were prescribed on admission in 76 (18%) subjects (simvastatine, atorvastatine, or pravastatine), mostly in the elderly. While 208 (50%) patients returned to baseline, 58 (14%) died. Multivariate ordinal logistic regression showed that statins use significantly correlated with a better outcome ( $p = 0.034$ ), after adjustment for the two most important SE outcome predictors (potentially fatal etiology, age;  $p < 0.001$  for both).

**Conclusion:** This study shows for the first time that previous treatment with statins might improve SE outcome, further suggesting a possible antiepileptogenic role. Other studies are warranted to confirm this intriguing finding.

### P381

#### NEW ONSET REFRACTORY STATUS EPILEPTICUS – "NORSE" – A CASE REPORT

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**Purpose:** We describe our experience with super-refractory status epilepticus in young woman of Korean origin.

**Method:** Woman, born 1983, South Korean origin. After a week of flu-like symptoms appeared first partial epileptic seizure with alteration of consciousness and its worsening. CT scans and lumbar puncture avoided acute organic intracranial focal lesion or viral and bacterial inflammation. Due to prolonged epileptic activity she was next transferred to ICU, pharmacological coma with highly dosage AED treatment and organ failure prevention therapy was accelerated. MRI scans were performed. EEG monitoring showed super-refractory SE. HLA B1502 negative. Although we have used modern pharmacological therapy the patient died after 1 month of first symptoms appeared.

**Results:** Laboratory results with no help for SE etiology. MRI scans: bilateral oedema of claustrum. EEG: Bilateral multifocal continual spikes with frontotemporal and right side maximum. Ictal EEG pattern of partial activity from left frontotemporal region with myoclonic jerks in right body side. Secondary generalization. Suppression -burst pattern in thiopental therapy with recurrence of epileptic activity after reduction of dosage repeatedly. Due to organ failure the patient dies. Autopsy was not performed due to family reasons.

**Conclusion:** We have established the diagnose of super -refractory SE as New Onset Refractory SE (NORSE) due to previously published papers. NORSE is a catastrophic type of status epilepticus. The question of etiology of super-refractory SE remains uncertain, immunologically mediated condition cannot be avoided, although plasmapheresis was not included into our treatment. There are no guidelines for treatment due to lack of clinical studies.

### P382

#### PSEUDOSTATUS EPILEPTICUS

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**Introduction:** Pseudostatus epilepticus (PE), is a clinical event that mimics epileptic seizure but is not associated with electroencephalographic discharges. PE generally being confused with true status epilepticus and treated as epileptic seizures cause unnecessary and inappropriate use of antiepileptic drugs.

**Aim:** Patients repeatedly resort to emergency clinics, unnecessarily repeated tests, thus the deterioration in quality of life as well as the economic burden become. PE is seldom reported in the literature and could be misinterpreted as convulsive status epilepticus.

**Method:** We report five patients with PE (simulated refractory convulsive status epilepticus). After several hospitalizations, the diagnosis of PE was established on the basis of clinical semiology, lack of EEG abnormalities during the seizures, and a positive provocation maneuver, which elicited and blocked the manifestations. The clinical spectrum of PE is wide and it is particularly difficult to differentiate psychogenic seizures from epileptic seizures, especially when occurring in patients, some of whom are already treated for epilepsy. It is important and necessary to make the diagnosis as soon as possible in order to rapidly begin appropriate treatment. PE was common in patients with pseudoseizures and was often misdiagnosed as status epilepticus. Complications of this misdiagnosis included eight episodes of anticonvulsant-induced respiratory arrest. Patients with pseudostatus commonly had multiple episodes of 'status'. They usually also had a history of other unexplained illness and of deliberate self-poisoning.

**Discussion and Results:** Management of these patients was difficult and emphasizes the need for specialist expertise for patients with epilepsy and apparent epilepsy. So, when we evaluating the patient with refractory convulsive status epilepticus; we must consider PE for differential diagnosis.

**P383**  
**STATUS EPILEPTICUS IN CHILDREN WITH POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: REPORT OF THREE CASES**

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**Purpose:** Posterior reversible encephalopathy syndrome (PRES) is often reported in children treated for hemato-oncological diseases. Patients frequently present headache, seizures, and visual disturbances. Neuroimaging studies typically reveal subcortical vasogenic edema over the posterior regions of the brain. Status epilepticus (SE) is rarely diagnosed in PRES.

**Method:** We report three cases of PRES presenting with SE in children submitted to allogeneic hematopoietic stem cell transplantation (AHSCT), and describe clinical, neuroimaging and EEG findings in these cases.

**Results:** Case 1 – a 15 year-old girl with sickle cell disease presented two SE episodes one and 3 months after AHSCT. Clinically she had brief generalized tonic-clonic seizures followed by sleepiness in both events. EEG showed continuous left parassagittal epileptiform discharges in the first episode and continuous bilateral posterior epileptiform discharges with frequent electrographic seizures in the second. Brain MRI showed subcortical hyperintensity (T2/FLAIR) in the left frontoparietal convexity and left occipitotemporal transition. Case 2 – a 12 year-old girl had four episodes of generalized tonic-clonic seizures, associated with vomiting and headache, 2 weeks after AHSCT for sickle cell disease. EEG revealed continuous right occipital epileptiform discharges. Brain MRI showed bilateral occipitotemporal subcortical hyperintensity (T2/FLAIR). Case 3 – a 3-year-old boy presented visual deficit, slurred speech and mental confusion after AHSCT for leukemia. EEG showed continuous occipital spikes. Brain MRI revealed subcortical hyperintensity (T2/FLAIR) in the parietooccipital region and meningeal hemorrhage over right temporal lobe.

**Conclusion:** SE may be the main manifestation in children with PRES following AHSCT, and should be promptly recognized and treated.

**P384**  
**LONG-LASTING FOCAL ONSET STATUS EPILEPTICUS RESPONDING TO ORAL AD-ON RETIGABINE TREATMENT: CASE REPORT AND LITERATURE OVERVIEW**

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**Purpose:** We present an interesting case of long lasting partial seizure status epilepticus fulfilling the criteria of epilepsia partialis continua (EPC) responsive to add-on retigabine (RTG) treatment.

**Method:** This was observational, non-interventional study.

**Results:** A 22-year-old, male with diagnosed focal onset epilepsy since childhood developed progressive deterioration of seizures, which transformed into EPC propagating from left frontal lobe, lasting for 8 months with only several short breaks. Extensive imaging techniques (including CT, MRI, PET) demonstrated unspecific signal change over the left frontal lobe, what necessitated further investigation. Brain biopsy confirmed the presence of cortical dysplasia as a primary cause of the epilepsy but no neoplastic or inflammatory changes except the features of neuronal damage and glial activation as, most probably, a consequence of long lasting seizures. Patient received extensive treatment including several different drug combinations including benzodiazepines, barbiturate, sodium valproate, carbamazepine, levetiracetam, topiramate but without clear effect. The introduction of retigabine added to levetiracetam and carbamazepine gave positive response leading to significant and sustained suppression of seizures, reduced down to 1–2 fits daily.

**Conclusion:** This is a first report demonstrating efficacy of additive treatment with RTG in long-lasting refractory focal onset status epilepticus.

**P385**  
**WORK, REST AND PLAY: THE CLINICAL SPECTRUM OF NON-CONVULSIVE STATUS EPILEPTICUS**

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**Introduction:** The absence of obvious motor features in non-convulsive status epilepticus (NCSE) undoubtedly is in part responsible for the fact it is probably an under recognised clinical entity. We present two clinical cases of NCSE which illustrate the subtly in diagnosis even in experienced hands.

**Case histories:** Case 1: A 55-year-old woman, with unclassified epilepsy well controlled on carbamazepine, presented with new onset "vague" episodes, difficulty talking and interacting, yet with retained awareness, lasting 4–48 h. She was able to continue working and continued to drive.

Case 2: A 52-year-old woman with learning disability and symptomatic focal epilepsy on levetiracetam presented with a 4-week history of declining social function and speech output. Over the previous 4 weeks she had become increasingly emotional, lost the ability to stand, had become incontinent of urine and had stopped playing card games; her favourite pastime.

**Results and conclusions:** NCSE was confirmed in both cases on an ictal EEG recording. Both cases help to illustrate the diverse clinical spectrum of NCSE, its disabling nature in those with learning disability, and often it's clinical subtly in high-functioning individuals. It also serves to highlight that continuous electrical activity in some cases of

NCSE although altering awareness; individuals may still be able to function at work and albeit unknowingly against DLVA guidelines, continue to drive while awaiting investigations and a diagnosis. These two clinical case vignettes raise the profile of the spectrum of NSCE and highlight the need for continued investment in the timely availability of EEG.

### P386

#### LEVETIRACETAM USE IN BENZODIAZEPINE REFRACTORY STATUS EPILEPTICUS AND POST-STATUS SEIZURES SECONDARY TO SUBARACHNOID HEMORRHAGE

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**Purpose:** There is limited literature on Levetiracetam use in subarachnoid hemorrhage (SAH) induced status epilepticus (SE) and post status seizures. The purpose of this study is to delineate the safety and efficacy of levetiracetam in SE and post SE seizures secondary to SAH.

**Method:** Over the course of a 45 month study period, 13 cases presented to Stony Brook University Hospital with benzodiazepine refractory SE secondary to aneurysmal and non-aneurysmal SAH. Our subjects consisted of six males and seven females between the ages of 29 and 78. Two cases were aneurysmal SAH, seven were non-aneurysmal secondary to trauma, while four were idiopathic. Levetiracetam was used as monotherapy in seven of the 13 cases and was adjunctive in 3/13 cases. In three cases we did not use levetiracetam.

**Results:** Levetiracetam alone was successful in seizure control in four patients, and as an adjunctive in three patients, having no more than one seizure episode during their hospitalization. The duration of SE was unknown in two patients. One patient continued to have intractable epilepsy requiring multiple AEDs and IV sedatives with eventual control of seizures at 3 months post SAH onset. Valproic acid and Phenytoin in combination controlled the seizures in one case by day 6. Dilantin monotherapy brought seizure control by day 2 in another case and combination lamotrigine and phenytoin suppressed seizures by day 1 in the third case. Six patients were discharged to acute rehabilitation facilities, four were discharged home and one was discharged to hospice while disposition for two others were unknown.

**Conclusion:** Based on a limited case review, effective doses of levetiracetam ranged between 1000 and 3000 mg/day, with a majority achieving seizure control within <24 h. Levetiracetam use was shown to be safe and effective for patients with status epilepticus and post-SE seizures secondary to SAH.

### P387

#### NEONATAL STATUS EPILEPTICUS: ARE THERE ANY DIFFERENT CHARACTERISTICS BETWEEN PRETERM AND TERM NEWBORNS?

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**Purpose:** In order to assess whether newborns with neonatal status epilepticus (NSE) showed homogeneous features or displayed clinical and/or instrumental differences depending on gestational age (GA), we compared preterm and term neonates with NSE.

**Method:** From the 154 newborns with video-EEG confirmed neonatal seizures consecutively admitted to the NICU of Parma University Hospital between January 1999 and December 2012, we collected a cohort of 47 newborns (19 preterm and 28 full-term) with NSE. NSE was defined as continuous seizure activity for at least 30 min or recurrent seizures lasting a total of 30 min without definite return to the baseline neurologic condition of the newborn between seizures. Outcome was assessed at 10 months with a follow-up from a minimum of 10 months to a maximum of 13 years according to clinical conditions. We applied the  $\chi^2$  test to compare the sample features (gender, delivery, Apgar score at 1, 5 and 10 min, aetiology, seizure onset, seizure type, cerebral ultrasound [US], EEG, neurologic examination) and the outcome.

**Results:** Only Apgar scores at any time and neurologic examination ( $p \leq 0.02$ ) showed differences between the two groups. None of the preterm newborns had a favorable outcome compared to 25% (7/28) of the full-term ones ( $p = 0.032$ ). Moreover, 52.6% (10/19) of preterm neonates died compared to 17.8% (5/28) of the full-term newborns ( $p = 0.01$ ).

**Conclusion:** Newborns with NSE represented a homogeneous group regardless of the GA. However, all preterm newborns presented an unfavorable outcome. NSE in preterm newborns is highly related to death and severe neurologic disability.

### P388

#### EFFICACY OF KETOGENIC DIET FOR SUPER-REFRACTORY STATUS EPILEPTICUS ASSOCIATED WITH FEBRILE INFECTION RELATED EPILEPSY SYNDROME (FIRES)

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**Purpose:** Febrile infection-related epilepsy syndrome (FIRES) is a severe epileptic encephalopathy in previously healthy children. FIRES was characterized by prolonged refractory status epilepticus (SE) which will evolve into refractory epilepsy associated with severe neuropsychological impairment, even death. Recent studies indicate ketogenic diet (KD) may terminate SE and improve the prognosis of FIRES.

**Method:** This study aimed to discuss the effect of KD in FIRES.

**Results:** Two months after onset, with super-refractory status epilepticus, the patient was assigned to receive KD with a 4:1 ratio of fat to protein and carbohydrate. The patient's seizures decreased dramatically and he was successfully weaned from phenobarbital, midazolam, diazepam and other anticonvulsants. Now after 8 months on the diet combined with ilepicimide (antiepilepsirine), he has >90% reduction in his seizure frequency.

**Conclusion:** Based on our case and review of the literature, KD has dramatic efficacy to FIRES, and we suggested that KD should be applied once diagnosis of the FIRES and super refractory status epilepticus has been made.

### P389

#### SAFETY AND EFFICACY OF LACOSAMIDE, LEVETIRACETAM AND SODIUM VALPROATE AS INITIAL TREATMENT OF POST-STROKE NON CONVULSIVE STATUS EPILEPTICUS

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**Purpose:** To compare the safety and efficacy of valproic acid (VPA), levetiracetam (LEV) and lacosamide (LCM) for initial treatment of post-stroke nonconvulsive status epilepticus (NCSE) in elderly patients.

**Method:** We reviewed clinical, EEG, and neuroimaging data of patients admitted to our Stroke Unit from 2010 to 2012 and receiving at least one dose of LCM, LEV, or VPA as initial treatment of NCSE. NCSE was defined as 30 min of continuous seizure activity without major motor phenomena.

**Results:** The incidence of post-stroke seizures within 24 h was 4.7%. A diagnosis of NCSE was made in 32/889 patients (3.6%). Twenty (62.5%) of them developed NCSE 7 days after stroke onset. Newer AEDs were used as initial treatment in 26/32 patients. VPA failed to control NCSE in 6/7 patients, LEV in 5/9 patients, LCM in 4/10 patients. Further treatment with diazepam failed to control NCSE in 3/6 patients. Overall, newer AEDs failed to control NCSE as initial treatment in 57.7% (15/26) of the patients. Univariate analysis revealed a significant difference between NCSE and no-NCSE group considering aetiology, clinical presentation, and the size of ischemic area ( $p < 0.001$  and  $p = 0.015$ , respectively). In multivariable analysis the extension of ischemic area was an independent risk factor of NCSE (OR: 2.764; 95 CI: 1.164–6.565).

**Conclusion:** VPA seems to be less efficient than LEV and LCM as initial treatment for post-stroke NCSE. LCM and LEV are good candidates to be an alternative choice drug to benzodiazepines against post-stroke NCSE. A prospective comparative trial is needed to confirm our observation.

### P390

#### ETIOLOGIC DIAGNOSIS AND IDENTIFICATION OF PERIICTAL CHANGES BY MR INVESTIGATION IN ADULT PATIENTS WITH STATUS EPILEPTICUS

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**Purpose:** Role of MRI in the etiologic diagnosis of epilepsy is well established. However its role in the status epilepticus (SE) is still not clear. We analyzed the MRI findings in various subtypes of SE and tried to find out whether the etiologic diagnosis is improved by MR investigation. In addition, the incidences of various periictal changes by MRI were investigated.

**Method:** One hundred and twenty adult patients (male = 79) with acute status epilepticus between March 2011 and October 2012 were included. The type and etiology of SE were analyzed with details of clinical, laboratory, EEG, CT, and MRI data. A neuroradiologist (NY Shin), blind to the data, interpreted MRI and CT scans independently. Remote and focal periictal changes were also investigated.

**Results:** Thirty patients (25%) had past history of seizures and acute symptomatic causes were found in 62% of the study patients. The most common etiology was infection (20%), and cerebrovascular events (16%). Abnormality was found in 69.7% of CT scans ( $n = 99$ ), but etiologic diagnosis by CT scan only were made in 36 patients (36.4%). 93.8% of MRI scan ( $n = 96$ ) had abnormal findings, and further improvement of the etiologic diagnosis was made by MRI (77.1%). From the 59 non-diagnostic CT scan, 39 reached to diagnosis after additional MRI (66.1%). Periictal changes on DWI were found in 36%

(32/89) of the patients. Focal cortical cytotoxic lesions were found in 27 patients (30.3%), and the hippocampal changes and diencephalic lesions were found in 11 and four patients (12.4% and 4.5%), respectively.

**Conclusion:** MRI was found to be superior to CT scan in identification of etiology of SE, and periictal changes were found in 36% of the patients. Early identification of etiology and parenchymal damage by MRI will help in appropriate treatment decision and improve the outcome of SE.

### P391

#### PERIICTAL BRAIN MRI ABNORMALITIES RELATED TO STATUS EPILEPTICUS

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**Purpose:** To determine the frequency, imaging characteristics, and clinical correlates of brain magnetic resonance imaging (MRI) abnormalities due to seizure activity in status epilepticus (SE).

**Method:** We reviewed the medical records of patients admitted to our hospital for SE from January 2008 to December 2012. Sixty-one (62.2%) of 98 patients diagnosed with convulsive and non-convulsive SE had brain MRI performed during the admission. We analyzed the clinical and imaging characteristics of these patients.

**Results:** Ten (16.4%) of 61 patients had periictal MRI abnormalities likely resulting from seizure activity. The most common MRI features (8/10) were increased T2 signal intensity and bright signal on diffusion weighted image with variable apparent diffusion coefficient values in the regions of seizure focus and ipsilateral hippocampus. Two of eight patients with these local MRI changes also showed the dilatation of ipsilateral cerebral arteries on magnetic resonance angiography and the hyperperfusion of affected areas on perfusion weighted image. One patient (1/10) had diffuse changes of increased T2 signal intensity and variably restricted diffusion in the cortex of bilateral cerebral hemispheres, and the other one (1/10) had the remote change of increased T2 signal intensity and restricted diffusion in the splenium. Patients with periictal MRI changes tended to have more generalized seizures and more vascular risk factors. The most characteristic EEG features accompanied with MRI changes were periodic epileptiform discharges, especially associated with hyperperfusion.

**Conclusion:** MRI performed during or immediately after SE showed the abnormalities resulting from seizure activity in 16.4% of patients in our study. These abnormalities could be observed in local, remote and diffuse areas; the most common findings were local changes with increased T2 signal and variably restricted diffusion confined to the area of seizure focus and ipsilateral hippocampus. Patients with generalized seizures and periodic epileptiform discharges had higher possibilities of periictal MRI abnormalities.

### P392

#### POST-ANOXIC MYOCLONIC STATUS EPILEPTICUS: IS IT TRULY EPILEPTIC?

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**Purpose:** Persistent myoclonus after cardiac arrest are thought to be epileptic when associated and synchronized with paroxysmic epileptiform

activity (spike) on the electroencephalogram (EEG) (Navarro et al. 2009). Looking for the delay between EEG spikes and myoclonic movement detected by electromyography (EMG), we tried to determine the cortical or sub-cortical origin of the myoclonus.

**Method:** Three patients suffering from post-anoxic myoclonic status epilepticus were registered with concomitant EEG and EMG derivations (sampling frequency = 256 Hz). We marked off-line the first 20 myoclonus jerks (M) observed on a randomly selected portion of the EEG traces, and then marked separately all the EEG spikes (S) registered during the same period of time. We calculated the latency between each myoclonus and the nearest spike.

**Results:** In all patients we observed a number of spikes far greater than myoclonus (respectively 30, 56 and 28 for patient 1, 2 and 3, for a period of time ranging from 8 to 60 s). The delay between S and M was  $0 \pm 7.86$  ms for patient 1,  $68.4 \pm 16.5$  for patient 2, and  $50.7 \pm 50.3$  ms for patient 3. Some myoclonus jerks in patient 1 and 3 were observed before spike occurrence, even sometimes without any EEG correlates.

**Conclusion:** Our results confirmed Hallett study in a patient suffering from Lance-Adams syndrome (Hallett et al. 1977). They support the hypothesis that post-anoxic myoclonus are generated subcortically, the generator sending pathological neural signals both to the periphery and the cortex, explaining that EEG spikes and EMG events seems visually synchronized.

### P393

#### CREUTZFELDT-JAKOB DISEASE: REPORTS OF SIX CASES AND EEG FINDINGS

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**Purpose:** Creutzfeldt-Jakob Disease (CJD) is a rare prion disease. Between the ages of 50–70, it is among the causes of rapidly progressive dementia, definitive diagnosis is made by brain biopsy. In this study, six patients who we have followed up with a diagnosis of probable CJD are presented with demographic and clinical characteristics, EEG and magnetic resonance imaging (MRI) findings.

**Method:** Between 2010 and 2013 years, six patients with the diagnosis of probable CJD (4 M, 2 F) who presented with rapidly progressive dementia examined according to their EEG, MRI, and laboratory findings.

**Results:** Patients aged between 54 and 71 (mean 61.8) and their clinical courses ranged from 3 to 11 months. First EEGs of two patients were nonconvulsive status epilepticus and they did not respond to treatment. Myoclonus and 'startle' response were observed in four patients. In the other four patients, in varying degrees, pyramidal, extrapyramidal, cerebellar signs and behavioral changes were presented. A relative of one patient had similar findings. Mini Mental Test (MMT) scores of the patients were between 18 and 25/30 (mean 21.5). In EEG recording, one patient had triphasic periodic epileptiform discharges, one had PLED, two patients had sharp slow wave activity which started from the lesion side and spread to the opposite hemisphere and two patients had slow background activity. In all the patients' MRI findings, diffusion restriction of caudate nucleus, putamen, insular cortex and ribbon-like hyperintensities in the parietal and temporal cortices were observed at one or more of them. In cerebrospinal fluid (CSF) examination, neuron-specific enolase (NSE) tested in five patients, four of them were at high level and one was at the borderline zone. 14.3.3 protein was negative in one patient.

**Conclusion:** CJD may be presented with NCSE have been reported. When investigating the etiology of NCSE, refractory to treatment, it should be considered CJD.

### P394

#### DEVELOPMENT AND VALIDATION OF SCALE PREDICTS MORTALITY IN NON-CONVULSIVE STATUS EPILEPTICUS IN ADULTS

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**Purpose:** Development and validation scale predicts mortality at day 30 in patients with non-convulsive status epilepticus (NCSE).

**Method:** In this prospective study we recorded all cases of NCSE between April 2007 and March 2012, in patients  $\geq 21$  years. The outcome analyzed was mortality at day 30.

**Development Model:** A cohort of 125 patients with SENC between April 2007 and March 2011. After analysis of all the aforementioned variables using stepwise logistic regression analysis, acute symptomatic etiology (OR: 7.2,  $p = 0.003$ ), partial SENC (OR: 3.9,  $p = 0.008$ ), delayed diagnosis (OR: 4.6,  $p = 0.001$ ) and refractoriness (OR: 5.3,  $p = 0.0008$ ) were independent predictors of mortality. We designed the scale predictive of mortality with the following score: acute symptomatic etiology (1 point), partial SENC (1 point), delayed diagnosis ( $\geq 72$  h: 2 points,  $\geq 48$  and  $< 72$  h: 1 point) and refractory SENC (1 point). The more certain forecast was obtained with a score  $\geq 4$ .

**Model Validation:** The scale was validated in a cohort of 33 patients with SENC collected between April 2011 and March 2012.

**Results:** When looking at different cutoff values of the scale, with values  $\geq 4$  yielded a moderate sensitivity of 81% (95% CI: 44–97) and high specificity of 96% (95% CI: 78–99) to predict mortality at day 30. The forecast accuracy was 91%. The area under the ROC curve was 0.94.

**Conclusion:** Data from the present study shows that this scale is a useful method in predicting mortality at day 30 in adult patients with SENC.

### P395

#### NONCONVULSIVE STATUS EPILEPTICUS IN THE ADULT: DIFFERENCES BETWEEN THE FORMS COMATOSE-CRITICAL AND PROPER

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**Purpose:** Describe the demographic and clinical characteristics, compare rates of refractoriness and mortality at day 30, days of hospitalization and delay in diagnosis, between patients with non-convulsive status epilepticus with critical disease or in coma (NCSE-CC) and patients referred to as outpatient or "proper" (NCSE-P).

**Method:** All the consecutive cases of NCSE between April 2007 and March 2012 among patients  $\geq 21$  years old, were prospectively recorded.

**Results:** the following results were recorded in 156 patients with NCSE: 75% ( $n = 117$ ) were proper and 25% ( $n = 39$ ) were critical-comatose. The mean age was similar in both groups (76 and 74 respectively). The patients with NCSE-CC presented fewer antecedents of epilepsy and a higher percentage of acute symptomatic etiology (97.5%), being the causes similar in both groups. The impairment of consciousness was the most common manifestation in both cohorts. A significant difference was observed in the NCSE-CC group between refractoriness rate (72%

vs. 40%,  $p = 0.0007$ ) and mortality rate (64% vs. 28%,  $p < 0.0001$ ), as well as delay in diagnosis (64 vs. 38 h,  $p = 0.03$ ) and days of hospitalization (21 vs. 7,  $p < 0.0001$ ).

**Conclusion:** The results of this study show significant statistical differences between patients with NCSE-CC and NCSE-P mainly in terms of higher rates of refractoriness and mortality. For this reason it is important to study and analyse the two groups separately. These findings should be confirmed in future prospective studies among different populations.

### P396

#### REFRACTORY STATUS EPILEPTICUS IN THE VETERAN POPULATION: CAUSES, TREATMENT AND OUTCOMES IN 22 PATIENTS

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**Purpose:** Refractory Status Epilepticus (RSE) can be defined as status epilepticus (SE) that continues despite treatment with benzodiazepines and one antiepileptic drug (AED). RSE has a mortality of 16–39% when compared with non-refractory status epilepticus (Non-RSE). Optimal treatment approaches for RSE are not clearly defined and major independent outcome predictors are age and etiology.

**Method:** To better understand RSE causes, treatment approaches, and associated outcomes we retrospectively reviewed all cases of SE treated at the Veterans Affairs Greater Los Angeles Healthcare System over a period of 8 years. SE cases were identified via an electronic electroencephalogram (EEG) consult service tracking list from July 1, 2001 to June 30, 2009.

**Results:** Four thousand five hundred and nine EEG reports were reviewed and 72 patients with SE were identified. Forty-four (44) of the 72 (61%) patients with SE failed the 1st line agent. 22 of the 44 (50%) of patients who failed the 1st line agent failed the 2nd line agent too and were considered to have RSE. Causes of RSE, efficacy of treatments used, and outcomes were assessed.

The average age of patients with RSE was 65 vs. 62 years for patients with Non-RSE. Mortality in the RSE group was higher at 55% vs. 20% in the non-RSE group. Anoxic/hypoxic brain injury and traumatic brain injury was identified as the etiology in 27% and 18% of the patients with RSE respectively. Lorazepam, phenytoin, and propofol were the most frequently used AEDs in patients with RSE. Lorazepam, phenytoin, propofol were successful in terminating RSE in 46%, 12% and 36% of the patients respectively. Other agents used in terminating RSE were midazolam, levetiracetam, and phenobarbital.

**Conclusion:** RSE is a serious condition and associated with higher mortality rates than SE as observed in our case-series.

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### P397

#### PREVALENCE, REASONS, AND CONSEQUENCES OF PRE-MARRIAGE DISCLOSURE OR CONCEALMENT OF EPILEPSY DISORDER IN THE MARITAL LIVES OF WOMEN IN KARACHI, PAKISTAN

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**Purpose:** The purpose of this study was to identify the rate of prevalence, reasons, and consequences of disclosure or concealment of epilepsy diagnosis at the time of women's marriage negotiations.

**Method:** This descriptive cross-sectional study included 381 married women with epilepsy, from a tertiary healthcare setting in Karachi, Pakistan. A purposive sampling method was used for the study. A self-reported questionnaire was administered to collect the data. Descriptive and inferential statistics were implied for data analysis.

**Results:** The present study shows that 64% of the participants disclosed the epilepsy diagnosis to their prospective spouse and in-laws, at the time of marriage negotiations. The three key reasons for the pre-marriage disclosure of epilepsy identified in this study include anticipating disruption in the matrimonial relationship, trustworthiness in the marital relationship, and acceptance from the prospective spouse after knowing the history of the disease. Whereas respondent have reported four major reasons for the concealment of epilepsy: to prevent proposal rejection, stigma, pressurized by their own family to hide, and myths and misperceptions regarding epilepsy. Study findings also revealed that married epileptic women who have disclosed or concealed are suffering from deleterious consequences. Furthermore, the study has shown a significant association of the socio-economic factors with the pre-marriage disclosure of epilepsy.

**Conclusion:** This study concludes that pre-marriage disclosure of epilepsy is a crucial and a complex decision because it carries numerous benefits as well as harms for women in the different domains of life. However, honestly sharing the history of epilepsy at the time of marriage negotiation is more helpful, as epilepsy requires follow-up in the clinic and compliance to medication for a prolonged period. Moreover, disclosure helps to get financial support, physical assistance, and affectionate support.

### P398

#### ASSOCIATION BETWEEN PARTICULAR FOETAL MALFORMATIONS AND ANTIEPILEPTIC DRUG EXPOSURE

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**Purpose:** To study associations between patterns of foetal malformations and individual antiepileptic drugs taken during pregnancy.

**Method:** Analysis of data related to 1733 fetuses from 1703 pregnancies (147 not exposed to antiepileptic drugs, by means of multiple variable logistic regression).

**Results:** There were statistically significant ( $p < 0.05$ ) associations between i. valproate exposure and spina bifida, malformations of the heart and great vessels, digits, skull bones and brain, but not hypospadias, cleft palate/lip and mouth abnormalities ii. topiramate exposure and hypospadias and brain maldevelopments, and iii. carbamazepine exposure and renal tract abnormalities.

**Conclusion:** The valproate findings are in keeping with the published literature, the topiramate finding regarding hypospadias, in conjunction with literature data pointing in the same direction, though not to a statistically significant extent support the idea that the drug is a teratogen, possibly with a specific pattern of organ maldevelopment. The finding needs to be confirmed in studies based on larger populations.

### P399

#### FOLLOW UP AND TREATMENT OF WOMEN WITH EPILEPSY DURING PREGNANCY

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**Purpose:** More than 90% of pregnant women who have epilepsy deliver healthy babies. However, antiepileptic drugs (AED) that were used, genetic and socio-economic causes of maternal seizures can adversely affect the health of the fetus. Here, epileptic pregnant women, who were followed up in our epilepsy outpatient department, were discussed.

**Method:** This study was included 87 pregnancies from 83 epileptic women who were following in our epilepsy department and had a child between June 2002-January 2012. All demographic data, medical and epileptic history, data about pregnancy, antiepileptic drugs malformations for each patient were evaluated.

**Results:** The mean age of patients was  $26.99 \pm 4.73$  and epilepsy duration was  $8.49 \pm 6.23$  years. There was focal onset seizure (with or without secondary generalization) in 52 patients (62.7%). The remaining 31 patients had generalized seizures. Fifty-one pregnancies were planned. Before pregnancy, AED or drug dosage was changed in 36 women, pregnancy was allowed after the discontinuation of AED in two patients. Six pregnancies were ended with spontaneous abortion in the first trimester and ectopic pregnancy was present in one patient, while 76 infants were healthy. Four patients had a major malformation (two gastroschisis, one ventriculoseptal defect, one meningocele). Five patients in spontaneous abortion and three patients who had major malformation infant were unplanned pregnancies.

**Conclusion:** Pregnancy in women with epilepsy must be planned and the regulation of treatment should be done before pregnancy.

#### P400

##### MATERNAL HEALTH AND EPILEPSY

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**Purpose:** Women with epilepsy rarely access antenatal services as required due to cultural beliefs and stigmatisation attached to epilepsy, thus an inferiority complex as a result of having epilepsy, a situation that jeopardises their maternal health. Only 36% of pregnant women deliver in health facilities, while 21% do not receive any care at all and in rural areas more than 20% of pregnant women deliver at home with neither a trained nurse nor a traditional birth attendant (UDHS REPORT 2006).

**Method:** In Uganda, after realizing the challenges women with epilepsy go through, ESAU joined a coalition of 14 civil society organisations whose aim is to contribute to the reduction of maternal mortality in Uganda.

**Results:** The proportion of mothers attending antenatal care (first visit) in Uganda has increased from 87% in 1988 to 94% in 2006. However, the proportion attaining full Antenatal Clinic (ANC) like 4 or more visits remained low; at 47% in 1995, 42% in 2000 and 47% in 2006.

**Conclusion:** It is believed that epilepsy affects all people despite of their gender. However, our Ugandan experience has shown that women are affected more. I would thus like to share with the world our experiences of epilepsy and maternal health, our interventions and our achievements.

#### P401

##### WOMEN'S EXPERIENCES OF PREGNANCY WHILST LIVING WITH EPILEPSY: A QUALITATIVE STUDY

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**Purpose:** As part of the EMPiRE (Anti-Epileptic drug Monitoring in PREGnancy) Randomised Controlled Trial (RCT), the authors conducted a qualitative study of women's experiences of pregnancy whilst living with epilepsy. The purpose of this research is to explore and capture the perspectives of pregnant women living with, and managing, epilepsy.

**Method:** Semi-focused interviews were conducted with 25 women who are enrolled in the EMPiRE RCT and 12 women who declined to take part in the trial. Participants are interviewed two to three times; once on recruitment into the trial, in the event of a seizure during pregnancy, and after giving birth. Interviews are analysed using narrative analysis.

**Results:** In this paper, the authors will present findings based on the initial interviews with women.

Themes that will be explored are:

- contextualising women's diverse experiences of pregnancy and epilepsy,
- how women "weigh up" the risks and benefits of having a baby whilst managing their condition,
- women's negotiations of anti-epileptic drug regimens,
- women's primary concerns and hopes for themselves and their babies,
- the nature of stigma as an influencing factor during this stage of women's lives.

The perspectives of women recruited into the trial and those who declined will also be compared.

**Conclusion:** Women living with epilepsy are "expert patients," and as such their perspectives on the management of epilepsy and pregnancy yield crucial insights for both health professionals and researchers. These key insights begin to address the critical gap in knowledge of women's experiences of pregnancy and epilepsy.

The EMPiRE trial was funded by the National Institute for Health Research Health Technology Assessment Programme (UK) (Ref 09/30/58) and ethical approval was granted by the National Research Ethics Committee, West Midlands (Ref 11/WM/0164).

#### P402

##### WOMEN WITH EPILEPSY AND INFERTILITY HAVE ABNORMAL REPRODUCTIVE HORMONAL PROFILE

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**Objective:** A third of women with epilepsy (WWE) may experience infertility (failure to conceive after 12 months of unprotected intercourse). We compared the hormone profile of WWE and infertility (WWE-I) with that of WWE who had conceived (WWE-F).

**Methods:** In the Kerala Registry of Epilepsy and Pregnancy we compared the hormone profile of 50 WWE-I and 40 age matched WWE-F. Morning blood samples were drawn in follicular phase (1–14 days) for 21 WWE-I and 18 WWE-F, in luteal phase (15–30 days) for 23 WWE-I and 15 WWE-F and beyond 30 days for 6 WWE-I and 5 WWE-F who had irregular cycles.

**Results:** The two groups were comparable regarding physical, epilepsy syndrome, duration of epilepsy, BMI and serum cholesterol levels. The WWE-I group (compared to the WWE-F group) had significantly higher level of Luteinizing Hormone -LH ( $26.4 + 37.3$  mIU/ml vs.  $9.9 + 14.5$  mIU/ml). LH/FSH ratio in follicular phase was abnormal ( $>2$ ) for WWE-I (OR 12.4, 95% CI 1.3–117.0). Their progesterone levels in luteal phase showed a trend towards low levels. They also had significantly ( $p < 0.01$ ) higher levels of Dehydro epiandrosterone ( $2.0 + 1.7$   $\mu$ g/

ml vs.  $1.0 \pm 0.7 \mu\text{g/ml}$ ). There was no significant difference in the levels of FT3, FT4, TSH, Prolactin, FSH, Testosterone or Androstenedione levels. WWE who were on AEDs (compared to WWE who were not on AEDs) had higher risk of elevated LH/FSH ratio.

**Conclusion:** WWE-I have significantly higher risk of abnormal reproductive hormone profile compared to WWE-F. The hormone profile high LH, elevated LH/FSH ratio (follicular phase), low progesterone (luteal phase) and high DHEA levels suggests a tendency for anovulatory cycles and or inadequate luteal phase in WWE-I.

#### P403

##### REPRODUCTIVE HEALTH PROBLEMS IN WOMAN'S EPILEPSY

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**Purpose:** To study influence of antiepileptic drugs (AEDs) on reproductive health (RH) at mono – and polytherapy of woman's epilepsy.

**Method:** The work was the part of prospective observation uncontrollable one-center research of side effects of AEDs on RH at 155 women at the age of 16–45. Three groups were allocated: 1 gr. – AEDs monotherapy, 2 gr. – polytherapy, 3 gr. – without AEDs. Social determinants of health included an assessment of an education level, employment and disability. Disturbances of RH in epilepsy were carried out to two stages: one stage was carried out by epileptologist, 2 – by gynecologist. The diagnosis was made in compliance with MKB-10. Definition of degree of reliability of interrelation “AEP – RH disturbances” was carried out by means of algorithm of Naranjo. STATISTICA for Windows system (version 5.5) was used.

**Results:** Average age was 25 years. 1 gr. – 70 (45%), 2 gr. – 65 (42%), 3 gr. – 20 patients (13%). Majority of patients had higher education, only 7% had secondary education. The indicator of employment better characterized the patient's social adaptation: 70% worked and studied, 30% didn't work and differences in groups weren't reliable. The fifth part of patients had disability, more in group of polytherapy ( $p < 0.001$ ). Disturbances of RH had 53%, 40% from them been caused by side effects of AEDs. Comorbid disturbance of RH was noted in 13% without differences in groups. Application of polytherapy by AEDs at epilepsy treatment at women enlarged the frequency of disturbances of RH ( $p < 0.001$ ).

**Conclusion:** Reproductive health in women with epilepsy is complex social, medical, pharmacological problem. Disturbances of reproductive health are frequent side effects of antiepileptic drugs. It is necessary to monitor a condition of reproductive health during treatment with antiepileptic drugs.

#### P404

##### POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES): A CASE REPORT

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**Introduction:** Posterior reversible encephalopathy syndrome (PRES), which is characterized by headache, mental disorder, epilepsy and visual impairment, often can not compensate for the sudden rising and is due to arterial pressure. The most common etiologies of PRES hypertensive encephalopathy, eclampsia, cyclosporine-A neurotoxicity and seizures

followed by postictal conditions, can be diagnosed clinically and radiologically.

**Case:** Sudden severe headache, nausea, vomiting, blurred vision symptoms admitted to the emergency department, 20-year-old female patient was hospitalized. Story, that gave birth a week ago, were diagnosed with preeclampsia in pregnancy obtained. Seizures at least once before admission to hospital, emergency services, follow-up is repeated two times during the day, waking, learned that generalized tonic-clonic seizures. MR imaging of the brain, the occipital cortex and basal ganglia hyperintensities on T2, diffusion-weighted MRI images consistent with vasogenic edema in PRES was diagnosed by detection of cases. Treating the patient, vasogenic edema regressed completely in about 10 days. Seizure cases to an improvement of clinical symptoms did not recur.

**Conclusion:** PRES variable and non-specific headache, nausea, vomiting, visual disturbances, seizure-like symptoms such as a more serious symptoms are also often seen alongside. With properly treatment, clinic patients show significant improvement and radiological resolution. In our case, to the improvement of the clinic as well as the recurrence of seizures and radiological findings seen declining.

#### P405

##### AUDIT OF WOMEN WITH AN INTELLECTUAL DISABILITY (ID) IN CORNWALL WHO ARE TAKING ANTIEPILEPTIC MEDICATION (AEDs) WITH CONCURRENT USE OF ORAL CONTRACEPTIVE PILLS (OCPs)

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**Purpose:** Improve the rationale, care, monitoring and treatment of women with ID who are on OCPs and taking AEDs.

**Method:** A questionnaire was developed from current good practice national guidelines for ID, OCPs & AEDs. These include “Valuing People Now”, Mental Capacity Act 2005 and NICE guidelines in Epilepsy. The questionnaire was sent to all surgeries in the county. Patients had to be on an OCP, AED and have an ID. Focus was on

- 1 Understanding the rationale for OCP (birth control/ behavior management)
- 2 Whether the GP had considered AED interactions, side effects etc and reviewed the patient regularly
- 3 Whether the patient had demonstrated the mental capacity to make an informed choice around this complex issue and if not a best interest process followed?

**Results:** Questionnaires were sent to 67 surgeries, 29 responded identifying 10 patients. All patients had a rationale for the OCPs and nine had “consented”. Decision making on the co-prescription of OCPs and AEDs and Capacity was unclear.

**Conclusion:** The long term effects of both OCPs and AEDs on bone density and concerns of OCPs reducing the efficacy of certain AEDs increasing vulnerability to seizures are well documented in literature. Our findings suggest that GP surgeries do not have a uniform process of consenting and managing vulnerable women with ID on this complex issue. This could lead to physical complications for the vulnerable woman in addition to financial and legal implications to the health community.

An easy read information leaflet for the patient and poster flow chart for the GP to highlight these issues was developed and disseminated to surgeries to support ID clients and GPs in making informed decisions. In cases where patients lack capacity, their “best interest” be considered as per the pathway. This will ensure uniformity of good practice across the county.

## P406

**HYPERPROLACTINEMIA AMONG WOMEN WITH EPILEPSY***Zhidkova IA<sup>1</sup>, Kaznacheeva TV<sup>2</sup>*<sup>1</sup>*Department of Neurology, Moscow State Medical Dental University named after A.I. Evdokimov, Moscow, Russian Federation,* <sup>2</sup>*Department of Reproductive Medicine, Moscow State Medical Dental University named after A.I. Evdokimov, Moscow, Russian Federation*

**Introduction:** Hormonal abnormalities among women with epilepsy are due to epilepsy-related hypothalamic-pituitary axis dysfunction or to side effects of antiepileptic drugs (Luef G. & Rauchenzauner M., 2009; Verotti A. et al., 2011). Postictal elevations in serum concentrations of prolactin (PRL) were assumed to be a marker of retrospective evidence of epileptic seizure (Bauer et al., 1996).

**Purpose:** To determine hormonal abnormalities among women with epilepsy (WWE), who were long-term treated with antiepileptic drugs (AEDs).

**Method:** Sixty-two women with epilepsy (WWE) of reproductive age (mean age 25.7 ± 0.6 years) were enrolled in the study. Group I included 14 WWE using valproate; group II consisted of 16 WWE taking carbamazepine; group III – included 21 WWE using new AED (lamotrigine, topiramate, levetiracetam, oxcarbazepine); group IV – 11 WWE taking polytherapy. All women were investigated: sex hormones – luteinizing hormone, follicle-stimulating hormone, prolactin, estradiol, progesterone, testosterone.

**Results:** Hyperprolactinemia revealed among 23% of women using valproate (786 (142.2) mIU/L); among 15% of WWE taking carbamazepine (786.3 (77.2) mIU/L); among 25% of WWE using new AED (802.9 (122.5) mIU/L); among 27% of WWE taking polytherapy (905.8 (109) mIU/L). Clinical manifestations of hyperprolactinemia associated with menstrual disorders (oligomenorrhea) in 6% of WWE. The level of prolactin was significantly higher in women with idiopathic generalized epilepsy in the 1 phase menstrual cycle (515.1 (296.3) mIU/L) than in symptomatic focal epilepsy (343.2 (238.2) mIU/L) (p = 0.016).

**Conclusion:** Hyperprolactinemia was revealed in about 1/4 of women with epilepsy, who were long-term treated with antiepileptic drugs, but serum concentrations of PRL were not more than 1000 mIU/L and were evaluated that functional hyperprolactinemia in women with epilepsy taking AEDs, and specific treatment was not needed.

## P407

**BIDIRECTIONAL INTERACTIONS BETWEEN PROGESTINS AND VALPROATE, LAMOTRIGINE AND CARBAMAZEPINE MONOTHERAPY IN WOMEN WITH EPILEPSY***Luef G<sup>1</sup>, Deichmann S<sup>1</sup>, Pittschieler S<sup>1</sup>, Rauchenzauner M<sup>2</sup>, Seger C<sup>3</sup>, Wildt L<sup>4</sup>*<sup>1</sup>*Department of Neurology, Medical University Innsbruck, Innsbruck, Austria,* <sup>2</sup>*Department of Paediatrics, Saint Vincent Hospital, Zams, Austria,* <sup>3</sup>*Institute of Medical and Chemical Laboratory Diagnostics, University Hospital, Innsbruck, Austria,* <sup>4</sup>*Department of Gynecological Endocrinology and Reproductive Medicine, Medical University Innsbruck, Innsbruck, Austria*

**Purpose:** Hormonal contraceptives in combination with antiepileptic drugs in women with epilepsy can lower the efficiency in both ways such as seizure susceptibility and unintended pregnancies.

**Method:** Ninety-one women on hormonal contraception were included. 61 women with epilepsy treated with LTG (n = 33), VPA (n = 23) and CBZ (n = 5) and 30 healthy women. Blood samples were drawn during menstruation and between day 14 and 21 of the menstrual cycle. The technique used for quantitative simultaneous determination of six progestins in human plasma was online solid-phase extraction-high performance liquid chromatography-tandem mass spectrometry (online SPELC-MS/MS). Since most variables were not normally distributed, results were calculated with non-parametric tests using Kruskal-Wallis-Test and Wilcoxon-Test.

**Results:** LTG serum levels were decreased significantly during on-phase compared to offphase (4.7 [1.1–21.3] vs. 1.8 [0–22.9] µg/ml, p = 0.002). On distribution of HC into progestins following differences occurred: LTG serum level decreased on drospirenon significantly (2.9 [1.6–4.8] vs. 1.4 [0.9–2.8] µg/ml, p = 0.018) and on levonorgestrel was a tendency for reduction (7.1 [3.5–17.1] vs. 2.1 [0–10.6] µg/ml, p = 0.068) during on-phase compared to offphase. On gestoden there was no change in LTG serum level (6.3 [1.1–21.3] vs. 1.9 [1–22.9] µg/ml, p = 0.59).

**Conclusion:** The study shows an inhibiting effect of particular progestins on AED serum levels which might increase seizure risks. In part the results for LTG serum concentration varied with different progestins. Of note, gestoden does not seem to interact with LTG and therefore could be a suitable progestin for WWE. Drospirenon and presumably levonorgestrel could increase seizure susceptibility and the risk of contraceptive failure due to reduction of LTG and their own serum concentrations.

## P408

**PEER TO PEER SUPPORT: NORMALISING PREGNANCY FOR THE MUM-TO-BE WITH EPILEPSY***Crosby-McKenna NM<sup>1</sup>*<sup>1</sup>*Epilepsy Action, PR and Campaigns, Leeds, UK*

**Purpose:** Normalising pregnancy in women with epilepsy is a key theme of papers and guidance in antenatal care. This poster identifies what information women with epilepsy receive, and suggests how information and peer-to-peer experiences can be used to normalise pregnancy.

**Method:**

- An online self-completed survey was posted on Epilepsy Action's website ([www.epilepsy.org.uk](http://www.epilepsy.org.uk)) between July and October 2012. Postal surveys were available on request. Total- 366 women of child bearing age completed the survey.
- Stimulated pregnancy discussions online.
- Created Pregnancy Diaries, a magazine that shares real-life experiences of pregnancy in seven women with epilepsy.

**Results:** The survey results showed that of women of child bearing age almost:

- 47% (171/366) said health professionals failed to discuss
- contraception
- teratogenicity of anti-epileptic drugs (AED)
- 65% (236/366) lacked advice relevant to maintaining child safety during a seizure.

Of women planning to becoming pregnant and those who have been pregnant during the last 5 years:

- Over a quarter said health professionals failed to discuss
- pregnancy (26% 53/204)
- teratogenicity of AEDs (28% 58/204)
- 49% (99/204) had not been told about the possibility of seizure change in pregnancy.

**Conclusion:** A lack of information about these issues represents a missed opportunity to reassure women about pregnancy, and normalise pregnancy for the patient. Providing information before and during pregnancy, and sharing peer experiences, can help to reduce anxiety and normalise pregnancy for the mum-to-be with epilepsy.

## P409

**MEDICATION ADHERENCE IN WWE VIA USE OF IPOD APPLICATION TRACKING DEVICE**

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**Purpose:** WEPOD is a multicenter prospective observational study evaluating fertility among women with epilepsy (WWE) compared to healthy controls. WEPOD utilizes a customized mobile electronic device (iPod) application to track fertility information, and in WWE, seizures and daily medication use. We determined medication adherence in the WWE group using the iPod application.

**Method:** WWE and healthy age-matched controls, seeking pregnancy, enrolled within 6 months of stopping birth control. Subjects were trained to use a customized iPod touch application (the WEPOD App™) for daily data tracking, which connects to a web-based program providing central data monitoring. All subjects tracked data daily until delivery or up to 12 months if they did not become pregnant.

**Results:** Of 61 WWE who enrolled before 12/1/12 and tracked AED usage, 51 (83.61%) tracked >90% of total enrolled days, and eight of 10 who did not eventually dropped out. WWE collectively tracked any data on 94.76% of 14,151 total enrolled days, and therefore missed tracking on 741 days. On the 13,410 collective days that they tracked, subjects reported 97.55% AED adherence. If these 51 subjects were not medication adherent on the 741 days not tracked, the maximum non-adherent rate could be 92.45%. The 28 WWE who tracked non-AEDs reported 89.57% non-AED medication adherence.

**Conclusion:** Overall, WWE in the WEPOD study tracked medication use in the vast majority of possible days, and reported over 90% AED adherence. Lack of tracking using the device was associated with study drop-out. Interestingly, WWE reported better compliance with AEDs than non-AEDs. Electronic diaries may be useful data capture tools for daily reporting on medication adherence.

## P410

**PREGNANT WOMEN WITH EPILEPSY: 43 PATIENTS RESULTS IN 1 YEAR PERIOD**

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**Purpose:** In the present study, we evaluated the epileptic pregnant women, who were followed up in our epilepsy outpatient clinic and discussed the antiepileptic drug usage and the effects of them on the fetus.

**Method:** Forty-three epileptic pregnant women who were followed in our epilepsy outpatient clinic between January 2012 and January 2013 were included in this study and the data about the patients are still continuing to collect. All demographic data, medical and epileptic history, seizure type, data about pregnancy, antiepileptic drug usage, and malformations were evaluated.

**Results:** The mean age of patients was 26.93 (18–38) and according to family and medical history, five patients have a history of family marriage, 10 patients have an epileptic relative in their family. Febrile convulsion has learned only eight of them. The beginning age of the seizure was between the 5 and 30 years of age. For seven patients, the first epileptic attack was occurred during the pregnancy and for one patient it was occurred in postpartum period. The seizure type in 67% of patients was

generalized tonic clonic. The most commonly chosen antiepileptic drugs were lamotrigine (34%) and carbamazepine (25%). Eight patients had lesion in MRI. In this 1 year period, 25 of 43 patients were delivered of a baby. Three pregnancies were ended with spontaneous abortion in the first trimester and ectopic pregnancy was present in one patient. One pregnancy was terminated because of cardiac defect, one baby died because of HELLP syndrome. Thirteen patients are carrying on their pregnancy. One kidney anomaly was observed in one born baby. There has not been living in a baby with a major malformation.

**Conclusion:** Pregnancy in epileptic patients must be planned and the regular visiting of these patients to the clinics can provide successful pregnancies and healthy offspring.

## P411

**PERICONCEPTIONAL FOLIC ACID SUPPLEMENTATION IN PREGNANCIES WITH ANTIEPILEPTIC DRUGS USE**

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**Purpose:** To investigate the evidence that periconceptional folic acid supplementation reduces the teratogenic risk of antiepileptic drugs. To investigate to what extent current guidelines or expert opinions are evidence based.

**Method:** Review of the available human and experimental literature.

**Results:** The effect of folic acid supplementation on teratogenic risks of antiepileptic drugs has never been tested in a randomized controlled clinical trial comparing folic acid supplementation with placebo, or low dose folic acid with high dose. Current professional guidelines turn out to be based on the assumption that teratogenic mechanisms of antiepileptic drugs are identical to the pathogenic mechanisms of idiopathic birth defects, which, however, are largely unknown. Recent animal studies and human observational data from the EURAP study demonstrated the possibility of an adverse effect of folic acid on pregnancy outcome.

**Conclusion:** Current guidelines and expert opinions promoting periconceptional high dose folic acid supplementation as an antidote for teratogenic risks of antiepileptic drug are not evidence based and even potentially hazardous. There is a strong need for randomized clinical trials comparing low vs. high dose folic acid in women on antiepileptic drugs with child wish. Population-based pregnancy registries and preconception outpatient clinics with focus on women on antiepileptic drugs may provide the best opportunity to conduct such studies.

**Poster Session: Adult Epileptology B  
Tuesday, 25 June 2013**

## P412

**PREVALENCE OF DRUG RESISTANT EPILEPSY IN PATIENTS WITH SYMPTOMATIC, IDIOPATHIC AND CRYPTOGENIC EPILEPSY IN A CANADIAN REFERRAL CENTER**

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**Purpose:** We analyzed the prevalence of Drug Resistant Epilepsy (DRE) in an epilepsy center using four definitions, including the definition provided by the International League against Epilepsy (ILAE).

**Methods:** We assessed 250 consecutive patients assessed in an epilepsy clinic. This clinic is the only available in the Canadian province of Saskatchewan. An independent chart reviewer previously trained applied four definitions of DRE. The definitions of DRE used in this study were as follows: Kwan and Brodie, Berg, Camfield and the recently provided by the ILAE. After the extraction of clinical information, the four definitions were applied.

**Results:** In our cohort the prevalence of DRE using the definition of Berg was 24%, Kwan and Brodie 34%, Camfield 36% and for the definition of the ILAE was 32%. There was no statistical difference between the rates provided by the four definitions ( $p > 0.05$ ). Using the definition of the ILAE, the prevalence of DRE was 36% in patients with focal epilepsy vs. 28% in patients with generalized epilepsy ( $p = 0.22$ ). The prevalence of DRE in patients with symptomatic epilepsy was 39%, idiopathic 31%, cryptogenic 26% and unknown 17%.

**Conclusions:** This is the first study of prevalence of DRE in a Canadian center. The prevalence of DRE was high, probably reflecting the referral pattern of a single epilepsy center in the province. No statistical differences were identified in the prevalence of DRE in patients with symptomatic, idiopathic, and cryptogenic epilepsy as other studies have showed.

#### P413

##### A PRELIMINARY DIAGNOSIS OF EPILEPSY BY LOGICAL DISJUNCTION FOLLOWING THE COMPLETE LISTING OF RELATED EPILEPSIES VIA GENUS AND DIFFERENTIA USING GOOGLE SEARCH ENGINE ON THE INTERNET TO MAKE AD HOC DATABASE OF WORKING KNOWLEDGE AT A PATIENT'S BEDSIDE

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**Purpose:** To develop the proven clinical tool, which will improve the diagnosis.

**Method:** Case report A woman aged 25, suffered convulsions which began in her teens. A gait disorder and impairment of visual activity began at age 20. A clinician must clarify the patient's symptoms by how the patient describes his convulsion. A questionnaire for a patient should be short and simple. It needs to be put in plain English. Eye fundus examination has revealed the macular cherry red spot. Use keywords such as "sudden brief muscle constructions" when using the Google search engine and it will find: myoclonic seizures. It is genus (class of things). By genus and differentia (in logic) it makes a distinction from one species to another -which is through this logical exclusive disjunction and googling search, following the complete listing of myoclonic epilepsies. Exclusive disjunction or alteration will be true when at least one of its parts is true. Exclusive disjunction means "this, or that, but not both." As a result, it is making an ad hoc full text database. It is included in an epileptic and non-epileptic myoclonic disorders, inherited myoclonic epilepsies with rare forms and acquired myoclonic epilepsies of others etiology. Use query keywords such as "macular cherry red spot" and "juvenile onset" in an ad hoc database of working knowledge when finding the myoclonic epilepsy sialidosis type I. The exact diagnosis can only be made by screening of urine for sialyloligosaccharides.

**Results:** We are able to diagnose 118 patients, both genders, between 18 and 60 years old with paroxysmal motor, sensory, and mental symptoms. And there is a 90% accurate diagnosis.

**Conclusion:** Using a logical exclusive disjunction with the Google search engine on the Internet, and making an ad hoc database, can be the clinician's tool.

#### P414

##### LONG-TERM PROGNOSIS OF JUVENILE MYOCLONIC EPILEPSY

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**Purpose:** To evaluate long-term prognosis and the related risk factors of patients affected by Juvenile Myoclonic Epilepsy (JME).

**Method:** This is an observational, open-label, long-term study. All patients affected by JME regularly followed by our Centers were recruited. Statistical analysis were performed using SPSS 6.0 for windows.

**Results:** Fifty-three patients affected by JME were recruited (29 F, mean age  $29.3 \pm 8.2$  yy [range 16–53]); in four cases JME was an evolution of Childhood Absence Epilepsy. 43 (81%) patients showed generalized tonic-clonic seizures (gtcs) and 19 (36%) absence seizures.

Mean follow-up was  $95 \pm 60$  months (16–239).

Forty (75%) patients resulted seizure-free for at least 2 years; an higher likelihood of refractoriness of JME was associated to: female sex, family history of epilepsy and febrile convulsions, gtc and absence seizures, focal abnormalities and photosensitivity on EEG, younger onset of epilepsy.

Twenty-one (39%) patients, after seizure-freedom, withdrew treatment, at a mean age of  $22.9 \pm 9$  yy (15–49); seizures relapse was observed in 20 (95%) cases and the patient remained seizure-free was the only one who withdrew drug treatment after the forth decade of life (49 yy).

**Conclusion:** Our study confirms good prognosis of JME and its tight relation to drug therapy, which should be maintained long-term.

#### P415

##### CLINICO-IMAGING AND EEG CHARACTERISTICS OF INTRACTABLE EPILEPSY FOLLOWING CLOSED HEAD INJURY

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**Purpose:** Post traumatic epilepsy (PTE) is seen in 2–20% following head trauma. Risk factors include injury severity, depressed skull fracture, intracranial hematoma, penetrating trauma, coma >24 h, early post traumatic seizures, focal EEG and neuroimaging abnormalities. However, not much data is available in such patients with intractable seizures following closed head injury (CHI).

**Method:** Consecutive patients with intractable (seizure freedom <1 year in spite of treatment with at least two AEDs) PTE following closed head injury were selected from our Epilepsy Clinic over past 1 year. Their demographic, clinico-imaging and EEG data were reviewed and correlated.

**Results:** Eleven patients (five males & six females) with mean age ( $\pm$ SD) 22 ( $\pm$ 9) years presented with intractable epilepsy of 29



(±33) months average duration, fulfilling the methodology. Age of CHI was 37.4 (±33.6) months with time to onset of seizures as 17.3 (±14.2) months following the injury. Etiologies of CHI were Motor Vehicle Accident in eight and fall in three patients. All but two patients had either physical or cognitive sequelae following CHI. Neuroimaging showed lesions in all, with multi-lobar involvement in 8/12 (66.6%) patients. The EEG revealed epileptogenic abnormalities in 9/12 (75%) that were multifocal in 6/9 patients.

**Conclusion:** All patients with intractable PTE following CHI revealed MRI abnormality and three quarter had epileptogenic abnormalities on EEG. Two-thirds of the patients had Motor Vehicle Accident as the etiology in our cohort.

#### P416 COMPARISON OF BIOMAKERS FOR DIFFERENTIATING SEIZURE

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**Purpose:** The need for a biological marker to diagnose seizure among the patients with a loss of consciousness has been emphasized from past studies. The elevation of creatine phosphokinase (CK), prolactin, neuron-specific enolase (NSE), ammonia has introduced as a tool, but each has its limitations in the clinical field. The purpose of this study is to analyze the effectiveness of biological markers to diagnose seizure in the emergency department.

**Method:** Adult patients who were admitted to the Department of Neurology at Gangnam Severance Hospital with final diagnosis of a generalized tonic-clonic seizure were eligible for this study and underwent analysis of serum biochemistry, including CK, prolactin, NSE and ammonia. These patients had blood test within 8 h after a seizure in the emergency department. We compared the sensitivities of each biochemical examination.

**Results:** We enrolled 36 patients who had final confirmed diagnosis of a generalized tonic-clonic seizure and underwent analysis of serum CK, prolactin, NSE and plasma ammonia (25 males, 11 females). NSE is the most sensitive biological marker to diagnose seizure in our study (Sensitivity: NSE 94.44% > ammonia 61.11% > prolactin 38.89% > CK 36.11%).

**Conclusion:** Serum NSE and plasma ammonia measurement during acute post-ictal period in emergency department may be useful tests for the identification and diagnosis of a seizure rather than serum CK and prolactin. Clinicians should consider the use of biological marker to differentiate seizure from many other disorders which can be altered mental status.

#### P417 INVESTIGATION OF AUTO-ANTIBODIES IN PATIENTS DIAGNOSED WITH FOCAL EPILEPSY

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**Purpose:** There is growing evidence that autoimmune mechanisms might contribute to the pathophysiology of some seizures. Our aim was to investigate anti-neuronal antibodies in a large series of adult cryptogenic focal epilepsy (CFE) patients.

**Method:** Serum NMDA receptor (NMDAR), leucine-rich glioma inactivated-1 (LGI1), contactin-associated protein 2 (CASPR2) and glycine receptor (GlyR) antibodies were investigated with cell-based assays and voltage-gated potassium channel (VGKC)-complex and glutamic acid decarboxylase (GAD) antibodies with radioimmunoassay. CFE patients were included and, as another focal epilepsy group, patients showing mesial temporal sclerosis (MTS) on the MRI were also investigated as controls.

**Results:** A total of 80 epileptic patients' sera were studied for all auto-antibodies, including 54 with CFE (mean age 39.2 ± 14 years, with normal MRIs) and 26 with MTS (mean age 32.5 ± 9.2 years). In CFE group, we found GlyR antibodies in 4, NMDAR antibodies at low levels in 2, VGKC antibodies at low levels in one. In MTS group, four patients were positive for antibodies to CASPR2, one had GlyR antibodies and one had VGKC antibodies at low levels. Only four of the total of 13 seropositive patients (seven female and six male, mean age 35.5 ± 8 years) had drug-resistant seizures; one in each antibody group.

**Conclusion:** GlyR auto-antibodies were determined in epileptic patients for the first time. Furthermore some MTS patients had antibodies to CASPR2. Our results suggest that the immune system might contribute to some forms of epilepsy. Further studies are needed to explore the potential pathogenic role of these antibodies.

#### P418 EPILEPSY IN DEMENTIA WITH LEWY BODIES (DLB): CORRELATION OF CLINICAL, EEG AND NEUROPATHOLOGICAL FINDINGS

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**Purpose:** Dementia with Lewy bodies (DLB) is one of the most common causes of neurodegenerative dementias. Even though some of the clinical features of the disease may be explained on the basis of epileptic seizures and post-ictal changes, reports of epilepsy among patients with DLB is scanty

We describe three patients with DLB whose main clinical manifestations were progressive dementia and epilepsy

**Method:** The three patients were men aged 70, 76 and 82 years. They were admitted, investigated and treated at the hospitals of the Eastern Health, St. John's, NL Canada, because of suspected epileptic seizures. Their investigations included CT scans of the head and multiple EEG recordings. Post-mortem examination was performed for two of the three patients

**Results:** During their hospital admissions, all the three patients were witnessed to have epileptic seizures followed by post-ictal confusion. CT scan of the brain was normal in each one of them

Their EEG recordings showed; (i) diffuse, asynchronous theta and delta waves which were most prominent in the parietal-posterior temporal-occipital regions, (ii) prolonged REM sleep features, (iii) focal interictal spikes in the parietal, posterior temporal or occipital regions and (iv) photic-elicited spikes at low stimulation frequency (PEST)

The two patients who had post-mortem examinations were aged 70 and 76 years. Classical Lewy bodies were identified in the substantia nigra, locus ceruleus and the dorsal motor nucleus of the vagus. Cortical lewy bodies were present in the frontal, temporal, parietal and occipital lobes. In the older patient, Alzheimer's changes consisting of neuritic plaques and neurofibrillary tangles were seen

**Conclusion:** The symptoms and signs of epileptic seizures arising from the occipital, posterior temporal and parietal cortices may underlie some of the manifestations of DLB. The presence of EEG findings such as described above may aid diagnosis of the disease.

## P419

## THE CAUSES OF EPILEPSY IN ADULTS

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**Purpose:** To study the presumptive etiology of epilepsy in adults at the hospital of the Tashkent medical Academy

**Method:** All patients underwent a clinical neurological examination, the study of somatic status, medical and psychological tests of higher cortical functions, neurophysiological tests, neuroradiological methods in the hospital of tashkent medical academy. All patients underwent a special survey which covered the following factors: age, sex, major etiological factors leading to an epileptic seizure, the frequency of seizures, types of seizures and antiepileptic drugs used by the patient.

**Results:** The study was conducted among 94 patients aged 16–70 years. Of these, 53 (57%) were men and 41 (43%) – women aged 16–70 years. By establishing the epilepsy causes found out a large role of brain injuries- 32.97%. head injury is a common and preventable cause of epilepsy and it turned out that the incidence of head injuries among men several times higher than the rate among women. Among the causes of epilepsy caused 38.29% of the occupied various unknown reasons, 11.7% – cerebrovascular disease, 10.64% – perinatal, 4.85% – mass lesions of the brain, 1.06% – neuroinfection.

**Conclusion:** Understanding the causes of epilepsy provides the key to epilepsy itself; such an understanding remains central to the appropriate management and to meaningful shared decision making for the individual with epilepsy.

## P420

## EPILEPSY ASSOCIATED WITH PRIMARY CENTRAL NERVOUS SYSTEM (CNS) IMMUNOGLOBULIN DEPOSITION DISEASE

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**Purpose:** Very little information exists about primary CNS immunoglobulin deposition disease. The relationship of the disease to epilepsy is unknown. We hereby describe a patient who had epilepsy for 18 years caused by immunoglobulin deposition disease of the brain.

**Method:** Our patient was evaluated and treated by physicians and surgeons of the Eastern Health, St. John's, NL, Canada. Unrestricted post-mortem examination was conducted at the hospital. Neuropathological examinations were performed at the Eastern Health, St. John's, NL and University Hospital, London, ON, Canada

**Results:** The main clinical features were epilepsy with partial-onset seizures, recurrent behavioral disturbances and personality change, severe motor deficits and progressive cognitive decline.

The CT and MRI were comprised of enhancing lesions of varying sizes in the brain parenchyma. Multiple areas of the cerebral hemispheres and brain stem were affected.

The EEG findings consisted of diffuse, asynchronous delta waves and focal spikes.

The pathology showed exuberant perivascular inflammatory cells, few giant cells and eosinophilic extracellular materials which were present within some blood vessels and within the brain parenchyma. The

inflammatory cells were composed mainly of mature plasma cells. There were few mature lymphocytes and eosinophils. The amorphous eosinophilic deposits showed a crystalline appearance, expressed lambda light chains and heavy chains (IgG) of immunoglobulin. They were weakly positive for beta amyloid.

**Conclusion:** Our patient's epilepsy was caused by immunoglobulin deposition disease of the brain. There was no involvement of any other organs or body parts.

Although rare, immunoglobulin deposition disease of the brain should be considered in the differential diagnosis of epilepsy with partial-onset seizures.

## P421

## EMOTIONAL SEMIOLOGY AND ITS LOCALIZING AND LATERALIZING VALUE IN FOCAL EPILEPSY

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**Purpose:** We attempted to determine a trend in seizure localization and lateralization for patients undergoing surgical epilepsy evaluations who have ictal laughter or crying.

**Method:** We searched the charts for patients admitted to the epilepsy monitoring unit at Thomas Jefferson Hospital for seizure descriptions with the words “laugh” or “giggle” or “cry”, and found data on their seizure localization and lateralization, including patients who had undergone intracranial monitoring.

**Results:** Sixteen patients were found with emotional semiology. Five underwent intracranial monitoring. Seven patients had onset of seizures in the left temporal lobe, and seven had onset of seizures in the right temporal lobe. One patient had a left frontal seizure onset, and one had bilateral temporal onsets. Most patients had ictal laughter, not crying.

**Conclusion:** Most of the patients with emotional semiology had temporal lobe seizures and the semiology seen was ictal laughter. Ictal laughter appears to have little lateralizing value.

## P422

## CONSEQUENCES OF MISDIAGNOSING OBSTRUCTIVE SLEEP APNOEA AS EPILEPSY

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**Introduction:** Epilepsy and obstructive sleep apnoea (OSA) may coexist, often recognised during sleep deprived EEG, with OSA first reported during epilepsy telemetry. Parasomnias have been reclassified as seizures but there is little data re OSA misdiagnosed as epilepsy.

**Case:** A 55 year old, obese (BMI 32) Caucasian male pilot was diagnosed with epilepsy, having been independently assessed by three neurologists/epileptologists. Further evaluation revealed doubtful history, normal EEG (awake and sleep deprived), normal imaging but he was trialled on two anti-epileptic medications by previous consultants. Polysomnography confirmed OSA (mean RDI @ 20 [41 in REM]; longest hypopnea 98 s; desaturation to 78% SAO<sub>2</sub>).

History from his sleeping partner cast great doubt on seizures, suggesting them to be OSA with prolonged apnoea. Treatment with CPAP aborted all episodes and re-diagnosis allowed return to flying initially with 1 year review and subsequently 2 years review plus, confirmation of CPAP compliance at review.

**Discussion:** Epilepsy and being a pilot are incompatible but compliant use of CPAP, in OSA, obviates risks. He was denied his licence, because OSA was misdiagnosed as epilepsy, but reclassification allowed successful return to flying and no further episodes nor problems with flying. This reinforces the need to have accredited sleep physicians, also versed in epilepsy, as an integral component of the evaluation of "seizures", especially within the context of being a pilot but also highly relevant to suspected epilepsy and driving. There is an absolute need for detailed history from sleeping partner and possible option for concurrent PSG with EEG telemetry.

#### P423

##### YOUNG ADULTS AND EPILEPSY

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In recent years, increasing the efficiency and quality of epilepsy contributed to increase the proportion of patients with epilepsy who are studying at the university, and having equal social opportunities with healthy people.

**Purpose:** To study the clinical course of epilepsy in young adults.

**Method:** Neurophysiological (EEG), statistical methods.

**Results:** Studied 67 patients, aged 18–24 years. Among them, the girls – 41 boys – 26. All representatives of Yakut nationality. The debut of epilepsy has primarily between the ages of 11 and 15 years – 27 patients, older than 15 years – 17 students, from 6 to 10 years – 14 patients, younger than 5 years – 9 patients.

Identified the following etiological factors: family history in 18 patients, the development of epilepsy after undergoing a traumatic brain injury – one patient, after meningoencephalitis – one student, arteriovenous malformation – 1, perinatal CNS lesions 1, in other cases, the cause is not established.

The shape of the disease the patients was as follows: with idiopathic epilepsy – 26.85%, with symptomatic – 26.85%, cryptogenic – 46.3%. Primary generalized epilepsy was present in 46.3% of patients, partial with secondary generalization – at 26.85%, forms, with the primary and secondary generalization – in 26.85% cases. One of the most important indicators is the frequency of epileptic seizures. Frequent attacks – in 9, the average frequency – 18, rare – 9, 31 seizures were observed. Most patients (46.3%) are in clinical remission.

**Conclusion:** (i) The debut of epilepsy in young without intellectual disabilities between the ages of 11 and 15 years. (ii) Family history (26.9%) plays a major role in the development of benign epilepsy. (iii) In most cases the diagnosis of primary or idiopathic generalized or cryptogenic epilepsy.

#### P424

##### HUMAN HERPES VIRUS 6B AND MESIAL TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS (MTLE-HS): IS THERE A LINK?

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**Purpose:** Human Herpesvirus 6 (HHV-6) is a ubiquitous virus acquired mainly during the first 2 years of life. Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis (MTLE-HS) is the most frequent pharmacoresistant epilepsy. One of the most common antecedents of MTLE-HS is febrile seizures (FS). Although the aetiology of MTLE-HS remains unclear, evidences suggest that HHV-6 infection could be implicated. The objective of this study was to investigate the presence of HHV-6B DNA in the hippocampus and adjoining temporal cortex of MTLE-HS patients submitted to surgery.

**Methods:** A total of 22 MTLE-HS (13 females and nine males) cases were studied. The mean age at surgery was  $39 \pm 9$  years and mean age at onset of seizures was  $10 \pm 6$  years. These study cohort was compared to a group of 10 epileptic patients without MTLE-HS (six females, four males; mean age =  $26 \pm 15$  years) and with autopsy material from nine individuals without neurological disease. HHV-6B DNA was identified by real-time PCR with specific TaqMan<sup>®</sup> probes.

**Results:** We detected HHV-6B DNA in only one hippocampus from a MTLE-HS patient. This patient had a disease duration of 36 years and a history of febrile seizures in childhood. None of the non-MTLE or controls specimens showed positivity for HHV-6B.

**Conclusions:** Our findings do not support a relevant etiologic role for HHV-6B in MTLE-HS, at least in this population. However, the possible role of viral infection in MTLE-HS epileptogenic process, in individual cases, cannot be excluded.

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#### P425

##### ICTAL UNILATERAL EYELID BLINKING – CASE REPORT AND REVIEW OF THE LITERATURE

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**Purpose:** Little is known about ictal unilateral eyelid blinking (UEB) as a lateralizing sign in focal seizures. We report a case study and give a short review on pathophysiology of UEB.

**Method:** We report a 38 year old, right-handed woman, who underwent prolonged non-invasive video-EEG monitoring. Ictal 99mTc-HMPAO-SPECT was performed during an episode with abdominal aura.

**Results:** We recorded a total of five seizures; one isolated abdominal aura and four evolving to complex focal seizures with UEB. Semiological signs in all of the seizures were forced bilateral blinking, in median starting 29 s after EEG-onset (range 18–37 s, lasting 9 s in median, range 6–11 s), followed by UEB in the right eye, in median starting 51 s after EEG-onset (range 30–71 s, lasting 17 s in median, range 10–34 s). UEB did not evolve in any clonic activity in the face. Other lateralizing seizure phenomena were ipsilateral head turn (2/4), contralateral eye deviation (3/4), aphasia (2/4), postictal impaired figural memory (1/4) and postictal nose wiping (2/4 partial complex seizures, respectively). Ictal EEG showed a right fronto-temporal seizure onset (F8, F8-Fp2 or Fp2-F4). Interictal EEG showed sharp waves right fronto-temporal (F8, F8-T4, F8-Sp2 or T2) and focal slowing left temporo-mesial.

**Conclusion:** UEB was ipsilateral to the right fronto-temporal EEG pattern in this patient and occurred only in seizures with clouding of consciousness and not during isolated epigastric auras.

The symptomatogenic zone generating UEB is still not clear. Ipsilateral fronto-temporal and cerebellar regions as well as trigeminal fibers may be involved in the evolution of UEB.

P426

**PROTECTIVE EFFECTS OF VAGUS NERVE STIMULATION ON CARDIAC ELECTRICAL INSTABILITY ASSESSED BY T-WAVE ALTERNANS IN PATIENTS WITH DRUG-RESISTANT EPILEPSY**

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**Purpose:** T-wave alternans (TWA), a beat-to-beat fluctuation in the amplitude and shape of the T wave in the electrocardiogram, has proven to be a noninvasive marker of risk for sudden cardiac death. At 30 min following secondarily generalized tonic-clonic seizures, TWA was markedly elevated to ~70  $\mu$ V (Strelczyk et al., *Epilepsia* 2011;52:2112–7), exceeding the 47- $\mu$ V criterion for life-threatening cardiac arrhythmia risk in patients with cardiovascular disease (TWA Consensus Guideline, *J Am Coll Cardiol* 2011; 58:1309–24). Our goal was to determine the impact of vagus nerve stimulation (VNS) on TWA and heart rate variability (HRV), an indicator of abnormal autonomic function implicated in sudden unexpected death in epilepsy (SUDEP).

**Method:** Ambulatory electrocardiograms of patients with VNS devices (N = 6) were analyzed for TWA using the Modified Moving Average method and for low- to high-frequency (LF/HF) ratio HRV during the interictal period. BIDMC's Committee on Clinical Investigations approved the study.

**Results:** The mean TWA was  $32.5 \pm 2.4 \mu$ V in lead V<sub>5</sub> for the six patients analyzed. In two patients monitored before device implantation, TWA was  $50.5 \pm 7.5$  in lead V<sub>5</sub> and decreased by 30.5% after VNS activation. There was a concomitant 12.5% decrease in LF/HF ratio, from  $1.6 \pm 0.2$  before to  $1.4 \pm 0.2$  after VNS activation, indicative of a shift toward increased parasympathetic tone.

**Conclusion:** Patients with VNS devices exhibit lower TWA levels than those without, suggesting a potential cardioprotective effect of this intervention. The corresponding decrease in LF/HF ratio suggests that enhanced parasympathetic tone may play a role, given its demonstrated capacity to suppress ventricular arrhythmias.

P427

**CHANGES IN SLEEP ARCHITECTURE AFTER SECONDARILY GENERALIZED SEIZURES THE DAY BEFORE**

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**Purpose:** This study was performed to investigate effects of (secondarily) generalized seizures during daytime on the sleep architecture the following night.

**Method:** Sleep of 425 long-term video-electroencephalography recordings were analysed and divided in two groups: *Seizure Free* (at start of the night a seizure free period of least 24 h) and *Daytime Seizure* (at least one (secondarily) generalized seizure occurred during the day before. *Seizure Free* (331 recordings) and *Daytime Seizure* (94 recordings) were compared for demographic data and sleep architecture variables: time in bed (TIB), total sleep time, sleep efficiency (SE), sleep onset latency, awakenings, wake after sleep onset (WASO), REM latency and sleep stages.

**Results:** In *Daytime Seizure* compared to *Seizure Free* more TIB (15.5 min,  $p = 0.001$ ), REM latency (17.8 min,  $p = 0.010$ ), NREM II (2.8 min,  $p = 0.023$ ), and less NREM III (-2.9,  $p = 0.012$ ) and REM

(-1.7,  $p = 0.037$ ) were seen. Comparison of recordings in 23 subjects with long-term recordings during nights with and without seizures the day before, resulted in longer TIB (26.0 min,  $p = 0.021$ ), WASO (22.8 min,  $p = 0.004$ ) and less SE (6.0%,  $p = 0.008$ ) in the night after daytime seizures.

**Conclusion:** Longer TIB and REM latency, more NREM II and less NREM III and REM were seen in the recordings in people with daytime (secondarily) generalized seizures compared to people without seizures. In people with recordings after days with and without seizures longer TIB and WASO and less SE were seen after daytime seizures. These differences were statistically significant, but their clinical relevance is doubtful.

P428

**RE-APPRAISAL OF CAUSATION OF EPILEPSY IN A DEVELOPING AFRICAN COUNTRY: ANALYSIS OF 342 NIGERIAN AFRICANS**

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**Purpose:** Epilepsy is common in sub-Saharan Africa. Studies are needed to determine the causes of epilepsy and in turn lower the incidence of epilepsy through the formulation and implementation of community and national preventive strategies and public health education programs. This observational, cross-sectional study assessed the possible causes of epilepsy in adult Nigerian Africans

**Method:** All adult patients (i.e. patients above 14 years of age) presenting to the clinic between January and December 2009 were recruited. The diagnosis of epilepsy was based on eye witness corroboration of recurrent afebrile seizures and EEG changes. The seizures were classified according to the International League against Epilepsy (ILAE) classification of 1981. Data was obtained through in-depth interview of patients' relations, review of medical records and results of investigations and telephone interview of medical personnel who treated these patients in the past. A structured interview schedule was used to obtain information on demographic information, seizure variables, health seeking itinerary and history of previous hospitalizations.

**Results:** A total of 342 patients were diagnosed with epilepsy during the study period comprising 202 males (59%) and 140 females (41%). The mean age of the patients was  $31.4 \pm 11.98$  years with a range of 16–76 years. One hundred and forty nine patients, comprising 43.6%, had no identifiable etiology. Of the remaining one hundred and ninety three, birth-related injuries (5%), recurrent childhood febrile convulsions (13.2%), neonatal sepsis/jaundice (7%), previous meningitis (7%), post stroke seizures 9.6% and post traumatic seizures (19.6%) were causes.

**Conclusion:** Preventable causes of epilepsy remain common in sub-Saharan African countries emphasizing the need for use of helmets and seat belts, standard efficient ante-natal services and intra-partum practices, implementation of immunization programs and primary prevention of stroke through risk factors modification and health education.

P429

**SEX DIFFERENCES IN ANTICONVULSANT THERAPY AND SIDE EFFECTS IN PATIENTS WITH EPILEPSY – A CROSS-SECTIONAL STUDY**

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**Purpose:** Differences in pharmacokinetics and reporting of adverse events between men (M) and women (W) have been described. This study evaluates sex differences in AED dosage, plasma concentration and adverse events.

**Method:** Using a semistructured interview, we obtained data regarding epilepsy syndrome, AED and side effects in epilepsy outpatients. Plasma levels of patients' current AED were routinely determined.

**Results:** Three hundred and two patients were included in the study (161 W, 53.3%). Idiopathic generalized epilepsies (IGE) were more frequent in women (W: 32.3%; M: 10.6%,  $p < 0.001$ ) and partial epilepsies in men (M: 85.1%; F: 58.4%;  $p < 0.001$ ). More women were treated in monotherapy ( $p = 0.008$ ). The average number of AED was  $1.62 \pm 0.98$  in men and  $1.41 \pm 0.75$  in women ( $p = 0.022$ ). In monotherapy, more women were treated with lamotrigine (W:  $n = 36$ , 36.4%; M:  $n = 13$ , 20%;  $p = 0.036$ ) and more men received oxcarbazepine (W: 3, 3%; M: 8, 12.3%;  $p = 0.027$ ). There were no differences in dosage and plasma concentration of any AED in monotherapy. Women and men reported different adverse events: men mentioned gait disturbances more frequently ( $p < 0.001$ ). Women more often complained about tiredness ( $p = 0.049$ ), impaired vision ( $p = 0.016$ ), skin reactions ( $p = 0.004$ ) and weight gain ( $p = 0.025$ ).

**Conclusion:** The epilepsy syndrome influences the choice of AED and hence could explain differences in substance and number of AED. We found significant differences in adverse events between men and women with epilepsy. Some are congruent with literature (skin reactions, weight gain), while others have not yet been described. Patient's sex should be considered when choosing the appropriate AED and evaluating reported side effects.

#### P430

##### NEUROIMMUNOLOGICAL CHARACTERISTICS OF EPILEPSY

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**Purpose:** We have studied immunological aspects of epilepsy with clarification their immunological pathomechanisms.

**Method:** This study included 52 patients with symptomatic epilepsy (SE) and idiopathic epilepsy (IE). Group I included 28 patients with SE and group II comprised of 24 patients with IE. Control group composed of 10 practically healthy subjects. The mean age of studied patients was  $36.2 \pm 14.7$  years. Immunological investigations were performed by method ELI-Neuro-test 12. We studied the level of neurotrop autoantibodies to NF-200, GFAP, S 100, Voltage-dependent Ca canals, glutamate receptors, GABA-, Dofamin, Serotonin and n-Choline-receptors. Thus we measured autoimmune responses directed to antigens of the neural tissue. Immunoreactivity of autoantibodies was measured with use of markers to double-stranded DNA and B2-cycloprotein which are products of disintegration of the neuron necrosis.

**Results:** Epilepsy is accompanied by changes in the immune system which are expressed by increase in autoantibodies to the receptors of choline, GABA, dofamine, serotonin and boderline deviations to protein B2 of glycoprotein. However, more reliable findings in comparison with data from control group were noted in contents of autoantibodies to such neurospecific proteins as: NF-200, S 100 and double-stranded DNA. Parameters of protein S 100 in the group I and group II were increased and had reliable differences in comparison with control group.

**Conclusion:** In the patients from group 2 there was noted increase in autoantibodies to double-stranded DNA that may be considered in this case as the sign of autoimmune process in the central nervous system.

#### P431

##### DIAGNOSTIC UTILITY OF VIDEO EEG MONITORING AT A TERTIARY EPILEPSY CENTER IN DENMARK

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**Purpose:** The purpose of this study was to analyze whether video EEG monitoring (VEM) had a clinical significance in establishing or changing the diagnosis in patients monitored by videoEEG at our department.

**Method:** We retrospectively analyzed data of all the adult patients who underwent inpatient VEM during a 3-years period between 2009 and 2011.

The indication for monitoring was either diagnostic purpose (in 94%) or presurgical evaluation. VEM was performed on average 2.7 days (2–5 days).

**Results:** All the 68 adult patients who have been monitored in the given period were included in the analysis. Fifty-three women and 15 men with the mean age of 38 years have been examined. The average disease duration was 10 years. At admission, the suspected diagnosis was epilepsy in 76.5% and 70.6% of all the patients were taking at least one antiepileptics (AED). There has been achieved at least one event during the monitoring in 86.3% of the patients. Psychogenic non-epileptic seizure (PNES) was the final diagnosis in half of the cases (48.5%).

Among patients with a final diagnoses of epilepsy, 16.7% were not treated with AED at referral. Conversely, 47.7% of the patients on AED at admission turned out with the diagnosis of PNES. The primary diagnosis of epilepsy was confirmed by VEM in 47% of the cases.

Psychiatric comorbidity was found in 42.6% of the patients significantly correlated with PNES, as expected (P-value: 0.002).

**Conclusion:** Our retrospective data showed that VEM was conclusive in 86.8% of all cases and in 39.7% led to changing the diagnosis. These results supports that VEM is a crucial diagnostic tool for diagnosing and classifying of epilepsy in order to improve its management.

#### P432

##### NATURAL EVOLUTION AND MORBIMORTALITY OF 75 PATIENTS WITH TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS AT CLEMENTINO FRAGA FILHO UNIVERSITY HOSPITAL, RIO DE JANEIRO

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**Purpose:** The morbidity of temporal lobe epilepsy associated with hippocampal sclerosis (TLE-HS) is contrasted with the excellent surgical response in about 85% of cases. Early identification of these patients impacts their lives improving in quality. The aim of this study is to describe the natural history and morbidity of dyscognitive seizures of a cohort of patients from Clementino Fraga Filho University Hospital in Rio de Janeiro.

**Methods:** Analysis of 75 patients with temporal lobe epilepsy associated with hippocampal sclerosis considering variables of demographic, clinical and morbidity.

**Results:** Thirty-four patients were men (47.2%). The average age of onset was 16.6 years. The average time of refractoriness was 30 years. 46 patients (63.8%) reported on initial precipitating incidents (IIP), which occurred on average at 24.16 months (about 2 years). Among the IIP 47.8% suffered febrile seizures, meningitis was found in 4.34%, 6.5% had neurocysticercosis, and 41.3% denied IIP. 36.1% of them could not

tell. The latency period was 12.86 years. 17% (13/75) had morbid events during dyscognitive seizures even when treated with antiepileptic drugs. Three (4%) suffered extensive burns, 8% suffered multiple trauma, 1.3% was involved in the murder which does not remember, and 4% had SUDEP.

**Conclusion:** The presence of IIP and latency period suggests the progressive aspect of ELT-EH. The average 30-year-refractory must have contributed to the high frequency of severe morbid events. Often dyscognitive seizures are not value however is associated with important adverse episodes. Early identification of patients with TLE-HS with surgical indication should prevent serious adverse events.

#### P433

##### SYMPTOMATIC EPILEPSY AS A RESULT OF STROKE

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**Objectives:** Cerebrovascular diseases are significant aetiological factors of epilepsy. Seizures may appear in acute phase of the insult, or during the reconvalescence. Our goal was to analyse the frequency and correlation between epileptic seizures and the type and size of cerebrovascular lesion.

**Methods:** In this prospective study, we evaluated patients with stroke who were hospitalised at the Department of Neurology in Nis, between January and December 2012. Witnessed epileptic seizures occurred in 129 patients. Patients with a previous history of epilepsy and pulmonary diseases were excluded. Patients were evaluated and had the same investigations with anamnestic, clinical, neurological, EEG and neuroimaging (CT, MRI) variables which were compared. Patients were treated with regular anti-oedematous and vasoactive therapy. After seizure appearance patients were instantly put on an anti-epileptic drug treatment.

**Results:** Of the 1386 patients with stroke who were admitted to the hospital, 482 (34.78%) had haemorrhagic stroke, and 904 (65.22%) had ischemic stroke. Mean age was  $52 \pm 30$  years. Of a total of 129 patients with witnessed epileptic seizures, 76 were male and 53 female. 46 (35.66%) patients with haemorrhagic and 83 (64.34%) patients with ischemic stroke developed seizures after 14 days of the stroke. Partial motor seizures (PMS) were registered in 73 (59.35%) patients, partial seizures with secondary tonic-clonic generalisation (GTC) in 39 (31.70%) patients and primary GTC seizures in 17 (13.82%) patients. Status epilepticus (SE) was registered in nine patients. 69 (53.49%) patients had EEG pathological changes (spike or sharp-waves) and 36 (27.90%) patients had focal or diffuse Theta-Delta waves. Normal EEG patterns were registered in 24 (18.60) patients.

**Conclusion:** Patients with ischaemic stroke and cortical lesions are at a higher risk of developing seizures. Partial motor seizures and partial seizures with secondary tonic-clonic generalisation are a dominant feature. Our results differ from the ones in literature, in which patients with haemorrhagic stroke are more likely to develop seizures. It may be the consequence of the fact that the mortality in haemorrhagic stroke patients is higher.

#### P434

##### SCREENING OF AUTO-ANTIBODIES AGAINST CALCIUM CHANNELS IN PATIENTS WITH ABSENCE EPILEPSY

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**Purpose:** Auto-immunity as a contributory mechanism of epilepsy has received increased attention in recent years. Since the relationship of idiopathic absence epilepsy (IAE) with calcium channels is well known and the presumed genetic etiology could not be uncovered, we aimed to study the possible role of antibodies against calcium channels in IAE patients.

**Method:** Antibodies against P-Q type voltage gated calcium channel (VGCC) and T type VGCC were investigated by ELISA technique. Patients diagnosed according to the 2010 International League Against Epilepsy classification with typical absence seizures either as childhood absence epilepsy (CAE) or juvenile absence epilepsy (JAE) showing typical generalized spike and wave discharges on electroencephalography (EEG) were included in the study. Patients with cryptogenic focal epilepsy (CFE) and healthy subjects comprised the control groups.

**Results:** Thirty-five idiopathic absence epilepsy (IAE) patients (mean age  $21 \pm 14.91$ ), 53 CFE patients (mean age  $38 \pm 13.92$ ) and 30 healthy persons (mean age  $29 \pm 12.25$ ) were investigated as the study groups. Thirteen of 35 patients of the IAE group had CAE and others had JAE. There was no antibody positivity against both types of the VGCCs in the IAE group and healthy subjects. One 47-year-old female CFE patient who also had systemic lupus erythematosus showed antibodies against P-Q type VGCC, interestingly.

**Conclusion:** Although the number of the cases was not high, it can be suggested that antibodies against VGCC does not play an important role in the pathophysiology of IAE. Further studies with large groups of other epileptic syndromes are needed to evaluate the exact role of autoimmunity in epilepsy.

#### P435

##### A PROPOSAL FOR CLASSIFICATION OF PSYCHOGENIC NON EPILEPTIC SEIZURES

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**Purpose:** To systematically study the semiology of psychogenic nonepileptic seizures (PNES) captured by video-EEG recording and categorize them according to a simplified clinical classification.

**Methods:** Video-EEG recorded PNES were visually analyzed by three epileptologists from two different tertiary care epilepsy centers, and by two psychiatrists, in a blinded manner. PNES were classified into five distinct groups according to a clinical classification proposed by one out of the five physicians (Magaudda), highly experienced with PNES.

**Results:** A total of 46 PNES from 45 patients were studied. Based on semiology, PNES were classified as follows: Hypermotor: with generalized motor phenomena, rhythmic or disordered, resembling grand

mal or hyperkinetic frontal lobe seizures (40%); Akinetic: without motor phenomena, with unresponsiveness, without or with fall (syncope-like; 36.3%); Hypertonic: main symptom is stiffness, of a variable degree, till to opisthotonus (arc en circle). Minor tremor can be associated (9%); With subjective symptoms: paresthesia, experiential phenomena (visual, acoustic; déjà-vu or veçu, anxiety, fear, confusional state, etc.; 4.5%); Focal motor: with partial clonic or tonic phenomena (9%).

According to the proposed classification, 87% of PNES entered within one of the five seizures' subtypes. 13% were not classified because of mixed phenomena. 69% out of PNES has been classified in the same manner by the five different observers.

**Conclusions:** We proposed a reliable and easy-to-use classification of PNES. Interestingly, stereotyped features either within or across patients in PNES were evidenced. A semiologically-focused classification of PNES may address proper diagnosis and standardization across different studies. Ultimately, etiological understanding and management of this important public health issue would be improved.

#### P436

##### INTER-TEMPORAL SEIZURE PROPAGATION

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Identified routes of inter-temporal seizure propagation depend heavily on sites of invasive electrode implantation. Studying patients with adequate bi-temporal and bi-frontal subdural electrode coverage, thus encompassing all published proposed routes, we found a variety of propagation pathways. Fifteen (15) electro-clinical seizures originated unilaterally in a mesial temporal lobe and propagated to the contralateral temporal lobe among eleven (11) patients with such ictal spread studied. The following three routes to the contralateral temporal region appeared:

- 1) direct mesial temporal-mesial temporal in 6 (40%),
- 2) mesial temporal-frontal-temporal in 4 (27%), and
- 3) mesial temporal – lateral temporal – temporal in 5 (33%).

Median latencies between seizure onset and propagation to the contralateral temporal lobe were:

- 1) direct: 4.75 s,
- 2) via frontal 28.5 s, and
- 3) via lateral temporal: 20.5 s.

Our findings suggest that at least three possible routes for contralateral temporal propagation exist. Additionally, the longer latencies through frontal and lateral temporal routes indicate that more than contralateral temporal receptiveness is requisite for some homotopic ictal involvement.

#### P437

##### EPILEPSY WITH GRAND MAL ON AWAKENING: SEIZURE OUTCOME 40 YEARS AFTER ONSET

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**Purpose:** Awakening epilepsy is an age related syndrome of idiopathic generalized epilepsy (IGE) characterized by generalized tonic clonic seizures occurring predominantly on awakening (independent of time of day) or at leisure time (almost at evening). Data on long-term outcome regarding seizure freedom are sparse.

**Method:** Based on charts of outpatients with IGE, patients with definite awakening epilepsy were identified and included into the study

when follow-up was  $\geq 20$  years. Diagnostic allocation was made on the basis of clinical and EEG data as documented in patient charts. Data were derived from direct patient interviews or from detailed outpatient charts. Terminal remission was defined as seizure freedom in the last 5 years.

**Results:** Forty-two patients (29 males, 69%) were included into the study (mean age,  $60 \pm 13$  years). Age at onset was  $21 \pm 9$  years. Eleven patients had died, age of death was  $74 \pm 11$  years. After follow-up of  $40 \pm 13$  years, 26 patients (62%) were seizure free, five without anti-epileptic drugs (AED). Following multivariate analysis, age at investigation (OR 0.939; CI95% 0.887–0.994;  $p = 0.029$ ) was an independent predictor for lack of remission. Twenty patients (48%) had withdrawn AED at least once, 12 of those (60%) suffered from seizure relapse.

**Conclusion:** Four decades after onset of awakening epilepsy, more than 60% of patients were seizure free in the last 5 years. Lack of remission was a function of patients' age, the younger patients were, the less likely they were seizure free. AED withdrawal was associated with significant relapse risk. Awakening epilepsy is not associated with premature mortality.

#### P438

##### CLINICAL CHARACTERISTICS AND PROGNOSIS OF AUTOIMMUNE DISEASE-RELATED EPILEPSY

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**Purpose:** There is a now well-established link between epilepsy and autoimmune processes, particularly with respect to certain neuronal autoantibodies. A sizeable subset of patients in this category is typically refractory to anti-seizure drug regimens and requires immunosuppressive therapy. We sought to characterize the electro-clinical features of such patients.

**Methods:** Autoantibodies were assessed in adult patients with late-onset epilepsy of unknown cause.

**Results:** Seventeen patients were identified with anti-thyroid (11), anti-phospholipid (3), anti-N-methyl D-aspartate (2), and anti-voltage-gated potassium channel (1) antibodies. Mean age was 46 years (range 20–72), and 11 patients were female. Four patients presented with status epilepticus. EEG recordings in 13 (76%) patients showed multifocal spikes, primarily in the temporal lobes. Only 23% had MRI anomalies consistent with mesial temporal sclerosis. Nine (53%) patients demonstrated a satisfactory response to anti-seizure medications only. Only three of five patients responded to immunosuppressive therapy.

**Conclusion:** Recognition of underlying autoantibodies in patients with late onset epilepsy is paramount. A significant proportion of these patients respond favourably to anti-seizure medications alone, but a relatively low threshold for use of immunosuppression is generally warranted.

#### P439

##### RELEVANCE OF SEIZURE WITH MORTALITY AND NEUROLOGIC PROGNOSIS OF OUT OF HOSPITAL CARDIOPULMONARY ARREST (OHCA) PATIENTS WHO WERE TREATED WITH THERAPEUTIC HYPOTHERMIA AFTER RETURN OF SPONTANEOUS CIRCULATION

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**Purpose:** To evaluate relevance of postanoxic seizure with prognosis in case of OHCA patients who treated with therapeutic hypothermia (TH) and research prognostic role of portable EEG.

**Method:** One hundred-eighty OHCA patients arrived during July of 2008 and June of 2011, and 144 patients who had been treated with TH were included. Portable EEG had been taken after 24 h after induction of TH and classified by neurologist. As outcome variable, overall mortality and neurological outcome after 6 month from discharge were evaluated (Good neurological outcome; Cerebral performance category [CPC] scale 1.2, Poor neurological outcome; CPC scale 3~5).

**Results:** Among 144 patients, 93 patients (63.9%) was male, mean age was 51. Eighty-two patients (56.9%) survived and almost 30% (43/144) of patients had a good neurological outcome. Sixty-five patients (45.1%) had seizures and among this group, 19 patients (29.2%) discharged with good neurological outcome. There was no statistical difference between seizure group and non-seizure group. Initial EKG rhythm, APACHE II score (acute physiology and chronic health evaluation), time from basic life support to return of spontaneous circulation (OR 2.169; 95% CI 1.158~4.063, OR 1.107; 95% CI 1.064~1.152, OR 1.014; 95% CI 1.006~1.022, respectively) had statistical importance, but seizure group (OR 0.67, 95% CI 0.356~1.032,  $p = 0.065$ ) had no statistical relevance with mortality. Grading of EEG by neurologist showed positive relation with neurological outcomes ( $p < 0.001$ ). Factors associated with good neurological outcome was initial EKG rhythm ( $p = 0.005$ ), cardiac cause of arrest ( $p = 0.001$ ), high initial body temperature ( $p < 0.001$ ), low APACHE II score ( $p = 0.010$ ), shorter time interval between arrest from basic life support ( $p = 0.005$ ).

**Conclusion:** In our study, seizure group showed no relevance with mortality and prognosis. We should treat more carefully in case of OHCA patient with seizure, hoping better outcome.

#### P440

##### STRUCTURAL ANALYSIS OF EPILEPSY IN ADULTS IN THE HOSPITAL OF TASHKENT MEDICAL ACADEMY

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**Purpose:** To study clinical and epidemiological characteristics of epilepsy and epileptic syndromes and their risk factors in patients in the hospital based on Tashkent Medical Academy.

**Method:** All patients underwent a thorough pre-clinical and anamnestic selection. Scope of the study included: a clinical neurological examination, the study of somatic status, medical and psychological tests of higher cortical functions, neurophysiological tests, neuroradiological methods.

**Results:** The results showed that (57%) of the 94 patients were male. It showed a more frequent incidence of men. Average age at which has the highest incidence was 30–49 years. In the study of the seizure frequency was found out that the main group consisted of focal seizures, that is, in 68 (72.34%) cases – partial seizures with secondary generalization, 4 (4.25%) – complex partial seizures, 3 (3.12%) – simple partial seizures, 10 (10.49%) – primary generalized tonic-clonic seizures, and the rest – other types of seizures (Fig. 2). Studies have shown that one-third of patients with epilepsy has less than one seizure per year, one-third about one to twelve a year and one-third more than one episode of seizures per month, of which one-fifth of patients have one episode of seizures in weeks. Acute symptomatic seizures usually have more favorable prognosis than symptomatic or idiopathic seizures. However, the second seizure in 80% of cases develop in individuals with history of single epileptic seizures. Among the causes of epilepsy caused 38.29% of the occupied vari-

ous unknown reasons, 32.97% – head injuries, 11.7% – cerebrovascular disease, 10.64% – perinatal, 4.85% – mass lesions of the brain, 1.06% – neuroinfection.

**Conclusion:** Core group of patients were symptomatic epilepsy, and the main reason was head injury. It has showed a frequent incidence in men.

#### P441

##### THE COMPLEX ISSUE OF VASCULAR EPILEPSY: TOWARD A DEFINITION BASED ON ANATOMO-ELECTRO-CLINICAL CORRELATIONS

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**Purpose:** Clinical and EEG features of vascular epilepsy are not entirely clear. Our aim was to study anatomo-electro-clinical correlations in patients with epilepsy and evidence of cerebrovascular disease.

**Method:** One hundred and sixty-six patients with epilepsy and evidence of cerebrovascular disease were consecutively seen in our Center from 2000 to 2012. Inclusion criteria were: history of one or more strokes and occurrence of one or more seizures after at least 1 month or a history of epilepsy and evidence of cerebrovascular disease at neuroimaging studies. Exclusion criteria were: insufficient data, psychogenic seizures or coexistence of non-vascular cerebral lesions. The endpoint was to establish the coherence between vascular lesion (imaging data) and epileptogenic focus (anamnestic and EEG data). The coherence was scored as: likely (concordance between cortical lesion and focus); unlikely (discordance between cortical lesion and focus, or subcortical lesions only regardless of focus localization); undetermined (cortical lesion and not localizable focus).

**Results:** One hundred and thirty patients were included and 36 excluded. The coherence was scored as likely in 29 subjects (22%), unlikely in 81 (63%) and undetermined in 20 (15%).

**Conclusion:** It seems that only a minority of patients with vascular lesions and epilepsy can be classified as having a true “vascular epilepsy”. The causal relationship between these two conditions cannot be proved in most cases. In these patients, the epileptogenic role of different or adjunctive factors needs to be elucidated.

#### P442

##### ECSTATIC SEIZURES: A STATE OF BLISS RELATED TO A SENSE OF SUBJECTIVE CERTAINTY?

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**Purpose:** Ecstatic seizures have been previously suggested to arise in the anterior insular cortex (Picard & Craig, 2009), although strong arguments are still lacking. We attempt to support the hypothesis of an insular involvement with the study of new cases, and according to the current stage of knowledge.

**Method:** We describe the cases of two new patients with ecstatic seizures, whose evaluation included a careful history, with significant details about their ictal symptoms which can help to better understand the origin of the sense of bliss. Ictal electroencephalographic and blood flow studies were performed in one patient.

**Results:** The description of the ictal symptoms by the two patients revealed a sense of absence of doubt. “Things suddenly seemed self-evi-



dent, almost predictable”, “all the ordinary facts about the environment seemed suddenly to become infused with certainty and a sense of inevitability”.

The ictal SPECT showed an increased blood flow maximal at the junction of the right dorsal mid-insula/central operculum.

**Conclusion:** We hypothesize that the abnormal insular activity during the seizures may prevent any prediction error processing, or ambiguous information processing, generated by the insula. Accumulative evidence has indeed recently highlighted an important role of the anterior insular cortex in this system, particularly as a comparator between prediction state and outcome, that detects mismatch (Preusschoff et al., 2008). The absence of detection of prediction errors could prevent any feeling of ambiguity (and the accompanying negative emotional component) during the seizure, which could lead to a blissful state.

#### P443

### ANTI-AMPA AND ANTI-GAD POSITIVE LIMBIC ENCEPHALITIS AND INTERMITTENT PLASMAPHERESIS THERAPY – A CASE REPORT

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**Background:** Limbic encephalitis is an inflammatory disorder that can be paraneoplastic with the existence of intracellular antibodies or autoimmune and related to the existence of antibodies to antigens located on the surface of cell membranes. These include anti-VGCK, anti-NMDA, anti-AMPA, anti-CASPAR and anti-GAD antibodies. Each of these antibodies are connected with some specificity in the clinical presentation and clinical course.

**Case Presentation:** A 24-year old patient initially manifested with complex partial epileptic seizures (CPS), myoclonus and then gradually developed mental decline and impairment of consciousness. After intensive-care treatment and immunoglobulin therapy, the state of consciousness improved but frequent generalized action-related myoclonus and CPS with damage to short-term memory remained. Diagnostic examinations found the existence of anti-AMPA and anti-GAD antibodies and additional treatment excluded the existence of an underlying malignancy. Despite several antiepileptic drugs and the first immunotherapy, corticosteroids and mycophenolate mofetil (Cell-Sept) there was no clinical improvement, and new active lesions on brain MRI were visualised. We decided to start with intermittent plasmapheresis therapy (each month three cycles) which lead to significant reduction of epileptic seizures and myoclonus and also mild cognitive improvement.

**Conclusion:** Anti-AMPA and anti-GAD limbic encephalitis are rare autoimmune disorders that tend to frequent relapses and there is a need for long-term immunotherapy. Our case shows the potential effectiveness of intermittent plasmapheresis in these patients, with extremely rare simultaneous occurrence of anti-GAD and anti-AMPA antibodies.

#### P444

### THE INFLUENCE OF ANTICONVULSANT DRUGS ON THE MAINTENANCE OF CIRCADIAN CHRONOFACOR IN PATIENTS WITH FOCAL SYMPTOMATIC AND CRYPTOGENIC EPILEPSY

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**Purpose:** To evaluate the alteration in urinary 6-sulfatoxymelatonin concentration (6-SOM) at patients with focal epilepsy in the time of achievable remission during therapy with different anticonvulsants.

**Method:** Forty-three patients (24 female, 19 male) with focal caused (symptomatic and cryptogenic) epilepsy with lasting seizures were studied at pilot investigation. Mean age was  $37 \pm 11.7$  years. Remoteness of diseases was limited from 4 month to 20 years. 22 patients received basic anticonvulsant monotherapy with valproate, 21 – with carbamazepine. Concentration of 6-SOM (ng/ml) the main melatonin metabolite, were determined twice using immunofluorescence method in evening and morning urine in the beginning of investigation and after 6 month as result of medication-dose correction.

**Results:** Medicament remissions were achieved in 31 from 43 patients in consequence of medication-dose correction during anticonvulsant therapy. Fifteen persons have got carbamazepine, 16 – valproate. On the whole the frequency of seizures reduced from  $1.285 \pm 0.45$  ( $n = 32$ ) to  $0.2925 \pm 0.13$  a week ( $p < 0.001$ ). Evening concentration of 6-SOM stayed of the same value. Anticonvulsants provoke reduction of 6-SOM concentration in morning urine, when achieved medicament remission, was more pronounced in carbamazepine by 35% ( $20.0 \pm 3.55$  and  $13.11 \pm 2.07$  ng/ml,  $p < 0.05$ ), than in valproate by 24% ( $49.28 \pm 6.72$  and  $37.09 \pm 5.43$  ng/ml,  $p < 0.05$ ).

**Conclusion:** In spite of lowering of seizures' frequency in consequence of medication-dose correction during anticonvulsant therapy, carbamazepine and less valproate provoked reduction of 6-SOM concentration in morning urine after 6 month. Carbamazepine and preparation of valproic acid need differential pathogenetic correction of levels of night melatonin.

#### P445

### WHICH HAND MOVES OUR PATIENTS WITH TEMPORAL LOBE EPILEPSY?

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**Purpose:** Seizure semiology plays an important role in localization and lateralization of seizure onset. Ipsilateral motor automatisms and contralateral dystonic posturing occurs typically in mesial TLE and it is one of the most useful lateralizing signs. Rhythmic Ictal Nonclonic Hand (RINCH) motions have been proposed as a new ictal sign in TLE. We aim to describe a new case of RINCH motions.

**Method:** RINCH motions are defined as low-amplitude milking, grasping, pill rolling motions. They appear to be a contralateral sign and are usually followed by dystonic posturing. We present a new case and analyzed seizure semiology, video-EEG recordings and neuroimaging as a result of a presurgical evaluation for refractory epilepsy.

**Results:** We present a right-handed male with pharmacoresistant TLE. During video-EEG 4 seizures were recorded which started with psychic aura followed by aphasia and a left hand motor automatisms with distal right upper limb dystonic posturing. Ten to 30 s before dystonic posturing, he presented right RINCH motions. Ictal EEG demonstrated left temporal seizure activity. 3T-MRI showed left medial temporo-occipital gliosis probably due to perinatal anoxia and in FDG-PET severe hypometabolism in left temporo-occipital cortex was observed. Seizure semiology, video-EEG and neuroimaging findings are consistent and localize the epileptogenic zone over left temporal region.

**Conclusion:** The originality of this case is the presence of RINCH motions, a recently described ictal sign in TLE. This lateralizing value is useful for presurgical evaluation in refractory epilepsies.

P446

**AUTOMATIC MOVEMENTS IN FRONTAL VS. TEMPORAL LOBE FOCAL EPILEPSY – ON WHAT EXTENT DO THESE TWO TYPES OF SEIZURES DIVERGE CONCERNING THEIR PATTERN OF COMPLEX MOTOR BEHAVIOR?**

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**Motivation:** Ictal automatism are purposeless or semi-purposeless movements, striking the examiner as remarkably similar to normal motor activity, yet deprived of some/any context (Mohammed M.S. Jan et al., 2008). This study aims to thoroughly investigate their diagnostic value as localizers of the epileptogenic area.

**Method:** We reviewed the ictal video-EEG recordings of 27 consecutive patients with focal pharmaco-resistant epilepsy that underwent presurgical evaluation in our center. One representative seizure for each patient was included in the analysis. Seizures were further divided into two groups: with frontal (14 patients), respectively temporal lobe (13 patients) origin. After carefully selecting and analyzing the clinical sequence of symptoms and signs that occurred during the recorded ictal episodes, we isolated 13 different classes of motor automatism as defined by the ILAE's Glossary of Terms (Blume et al., 2001). The final analysis was based on several other factors, besides the difference in the frequencies of appearance: number of similar events per seizure, relative moment of onset and finally, the total and medium duration of each class, all applied both to the ictal and the post-ictal period.

**Results:** Verbal, oculo-motor, cephalic, oro-alimentary, gestural and manual automatism appeared with important differences between the two groups, favoring the temporal origin, the last three being the most striking (70% vs 36%, OR = 4; 39% vs 7%, OR = 8.125; 100% vs 63%, OR = 6.1; P < 0.05). In contrast vocal, mimetic and dyspraxic behavior ended up having no particular association power. Pedal and dacrytic automatism appeared exclusively during frontal seizures.

**Conclusion:** Regarding automatic behaviors, temporal lobe seizures could be distinguished from seizures originating in the frontal lobes, by a greater frequency and diversity of these phenomena. Manual, gestural and oro-alimentary automatism, with an early onset, can reliably guide the clinician regarding the seizures' origin.

**Poster Session: Basic Sciences B  
Tuesday, 25 June 2013**

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**THE EPILEPSY-RELATED PROTEIN SKYWALKER/TBC1D24 CONTROLS SYNAPTIC VESICLE REJUVENATION AND RESTRICTS NEUROTRANSMITTER RELEASE**

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Currently available Anti-epileptic drugs (AED) are ineffective with more than 30% of the patients. The model organisms used to screen for AED are mainly based on drug-induced seizures or random mutations that elevate seizure susceptibility. Ideally, models that harbor specific mutations are used. Existing models include animals with mutations in ion channels or neurotransmitter receptors, however, recent evidence also implicates additional presynaptic pathways in specific forms of epilepsy.

In an unbiased genetic screen in fruit flies we isolated loss of function mutations in a novel gene we named “skywalker” because mutant animals undergo massive seizures that result in the larvae to erect themselves in the food. Interestingly, mutations in the human orthologue of Skywalker, TBC1D24, cause epilepsy. Sky/TBC1D24 encodes a synaptically expressed GTPase activating protein (GAP) and we show that Sky facilitates endosomal trafficking of synaptic vesicles, chiefly by activating the GTPase activity of Rab35. Analyses of genetic interactions with the ESCRT machinery and components of the VPS/HOPS complex that control endo-lysosomal traffic, as well as chimeric ubiquitinated synaptic vesicle proteins, indicate that endosomal trafficking facilitates the replacement of dysfunctional synaptic vesicle components. Consequently, sky mutants harbor a larger readily releasable pool of synaptic vesicles and show a dramatic increase in basal neurotransmitter release, in line with the protein to restrict synaptic activity. Thus, the trafficking of vesicles via endosomes uncovered using sky mutants provides an elegant mechanism by which neurons may regulate synaptic vesicle rejuvenation and neurotransmitter release and we believe this mechanism is may prove to be an important pathway in epilepsy as well. In future work, we are developing novel molecular genetics tools to generate “clean” knock-in alleles of human TBC1D24 clinical mutants in the fly sky locus to assess the effect of these mutants on vesicle trafficking, neurotransmitter release and the development of seizures.

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**SODIUM SELENATE REDUCES NEURODEGENERATION AND BEHAVIOURAL IMPAIRMENTS IN THE POST-KAINIC ACID STATUS EPILEPTICUS RAT MODEL OF TEMPORAL LOBE EPILEPSY**

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**Purpose:** Hyperphosphorylated tau has been implicated in the pathogenesis of a variety of neurodegenerative disorders, including epilepsy. Here we investigated whether treatment with sodium selenate, a drug that reduces the pathological hyperphosphorylation of tau by increasing PP2A activity, would reduce neurodegeneration and functional impairments in a rat model of mesial temporal lobe epilepsy (mTLE).

**Method:** After 4 h of status epilepticus induced by systemic kainic acid injections, or control-saline injections, young-adult male Wistar rats (n = 9/group) were given continuous sodium selenate treatment (1 mg/kg/day), administered via subcutaneous osmotic mini-pump, for 2 months. In-vivo imaging with T2-weighted MR, diffusion weighted imaging, diffusion tensor imaging and magnetic resonance spectroscopy were used to assess structural and metabolism damage 1 month post-injury. Cognitive, motor, and emotional impairments were also assessed at 1 month post-injury. Video-EEG recording was used to evaluate the seizure frequency and duration. Immunohistochemical and western-blot analyses were used to assess levels of hyperphosphorylated tau and related pathologies.

**Results:** The results demonstrated that sodium selenate treatment reduced markers for neurodegeneration and behavioural impairments after a post-SE excitotoxic injury in the rat.

**Conclusion:** These data indicate that sodium selenate has neuroprotective effects against KA induced epilepsy and neurodegeneration in a rat model of mTLE, and may represent a novel disease modifying approach to preventing epilepsy that is translatable to the clinical setting.

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### EFFECTS OF RECOMBINANT ADENO-ASSOCIATED VIRUS MEDIATED NEUROPEPTIDE Y GENE TRANSFECTION ON THE EXPRESSION OF N-METHYL-D-Aspartate Receptors in the Hippocampus of Epileptic Rats

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**Purpose:** To explore the effects of recombinant adeno-associated virus mediated neuropeptide Y gene transfection on the expression of N-methyl-D-aspartate receptors in the hippocampus of epileptic rats.

**Method:** NPY gene was transfected into brain tissue of kainic acid-induced epilepsy rats through stereotactic methods with recombinant adeno-associated virus vectors.

At 2, 3, 4 weeks after vectors injection respectively, the seizure severity were observed and graded according to a modified Racine six evaluation criteria. The mRNA and protein expressions of NPY and NMDA receptor subunits in the hippocampus tissues detected by quantitative PCR and western blot analysis.

**Results:** Research results show that NPY gene overexpression can be realized in the epileptic brain; EEG results show that NPY gene expression 4 weeks after vector transfection significantly inhibited seizure severity in rats and prolonged seizure latency; quantitative PCR and Western blot detection show that the mRNA and protein expression of NMDA receptor subunit NR1, NR2A, NR2B was inhibited in the epileptic rat hippocampus.

**Conclusion:** These results demonstrate that NPY may subserve the inhibitory effects on seizure via down-regulation of the functional expression of the NMDA receptors.

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### HYPOXIA-INDUCED SEIZURES AFFECT INTERNEURONAL NETWORK MATURATION IN THE MOUSE HIPPOCAMPUS AND NEOCORTEX

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**Purpose:** Perinatal hypoxic-ischemic encephalopathy is the most important cause of acute mortality and morbidity in newborns. The most common acute effect of hypoxic-ischemic encephalopathy is neonatal seizures, which are very often refractory to conventional seizure medications. Hypoxia-induced seizures (HIS) are associated with a high incidence of epilepsy as well as cognitive disabilities later in life. Despite the significant long-term morbidity of HIS in the neonates, there is currently no specific treatment. Further, our understanding of how HIS changes the developmental trajectory of neuronal circuit development, and ultimately results in epileptogenesis and cognitive dysfunction, is still mostly unknown.

**Methods:** Our studies characterize the effects of HIS on the development of cortical inhibitory GABAergic circuits, a critical yet poorly understood aspect of neonatal seizures, using a mouse model.

**Results:** We determined that HIS affects the maturation and function of distinct GABAergic interneuron populations, parvalbumin (PV)-positive (Basket cells) and somatostatin (SOM)-positive interneurons differentially in the neocortex and in the hippocampus. In particular, we show that Basket interneurons in the neocortex remain immature at the level of transcription factor expression. This correlates electrophysiologically

with a diminution of mIPSC amplitude and frequency in hippocampal pyramidal cells.

**Conclusion:** Our data demonstrate that HIS have significant consequences on inhibitory networks, leading to increased excitability of the cortex and/or hippocampus. We believe that targeting these developmental changes will pave the way for developing novel pharmacological interventions to prevent the severe and lasting consequences of perinatal HIS.

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### THE PROTECTIVE EFFECTS OF AN DBS AGAINST SPONTANEOUS RECURRENT SEIZURES

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**Purpose:** Many patients with epilepsy are refractory to drug treatment. For those who are not good candidates for conventional surgery, deep brain stimulation (DBS) has been proposed as alternative treatment. The anterior nucleus of the thalamus (AN) has been one of the most studied targets for seizure control. Despite the encouraging results of recent clinical and preclinical studies, the most appropriate parameter for seizure control is still unknown. We investigate whether 100 and 500 mA AN DBS reduces seizures in epileptic rats in pilocarpine model.

**Method:** SE was induced with Pilo injections (320 mg/kg i.p.) and attenuated 90 min later with thionembatal (25 mg/kg i.p.). After the first spontaneous seizure the rats were divided into three groups: SHAM, 100 mA DBS and 500 mA DBS. DBS treated animals were implanted with AN electrodes 1 week before stimulation and had their preoperative seizure rate compared to that recorded during DBS (130 Hz, 90 µs pulse width).

**Results:** DBS at 100 mA has anticonvulsant effect whereas 500 mA is proconvulsant. In sham-treated controls, the frequency of seizures before and after surgery remained unaltered. In contrast, rats given AN DBS at 100 mA had a 65% reduction in seizure rate as compared to sham-treated controls (p = 0.09) and 68% less seizures than its own baseline (p = 0.05). In addition, 10 out of the 15 animals treated with 100 mA (67%) had a decrease in seizure rate, 4 (26%) did not have seizures before or after DBS and only 1 (7%) had more seizures while receiving DBS than at baseline (p = 0.05). On the other hand, animals treated with 500 mA had a 3.5-fold increase in seizure rate as compared to controls (p = 0.07) and 4.8 times more seizures than at baseline (p = 0.04).

**Conclusion:** The protective effect of AN DBS against spontaneous recurrent seizures is current-dependent, 100 mA has anticonvulsant effect whereas 500 mA is proconvulsant.

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### HIPPOCAMPAL GABA TRANSPORTER DISTRIBUTION IN PATIENTS WITH TEMPORAL LOBE EPILEPSY AND HIPPOCAMPAL SCLEROSIS

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**Purpose:** The purpose of this study was to determine hippocampal expression of neuronal GAT (GAT-1) and glial GAT (GAT-3) in patients with temporal lobe epilepsy (TLE) and hippocampal sclerosis (HS).

**Method:** Hippocampal specimens were obtained from patients who underwent surgery for TLE and from autopsy controls. Patients were divided into a mild and a severe HS group. Sections were immunohistochemically stained for GAT-1 and GAT-3, followed by quantification of the immunoreactivity in the hilus by optical density measurements. Additionally, GAT-3 positive hilar cells were counted and GAT protein expression in sections that included all hippocampal subfields was quantified by Western blot.

**Results:** The hilar GAT-1 expression of patients with severe HS was about 7% lower compared that in the mild HS / control group ( $p < 0.001$ ). The hilar GAT-3 expression was about 5% lower in the severe HS group than in the mild HS / control group (nonsignificant). Mild and severe HS samples contained 25–34% less GAT-3 positive cells compared to that in controls (nonsignificant). Protein expression as assessed by Western blot showed that GAT-1 was equally expressed in mild and severe HS samples, whereas GAT-3 was reduced by about 62% in severe HS samples ( $p < 0.0001$ ).

**Conclusion:** These data confirm previous observations that GAT expression is spatially and isoform-specific reduced in HS. In addition, we show that GAT-3 positive cell numbers are unchanged. Implications for the use of GABAergic antiepileptic therapies in HS vs nonHS patients remain to be studied.

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#### P453

##### INTERACTIONS OF RETIGABINE WITH PHENYTOIN, LACOSAMIDE, OXCARBAZEPINE, AND TOPIRAMATE IN THE MOUSE MAXIMAL ELECTROSHOCK-INDUCED SEIZURE MODEL – A TYPE I ISOBOLOGRAPHIC ANALYSIS

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**Purpose:** Rational combinations of antiepileptic drugs may help control drug-resistant epilepsy. Consequently, the aim of this experimental study was to evaluate interactions of a novel antiepileptic, retigabine, with phenytoin, and three newer antiepileptics, lacosamide, oxcarbazepine, and topiramate against maximal electroshock-induced convulsions in mice.

**Method:** The criterion to indicate seizure activity was the tonic extension of the hind limbs, following maximal electroshock (25 mA, auricular electrodes, 0.2 s stimulus duration). Brain concentrations of retigabine were measured by HPLC, whilst neurotoxicity was evaluated in the chimney test.

**Results:** Isobolography for the combinations of retigabine with the studied antiepileptic drugs revealed additive interactions in the maximal electroshock test, a tendency towards supraadditivity (synergy) being observed for retigabine+lacosamide at the fixed ratio of 1:1. In the chimney test, the combination of retigabine with lacosamide at the fixed ratio

of 1:1 exerted antagonistic interaction, whilst a tendency towards antagonism was evident for the fixed ratios of 1:3 and 3:1. Also, this tendency was seen in combinations of retigabine with phenytoin (at the fixed ratios of 1:3, 1:1, and 3:1) and retigabine with topiramate (at 1:1). As regards the combined treatment of retigabine+oxcarbazepine, additivity was found at the ratio of 1:1. In no case, brain retigabine concentration was affected by the combined treatments at the fixed ratios of 1:1.

**Conclusion:** The obtained results indicate that all evaluated drug combinations possessed good anticonvulsant and neurotoxic profiles. The most favorable profile may be ascribed to the combination of retigabine with lacosamide.

#### P454

##### SERUM BRAIN-DERIVED NEUROTROPHIC FACTOR LEVELS IN EPILEPSY

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**Purpose:** Serum brain-derived neurotrophic factor (BDNF) levels have not yet been examined in patients with epileptic seizures. The goal of this study was to clarify the utility of serum BDNF as a biomarker of epilepsy diagnosis and/or severity.

**Method:** We assessed the serum BDNF levels in 135 consecutive patients with epilepsy who met our criteria. Thirty-four healthy individuals who were evaluated for 12 months or longer and did not demonstrate any symptoms or signs of neurological disorders, served as controls. The serum BDNF concentrations were measured using Luminex technology.

**Results:** Our results identified gender, but not age, as a significant factor related to the BDNF levels in serum in both controls and epileptic patients. In addition, the serum BDNF levels of epileptic patients ( $8798.5 \pm 321.5$  pg/ml) were not different from those of controls ( $8919.5 \pm 709.0$  pg/ml); however, a multiple linear regression analysis revealed that the frequency of epileptic seizures and disease duration negatively correlated with the serum BDNF levels ( $p = 0.002$  and  $0.047$ , respectively) and were independent from other factors. When the cut-off values of 6260 pg/ml was chosen for BDNF, the sensitivity and specificity for distinguishing epileptic patients with daily or more frequent seizures from the ones with lower frequency of seizures were 80% and 90%.

**Conclusion:** The concentration of BDNF in serum is associated with disease severity (which was approximated by the frequency of epileptic seizures and disease duration) in patients with epilepsy and is a helpful marker for epileptic severity.

#### P455

##### VALIDATION OF AN ALLYLGLYCINE MODEL OF PHARMACORESISTANT EPILEPSY IN ZEBRAFISH

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**Purpose:** The zebrafish (*Danio rerio*) is increasingly accepted as an in vivo model for epilepsy. To establish a zebrafish model of pharmacoresistant epilepsy, we investigated the effects of allylglycine, a competitive inhibitor of gamma-aminobutyric acid biosynthesis, on the behavior, electrical brain activity, and *c-fos* expression of 7-day-old zebrafish larvae.

**Method:** Allylglycine dose-dependently increased locomotor activity (automated video tracking analysis), electrographic changes (open field

recordings from midbrain) and *c-fos* expression (whole-mount in situ hybridization, WISH). Five antiepileptic drugs (AEDs) with different mechanisms of action were tested for prevention of allylglycine-induced seizures: diazepam, levetiracetam, phenytoin, topiramate, and sodium valproate.

**Results:** In bath co-exposure experiments with 50–300 mM allylglycine only sodium valproate significantly ( $p < 0.01$ , 1-way ANOVA) decreased seizure-like movements. Diazepam showed a protective effect in the behavioural assay against the highest (300 mM), but not the lower concentrations of allylglycine. Other AEDs were not active in all conditions tested. Higher concentrations of allylglycine produced a more uniform electrographic response. Sodium valproate significantly decreased the incidence of electrographic seizure-like paroxysms (Fisher exact test, 10 animals per treatment), whereas levetiracetam significantly increased it. WISH analysis revealed that sodium valproate prevented *c-fos* upregulation induced by allylglycine. None of the AEDs prevented or delayed death within 8 h as a final endpoint at 100–300 mM allylglycine.

**Conclusion:** These data suggest that an allylglycine acute seizure model in zebrafish may have potential as an in vivo screening assay for novel molecules against pharmacoresistant epilepsies.

Ethics Committee of the University of Leuven (approval number P112/2012).

#### P456

### THE EXPRESSION OF GABA<sub>B</sub> R1A mRNA IN EXPERIMENTAL EPILEPSY INDUCED BY KAINIC ACID

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**Purpose:** To explore the expressions of GABA<sub>B</sub> R1a mRNA in experimental epilepsy induced by KA, and explore the possible mechanism of GABA<sub>B</sub> R1a mRNA in neuroprotection of epileptic rat models.

**Method:** Experiments were performed on 28 male Wistar rats weighting about 250 g. All rats were divided into four groups: control group, KA 2 h group, KA6 h group, KA 24 h group, seven rats in each group, the bipolar electrode, used for EEG recording were placed stereotaxically on the left of hippocampus, epilepsy were induced firstly by injecting stereotaxically kainic acid 1 μg into the right amygdala, observed the epileptic behaviour. The gene expression of GABA<sub>B</sub> R1a mRNA in the brain tissue were examined by in situ hybridization, then analysis the all the results with T test.

**Results:** The results show that the expression of GABA<sub>B</sub> R1a mRNA in KA group began to decrease since 2nd hour after epilepsy, however, began to increase significantly since 6th hour and kept increasing to the 24th hour ( $p < 0.001$ ). There were the pathologic changes after epilepsy as following: shrunk, acidophilic neurons, pyknotic, nuclei, and edematous perinuclei had been seen in the early time of epilepsy, then necrosis, detachment would be observed.

**Conclusion:** The up-regulation expression of GABA<sub>B</sub> R1a mRNA may be associated with epilepsy control.

#### P457

### IONOTROPIC GABA<sub>A</sub>ERGIC NEUROTRANSMISSION IN THE BRAIN: A SYSTEMS BIOLOGY APPROACH TO IDIOPATHIC GENETIC EPILEPSY

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**Purpose:** To examine mammalian CNS ionotropic GABA<sub>A</sub>ergic neurotransmission in the context of the idiopathic genetic epilepsies (IGE).

**Method:** Integration of the proteome of Slc32a1-enriched vesicles, with neurochemistry of GABA<sub>A</sub>ergic nerve terminals, trans-synaptic adhesion molecules, and the post-synaptic proteome of ionotropic GABA<sub>A</sub> receptors and interactants, with protein mutations predicted via recent exome sequencing (Heinzen et al. 2012, marked in bold).

**Results:** In mammalian brains, GABA<sub>A</sub>ergic neurotransmission requires the coordination of hundreds of proteins, often combined in large multi-meric complexes. These proteins include, but are not limited to:

**Presynaptic terminal proteins/protein complexes:** Rate-limiting enzymes of GABA synthesis: **Gad1/2**; the GABA vesicular transporter Slc32a1; vesicular ATPase, containing multiple subunits eg **Atp6v0d2**, Atp6v1e1, **Atp6v1g2**; voltage-gated ion channel alpha subunits eg Scn2a, **Scn5a**, Kcna1, Kcna2, Kcna6, Kcnq2, Kcnq5, Cacna1a, Cacna1b; and multiple associated/regulatory subunits

**Trans-synaptic adhesion proteins: eg Nrnx1, Nlgn2, Nlgn3, Cdh8, Cdh9, Cdh13, Dmd:** Post-synaptic proteins/protein complexes: ionotropic GABA receptor subunits Gabra1-6, **Gabrb1/2/3**, Gabrg1-3, Gabrd/e/p/q, Gabrr1-3; Nbea; scaffolding proteins for receptor subunits: Gphn for Gabra1-3, **Rdx** for Gabra5; trafficking proteins and post-translational modifiers of subunits eg. Gapdh and Ppp3ca for Gabra1; **Trak2** and Arfgef2 for Gabrb2; Camk2, Fyn, Src for Gabrg2

These proteins have specific anatomic distributions: eg Atp6v1g2 is brain-specific, and expressed in cerebral cortex, in cerebellar Purkinje cells, and in hippocampal dentate gyrus, while Scn5a is expressed in GABA<sub>A</sub>ergic striatal projection fibres, and in the limbic system. Some of the ionotropic GABA receptor subunits are very widely distributed throughout the mammalian brain (eg Gabra1, **Gabrb2**, Gabrg2) while others are more restricted.

#### Conclusions:

- 1 Diverse GABA<sub>A</sub>ergic protein mutations would be predicted to affect functioning in specific regions or networks of the mammalian brain.
- 2 Because large numbers of proteins interact together, the number of susceptibility loci in genetically complex epilepsy would be predicted to be large, as demonstrated by Heinzen et al.

#### P458

### SPIKE-AND-WAVE DISCHARGE MEDIATED REDUCTION IN HIPPOCAMPAL HCN1 CHANNEL FUNCTION ASSOCIATES WITH LEARNING DEFICITS IN A GENETIC MOUSE MODEL OF EPILEPSY

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**Purpose:** Although absence seizures are derived from cortico-thalamic networks associated co-morbidities including learning problems may result from hippocampal deficits. Mice with a DBA genetic background heterozygous for the human GABA<sub>A</sub>γ2R43Q mutation have a spike-and-wave discharge (SWD) phenotype that recapitulates absence epilepsy observed in patients. However, mice harbouring the mutation on the C57 seizure-resistant background have no SWDs acting as a control. In this study we determine if SWDs engage the hippocampus. Specifically, we assess expression of the Hyperpolarization-activated-Cyclic Nucleotide-gated 1 (HCN1) channel that is known to be transcriptionally regulated in several forms of epilepsy.

**Method:** HCN1 mRNA in the hippocampus was assayed by qPCR in DBA and C57 mice with the R43Q mutation. The effect on Ih was measured using whole-cell voltage clamp of CA1 pyramidal cells. Spatial learning was assayed in the Morris Water Maze.

**Results:** Hippocampal HCN1 was reduced in DBA (R43Q) mice displaying SWDs ( $p = 0.0049$ ), but not in young pre-SWD or in the adult SWD-free C57strain. Voltage clamp studies of CA1 pyramidal neurons revealed reduced Ih in mice with SWDs. Further a left-shift in  $V_{1/2}$  was consistent with a larger proportion of HCN2 relative to HCN1 current.

Spatial learning defects were apparent in adult DBA but not in SWD-free C57 strain. (Note:  $n \geq 12$  in all studies).

**Conclusion:** Cortico-thalamic derived SWDs alter HCN1 expression and function in the hippocampus, with accompanying spatial learning deficits. HCN1 channel reduction is a biomarker of SWD-mediated changes in the hippocampus and may be part of the underlying mechanism of co-morbid states.

#### P459

### THE EFFECTS OF ESLICARBAZEPINE ON PERSISTENT $Na^+$ CURRENT AND THE ROLE OF THE $Na^+$ CHANNEL $\beta$ SUBUNITS

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**Purpose:** Eslicarbazepine is the major active metabolite of eslicarbazepine acetate, a once-daily antiepileptic drug approved in Europe as adjunctive therapy for refractory partial-onset seizures in adults. This study was aimed to determine the effects of eslicarbazepine on persistent  $Na^+$  currents ( $I_{NaP}$ ) and the role of  $\beta$  subunits on the  $Na^+$  channel.

**Method:** To study the role of  $\beta$  subunits of the  $Na^+$  channel we used a mouse line lacking either the  $\beta_1$  or  $\beta_2$  subunit, encoded by the *Scn1b* or *Scn2b* gene, respectively. Whole cell patch-clamp recordings were performed on CA1 neurons in hippocampal slices under control conditions and application of 300  $\mu M$  eslicarbazepine.

**Results:** We examined  $I_{NaP}$  in acutely isolated CA1 neurons and repetitive firing in 300  $\mu M$  hippocampal slices of mice. We found that eslicarbazepine caused a significant reduction of maximal  $I_{NaP}$  conductance and an efficient reduction of the firing rate in wildtype mice. In mice lacking  $\beta_1$  subunits, carbamazepine causes a paradoxical up-modulation of  $I_{NaP}$  in the subthreshold range, leading to a failure in affecting neuronal firing (Uebachs M et al., J Neurosci. 2010 Jun 23; 30 (25):8489–501). In contrast, eslicarbazepine did not cause a paradoxical up-regulation of  $I_{NaP}$  in *Scn1b* null mice. Consequently, the effects of eslicarbazepine on repetitive firing were maintained in these animals.

**Conclusion:** These results indicate that eslicarbazepine exerts effects on  $I_{NaP}$  similar to those known for carbamazepine. However, in animals lacking the  $\beta_1$   $Na^+$  channel subunit these effects are maintained. Therefore, eslicarbazepine potentially overcomes a previously described putative mechanism of resistance to established  $Na^+$  acting antiepileptic drugs.

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#### P460

### INFLUENCE OF LOW-FREQUENCY REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION ON THE EXPRESSIONS OF KCA1.1, NAV1.6, NMDAR1, GAD65 PROTEINS IN HIPPOCAMPUS CA3 OF SD RATS

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**Purpose:** To investigate whether low-frequency repetitive transcranial magnetic stimulation (rTMS) can affect the expressions of KCA1.1, Nav1.6, NMDAR1 and GAD65 proteins in the rat CA3 region pyramid layer.

**Method:** Fifty rats were randomly divided into the experimental group and the sham group. The former was administered with low-

frequency rTMS for 14 consecutive days; the latter was given sham stimulation for also 14 days. After finished the rTMS protocol, each group was further divided into five subgroups according to time point (6, 24 h, 1, 3, 6 weeks). The animals were killed at corresponding time points respectively, and the expressions of KCA1.1, Nav1.6, NMDAR1 and GAD65 in the CA3 region of hippocampus were examined by immunohistochemistry.

**Results:** Compared with the sham group, the KCA1.1-positive neuron densities were significantly increased in the period of 6 h–3 weeks after rTMS ( $P < 0.01$ ), the GAD65-positive neuron densities were also obviously elevated at 6 h ( $P < 0.05$ ), especially in the duration of 24 h–3 weeks following rTMS ( $P < 0.01$ ); the Nav1.6-positive neuron density was transiently decreased at 6 h after rTMS protocol ( $P < 0.05$ ); similarly, the NMDAR1-positive neuron density was also shortly decreased at 6 h following rTMS treatment ( $P < 0.01$ ).

**Conclusion:** The study shows low-frequency rTMS can upregulate the expressions of KCA1.1 and GAD65 and last for at least 3 weeks; but transiently downregulate the expressions of Nav1.6 and NMDAR1 in the rat hippocampal CA3. These changes might be one of its anti-epileptic mechanisms.

#### P461

### EXPERIMENTAL MODEL OF CHRONIC EPILEPTOGENESIS

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**Purpose:** The number of chronic epileptogenesis models is restricted. Important that none of the available chronic epileptogenesis models has been clinically validated. The spontaneous seizures development is considered as the crucial feature of the models. The aim of our work was to test the new experimental condition resembled chronic epileptogenesis.

**Method:** Adult Wistar rats underwent brain fluid percussion trauma (FPT) according to method of McIntosh et al. (1989). One week after FPT animals were kindled using pentylenetetrazol (PTZ). Video-monitoring started 24 h after kindling termination.

**Results:** 28% of the rats subjected to brain FPT died that corresponded known data. 7.5% rats after FPT revealed immediate clonic seizures lasted 7–12 s. One rat experienced convulsions that lasted during 70 days. All rats subjected to PTZ kindling showed repetitive generalized clonic-tonic seizures development on 18–21 days. 41% of the rats alive after brain FPT developed spontaneous seizures lasted by 8–15 s with the latency 47–63 days after kindling termination. None of the PTZ-kindled rats and 33% traumatized animals developed spontaneous seizures within 200–230 days after FPT induction in control observations.

**Conclusion:** Step-wise FPT and kindling procedure represent animal model of chronic epileptogenesis that reproduced features of focal and diffuse brain injuries and characterized by spontaneous seizures development. Spontaneous seizures latency was significantly shorter compared with the FPT alone and the number of rats with such convulsions corresponded to the known data.

#### P462

### REPEATED STROBE EXPOSURE FACILITATES DORSAL HIPPOCAMPAL KINDLING IN RATS

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**Purpose:** It is well known that visual stimuli can trigger seizures in some epileptic patients. But less well understood is whether visual stimulation can alter natural neural circuitry to precipitate seizures. There is evidence that repeated strobe exposure contribute to heightened seizure susceptibility in some animal models. This work is to test whether strobe stimulation can also facilitate hippocampal kindling in normal rats.

**Methods:** The eight chronic recording electrodes were implanted into bilateral somatomotor cortex (SM), primary visual cortex (V1), mediodorsal thalamic nucleus (MD) and hippocampus CA1 area in normal adult Sprague-Dawley rats. The stimulating electrode was implanted into right dorsal hippocampus. Experimental group rats were exposed to repetitive 8 Hz strobe stimulation for 3–5 days until visual evoked response magnitude of V1 stabilized at its highest plateau. These rats then received electrostimulation of right dorsal hippocampus until the rats reached kindled state. Control group rats were treated identically but not exposed to strobe stimulation. Seizure kindling rates were compared between strobe exposed rats and unexposed rats, and EEG average evoked response amplitude to strobe stimulation was analyzed.

**Results:** The result shows that seizure kindling rates of experimental group rats were significantly faster than of control group rats. Moreover, positive correlation was found between evoked response amplitude of SM and seizure kindling rates.

**Conclusion:** Our work suggests that strobe stimulation can facilitate seizure in normal rats. Furthermore, SM may play a key role in facilitate course and serve as a predictive method for vulnerability to seizure.

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#### P463 NETWORKING TOPOLOGY DURING PILOCARPINE INDUCED EPILEPTIC SEIZURE

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**Purpose:** Neuronal networks with small-world topography are known to facilitate synchronization and possibly seizure generation. Large scale synchronization is an underlying mechanism of epileptic seizures. EEG recordings are widely used in epilepsy research. In this work, we intend to address a question whether the change of small world network property exists in neural networks when epileptic seizures occur.

**Methods:** Under anesthesia with pentobarbital sodium, the sixteen recording electrodes were surgically implanted respectively into bilateral hippocampus, thalamus and different cortex regions of Sprague-Dawley rats in order to gain brain activity in a more large scale. Local field potentials (LFP) of pilocarpine-induced epileptic rats were recorded during freely moving state. Functional connection changes of different frequency bands were estimated with the phase locking value (PLV) and network property.

**Results:** The results show that the brain network appear to be significant desynchrony during preictal period, but significant synchrony during ictal period in theta frequency band. Moreover, network parameter analysis based on graphic theory find that mean weighted clustering coefficient (C<sub>w</sub>) and mean weighted path length (L<sub>w</sub>) were increased during preictal period, but decreased during ictal period in theta frequency band.

**Conclusion:** Our research demonstrate that the epileptic brain network represent different changes following epileptic seizure. The brain network shifts to regular network during preictal period and shifts to random network during ictal period. These results suggest that the changes of brain network topology might play a crucial role in epilepsy.

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#### P464 ABSENCE EPILEPSY REGULATED BY BASAL GANGLIA: A MODELING STUDY

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**Purpose:** Increasing evidence revealed that besides the direct coupling, thalamus and cerebral cortex are also connected through an intermediate bridge—basal ganglia. Such indirect pathway may play key roles in the modulation of absence epilepsy, but the relevant mechanisms are still poorly understood. Using computer simulations, we investigated here how basal ganglia regulate the absence epilepsy.

**Methods:** We developed a neural mass model to study the modulation of basal ganglia on the absence epilepsy. This model includes three parts: thalamus, cerebral cortex, and basal ganglia. All simulations and data analysis were performed in Matlab.

**Results:** The model successfully reproduced the slow spike-wave discharges (SWDs) in cerebral cortex. Enhancing the connection strengths of nigrothalamic pathway and cortico-STN (subthalamic nucleus) pathway greatly suppress the SWDs, thus leading to the inhibition of absence epilepsy. It was also observed that strong deep brain stimulus on STN can kick our model from the seizure state to normal discharge state, which is in agreement with previous experimental findings. Interestingly, further simulations demonstrated that increasing the dopaminergic neurotransmitter in striatum can assist the cortico-STN pathway to modulate and suppress the SWDs, primarily through the indirect pathway but not through the direct pathway.

**Conclusion:** Our results provide theoretical evidence that the absence epilepsy might be significantly regulated by several important pathways of basal ganglia. We hope that these findings can inspire further research on this topic, through both experimental and computational approaches.

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#### P465 TEMPORAL PROFILE OF mIRNA EXPRESSION IN HIPPOCAMPAL SUBREGIONS DURING EPILEPTOGENESIS IN POST-STATUS EPILEPTICUS MODEL FOR TEMPORAL LOBE EPILEPSY INDICATES POTENTIAL NEW ANTI-EPILEPTOGENIC TARGETS

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## Abstracts

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**Purpose:** MicroRNAs (miR) offer a route to novel understanding and treatment options for epilepsy.

**Method:** In the present study we have analyzed the temporal profile of miR expression in three brain regions (CA1; dentate gyrus, DG; temporal lobe, TL) associated with epileptogenesis in a rat model of temporal lobe epilepsy. Tissue was obtained after electrically-induced status epilepticus (SE) at 1 day, 1 week and 3 months, and compared with control tissue using Exiqon microRNA Arrays which contain capture probes targeting all miRNAs for rat (n = 5 each, p < 0.05, and a 1.5-fold up- or down regulation). Identification of involved pathways was performed using DIANA, a web program that can identify molecular pathways which are potentially altered by the expression of multiple miRNAs.

**Results:** In the latent and chronic phase, the most important pathways involved based upon changed miRs were: axon guidance, ErbB signaling pathway, MAPK signaling pathway and focal adhesion. Ubiquitin-mediated proteolysis and ECM interaction were associated with miR downregulation at 1 week in all three regions. The miRs that were exclusively upregulated in the DG during the chronic phase pointed also to Wnt signaling and regulation of actin skeleton. In the acute phase the same pathways were indicated, but also included TGF $\beta$  and mTOR signaling.

**Conclusions:** This study points to several signaling pathways suspected to be involved in epileptogenesis but not previously indicated by RNA microarray studies. miRs regulating the ErbB pathway and focal adhesion may be interesting new targets that should be further explored.

## P466

### ROLE OF SUBSTANTIA NIGRA RETICULATA IN KINDLING RESISTANCE IN GAERS

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**Purpose:** Genetic Absence Epilepsy Rats from Strasbourg (GAERS) show a failure to develop stage 3–5 seizures during amygdala kindling with maximum number of stimulation. One of the mechanisms that control epileptic seizures involves the neural network in the substantia nigra pars reticulata (SNR). In the present study, we aimed to determine the role of the SNR<sub>anterior</sub> and SNR<sub>posterior</sub> regions in mediating the resistance to limbic epilepsy in adult GAERS.

**Method:** A unilateral stimulation electrode in the right basolateral amygdala, bilateral injection guide cannulas in the SNR (SNR<sub>anterior</sub> or SNR<sub>posterior</sub>), and bilateral recording electrodes over the cortex were stereotaxically implanted in male GAERS. After a recovery period lidocaine, a Na<sup>+</sup> channel blocker, or vehicle was given through the cannulas 30 min before each kindling stimulation. Twice daily stimulations continued until the animals reached stage 5 or the maximum number of 30 stimulations. Behavioral changes according to Racine's scale and after-discharge durations were evaluated. Injection sites were histologically verified using thionin staining after the experiments.

**Results:** GAERS treated with lidocaine injections into the SNR<sub>posterior</sub> reached stage 5 with repeated kindling stimulations, whereas none of the animals treated with lidocaine into the SNR<sub>anterior</sub> failed to reach stage 3, 4, or 5 and stayed at stage 2 after the application of 30 stimulations. The

mean of the afterdischarge durations following the stimulations showed no significant differences in the GAERS SNR<sub>anterior</sub> and SNR<sub>posterior</sub> groups.

**Conclusion:** The lidocaine injections into the SNR<sub>posterior</sub> obliterate the resistance to kindling, suggesting that the SNR<sub>posterior</sub> is an important site underlying this resistance.

## P467

### GARODERMA LUCIDUM POLYSACCHARIDES IMPROVE EPILEPTIC BEHAVIOR, INCREASE CAV-1 EXPRESSION AND INHIBIT NF- $\kappa$ B EXPRESSION IN HIPPOCAMPUS OF EPILEPTIC RATS

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**Purpose:** To investigate the effect of garoderma lucidum polysaccharides (GLP) on epileptic behavior, Cav-1 and NF- $\kappa$ B protein expression in hippocampus of epileptic rats induced by injection kainic acid into hippocampus.

**Method:** Sixty male Wistar rats were randomly divided into six groups. They are: A) Control group, no treatment given; B) PBS group, PBS was injected into hippocampus; C) Epilepsy group, kainic acid (1.5  $\mu$ g/ $\mu$ l) was injected into hippocampus; GLP treatment groups: rats were given kainite treatment same as group C, and then given GLP (i.p.) once a day for 7 days, GLP doses are D) low dose (25 mg/kg), E) medium dose (50 mg/kg) and F) high dose (100 mg/kg) respectively. Rat behavior and brain EEG were recorded. The number of immunohistochemical staining Cav-1 and NF- $\kappa$ B positive cells were counted.

**Results:** Epileptic symptoms in rats of group C, D, E and F was observed in 7 min after kainic acid injection. On day 7, normal EEG, with lower wavelength of  $\alpha$  and  $\beta$  waves, was observed in group A and B. But, sharp and frequent wavelength was showed in C, D, E and F groups, however, compared to C group, more waves with lower wavelength existed in D, E and F groups. The frequency of epilepsy discharge from initial 10–15/min reduced to 1/min after GLP treatment. Cav-1 positive cells in group C (118.45  $\pm$  2.13) are significantly higher compared with group A (70.23  $\pm$  0.87), B (71.96  $\pm$  2.03) (p < 0.01). GLP treatments (D, 212.15  $\pm$  2.14; E, 318.25  $\pm$  2.06; F, 319.14  $\pm$  1.82) further increased Cav-1 positive cells compared with group C (p < 0.05). NF- $\kappa$ B positive cells of group C (21.32  $\pm$  1.95) increased significantly compared with group A (3.11  $\pm$  1.54), B (2.81  $\pm$  0.74) (p < 0.01). GLP treatments (D, 16.51  $\pm$  2.42; E, 10.76  $\pm$  1.89; F, 9.82  $\pm$  2.03) decreased NF- $\kappa$ B positive cells compared with group C.

**Conclusion:** GLP can improve the epileptic symptoms and EEG, stimulate the Cav-1 expression and inhibit NF- $\kappa$ B expression.

## P468

### GANODERMA LUCIDUM POLYSACCHARIDES INHIBIT CALCIUM OVERLOAD AND INCREASE THE EXPRESSION OF CAMKII IN A MODEL OF EPILEPTIFORM DISCHARGE OF HIPPOCAMPAL NEURONS

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**Purpose:** To investigate the effects of Ganoderma lucidum polysaccharides (GLP) on calcium turnover and CaMKII  $\alpha$  expression, in a model of epileptiform discharge of hippocampal neurons.

**Method:** Primary hippocampal neurons from <1 day old rats were cultured using Neurobasal medium for 9 days. The neurons were divided into, (i) control group: cells cultured with normal medium for 3 h; (ii) model I group: neurons were incubated with Mg<sup>2+</sup> free medium for 3 h; (iii) model II group: neurons were incubated with Mg<sup>2+</sup> free medium for 3 h, then cultured with the normal medium for an extra 3 h; (iv) GLP group I: neurons were incubated with Mg<sup>2+</sup> free medium containing GLP (0.375 mg/ml) for 3 h; (v) GLP group II: neurons were incubated with Mg<sup>2+</sup> free medium for 3 h then cultured with a normal culture medium containing GLP (0.375 mg/ml) for extra 3 h. The CaMK II  $\alpha$  protein expression in control group, model I group, GLP group I was analysed by confocal laser microscopy, Western blotting. Calcium<sup>2+</sup> turnover in neuron of all groups was measured by labeled fluo-3/AM and observed/recorded by laser confocal microscopy.

**Results:** The fluorescence intensity of CaMKII $\alpha$  in model group (327  $\pm$  44) was less than control group (826  $\pm$  70); CaMKII $\alpha$  fluorescence intensity in GLP I group (573  $\pm$  85) was higher than model group. The result of CaMKII $\alpha$  expression showed the same trend as the fluorescence intensity; Ca<sup>2+</sup> fluorescence intensity, in GLP group, was significantly lower than model I group; in GLP group II, it was reduced significantly compared to model II group.

**Conclusion:** GLP may inhibit calcium overload, promote CaMKII alpha expression to protect neurons injured by epilepsy.

#### P469

##### EFFECT OF BETAINE ON SERUM HOMOCYSTEINE, $\gamma$ -AMINOBUTYRIC ACID AND ITS RECEPTORS IN BRAIN OF AN EPILEPTIC RAT MODEL

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**Purpose:** To study antiepileptic effect of betaine and its effect on serum homocysteine level, and  $\gamma$ -aminobutyric acid (GABA) and its receptor expression in hippocampus in an epileptic rat model.

**Method:** Healthy male Wistar rats were randomly divided into, control group A (1.0 ml saline, i.o.); epilepsy group B, (pentylene-tetrazol, 35 mg/kg, i.p. once a day, for 28 days); group C, D, E and F which were given same treatment as group B, but group C, D, E were also given betaine treatment with daily doses (mg/kg) of 450, 225 and 112.5 respectively. Group F was given extra 200 mg/kg sodium valproate. Rat behavior was recorded. Serum homocysteine level was measured. GABA and its receptors in hippocampus were measured by ELISA and Western blot respectively. Morphology of liver tissue was examined.

**Results:** There was no difference in incubation time (second) of grand mal seizures among groups, however, betaine treatment significantly decreased duration time (second) of grand mal seizures (C, 180.94  $\pm$  9.75; D, 160.11  $\pm$  4.11; E, 180.39  $\pm$  4.03) compared to with-

out treatment (240.58  $\pm$  10.42). Serum homocysteine level ( $\mu$ mol/L) in epilepsy group (B, 9.30  $\pm$  1.24,  $p$  < 0.01) was significantly lower compared to the control group (A, 11.90  $\pm$  1.07), and further decreased after betaine treatment (C, 7.91  $\pm$  0.64; D, 8.69  $\pm$  1.13; E, 7.47  $\pm$  0.89,  $p$  < 0.05); GABA in epilepsy group (B, 3.47  $\pm$  0.59) was significantly lower compared to control group (A, 6.31  $\pm$  0.96,  $p$  < 0.01). GABA increased after betaine treatment (C, 5.18  $\pm$  0.36; D, 5.90  $\pm$  0.67,  $p$  < 0.05). GABA receptor changes has same trend as its content. There was no change in liver histology after betaine treatment.

**Conclusion:** Betaine treatment showed antiepileptic effect, this may be due to its effect on the metabolites of homocysteine and GABA.

#### P470

##### INHIBITION OF RECOMBINANT ADENO-ASSOCIATED VIRUS MEDIATED NEUROPEPTIDE Y GENE TRANSFECTION TO HIPPOCAMPAL SYNAPTIC RECONSTRUCTION IN EPILEPTIC RAT

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**Purpose:** To investigate the effect of recombinant adeno-associated virus mediated neuropeptide Y gene transfection on hippocampal synaptic reconstruction in epileptic rat.

**Method:** Recombinant adeno-associated virus carrying neuropeptide Y gene was injected to lateral ventricle in epileptic rat induced by kainic acid, then the mossy fiber sprouting in epileptic rat hippocampal CA3 region and expression of synaptophysin p38mRNA and protein were observed and analyzed.

**Results:** After the recombinant adeno-associated virus neuropeptide Y gene transfection, mossy fiber sprouting in rat hippocampal CA3 region is significantly suppressed and synaptophysin p38mRNA and protein expression also are inhibited.

**Conclusion:** Recombinant adeno-associated virus mediated neuropeptide Y gene transfection could reduce the degree of mossy fiber sprouting and inhibit the synaptophysin abnormal expression, thereby inhibiting the synaptic reconstruction in epileptic rat.

#### P471

##### THE ANTIEPILEPTOGENIC AND NEUROPROTECTIVE EFFECTS OF LAMOTRIGINE AND ETHOSUXIMIDE IN TEMPORAL LOBE EPILEPSY

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**Purpose:** The putative neuroprotective and antiepileptogenic effects of lamotrigine (LTG) and ethosuximide (ETX) were investigated in the lithium-pilocarpine (Li-Pc) model of temporal-lobe epilepsy (TLE) in rats. Next to spontaneous recurrent epileptic seizure (SRS), EEG and pathology were investigated.

**Method:** Status Epilepticus (SE) was induced by Li-Pc in five experimental groups, 24 h after SE these rats received either a low (10 mg/kg) or high (20 mg/kg) dose of LTG, or a low (25 mg/kg) or high (50 mg/kg) dose of ETX, or solvent. The sixth group was not given Li-Pc and they received solvent. Dosing began 24 h after SE and lasted 10 days. SRS, EEG, loss of neurons, hyperplasia of astroglia and mossy fiber sprouting (MFS) were measured in all groups.

**Results:** The low and high dose LTG decreased the frequency of SRS, reduced the frequency of spike wave or sharp wave, and restrained the neuronal loss, astroglial hyperplasia and mossy fiber sprouting in the hippocampus compared to the untreated control group. Moreover, the effects were larger in the high dose LTG group compared to the low dose LTG group. However, ETX had none of the above mentioned effects.

**Conclusion:** LTG dose-dependently reduced seizures and neuronal damage. These findings suggested that LTG had neuroprotective and antiepileptogenic effects. Ethosuximide was without any neuroprotective and antiepileptogenic effects, in contrast to what can be found in other epilepsy models.

#### P472

### AUTOMATED PLANAR PATCH CLAMP REVEALS DIFFERENTIAL MODULATION OF $Na_v1.1$ AND $Na_v1.2$ SODIUM CHANNELS BY THE $\beta_1$ AUXILIARY SUBUNIT

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**Purpose:** Voltage-gated sodium channels are composed of an alpha ( $\alpha$ ) subunit and, typically two auxiliary beta ( $\beta$ ) subunits. As different  $\alpha$ -subunits are differentially expressed in excitatory and inhibitory neurons, it is important to understand the differential effects  $\beta$ -subunits may have on  $\alpha$ -subunits, to assist in understanding how they modulate neuronal function in health and disease. In the present study we used automated planar patch clamp recording to investigate the effect of  $\beta_1$  subunit modulation on the “excitatory neuron”  $Na_v1.2$   $\alpha$ -subunit, and the “inhibitory interneuron”  $Na_v1.1$   $\alpha$ -subunit.

**Method:** Automated patch clamping using the Nanion patchliner in voltage clamp was used analyse different  $\alpha\beta$  subunit combinations transiently expressed in HEK293T cells.

**Results:** Analysis of  $Na_v1.2$  with  $\beta_1$  revealed a depolarising shift in the voltage-dependence of inactivation ( $p < 0.001$ ), larger time constants of inactivation ( $p < 0.001$ ) and more rapid recovery from inactivation ( $p < 0.001$ ). Additional co-expression of  $\beta_2$  elicited a shift in the hyperpolarising direction for the voltage dependence of inactivation compared to  $\beta_1$  expressed alone ( $p < 0.01$ ), shorter time constants of inactivation ( $p < 0.05$ ), and slower recovery from inactivation ( $p < 0.0001$ ). In contrast,  $\beta_1$  co-expressed with  $Na_v1.1$  displayed no modulation of these parameters. Additional co-expression of  $\beta_2$  elicited a slower recovery from inactivation ( $p < 0.001$ ).

**Conclusion:** We observed a differential effect of  $\beta_1$  on the “excitatory neuron”  $Na_v1.2$   $\alpha$ -subunit, and the “inhibitory interneuron”  $Na_v1.1$   $\alpha$ -subunit. This will have implications for CNS disorders such as genetic epilepsy, where knowledge of neuron type specific dysfunction caused by  $\beta_1$  mutation is important for understanding of disease mechanisms and devising therapeutic strategies.

#### P473

### NEUROSTEROIDS MODULATE INTERICTAL ACTIVITY AND HIGH FREQUENCY OSCILLATIONS IN THE CA3 SUBFIELD

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**Purpose:** Application of 4-aminopyridine (4AP; 50  $\mu$ M) induces short- (0.2 s) and long-lasting (1.4 s) interictal discharges in the rat CA3 sub-

field. Short-lasting discharges presumably reflect glutamatergic mechanisms whereas long-lasting discharges are largely contributed by GABAergic conductances. Here, we addressed whether neurosteroids modulate these interictal events as well as their associated, ripples (80–200 Hz) and fast ripples (250–500 Hz).

**Method:** Epileptiform activity was induced in rat brain slices. Allotetrahydrodeoxycorticosterone (THDOC; 100 nM and 5  $\mu$ M) was applied during continuous 4AP application. Local field potentials were recorded from CA3 with glass micropipettes.

**Results:** Following 4AP bath application, ripples and fast ripples were detected during 6% and 14% of short-lasting interictal discharges, respectively. In contrast, ripples and fast ripples co-occurred with <2% of long-lasting interictal discharges. Addition of THDOC (100 nM or 5  $\mu$ M) to 4AP applied slices increased the duration of the long-lasting interictal discharges by 15% but had no effect on short-lasting interictal events. THDOC also led to an increase of short-lasting interictal events (20%) and long-lasting interictal events (5%) coinciding with ripples, but there was no change in fast ripples co-occurrence. Finally, blocking glutamatergic transmission disclosed ripples and fast ripples occurring during background activity.

**Conclusion:** Our results show that neurosteroids can differentially modulate the short-lasting and long-lasting interictal discharges, and high frequency oscillations occurrence in CA3. These effects are presumably due to the potentiation of GABA<sub>A</sub> receptor mediated activity.

#### P474

### ATORVASTATIN AMELIORATES COGNITIVE IMPAIRMENT SUBSEQUENT TO PENTYLENETETRAZOL-INDUCED SEIZURES IN RATS

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**Purpose:** Cognitive impairment is known to occur after epilepsy and anti-epileptic drugs. In acute experiments, the control of seizures by sodium valproate can mask the cognitive impairment. Rho kinase signaling is involved in both epilepsy and cognitive impairment and atorvastatin is known to modulate this pathway. In present study, the effect of graded doses of atorvastatin pretreatment, which does not produce 100% protection in pentylenetetrazole (PTZ)-induced seizures, was evaluated for seizure induced cognitive impairment in rats.

**Method:** Pretreatment with vehicle/atorvastatin (2.5, 5 and 10 mg/kg/day, orally) was given daily for 5 days to male Wistar rats. Sodium valproate (150 mg/kg single dose, i.p.) was taken as positive control group for seizures. On day 5, myoclonic jerk and generalized tonic clonic seizure (GTCS) latencies were noted for 30 min in PTZ (60 mg/kg i.p.) induced seizures. Cognitive impairment was assessed using Morris water maze 24 h after the seizures.

**Results:** Atorvastatin (5 and 10 mg/kg/day) significantly increased myoclonic jerk and GTCS latencies as compared to vehicle control group. In vehicle control group, significant cognitive impairment was observed in comparison to normal control group as indicated by increase in escape latency ( $5.5 \pm 0.8$  vs.  $24.4 \pm 0.8$  s) and total distance traveled to reach the platform ( $10.5 \pm 1.3$  vs.  $33.5 \pm 3.0$  m); which was significantly ameliorated with atorvastatin (5 and 10 mg/kg/day) ( $p < 0.05$  and  $p < 0.001$  respectively).

**Conclusion:** The present study indicates that atorvastatin in doses that are only partially effective in seizure control, ameliorates seizure induced cognitive impairment and can be considered as a potential adjuvant to anti-epileptic therapy.

P475

### AN EXAMINATION OF COGNITIVE DEFICITS FOLLOWING EXPERIMENTAL FEBRILE STATUS EPILEPTICUS IN RAT PUPS: NEUROBIOLOGY AND BIOMARKERS

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**Purpose:** To test the hypothesis that cognitive deficits can be measured in a subset of rats that have experienced prolonged EFS. Deficits in performance in a spatial task are examined in relation to cellular function as well EEG in the hippocampus in search of biomarkers for cognitive performance. The results of the study may create biomarkers for those at risk for cognitive deficits following febrile seizures and set the stage for intervention.

**Method:** EFSE is induced in rat pups at P10 through prolonged hyperthermia while controls are kept at room temperature. At 8 weeks old the rats are trained to perform a spatial task involving avoidance of a shock zone on a rotating arena. After 12 weeks the rats undergo chronic implantation of four separately drivable tetrodes in left and right hippocampus. Cellular activity as well as local field potentials are recorded simultaneously from each hippocampus while the rat forages for food pellets on a stable arena or avoids a shock zone on a rotating arena.

**Results:** Preliminary data examine the stability of firing fields for both EFSE and control rats on the stable arena as well as potential differences in firing activity in the transition between the stable and rotating arena conditions. Oscillatory phenomena, such as the power and frequency of sharp wave ripple complexes as well as theta gamma comodulation are examined for both groups in both recording conditions.

P476

### PROTECTION AGAINST CONVULSIVE SEIZURE AFTER HIPPOCAMPAL TRANSPLANTATION OF MESENCHYMAL CELLS FROM ADIPOSE TISSUE IN MICE

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The use of mesenchymal stem cells is an innovative and accessible strategy for the treatment of epileptic disorders due to their involvement in immunoregulatory mechanisms and anti-apoptotic action. Based on this, we evaluated the protective effect of mesenchymal cells from adipose tissue (MCAT) against convulsive seizure induced by PTZ and maximum electroconvulsive shock (MES). The MCAT from C57/B6 mice were isolated from the supra-epididymal region and cultured in DMEN Low 10% SFB and used between 15 and 18 passages. The cells were transplanted into the hippocampus of adult male mice C57/B6 (PTZ n = 8; MES n = 12). Control groups (n = 6; n = 12) received the same volume of culture medium in the same location. Ten days after the surgery, PTZ or MES was applied to induce acute tonic-clonic seizures. The parameters used to evaluate the anticonvulsant activity of the MCAT were protection against seizure, reduction in the duration of each convulsive phase, and decreased mortality. Animals transplanted with MCAT showed a significant reduction in the PTZ-induced seizure intensity (p < 0.05) and in the duration of tonic seizure and in the mortality rate induced by MES (p < 0.05). Immunofluorescence analysis confirmed the presence of MCAT in the hippocampus. These neuroprotective effects on seizure

induced by both models may be related to inhibitory factors and immunomodulatory mechanisms assigned to MCAT present in the hippocampus. This study contributes to the understanding of the MCAT anticonvulsant mechanisms, and has strong therapeutic implications for the control of epileptic seizures.

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### PREVENTIVE TREATMENT WITH LEVETIRACETAM AGAINST THE PATHOLOGICAL CHANGES IN HIPPOCAMPUS OF TEMPORAL LOBE EPILEPSY MODEL MICE

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**Purpose:** Temporal lobe epilepsy (TLE) tends to be drug-resistant. Surgical resection is accepted as a standard treatment for intractable TLE, while there is a risk of postoperative cognitive dysfunction. It is advocated the first epileptic seizure causes continuously pathological and electrophysiological change in hippocampus leading to the development of epileptogenesis. The preventive treatment with anti-epileptic drugs has a prospect against the development of epileptogenesis. We detected the effect of preventive treatment with levetiracetam (LEV) on pathological changes in epileptic mice hippocampi.

**Method:** Eight week-old male C57BL6 mice were used in our study. We classified them into three groups: Group A was treated with saline injection for 5 days after the development of status epilepticus (SE), Group B was treated with LEV (200 mg/kg/day i.p.) for 5 days after SE, and Group C was injected saline for 5 days without SE. SE was induced by pilocarpine injection (280 mg/kg i.p.), and all animals were treated with diazepam (10 mg/kg i.p.) to sedate SE. We injected Green Fluorescence Protein (GFP)-labeled retrovirus into bilateral hippocampal dentate gyrus (DG) stereotactically 2 days after pilocarpine injection to visualize mitotic newborn neurons. All mice were sacrificed 14 days after development of SE and then removed a brain.

We compared the number of GFP-labeled newborn neurons in DG among three groups and performed statistic analysis with ANOVA (p-value < 0.05).

**Results:** The number of GFP-positive newborn neurons in DG was significantly lower in group B comparing to group A (p < 0.01). There was no difference between group B and C, suggesting that continuous treatment with LEV inhibited epilepsy-induced neurogenesis.

**Conclusion:** Continuous treatment with LEV suppressed epilepsy-induced neurogenesis in mice hippocampus. Preventive treatment with LEV has potentials to inhibit pathological changes in hippocampus.

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### ADLTE-CAUSING LGII MUTATIONS IMPAIR EXTRACELLULAR BINDING OF LGII PROTEIN TO ADAM RECEPTORS

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**Purpose:** The vast majority of LGII mutations responsible for autosomal dominant lateral temporal epilepsy (ADLTE) inhibit Lgi1 protein

secretion (loss-of-function effect), and only one exception has been reported so far. We investigated three nonsynonymous LGI1 mutations to determine their effects on protein secretion and extracellular interactions.

**Method:** Mutant LGI1 cDNAs transfected into HEK293 cells were analyzed by immunoblot in both cell lysates and media. Cotransfected mutant LGI1 and wild type ADAM 22/23 receptors were analyzed by immunocytofluorescence and coimmunoprecipitation. In silico modelling of the Lgi1 protein EPTP domain was carried out using the structure of WD repeat protein and manually refined.

**Results:** All three LGI1 mutations investigated, T380A (unpublished), S473L, and R474Q did not inhibit protein secretion in HEK293 culture cells, as already observed for the R407C mutation. This likely results from the lack of effects of these mutations on Lgi1 protein folding, as suggested by a 3D protein model. In addition, immunocytofluorescence and coimmunoprecipitation experiments showed that all four mutations remarkably reduced affinity of Lgi1 protein for ADAM22/23 receptors.

**Conclusion:** We have shown that a class of ADLTE-causing LGI1 mutations do not interfere with protein secretion. These mutations exert their loss-of-function effect extracellularly by considerably reducing Lgi1 binding affinity for ADAM22/23 receptors.

#### P479

### HIGH DOSES OF mTOR INHIBITOR TREATMENT CANNOT SUPPRESS EPILEPTOGENESIS IN A MOUSE MODEL OF MESIO-TEMPORAL LOBE EPILEPSY

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**Purpose:** Recent studies showed that the mammalian target of rapamycin (mTOR) pathway is involved in some features of MTLE epileptogenesis. Here, we examined the efficacy of a high-dose mTOR inhibitor treatment on epileptogenesis following intrahippocampal injection of kainate (KA) in a mice model of MTLE.

**Method:** Male C57/bl6 mice were injected with KA (1 nmol) in the dorsal hippocampus and were treated with vehicle or high-dose rapamycin (80 mg/kg i.p. 5 h after KA injection; 40 mg/kg/day i.p. from 1 to 20 days after KA). Electroencephalography was recorded for 3 h at 25 days after KA injection.

**Results:** The expression of p-S6, the product of mTOR, was increased markedly in granule cell layer 21 days after KA injection in vehicle-treated mice whereas it was decreased when mice were treated with rapamycin. In addition, the granule cell dispersion that is observed in vehicle-treated KA-injected mice, was suppressed by the rapamycin treatment. However, the total time of hippocampal discharges of spikes was not significantly different between the vehicle-treated group (1471 ± 73 s/60-min) and the rapamycin-treated group (1458 ± 110 s/60-min).

**Conclusion:** These findings suggest that mTOR inhibition reduces morphological features of MTLE, but cannot effectively impair epileptogenesis.

#### P480

### SLOW AND FAST INACTIVATION OF HNA<sub>v</sub>1.3 VOLTAGE-GATED SODIUM CHANNELS BY ESLICARBAZEPINE, OXCARBAZEPINE AND CARBAMAZEPINE

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**Purpose:** This study aimed at determine the effects of eslicarbazepine, the major active metabolite of eslicarbazepine acetate, oxcarbazepine (OXC) and carbamazepine (CBZ) on the fast and slow inactivated states of the human Na<sub>v</sub>1.3 sodium channels expressed in CHO-K1 cells.

**Method:** CHO-K1 cells were transfected with human Na<sub>v</sub>1.3 sodium channel cDNA. The whole-cell patch-clamp technique was used to investigate the effects of eslicarbazepine, OXC and CBZ (all at 250 μM), in conditions of fast and slow inactivation of sodium currents.

**Results:** Steady state fast inactivation curves were shifted in the hyperpolarizing direction by OXC (-8.97 mV) and CBZ (-14.35 mV), but not by eslicarbazepine (-0.83 mV). Eslicarbazepine-treated fast-inactivated channels recovered similarly to control conditions (Δt = 3.3 ms), whereas OXC- and CBZ-treated channels required longer pulses to recover (Δt = 391.35 and 1291.47 ms, respectively). The time constant for entering the slow inactivated state of Na<sub>v</sub>1.3 channels was not affected by CBZ and OXC, but reduced by eslicarbazepine (from 20.29 to 14.02 s). OXC and CBZ shifted by -1.99 and -4.64 mV, respectively, the voltage dependence of the slow inactivation, whereas for eslicarbazepine the shift V<sub>0.5</sub> was -14.40 mV. For eslicarbazepine, OXC and CBZ, the affinity to the slow inactivated state was 2.6, 2.0 and 1.6 times higher than to the channels in the resting state, respectively.

**Conclusion:** Eslicarbazepine does not share with OXC and CBZ the ability to alter fast inactivation of human Na<sub>v</sub>1.3, but rather appears to modify the kinetics and voltage-dependence of slow inactivation states.

*These studies were sponsored by Bial – Portela & C<sup>a</sup>, S.A.*

#### P481

### SLOW AND FAST INACTIVATION OF HNA<sub>v</sub>1.3 VOLTAGE-GATED SODIUM CHANNELS BY ESLICARBAZEPINE, R-LICARBAZEPINE AND LACOSAMIDE

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**Purpose:** This study was aimed to compare the effects of eslicarbazepine and R-licarbazepine, major (94.5%) and minor metabolites (5%) of eslicarbazepine acetate, and lacosamide (LCM) on the fast and slow inactivated states of the human Na<sub>v</sub>1.3 sodium channels expressed in CHO-K1 cells.

**Method:** CHO-K1 cells were transfected with human Na<sub>v</sub>1.3 sodium channel cDNA. The whole-cell patch-clamp technique was used to investigate the effects of eslicarbazepine, R-licarbazepine and LCM (all at 250 μM), in conditions of fast and slow inactivation of sodium currents.

**Results:** Steady state fast inactivation curves were shifted in the hyperpolarizing direction by R-licarbazepine (-4.03 mV), but not by eslicarbazepine (-0.83 mV) and LCM (-1.90 mV). Eslicarbazepine- and LCM-treated fast-inactivated channels recovered similarly to control conditions (Δt = 3.3 ms), whereas R-licarbazepine-treated channels required longer pulses to recover (Δt = 1291.47 ms). The time constant for entering the slow inactivated state of Na<sub>v</sub>1.3 channels was reduced by eslicarbazepine, R-licarbazepine and LCM (from 20.29 to 14.02, 13.26 and 10.91 s, respectively). R-licarbazepine shifted by -4.50 mV the voltage dependence of the slow inactivation, whereas for eslicarbazepine and LCM the shift V<sub>0.5</sub> was -14.40 and -16.90 mV, respectively. For eslicarbazepine, R-licarbazepine and LCM, the affinity to the slow inactivated state was 2.6, 2.0 and 4.8 times higher than to the channels in the resting state, respectively.

**Conclusion:** Both eslicarbazepine and LCM preferentially enhance the slow inactivation of human Na<sub>v</sub>1.3, whereas R-licarbazepine appears to modify kinetics and voltage-dependence of fast inactivation states.

*These studies were sponsored by Bial – Portela & C<sup>a</sup>, S.A.*

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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 orally administered 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  $\mu\text{M}$ , 1  $\mu\text{l}/\text{min}$ , 7 h/day) with continuous EEG and videotape recording for three consecutive days. Microdialysate samples were analysed 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 behavioural changes. Control EEG recordings (8 h) were performed in all animals at least once a week for a minimum of 1 month.

**Results:** Oral administration of ESL (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 treatment reduced the increased 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:** ESL treatment prevented acute latrunculin A-induced seizures as well as chronic seizures and all EEG chronic signs of paroxysmal activity, supporting a possible anti-epileptogenic effect in mice.

*These studies were sponsored by Bial – Portela & C<sup>a</sup>, S.A.*

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### EFFECTS OF ESLICARBAZEPINE AND CARBAMAZEPINE ON ION TRANSMISSION THROUGH CA<sub>v</sub>2.1 (P/Q-TYPE) AND CA<sub>v</sub>3.2 (T-TYPE) CALCIUM CHANNELS

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**Purpose:** To evaluate the effect of eslicarbazepine (major active metabolite of eslicarbazepine acetate) and carbamazepine (CBZ) on human hCa<sub>v</sub>2.1 and hCa<sub>v</sub>3.2 currents.

**Method:** The whole-cell patch-clamp technique was used to investigate the effects of eslicarbazepine CBZ on hCa<sub>v</sub>2.1 and hCa<sub>v</sub>3.2 calcium channels stably expressed in CHO and HEK 293 cells, respectively. Compounds were tested (0.3–1000  $\mu\text{M}$ ; n = 3–5 cells) on hCa<sub>v</sub>2.1 and hCa<sub>v</sub>3.2 currents upon depolarisation of the cell membrane to –10 or –25 mV for 500 or 50 ms from a holding potential of –80 mV, respectively. Ca<sub>v</sub>2.1 and Ca<sub>v</sub>3.2 blockers cobalt chloride, valproic acid and mibefradil were used as reference.

**Results:** Eslicarbazepine did not affect hCa<sub>v</sub>2.1 calcium peak currents (IC<sub>50</sub> = 7836.80  $\mu\text{M}$ ), but CBZ inhibited hCa<sub>v</sub>2.1 calcium peak currents

(IC<sub>50</sub> = 452.46  $\mu\text{M}$ ). Eslicarbazepine potently inhibited hCa<sub>v</sub>3.2 calcium peak currents, but CBZ did affect hCa<sub>v</sub>3.2 calcium peak currents at much higher concentrations. A block of high affinity occurs with an IC<sub>50</sub> of 0.43 and 27.10  $\mu\text{M}$  for eslicarbazepine and CBZ, respectively. A further block occurs at higher concentrations of the test agents, with an IC<sub>50</sub> of 62.61  $\mu\text{M}$  for eslicarbazepine and 711.20  $\mu\text{M}$  for CBZ, respectively.

**Conclusion:** These results demonstrated that eslicarbazepine effectively inhibits high and low affinity hCa<sub>v</sub>3.2 inward currents with greater affinity than CBZ. These findings may have implications for the clinical activity of eslicarbazepine acetate.

*These studies were sponsored by Bial – Portela & C<sup>a</sup>, S.A.*

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### NEUROSTEROID MODULATION OF SYNCHRONOUS ACTIVITY IN THE PIRIFORM CORTEX OF PILOCARPINE-TREATED EPILEPTIC AND NON-EPILEPTIC CONTROL RATS

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**Purpose:** Neurosteroids modulate GABA<sub>A</sub> receptor-mediated neurotransmission in various regions of the brain. The piriform cortex (PC) is a region of high seizure susceptibility. We examined the effects of the neurosteroid allotetrahydrodeoxycorticosterone (THDOC) on the epileptiform discharges generated by the PC network treated with 4-aminopyridine (4AP). Brain slices were obtained from pilocarpine-treated epileptic and age-matched non-epileptic control rats.

**Method:** Status epilepticus (SE) was induced by i.p. injections of pilocarpine (380 mg/kg) in adult Sprague Dawley rats. SE was terminated after 1 h using diazepam (5 mg/kg) and ketamine (50 mg/kg). The in vitro electrophysiology experiments were carried out 4–5 weeks following injection. Transverse brain slices were obtained and bathed in 4AP (50  $\mu\text{M}$ ) to induce seizure-like events (SLEs). THDOC (5  $\mu\text{M}$ ) was bath applied and local field potential (LFP) recordings were obtained from the PC network.

**Results:** In non-epileptic controls, THDOC:

- i) did not affect the frequency of ictal and interictal discharges,
- ii) decreased the duration of ictal events, and
- iii) increased the duration of interictal events.

In pilocarpine-treated epileptic slices, THDOC:

- i) increased the interval of occurrence of ictal and interictal discharges,
- ii) did not affect the duration of ictal events, and
- iii) increased the duration of interictal events.

**Conclusion:** THDOC reduced the frequency of ictal and interictal discharges in pilocarpine-treated epileptic rats but failed to induce any significant change in age-matched non-epileptic controls. In spite of these differences, we conclude that neurosteroids may maintain their ability to control epileptiform synchronization in pilocarpine-treated epileptic rats.

## Poster Session: Clinical Neurophysiology A Tuesday, 25 June 2013

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### EEG AS A PROGNOSTIC TOOL FOR ABSENCE SEIZURE

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**Purpose:** The main purpose of this paper is to offer some guidance to expect the prognosis of classical absence from the EEG.

**Method:** This was an observational study conducted from July 2006 to July 2012. Data of 42 newly diagnosed patients with typical absence seizures was collected retrospectively and analyzed.

**Results:** The mean time until seizure and EEG control for those with +ve 3 Hz. SWC during routine EEG recording was  $(9.9 \pm 14.4)$  months. While the mean total follow up period for all cases were  $(19.3 \pm 20.5)$ . 100% of patients with +ve 3 Hz. SWC during the 3rd minute and after HV were controlled and 80% of the overall no. of controlled patients in this study was found during 3rd min HV ( $p$  value = 0.049). The majority of the controlled patients with 3 Hz. SWC after HV and during 2nd or 3rd minute HV was prescribed only monotherapy.

**Conclusion:** Overall prognosis of typical absence was good yet the presence of the 3 Hz. SWC with late onset either during the 3rd minute HV or even after had a better prognosis as regard; All of this group were controlled, monotherapy was used to control the majority of patients with late onset 3 Hz. SWC. These data was only significant for the association between the 3 Hz. SWC and the percentage of control of absence seizures during the 3rd minute HV (80%) ( $p$  value = 0.049). A multicenter study should be done in the nearby future to confirm these results.

#### P486

### THE DETERMINATION OF VEP IN PATIENTS WITH NON-OCCIPITAL LOBE EPILEPSY

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**Purpose:** To explore the impairment of visual passway in patients with non-occipital lobe epilepsy (NOLE) and the possible mechanism of damage.

**Method:** The patients with NOLE were selected in this study including 43 cases (Group 1) with drug-responsive epilepsy and 34 cases with drug-resistant epilepsy (Group 2). And other 34 normal people served as the controls (Group 3). The evoked potential machine was used to check visual evoked potential (VEP) in the three groups. Indexes of visual evoked potential (VEP) including latency and amplitude of N75 and P100 waves were determined.

**Results:** The latencies of N75 and P100 in the first two groups were longer than that in the Group 3 ( $p < 0.05$ ), but there was no difference between Group 1 and 2 ( $p < 0.05$ ). The amplitudes of P100 in the second group were higher than that in Group 3 ( $p < 0.05$ ), but there was no difference between Group 1 and 2 ( $p < 0.05$ ). There was no difference in amplitude of N75 in all the three groups ( $p < 0.05$ ).

**Conclusion:** There is visual pathway impairment in NOLE, which shows the latencies of N75 and P100 are longer and amplitude of P100 is higher, but there is no difference between patients with drug-responsive epilepsy and patients with drug-resistant epilepsy.

#### P487

### SPIKE FREQUENCY AFFECTS THE OCCURRENCE OF SCALP-RECORDED HIGH FREQUENCY OSCILLATIONS, BUT NOT THEIR ROLE AS EPILEPTOGENICITY MARKER

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**Purpose:** We aim to analyze the high frequency oscillations (HFOs) in the scalp EEG of focal epilepsy patients with different spiking rates, to determine how this feature influences HFO activity and their significance as markers of the seizure onset zone (SOZ).

**Method:** Thirty-two patients were studied, subdivided in four categories based on spike frequency: groups A, B, C and D (respectively with high, intermediate, low spike rate and with no spike). Thirty minutes of slow-wave sleep, low-pass filtered at 300 Hz and sampled at 1000 Hz, were reviewed. Spikes, gamma (40–80 Hz) and ripples (>80 Hz) were marked. Each channel was classified as inside/outside the irritative zone and the SOZ. The rates and co-occurrence of spikes and fast oscillations, the frequency in the irritative zone and SOZ, the specificity, sensitivity and accuracy to determine the SOZ were calculated, in the overall population and separately for each group.

**Results:** We analyzed 984 channels. Group A showed the highest HFO rate, followed by group B, C and finally group D. Gamma co-occurred with spikes in 46.2%; ripples in 44.4%. The HFOs were more frequent inside the irritative zone and the SOZ ( $p < 0.001$ ). Compared to the spikes, the fast oscillations were less sensitive (spikes: 78%; gamma: 66%; ripples: 48%) but more specific (spikes: 50%; gamma 76%; ripples: 83%) and accurate (spikes: 54%; gamma: 74%; ripples: 77%) in identifying the SOZ; the same results were reproduced for the different groups separately.

**Conclusion:** This study confirms that HFOs can be recorded from the scalp. Gamma and ripples are more frequent in patients with frequent spikes, particularly inside the irritative zone. Compared to spikes, gamma and ripples are less sensitive but more specific and accurate in identifying the SOZ, also in patients with low HFO rates, appearing to be a better biomarker of epileptogenicity.

#### P488

### ELECTROENCEPHALOGRAPHIC FEATURES OF BENIGN ADULT FAMILIAL MYOCLONIC EPILEPSY

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**Purpose:** To investigate electroencephalographic features of benign adult familial myoclonic epilepsy (BAFME).

**Methods:** We reviewed interictal electroencephalography (EEG) findings of BAFME patients who were treated between April 2005 and November 2012 at a tertiary referral center. The diagnostic criteria for BAFME were the presence of infrequent generalized tonic-clonic seizures, myoclonus or myoclonic seizures, positive family history of epilepsy suggesting autosomal dominant inheritance, and absence of known neurological disorders that causes myoclonic epilepsy. Interictal EEG findings of epilepsy with generalized tonic-clonic seizure only (EGTCS) as a subgroup of idiopathic generalized epilepsy were reviewed for comparison. We selected 10 generalized spike and wave complexes (GSW) or generalized polyspike and wave complexes (GPSW) per BAFME patient randomly. We measured duration of the spike-and-wave complex or polyspike and wave to calculate the frequency. EGTCS patients had fewer GSW than BAFME, so we selected GSW per EGTCS patient as many as possible when they had <10 GSW. Photoc stimulation using stroboscopic diffuse light stimulation with the frequency of 3, 6, 9, 12, 15 and 20 Hz for 10 s was performed in all patients.

**Results:** Fourteen (five men, nine women) BAFME patients were included in this study. The mean frequency of GSW was  $4.3 \pm 1.0$  Hz (mean  $\pm$  SD) in BAFME and  $3.2 \pm 0.8$  Hz in EGTCS. There was a sta-

tistically significant difference ( $p = 0.008$ ) between the two groups. Photoparoxysmal responses were noted in all BAFME patients but one in EGTCs patients.

**Conclusion:** Faster frequency of GSW than EGTCs accompanied with photoparoxysmal response may be the EEG features of BAFME. When these EEG findings are seen in patients with adult onset generalized epilepsy, BAFME should be included in the differential diagnoses.

#### P489

##### MULTICENTER STUDY OF AN AUTOMATIC SEIZURE DETECTION SYSTEM

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**Purpose:** Long-term video-EEG recordings for pre-surgical evaluation in cases of refractory epilepsy demand high effort from staff and patients. A prospective multicenter study is being performed in three epilepsy monitoring units (EMUs) to evaluate the added value of an automatic seizure detection system. Sensitivity and specificity of the detection system EpiScan are analysed in respect to increasing patient safety and reduction of evaluation time.

**Method:** The study will include 180 consecutive patients over the age of 18 attending EMUs as part of their treatment. EpiScan evaluates the surface EEG during recording and generates seizure alarms and EEG markings. A true positive (TP) is defined as marker within 3 min after seizure onset. A marker outside of a seizure period is defined as false positive (FP). Sensitivity is the ratio of the number of TPs to the number of all seizure. Specificity is defined as the average number of hours between two FPs.

**Results:** Preliminary results of 149 patients with 11,453 h of EEG are shown, including 64 patients with seizures. EpiScan reached 100% sensitivity at 33 patients, a good sensitivity between 99% and 33% at 19 patients, and lower sensitivities at only 12 patients. The average sensitivity was 70%. The average specificity of 3.4 h between false alarms results in seven markers per day.

**Conclusion:** The seizure detection system EpiScan showed high overall sensitivity and low false alarm rate. The application as surveillance support system in EMUs becomes feasible and increases patient safety while reducing EEG evaluation time.

#### P490

##### CAPTURING THE EPILEPTIC TRAIT: A CORTICAL EXCITABILITY STUDY OF PATIENTS AND THEIR UNAFFECTED SIBLINGS

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**Purpose:** We used transcranial magnetic stimulation (TMS) to investigate whether the cortical excitability changes observed amongst the different generalized and focal epilepsy syndromes are reflected in their asymptomatic siblings and if these changes depended on the clinical phenotype.

**Method:** 157 patients with epilepsy (95 generalized and 62 focal) and their asymptomatic siblings (138 and 82 respectively) were studied. Motor threshold (MT) and paired pulse TMS at short (2, 5 & 10, 15 ms) and long (100–300 ms) interstimulus intervals (ISIs) were measured. Results were compared to those of 12 controls and 20 of their siblings.

**Results:** There were no differences in cortical excitability between healthy controls and their siblings. Compared to controls, cortical excitability was higher in siblings of patients whether generalized ( $p < 0.05$ ; short and long ISIs) or focal ( $p < 0.05$ ; long ISIs). Compared to epilepsy, MT was lower ( $p < 0.05$ ) in patients with juvenile myoclonic epilepsy compared to their siblings only early at onset in the drug naïve state. In all groups (generalized and focal) cortical excitability was lower in siblings only at the long ISIs (250 and 300;  $p < 0.05$ ).

**Conclusion:** Cortical excitability is higher in asymptomatic siblings of patients with generalized and focal epilepsy in a similar manner. The disturbance seems to involve intracortical inhibitory circuits even in the siblings of patients with a structural abnormality (acquired epilepsy). This implies there are certain genetic factors that predispose to both generalized and focal epilepsies and a complex genetic/environmental interaction then determines the clinical phenotype.

#### P491

##### THE CLINICAL STUDY ON THE ATYPICAL PRESENTATION OF BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES

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**Purpose:** To explore the atypical clinical presentation, electroencephalography (EEG) characteristics, treatment and prognosis of benign childhood epilepsy with centrotemporal spikes (BECT).

**Method:** We collected 122 cases of BECT Children in Qilu Hospital from 2006 to 2012, ambulatory EEG or video EEG monitoring was performed for 11 cases BECT Children who had some atypical symptoms. The seizure semiology, neuropsychological impairments and response to antiepileptic drugs were analyzed and followed up.

**Results:** All 11 cases had seizure changes or EEG deterioration. Sodium Valproate was only effective in two cases. Valproate combined with clonazepam was effective in four cases. Topiramate were effective in three cases. There was still electrical status epilepticus during sleep after various antiepileptic drug therapy in two cases.

**Conclusion:** BECT had atypical presentations and some different seizure semiology. The clinical presentations were associated with EEG deterioration and cognitive deficits, and the seizures were relatively difficult to control.

#### P492

##### QUANTITATIVE ANALYSIS OF SURFACE ELECTROMYOGRAPHY SIGNALS DURING EPILEPTIC AND NON-EPILEPTIC SEIZURES

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**Purpose:** To investigate the characteristics of sustained muscle activation during tonic seizures (TS), tonic-clonic seizures (TCS), and psychogenic non-epileptic seizures (PNES).

**Methods:** Surface electromyograms (EMG) were recorded from the deltoid muscles, on both sides, during seizures in 13 patients with TCS, 12 patients with TS and 10 patients with PNES. To characterise the signal properties we calculated the root mean square of the amplitudes (RMS), the median frequency (MF) and the coherence. The duration of the seizures and of the various seizure-phases has been determined using a standardised automatic method based on the results of the wavelet analysis.

**Results:** The quantitative parameters differentiated well between the three seizure types. TS were characterised by increase in the frequency, TCS by increase in the amplitude of the signal, while the PNES were characterised by longer duration and fragmentation of the EMG activity. Exponential increase in duration of the silent-periods interrupting the EMG-bursts was observed during TCS, but not during PNES.

**Conclusion:** The pathophysiology of sustained muscle activation during PNES is different than the muscle activation during epileptic seizures. Quantitative analysis of surface EMG data can help in differentiating PNES from the epileptic ones.

#### P493

### SOURCE LOCALISATION OF RHYTHMIC ICTAL ACTIVITY: A STUDY OF DIAGNOSTIC ACCURACY FOLLOWING STARD CRITERIA

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**Purpose:** To estimate the accuracy of source localisation of rhythmic ictal EEG discharges using a distributed source model.

**Methods:** Source localisation of rhythmic ictal activity was performed in 42 consecutive cases, according to recommendations for studies on diagnostic accuracy (STARD). The initial ictal EEG signals were selected using a standardised method, based on frequency analysis and voltage distribution of the ictal discharges. A distributed source model (LAURA) was used for the source localisation. In 20 patients, additional, functional neuroimaging tests were done. Sensitivity, specificity and measurement of agreement (kappa) were determined based on the reference standard – the consensus conclusion of the multidisciplinary epilepsy surgery team. Predictive values were calculated from the surgical outcome of the operated patients. The source localisation was performed blinded to the clinical data, and before the surgical decision.

**Results:** The ictal source localisation had a sensitivity of 70% and a specificity of 76%. The mean measurement of agreement (kappa) was 0.61 corresponding to substantial agreement (95% CI: 0.38–0.84). Twenty patients underwent resective surgery. The positive predictive value for seizure-freedom was 92% and the negative predictive value was 43%. The sensitivity, specificity of the ictal source localisation was similar to the functional neuroimaging tests.

**Conclusion:** Source localisation of rhythmic ictal activity using a distributed source model for the ictal EEG signals selected with a standardised method is feasible in the clinical practice. It yields a good diagnostic accuracy. Our findings encourage clinical neurophysiologists assessing ictal EEGs to include this method in their armamentarium.

#### P494

### EPILEPSY: ELECTROENCEPHALOGRAM AND BRAIN MATURATION

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**Purpose:** The objective of this study was to emphasize the why and how the change in brain electrical activity in children, adolescents, adults and the old man and take, therefore, a relationship between the evolution of the EEG and epilepsy related to cerebral maturation.

**Methods:** A clinical study based on analysis of 100 electroencephalograms (EEGs) of epileptic and normal subjects of different ages was carried out at the hospital Al-Kortobi of Tangier, Service of Neurology (Morocco).

**Results:** Analysis of electroencephalograms showed, first, that during childhood the EEG is characterized by the gradual transformation of brain waves (Delta-Theta-Beta-Alpha) in time reflecting the different stages of brain maturation. On the other hand, there is a regional component of brain maturation in a posterior-anterior gradient chronological. Completion maturation is set between 12 and 14 years.

**Conclusions:** One thus understands why the newborn babies make mainly motor seizures and why the occipital epilepsy begin preferentially in the very first months from life, while the frontal epilepsy appear only seldom before the 2 years age, and the temporal epilepsy seldom before 8–10 years.

#### P495

### SLOW SPINDLES CORTICAL GENERATORS OVERLAP WITH THE EPILEPTOGENIC ZONE IN TEMPORAL EPILEPTIC PATIENTS: AN ELECTRICAL SOURCE IMAGING STUDY

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**Purpose:** To determine whether temporal epileptic patients and normal volunteers display similar sleep spindles' cortical generators as determined by electrical source imaging (ESI), and whether such generators overlap in epilepsy patients with the epileptogenic zone identified by ESI.

**Method:** Thirteen healthy subjects and eight temporal lobe pharmacoresistant epileptic patients underwent a 256-channel EEG recording during a daytime nap. Spindles were visually scored and marked; categorization in slow (10–12 Hz) and fast (12–14 Hz) ones was done by independently bandpass filtering in the appropriate frequency band. EEG was segmented on the marker position, and segments separately averaged for each category. Cortical sources were estimated using LORETA on the MNI brain. Maximal intra- and inter-individual intensities were compared through the Wilcoxon matched pairs test ( $p < 0.05$ ). The same procedure was performed for averaged epileptic spikes, obtaining their cortical source. Source generators localizations were statistically compared between epileptics and controls via a  $\chi^2$  test, and source intensities through a Mann-Whitney t test for independent samples ( $p < 0.05$ ). Overlap of spindles generators and spike generator was performed via a binomial distribution test ( $p < 0.05$ ).

**Results:** Multiple, concomitant and equipotent generators were detected in both populations for slow and fast spindles. While in normal subjects slow spindles had a persistent source over the frontal cortex, in temporal epileptic they displayed a preferential localization over the temporal cortices ( $p = 0.035$ ), as well as higher source amplitude in comparison to



healthy volunteers ( $p = 0.042$ ). Interestingly, at least one of slow spindles' generators overlapped with the epileptogenic zone ( $p = 0.016$ ) as obtained by ESI.

**Conclusion:** Slow spindles, but not fast ones, in temporal epilepsy are mainly generated over the affected temporal lobe cortex, and display overall higher intensities than spindles generators in healthy individuals. These results point to the strict relation between physiological sleep and epilepsy, and could underlie cognitive implications.

#### P496

##### EEG SEIZURE MONITORING AND NURSING

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**Purpose:** To ensure the accuracy of EEG Seizure monitoring and the safety of the patients by discussing the methods of monitoring and nursing.

**Method:** The patient did some sports or others before monitoring to bring out seizures. Located every electrode by measuring the head of the patient. Fixed the electrodes with adhesive plaster or celloidin. Clear away all the danger factors in the monitoring room and take protective measures.

**Results:** Four hundred and fifty-five patients suffered from epilepsy were monitored from 2006 to 2010. Epileptiform discharges are highly identified under the EEG monitoring and there is no electrode fell off and no accident happened for the patients, although there were some seizures occurred.

**Conclusion:** According to the results above, we can draw a conclusion that the methods of monitoring and nursing were worth to spread.

#### P497

##### BILATERAL CORTICAL REPRESENTATION OF ORGASMIC ECSTASY LOCALIZED BY DEPTH ELECTRODES

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**Introduction:** While in the past, sexual arousal has been evoked during direct electrical stimulation (DES) of the right mesial temporal lobe and the septal region, isolated orgasmic ecstasy has not been reported in the literature. We report the first case of isolated bihemispheric reproduction of orgasmic ecstasy by stimulation via depth electrode in a patient implanted for epilepsy.

**Case report:** To better define the epileptogenic zone(s), an invasive electrode study was performed in a 49 year-old, right-handed woman. In the course of DES for cortical mapping the patient reported orgasmic ecstasy following the stimulation of the left hippocampus at 3 mA. This stimulation was followed by an 18-s afterdischarge over the left hippocampus, the parahippocampal gyrus and the anterior-inferior insula. Stimulation of the right hippocampus at 1 mA generated the same orgasmic sensation and triggered a 45 s seizure discharge over the right hippocampus, parahippocampal gyrus, temporal pole and anterior insula.

**Discussion:** Orgasmic ecstasy can be evoked bilaterally. Activation of a large network (hippocampus, parahippocampal gyrus, temporal pole and anterior insula) appears to be necessary in order to generate such sensa-

tions. The latter is in line with the recent hypothesis of participation of the anterior insular cortex in ecstatic states.

**Conclusion:** Observation from this case study and previously reported cases suggest that isolated orgasmic ecstasy involve the activation of a network comprising the amygdala, the hippocampus, the parahippocampal gyrus, the temporal pole, the anterior inferior insula and the septal area.

#### P498

##### BUILDING A PATIENT-SPECIFIC SEIZURE DETECTOR WITHOUT EXPERT INPUT USING USER-TRIGGERED ACTIVE LEARNING STRATEGIES

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**Purpose:** Patient-specific seizure detectors outperform general seizure detectors, but building them requires lots of consistently marked electroencephalogram (EEG) of a single patient, which is expensive to gather. This work presents a method to bring general seizure detectors up to par with patient-specific seizure detectors without expert input. The user/patient is only required to push a button in case of a false alarm and/or missed seizure.

**Method:** For the experiments the 'CHB-MIT Scalp EEG Database' was used, which contains pre-surgically recorded EEG of 24 patients. The seizure detector used is based on (Buteneers et al. Epilepsy Research 2012: in press) combined with the preprocessing technique presented in (Shoeb et al. Epilepsy & Behavior 2004; 5:483–598). Button presses mark the corresponding data and add it to the training set of the system. The performance is evaluated using leave-1-h-out cross-validation to attain statistically relevant results.

**Results:** For the patient-specific seizure detector 34 (32%) (average [standard deviation]) of the detections are false, 8 (14%) of the seizures are missed and a detection delay of 11 (10) s is reached. The general seizure detector achieves: 86 (89)%, 28 (41)% and –35 (82) s, respectively. Adding only false positives, the patient specific performance is achieved in nine of the 24 patients. Adding missed seizures allows the patient-specific performance to be reached in 21 patients (about 90%).

**Conclusion:** This work shows that in order to build a patient-specific seizure detector, no patient-specific EEG data is required for up to 90% of the patients using the presented technique.

#### P499

##### MULTIMODAL NEUROIMAGING ASSESSMENT IN NONLESIONAL TEMPORAL LOBE EPILEPSY

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**Purpose:** To combine the information provided by structural and functional techniques during pre and intraoperative evaluation in Magnetic Resonance Imaging (MRI) – negative temporal lobe epilepsy patients underwent epilepsy surgery

**Method:** Quantitative methods for characterizing MRI (volumetric and voxel based morphometric), and time variant EEG spectral analysis for determining ictal Electroencephalographic (EEG) onset were used in a

total of 30 TLE patients during preoperative evaluation. Bayesian Model Averaging (BMA) was calculated on the individual's brain space. Intraoperative Electroencephalography (ECoG) recordings were also analyzed for epileptiform discharge frequency and morphology. Associations between multimodal assessment and histological findings in operated patients were examined

**Results:** In TLE patients with MRI- negative the functional assessment using BMA solutions clearly estimated a mesiolateral temporal generator. This coincided with regions of structural abnormalities evidenced by Morphometric methods (volumetry and voxel-based morphometric). On the other hand, during the intraoperative electrocorticographic interictal spike frequency (SF) recorded in the neocortical inferior temporal gyrus there was a tendency to higher SF and lower amplitude in areas with microscopic Focal Cortical Dysplasia (FCD) histopathologic subtype IB in relation with IA. It was also found that SF was significantly higher in patients with temporal neocortical atrophy evaluated by volumetric MRI.

**Conclusion:** Pre and intraoperative multimodal neuroimaging assessment helps to distinguish subtypes of TLE and to characterize the histopathologic subtypes of mild Palmini Type-I FCD. Our data also support the epileptogenicity of neocortical structures in TLE.

#### P500

##### EFFECTS OF VAGAL NERVE STIMULATION ON HEART RATE OF PATIENTS WITH REFRACTORY EPILEPSY

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**Purpose:** There is little information about the real effect in humans of vagal nerve stimulation (VNS) on heart rate (HR). The aim of this investigation is to observe this effect in patients with refractory epilepsy in three states: basal state, programmed stimulation and magnetic overstimulation.

**Method:** We used a Grass<sup>®</sup> technologies EEG machine to register VNS activity and HR using ground electrodes, two heart electrodes placed in 2nd and 6th left intercostal spaces and two VNS electrodes over the VNS cable in the neck. R-R intervals were manually measured to obtain the value in milliseconds during 120 s without stimulation (basal); 60 s with programmed stimulation and 60 s with magnetic overstimulation. All patients underwent to sympathetic skin response test to discard disautonomy. HR variability was obtained using Excel software and spectral analysis was obtained using Kubios<sup>®</sup> software. We use as Statistical methods student T or Mann-Whitney U and Stata<sup>®</sup> software.

**Results:** In 100% of patients (five men and four woman) there was a significant reduction on HR (< 0.05) with both programmed stimulation and magnetic overstimulation compared to basal HR. The mean difference was of three beats per minute (bpm) with programmed stimulation and 6 bpm with magnetic overstimulation. In 66% the difference was >5 bpm and in 11% >10 bpm. Spectral analysis (basal vs magnetic overstimulation) showed Low frequency (LF) 40.05 ± 7.02 vs 65.76 ± 6.80 (p < 0.05). High frequency (HF): 59.94 ± 7.02 vs 34.23 ± 6.8 (p < 0.05).

**Conclusion:** There is a reduction on HR with the use of left VNS, which could benefit patients with tachycardia during seizures. Spectral analysis show sympathetic dominance over parasympathetic during magnetic stimulation.

#### P501

##### EEG PHASE RELATIONSHIP AMONG ELECTRODES FOR CHILD ABSENCE EPILEPSY

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**Purpose:** To investigate the EEG phase relationship among electrodes in child absence epilepsy (CAE) and compare it with that of normal controls.

**Method:** The transient digital EEG signals of 10 clinical seizures with 20 subclinical epilepsy-form discharge in 15 cases of children absence epilepsy and 12 normal controls are recorded at awake and eye-closed state. Wavelet transform is employed to unfold the digital EEG signals into multi-scale components. The phase-lock average waveforms (PLAW) among different electrodes are obtained by phase-lock conditional sampling and phase-lock average techniques. The phase differences among electrodes are determined by correlation functions for PLAW. The phase relationships among electrodes of PLAW in CAE are compared with that of the 12 normal children at the same age.

**Results:** There exists phase-difference in PLAW among electrodes of normal controls. A phase-difference of PLAW between forehead lead and occipital lead is about  $\pi/2$  for normal controls. There are two types of phase-difference for CAE. One type is the PLAW of all electrodes are synchronised while another type is that the phase-difference between forehead lead and occipital lead is about  $\pi$ .

**Conclusion:** Phase-lock conditional sampling and phase-lock average techniques are employed to obtain the phase-difference of the PLAW among electrodes. The study result shows that the phase-difference among electrodes for CAE is different from that of normal controls and there are two types of phase-difference for CAE, while whose mechanism remains to be furtherly explored.

#### P502

##### A CASE OF NOVEL ICTAL PHENOMENA: ICTAL EVENTS CHARACTERIZED BY RHYTHMIC INFRA-SLOW DELTA ORIGINATING FROM A FRONTAL LOBE THAT PROPAGATE TO BILATERAL HEMISPHERE

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**Purpose:** A unique case presentation of a 46 year old black female with history of closed head injury experiencing stereotypical ictal attack consisting of internal pressure sensation and light headedness without loss of consciousness or migraine symptom. Brain MRI was non-lesional. She had EMU evaluation 2010 in other epilepsy center and was diagnosed as psychogenic seizure because of absence of IID during recorded events. The patient requested us the second opinion.

**Method:** The patient was admitted to Beaumont EMU and recorded video-EEG. The stereotypical ictal events were recorded in 10–20 scalp recording system and reviewed in broad band EEG parameter settings.

**Results:** During the recurrent episode of her seizure attack, 60 s per page segment EEG demonstrated right frontal rhythmic infraslow delta with frequency of 1/8 to 1/2 Hz, and 80–120  $\mu$ V in amplitude. This finding may not be clear in routine 10 s per page segment

EEG reading. The activity sustained for 3–25 min and the patient experienced reproduced stereotypical feeling of internal pressure and light headedness, but no alternation of consciousness or amnesia. In one attack, EEG recording demonstrated crescendo progression of infraslow rhythmic delta slow activity with maximum negativity at Fp2 and F8 which propagate to contralateral Fp1 and F7 and showed bifrontal synchronization which is comparable with frontal hypersynchrony.

**Conclusion:** There was no previous case report of infraslow rhythmic electrographic seizure. Her symptom correlated with reproducible EEG findings of right frontal infraslow delta which propagate to bilateral frontal lobe. The origin of the infraslow delta has not been determined if it is glial origin or neuronal origin. Mechanism of bifrontal synchrony of infraslow delta is in speculation. Nevertheless, in term of the nature of rhythmicity, novel seizure classification may be considered for this case.

### P503

#### ICTAL CHANGES IN HEART RATE AND HEART RATE VARIABILITY IN MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Ictal tachycardia may occur in patients with complex partial seizures (CPSs), especially with right hemispheric onset. However, the relationship between side of seizure onset and heart rate (HR) changes, and the ictal changes in HR variability (HRV), an indicator of cardiac autonomic function, are unclear. Ictal HR and HRV changes were investigated in patients with CPSs arising from the left and right temporal regions.

**Method:** Long-term video electroencephalographs were retrospectively reviewed in 20 patients, seven men and 13 women aged 13–67 years, with mesial temporal lobe epilepsy with MRI lesions. Peri-ictal time-series of electrocardiographic RR intervals were extracted from 77 CPSs (29 with right temporal onset). The high frequency (HF, 0.15–0.4 Hz) component of HRV was measured as vagal activity.

**Results:** All 29 right temporal seizures were accompanied by abrupt increase in HR and suppression of HF power followed by gradual recovery. In contrast, HR and HF changes during the 48 left temporal seizures had three subtypes: same pattern as right temporal seizures (n = 36); longer suppression of HF (n = 4); and no obvious changes (n = 8). The onset of HR increase was approximately 20 s earlier in the right than in the left temporal seizures (p < 0.0001).

**Conclusion:** Right temporal seizures showed the same pattern of ictal changes in HR and HF power, whereas left temporal seizures had various patterns. Right temporal seizures showed HR increase at an earlier phase. Cardiac autonomic dysregulation during seizures is closely associated with seizure lateralization.

### P504

#### CORTICAL AND SUB-CORTICAL EXCITABILITY DURING SPINDLES AND K-COMPLEXES, PUTATIVE ATTRACTORS OF EPILEPTIC ACTIVITY

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**Purpose:** The ARMOR project ([www.armor-project.eu](http://www.armor-project.eu)) is developing a platform for home monitoring of epilepsy patients. During sleep stage II (SS2) the frequency of specific types of epileptic activity is high. It is believed that large graphoelements of SS2, spindles and K-complexes act as attractors of epileptic activity.

**Method:** We studied high quality whole night sleep MEG recordings of four normal subjects [1]. The brain activity during K-complexes and spindles was compared with activity shortly during targeted baseline periods that included periods before (1–2 s) the graphoelements, quiet core periods of sleep stages [1], including SS2 and the awake state, with separate comparisons performed in the time and frequency domains.

**Results:** We showed widely distributed cortical foci of activity with hot spots during spindles around the central sulcus, parietal and prefrontal cortex, and during K-complexes the strongest hot spots in the anterior and motor cingulate. The statistical comparisons between periods of large K-complex and spindle activity with targeted baseline periods confirmed these findings with very high statistical significance (p < 0.0001) for each subject. However, the same comparisons showed distinct sub-cortical areas for each baseline period, suggesting significant changes in sub-cortical excitation in different sleep stages, even in the quiet periods, consistent with our earlier study [1].

**Conclusion:** Our results highlight the need to monitor epileptic activity during sleep with simultaneous characterization of sleep stages. This need will be satisfied by the output of the ARMOR project that has home monitoring capability, allowing such a characterization to be followed over extended periods and thus probe the evolution of epilepsy with unprecedented detail.

**Acknowledgment:** The work was partially funded by the European Commission under the Seventh Framework Program with grant ARMOR, agreement number 287720.

**References**[1] Ioannides AA et al. (2009) MEG identifies dorsal medial brain activations during sleep, *NeuroImage* 44:455–68.

### P505

#### CHARACTERIZATION OF POSTICTAL GENERALIZED EEG SUPPRESSION IN CHILDREN

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**Objective:** Postictal generalized EEG suppression (PGES) has been reported in adult with sudden unexpected death in epilepsy (SUDEP). We characterize PGES in children undergoing video EEG (vEEG).

**Methods:** A retrospective review of vEEG at SickKids (2009–2011) was performed to identify episodes of PGES. PGES was defined as generalized voltage attenuation <10  $\mu$ V and >1 s. Age, duration of PGES, type and duration of seizures, and EEG background features were analyzed.

**Result:** A total of 977 vEEG reports (<18 years old) were reviewed including 399 (41%) with electroclinical seizures. Twenty-seven children (7%; 16 male; mean 10 years old) demonstrated 49 seizures with PGES (37%) from a total of 134 seizures. Duration of PGES ranged 2–54 s (mean 30 s). 42 of 49 (86%) seizures associated with PGES were generalized tonic clonic seizures (GTCS). Forty-nine seizures with PGES were longer (mean 92 s) than 85 seizures without PGES (35 s) (p < 0.01). Older children demonstrated longer duration of PGES (R = 0.67, p < 0.01). Duration of 42 PGES with GTCS (mean 40 s) was longer than that of seven PGES without GTCS (3 s) (p < 0.01). Duration of PGES was longer in 10 children with normal awake EEG background; 20 with normal sleep spindles and 19 with normal REM sleep than in 17 with disorganized awake background, seven with disorganized sleep spindles and eight without REM sleep, respectively (p < 0.05).

**Conclusion:** PGES was more often associated with longer seizure duration and GTCS in children. Longer duration of PGES was associated with older age, GTCS and normal EEG background activity and sleep features.

## P506

### CLINICAL AND GENETIC ASPECTS OF 18 JAPANESE PATIENTS WITH HYPEREKPLEXIA: HOW TO DISTINGUISH FROM EPILEPSY

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**Purpose:** To determine clinical features of patients with hyperplexia (HPX) and how to distinguish between HPX and epilepsy.

**Method:** We investigated in 18 Japanese patients with HPX confirmed by gene analysis.

**Results:** The age at diagnosis was before 15 years in 15 of 18 cases, of which seven cases were before 1 year. Six of 18 cases (33%), however, had been misdiagnosed as having epilepsy, resulting in delayed diagnosis. Muscle stiffness and startle responses were observed soon after birth in all cases. Only one patient had epileptic seizures along with non epileptic startle response. Abdominal hernias were common complications. Nose-tapping test was positive for all patients. Localized spikes or spike and waves were found in interictal electroencephalograms (EEG) in three of 15 cases (20%). Clonazepam (CZP) was the most effective drug for muscle stiffness and startle responses. In the clinical courses, muscle stiffness disappeared until 5 years in 16 of 18 cases (88%), but startle responses remained in 12 (66%) even after the age of 8 years. On gene analysis, heterozygous *GLRA1* mutations (p.R299Q: 10 cases, p.A300P: 2, p.K304E: 1, p.Y307C: 1) were identified in 14 of 17 cases, compound heterozygous *GLRA1* mutations were in three (each of p.A412P/R420H, p.R344X/R420H, and p.171T/p.L319del), and compound heterozygous *GLRB* mutations were identified in one (p.R50X/p.Q216fsx222).

**Conclusion:** Generalized stiffness and excessive startle reflex soon after birth, nose-tapping test, and genetic test may be essential in differential diagnosis between HPX and epilepsy although some patients with HPX had abnormal EEG findings and remained in startle response.

## P507

### PHASE-DIFFERENCE-ZERO GAMMA OSCILLATIONS FLUCTUATE PRECEDING POLY SWCS IN A CASE WITH JME

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**Purpose:** Gamma oscillations (40–100 Hz) are considered as a binding measure of the neuronal activities between remote cortical areas. Poly spike-and-wave complexes (SWCs), which are found in juvenile myoclonic epilepsy (JME), are the prototype of diffuse synchronized epileptic discharges in human generalized epilepsies. Here, we investigated the changes of gamma oscillations preceding poly SWCs in a case with JME to evaluate whether they could predict the emergence of poly SWCs.

**Method:** Eight-channel EEGs (Fp1-C3, C3-T3, T3-O1, Fp2-C4, C4-T4, T4-O2, C3-Cz and Cz-C4) were recorded, and sampled (1.25 kHz) in a 12-year-old boy with JME. Twenty-four sequences of poly SWCs were selected. The EEG data were notch-filtered at 50 Hz, then 12 segments (2048 points/segment) were selected for the 8-th segment to cover the onset of poly SWCs.

**Results:** The average of wavelet analyses on bilateral fronto-central leads showed three frequencies of gamma oscillations (around 60, 70 and 85 Hz) pre- and during the poly SWCs. The gamma oscillations were extracted. Hilbert transform gave two parameters (instantaneous ampli-

tude and phase) of the gamma oscillations. Multiplied products of the instantaneous amplitudes between the leads are the measure for their synchronization. The data exceeding a threshold ( $>7.5 \mu V^2$ ) were collected, and the instantaneous phase differences were calculated and distributed on a time-series histogram. Time-series phase differences were evaluated by one-way repeated measures of ANOVA. Results showed fluctuations of phase-difference-zero synchronized gamma oscillations (around 70 Hz) before the onset of poly SWCs.

**Conclusion:** The preceding, phase-difference-zero synchronized gamma oscillations probably bind the widespread cortical activities, then trigger the seizure activities in human JME.

## P508

### CLINICAL SIGNIFICANCE OF HIGH-FREQUENCY OSCILLATIONS RECORDED BY SCALP ELECTROENCEPHALOGRAPHY ON CHILDREN IDIOPATHIC PARTIAL EPILEPSY

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**Purpose:** To analyze the relationship between high-frequency oscillations (HFOs) recorded by scalp electroencephalogram (EEG) and prognosis on children idiopathic partial epilepsy (IPE).

**Method:** Thirty cases of benign childhood epilepsy with centrotemporal spike (BCECTs) and 15 cases of benign childhood epilepsy with occipital paroxysms (BCEOP) were enrolled and followed up for 2 years. The scalp EEG and intelligence examination were performed every 6 months. HFOs were recorded by scalp EEG with high sampling rate. The seizure condition and cognition impairment were compared between the cases with HFOs and without HFOs.

**Results:** HFOs were recorded on six cases of BCECTs and four cases of BCEOP. Four cases of BCECTs and one case of BCEOP with HFOs developed to epilepsy with continuous spike-waves during slow-wave sleep (CSWS) during the term of following up. The average number and time of taking anti-epilepsy drugs of the patients with HFOs were more and longer than the ones without HFOs. The average scores of intelligence of the patients with HFOs were lower than the ones without HFOs. The differences are both significant by statistic analysis ( $p < 0.05$ ).

**Conclusion:** HFOs (80–160 Hz) can be recorded by scalp EEG with high sampling rates. They superimposed on the sharp or spike waves. HFOs have significant sense to judge the prognosis of children IPE. The emerging of HFOs indicates children IPE could develop to CSWS.

## P509

### POSTICTAL GENERALIZED ELECTROENCEPHALOGRAPHY SUPPRESSION IS COMMON IN TEMPORAL LOBE EPILEPSY PATIENTS WITH SECONDARY GENERALIZATION

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**Purpose:** Postictal generalized electroencephalography (EEG) suppression (PGES) may be associated with sudden unexpected death in patients with epilepsy. However, which type of epilepsy is likely to show PGES remains unclear. This study investigated the clinical characteristics of patients presenting with PGES.

**Method:** We retrospectively reviewed 24 consecutive epilepsy patients, eight men and 16 women aged 13–43 years, who presented with generalized tonic-clonic seizures (GTCSs) during long-term video EEG monitoring. A total of 38 GTCSs were recorded during monitoring. PGES was determined using the previously published criterion of generalized absence of EEG activity  $>10 \mu\text{V}$  in amplitude. We compared clinical parameters including age, sex, epilepsy classification, side of seizure onset, duration from EEG to GTCS onset, and duration of GTCS. The occurrence rate of PGES was also calculated for each epilepsy classification.

**Results:** PGES was observed in 14 of the 24 epilepsy patients with GTCSs. The occurrence of PGES was not associated with age, sex, side of seizure onset, duration from EEG to GTCS onset, or duration of GTCS. PGES occurred in eight of nine patients with temporal lobe epilepsy, two of eight with frontal lobe epilepsy, and four of four with generalized epilepsy. The occurrence rate of PGES was significantly higher in patients with temporal lobe epilepsy than in patients with frontal lobe epilepsy ( $p < 0.05$ ).

**Conclusion:** The incidence of PGES occurrence is significantly higher in patients with temporal lobe epilepsy. Propagation pathways leading to GTCS may be important in the occurrence of PGES.

## P510

### TRANSCRANIAL MAGNETIC STIMULATION AND EPILEPSY

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**Purpose:** To investigate of interaction of epileptic discharges by TMS in PWE with different type of seizure.

**Method:** 43 PWE: (mean age  $27.9 \pm 4.3$  years) were investigated with single pulse (TMS). Patients divided in 3 groups according to the type of seizure. 1 group-18 patients with GTCS, the 2 group – 13 patients with absence seizures (AS), the 3d group – 12 patients with partial motor and sensorimotor seizures (PM & SMS).

The single pulse (TMS) were performed by maximum output at single pulse was 2.2 Tesla. 19 channel scalp EEG was recorded 20 min before and after the TMS.

Interictal index of epileptiform discharges were counted for each patient before and after TMS.

Wilcoxon matched paired test was used for comparisons EEG changes before and after TMS.

**Results:** In 14 (78%) patients with GTCS was observed the suppression of epileptiform activity, in 12 (92%) patients with AS increased the duration and frequency of 3 Hz spike-wave discharge (statistically significant  $p < 0.001$ ). In patients with PM&SMS there were different EEG changes: in 50% patients – reduction, in 50% patients- increase of epileptic discharges.

**Conclusion:** TMS impact on scalp EEG has different influence on epileptiform activity depending on type of seizure: in patients with GTCS – they suppression, in AS – activation. We suggest that TMS triggering the thalamus via fibres connecting thalamus and cortex, according to the thalamocortical concept GE. Suppression of epileptiform activity in patient with GTCS would be due to cortical inhibition effects induced by TMS.

Our preliminary data show that single-pulse TMS may have therapeutic effect in patients with GTCS and may be contraindicate in patients with AS.

## P511

### ACCURATE LOCALISATION OF FOCAL EPILEPTIC ACTIVITY: VALIDATION OF HIGH DENSITY ELECTRIC SOURCE IMAGING USING INTRACRANIAL RECORDINGS

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**Purpose:** Electric source imaging (ESI) is an increasingly validated non-invasive approach for localising the epileptogenic focus in patients with drug-resistant epilepsy undergoing evaluation for surgery. While ESI has been shown to be concordant at a sub-lobar scale with the gold standards of intracranial EEG and the resected brain volume, a direct measure of its localisation accuracy is missing.

**Method:** We evaluated the accuracy of ESI in localising the cerebral generators of interictal spikes and in delineating the seizure onset zone, as compared to the gold standard of intracranial EEG. Thirty-eight patients underwent both ESI and intracranial EEG, and 32 of them subsequently underwent resective surgery.

**Results:** The median distance from the ESI maximum to the nearest intracranial electrode involved in the irritative zone was 15 mm (interquartile range 8–21 mm) and was below 30 mm in all patients but one. The distance to the nearest electrode involved in the seizure onset zone was 17 mm (9–27 mm) and was below 35 mm in all but six patients; in these patients, the ESI accurately identified an irritative zone that in fact did not participate in seizure generation. The irritative zone and seizure onset zone electrodes nearest the ESI maximum co-localised in a majority of patients, indicating that the irritative zone is a valid surrogate for localising the seizure onset zone. There was no difference in accuracy among patients with temporal or extra-temporal lobe epilepsy. In the 32 patients who underwent resective surgery, the inclusion of the ESI maximum in the resected brain volume was associated with a favourable post-operative outcome.

**Conclusion:** The high accuracy of ESI allows this technique to play an important role in planning the implantation of intracranial electrodes as well as resective surgery.

## P512

### TIME FREQUENCY ANALYSIS OF ICTAL MEG SIGNALS USING WAVELET-BASED MAXIMUM ENTROPY OF THE MEAN (wMEM)

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**Purpose:** When seizures are captured in MEG, rhythmic activity with low signal-to-noise ratio imposes a challenge to source localization methods. We present wMEM source localization as an alternative to determine sources of oscillatory components in the time frequency domain.

**Method:** Three seizures from three patients were analyzed. wMEM was performed within  $-1$  to  $+2$  s from seizure onset in three frequency bands: alpha (10–20 Hz), beta (20–30 Hz), and gamma (30–80 Hz). Principal Component Analysis was applied to source maps obtained for each band, at 0–400 ms from seizure onset. The first spatial component of the source maps was visually analyzed over the cortical-subcortical interface extracted from each patient's MRI. Results were compared to clinical information from ictal scalp and intracranial EEG (iEEG).

## Abstracts

**Results:** Patient #1 had a right orbitofrontal focal cortical dysplasia (FCD). Scalp EEG suggested an anterior temporal focus. Interictal MEG localized to the right inferior frontal cortex, this being confirmed with iEEG. Ictal MEG sources in the beta band showed concordance with iEEG. Gamma also showed concordant sources alongside secondary sources seen diffusely in both hemispheres.

Patient #2 had a left anterior cingulate FCD. Scalp and iEEG abnormalities with a widespread epileptogenic area involving the left temporal pole and anterior cingulate region. In ictal wMEM analysis, only alpha showed a clear maximum over the mid superior frontal gyrus, immediately above the lesion topography.

Patient #3 presented scalp EEG abnormalities involving the right posterior quadrant. wMEM in beta and gamma bands localized to the temporo-occipital and temporo-parietal regions, respectively. This patient has not undergone surgery.

**Conclusion:** wMEM ictal MEG source localization is coherent with scalp/intracranial EEG findings. Secondary sources likely correspond to contribution from baseline physiological activity.

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## P513

### THE CHANGES IN CYCLIC ALTERNATING PATTERN (CAP) OF EPILEPSY PATIENTS

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**Purpose:** The aim of this study was to determine the changes in the polysomnographic parameters and the cyclic alternating pattern (CAP) in generalized and partial epilepsy patients (with and without epileptiform discharges on EEG) using video-EEG-PSG recording.

**Method:** Seventy-three patients diagnosed with epilepsy and 19 healthy controls within the same age group (control group) underwent an 8-h long sleep video-EEG-PSG recording. After the first evaluation, the CAP parameters were scored in 57 patients (31 generalized and 26 partial epilepsy) and 16 healthy subjects who had no sleep diseases and the results were compared within the groups.

**Results:** The total sleep time and the NREM I phase were found to be longest in the partial epilepsy group and shortest in the control group, while the REM phase was found to be exactly the opposite to this. The mean CAP ratios were found to be statistically higher in the generalized epilepsy group when compared to the other two groups. This difference was also found in the control group and the generalized epileptic patients who had no abnormality on EEG. No difference was found between the partial epilepsy and the control group regarding CAP ratios.

**Conclusion:** Patients with generalized epilepsy have differences compared to healthy individuals regarding the macro- and micro-structure of sleep, and it seems that these differences are independent from the epileptiform discharges. In partial epilepsy patients, no microstructural differences were detected, while macrostructural changes were evident.

## P514

### THE EFFECTS OF SLEEP DEPRIVATION ON FUNCTIONAL EEG NETWORK CHARACTERISTICS IN CHILDREN WITH PARTIAL EPILEPSY

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**Objective:** Sleep deprived EEG recordings are often performed to increase the diagnostic yield in patients suspected of epilepsy, when routine EEGs have not confirmed the diagnosis or the classification of the epilepsy syndrome. Both sleep itself and sleep deprivation are associated with an increase of interictal EEG activity. The exact mechanism remains unclear. In this pilot study, we aimed to elucidate how sleep deprivation influences interictal functional brain networks, as derived from EEG data.

**Methods:** All children referred to the outpatient clinic with suspected new onset partial epilepsy, in whom both a routine interictal EEG recording and a sleep deprivation EEG (SD-EEG) were performed, were included in this study. The children were off-drugs at the moment of either EEG. Functional connectivity was analysed in artefact free epochs and was used to create weighted functional network characteristics. We compared normalized path length and cluster coefficient of EEG and SD-EEG recordings.

**Results:** Thirteen children with partial epilepsy were included. In the broadband frequency (0.5–45 Hz) we found a significantly decreased normalized cluster coefficient after sleep deprivation ( $p < 0.05$ ,  $t = 2.195$ ) and a trend towards a decreased normalized path length ( $p = 0.066$ ,  $t = 2.020$ )

**Conclusion:** These results suggest a shift towards a less segregated and a more integrated network after sleep deprivation in patients with partial epilepsy. Possibly, these alternations in the functional networks explain the increased interictal EEG activity after sleep deprivation.

## P515

### AUTOMATIC DETECTION OF EPILEPTIC CRISIS IN EEG

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**Purpose:** Develop and design a program that can detect epileptic crisis in a simple way, without the use of complex mathematical methods that require powerful hardware and as a first study is based on a heuristic method allowing enrichment of signal behavior in presence of crisis.

**Methods:** The creation of an automatic detection algorithm using basic concepts and procedures of digital signal processing, with direct and complementary measures, supported by a heuristic and iterative methodology of work.

**Results:** It was determined the execution time of each used segment. It was quantitatively evaluated the results of the algorithm by the sensitivity and selectivity parameters, showing a considerable quantitative analysis records analyzed, including EEG signals in the presence of crisis.

**Conclusion:** It was developed an automatic detection algorithm for identifying epileptic crisis, in which it was analyzed that the direct measures are rarely implemented with highly efficient if they are not accompanied by measures that complemented the first.

## P516

### EFFECT OF ELECTROENCEPHALOGRAPHIC SEIZURE PATTERNS ON HEART RATE VARIABILITY IN PARIETAL LOBE EPILEPSY

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**Purpose:** To investigate whether electrographic seizure patterns (EEG-Sz) affect heart rate variability in a patient with parietal lobe epilepsy.

**Method:** Data were obtained from a 52-year-old right handed male with parietal lobe epilepsy, who had medically-intractable daily partial seizures starting with numbness of the left upper trunk. The patient had implanted chronic subdural electrode grids (inter-electrode distance: 1 cm) for preoperative evaluation. Electroencephalogram and electrocardiography were recorded by a digital EEG machine with sampling rate of 200 Hz. EEG-Sz events lasting longer than 3 s with inter-event interval of more than 10 min were selected for analysis. All EEG-Sz showed bursts of fast (20–25 Hz) activities clearly restricted to one electrode in the right parietal cortex. Heart rate variability indices of high frequency component (HF), low frequency component (LF), and their ratio (LF/HF), were analyzed using ECG of 5 min each before and after events.

**Results:** LF significantly increased 2 min before the onset of EEG-Sz and decreased 1 min after the end of EEG-Sz ( $p < 0.05$ ). HF showed a tendency to decrease during 1 min after the end of EEG-Sz and to increase thereafter.

**Conclusion:** Our data suggest that cardiac autonomic modulation increase with sympathetic predominance before the onset of EEG-Sz in right parietal lobe.

#### P517

##### ANALYSIS OF FREQUENCY AND INTERHEMISPHERIC TIME DIFFERENCE OF MEG SPIKES AFTER ANTERIOR CORPUS CALLOSOTOMY IN PATIENTS WITH INTRACTABLE EPILEPSY AND DROP ATTACK

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**Purpose:** We evaluated the effects of anterior corpus callosotomy (ACC) on the frequency and interhemispheric time difference (ITD) of magnetoencephalography (MEG) spikes in patients with intractable epilepsy and drop attacks.

**Method:** We analyzed pre- and post-ACC interictal MEG spikes in five patients (11–33 years) with multiple seizure types, including drop attacks using gradient magnetic-field topography (GMFT) (Hashizume, 2007). We selected bilateral synchronous (BS) MEG spikes with peaks located on GMFT in the frontal, central, or anterotemporal regions (anterior distribution). We classified patients into anterior dominant (AD) and non-AD groups with anterior-distributed BS (ADBS) spikes  $\geq 50\%$  and  $< 50\%$  of all MEG spikes, respectively. We measured the BS spikes and ITD of the BS-spike peak in each hemisphere, and compared with results of drop attacks.

**Results:** In all three AD patients, ADBS spikes were postoperatively reduced in frequency (one patient had no spikes after ACC), and their pre- vs postoperative mean ITDs in two patients with postoperative ADBS spikes changed: i.e.  $15.0 \pm 13.9$  vs  $32.3 \pm 13.8$  and  $12.1 \pm 11.2$  vs  $38.3 \pm 1.37$  ms. Two of 3 AD patients portrayed cessation of drop attacks after ACC. However, ADBS spikes in one of two non-AD patients were unaffected although the frequency increased after ACC. Posterior-distributed (parietal, occipital, and posterotemporal regions) BS spikes were slightly increased in frequency of non-AD patients. The pre- vs

postoperative mean ITD of ADBS spikes in two non-AD patients were also changed: i.e.  $12.3 \pm 15.5$  vs  $33.7 \pm 22.3$  and  $17.3 \pm 6.47$  vs  $31.3 \pm 14.1$  ms, respectively. None of the two non-AD patients displayed cessation of drop attack after ACC.

**Conclusion:** ITD of ADBS spikes was prolonged after ACC in all patients. ACC reduced more of the frequency of ADBS spikes in the AD than non-AD patients. These findings may be relevant to the cessation mechanism of drop attacks after ACC.

#### P518

##### PREICTAL TEMPORAL PATTERN OF HIGH-FREQUENCY ACTIVITIES AND PREICTAL DISCHARGES

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**Purpose:** In previous experimental studies, preictal decrement of inhibitory activities were suggested especially in mesial temporal lobe epilepsy patients. In contrast, preictal discharge, preictal high-amplitude spike with glutamatergic mechanism was suggested to increase. However, these activities were not well identified in clinical data. We investigated the relationship between temporal pattern of high-frequency activities and preictal discharges and epilepsy types. Underlying mechanisms may be speculated by comparing temporal patterns.

**Methods:** Eighteen patients with medically intractable epilepsy underwent chronic electrocorticography using subdural electrodes. The ictal onset were defined by continuous ictal rhythms. Periods from -15 to 5 s from the ictal onset were investigated. Preictal high-frequency activities and discharges were visually marked. Temporal changes were compared between mesial temporal lobe epilepsy and neocortical epilepsy.

**Result:** Seven mesial temporal lobe epilepsy and 11 neocortical epilepsy patients were recruited. Nine out of 11 neocortical epilepsy patients had cortical dysplasia. No consistent temporal pattern was found in all patients with neocortical epilepsy and in four out of seven patients with mesial temporal lobe epilepsy. In three out of seven mesial temporal lobe epilepsy patients, progressive decrement of high-frequency activities and increment of preictal discharges were found.

**Conclusion:** Progressive decrement of high-frequency activities may suggest preictal decrement of inhibitory activities. This difference between epilepsy types may suggest that the mechanism underlying ictogenesis is potentially different between neocortical epilepsy patients and mesial temporal lobe epilepsy patients. Further studies using recording at smaller scales are warranted to elucidate the underlying mechanisms of ictogenesis.

#### P519

##### INDUCED VISUAL CORTICAL OSCILLATIONS SHOW ALTERED BETA AND GAMMA POWER CHANGES IN PHOTOSENSITIVE EPILEPSY

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**Purpose:** Induced oscillations in the visual cortex are potential markers of disease states and cortical excitability. They show remarkable

repeatability, are age related, appear heritable, and correlate with MRS measured GABA levels. We investigated these cortical responses in patients with photosensitive epilepsy using magnetoencephalography (MEG).

**Method:** We acquired MEG data from 12 patients with photosensitive epilepsy (PSE), and two age matched control groups (nine non-photosensitive epilepsy and 12 controls) during achromatic contrast grating visual stimulation with three contrasts, (40%, 60%, 100%) and two sizes, (4 and 8 degrees). Synthetic aperture magnetometry was used to localise power changes in beta (15–30 Hz) and gamma (30–70 Hz) bands. Time-frequency data was extracted from a source space virtual electrode reconstruction at the beamformer peak, for sustained and pattern onset visual responses.

**Results:** We found visual cortex alpha suppression, gamma enhancement and, in some, a beta response during stimulation in all three groups. For the photosensitivity patients, we found a trend for increased amplitude in the gamma range (40–70 Hz) as well as in the high-beta/low-gamma range (~30 Hz). In one patient tested prior to the commencement of anti-epileptic medication there was a 6-fold higher gamma power response compared to controls, that was significantly reduced after sodium valproate. A further patient with frequent spike-wave during stimulus presentation showed an atypical high beta band response above that of the gamma band. There were no differences in peak frequency or pattern onset response between groups.

**Conclusion:** The linking of photosensitivity to differences in neuronal oscillations at specific frequencies may help to identify the neurophysiological abnormalities that lead to seizures in photosensitive epilepsy. Induced visual gamma oscillations may also be useful in identifying hyper-excitability in individual patients, evaluating the efficacy of antiepileptic drugs and predicting which patients will respond to specific drugs.

## P520

### SOMATOSENSORY CORTICAL EXCITABILITY IN JUVENILE MYOCLONIC EPILEPSY

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**Purpose:** Studies suggest that elaborated movements of constructive character, defined as praxis, can evoke epileptiform discharges and/or reflex seizures in juvenile myoclonic epilepsy (JME). The somatosensory cortex provides information to the motor cortices modulating the planning and execution of the motor behaviors. This study aims to evaluate the somatosensory cortical excitability in JME patients with epileptiform discharges and/or reflex seizures induced by praxis.

**Method:** The sample (n = 30) was composed by 21 patients with JME divided in two groups. A group with 10 patients (four females) with epileptiform discharges and/or reflex seizures induced by praxis (JME-Praxis), another with 11 patients (six females) without induction by praxis (JME-WP); and a healthy control group (CG) with nine volunteers (six females). JME patients were screened by Video-EEG Neuropsychological Protocol (VNPP) associated to habitual methods of activation with duration of 4–6 h. The three groups were submitted to somatosensory evoked potential (SEP) evaluating the peak to peak amplitude (μV) of N20-P27 and P27-N35.

**Results:** Statistical analysis was performed by Mann-Whitney Test, considering p < 0.05. The amplitudes (median), in the three groups for

N20-P27 and P27-N35, were respectively: JME-Praxis (1.9), (-1.6); JME-WP (1.9), (-1.3); CG (1.3), (-0.6). The P27-N35 amplitude was significantly increased in the JME group (p < 0.044) when compared to the CG. P-value was significant in JME-Praxis (p < 0.017) but not in JME-WP (p < 0.239). No other significant differences were detected.

**Conclusion:** The increase of excitability in the primary somatosensory cortex was detected just in JME patients with discharges and/or seizures induced by praxis.

## P521

### IS THERE A DIFFERENT EZ ORGANIZATION IN BILATERAL AND UNILATERAL MTLT? A QUANTIFIED STUDY FROM SEEG SIGNALS

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**Purpose:** We aimed at better delineate the functional anatomical organization and the clinical context of bilateral temporal lobe epilepsy.

**Method:** We studied the epileptogenic zone (EZ) by quantifying the epileptogenicity of brain structures explored by depth electrodes in patients investigated by stereoelectroencephalography (SEEG). We compared patients having bilateral mesial temporal lobe epilepsy (B-MTLE, n = 15), with patients with unilateral mesial temporal lobe epilepsy (U-MTLE, n = 15). This quantification was performed using the "Epileptogenicity Index"(EI) method, that accounts for both the propensity of a brain area to generate rapid discharges and the time for this area to get involved in the seizure. We determined EI from signals recorded in the mesial part of the temporal pole, the amygdala, the anterior and posterior part of the hippocampus and subhippocampal regions (the entorhinal cortex and the posterior part of the parahippocampal gyrus), on the left and right sides.

**Results:** The EZ organization was statistically different in the two groups: U-MTLE patients displayed more frequently maximal epileptogenicity in hippocampal structures, whereas B-MTLE patients had maximal values in subhippocampal areas.

**Conclusion:** Results suggest a different organization of the EZ in the two groups. This raises the question of the functional connectivity between the two temporal regions and the origin of the bilateralization (etiology, secondary epileptogenesis).

## P522

### EPILEPSY AND SLEEP DISORDERED BREATHING

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**Introduction:** Sleep disorders may be associated with in many diseases like epilepsy. The presence of sleep disorders and respiratory disorders may increase the frequency of seizures and make difficult to treatment of seizures. Reduced seizure frequency and severity of seizures at CPAP therapy.

**Method:** We retrospectively reviewed the database of our sleep centre to identify 10 patients with both epilepsy and sleep disordered breathing (SDB). Recording were done using an Embla Recording System with somnologica software (RemLogic©) which was included continuous video-EEG monitoring and polysomnography.

**Results:** Generalized epileptiform discharges in six cases, three cases of paroxysmal epileptiform activity disorder, and one patient CAP (cyclic alternating pattern) showed activity disorder. Examination of these cases, polysomnography sleep fragmentation, reduction in REM, N1 and N2 were also increased. The most common symptom of excessive daytime sleepiness 80%, wake after sleep onset (WASO) 70%, parasomnias 40% and sleep movement disorder 20%. Six patients were treated with CPAP titration or dental devices, therapy reduce the seizures and interictal epileptiform discharges at the epileptic patients with SDB.

**Discussion and Conclusion:** CPAP led to significant reduction of both Epworth sleepness score and seizure frequency in the patients with epilepsy and SDB. Our data show that SDB treatment reduces the interictal epileptogenic activity, suggesting that SDB plays a role in increasing epileptogenicity. Further studies will be necessary to clarify the mechanisms whereby this reduction in epileptogenicity occurs, although improved sleep stability seems to play an important role.

## P523

### DIAGNOSTIC VALUE OF VIDEO EEG PSG IN EPILEPSY DIAGNOSIS

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**Introduction:** Differential diagnosis of nocturnal paroxysmal events is very important in terms of approach to these events and determination of the treatment. It is very difficult to clarify the differential diagnosis by means of history, seizure semiology, and examinations carried out in interictal period. There is a need for objective measurement and assessment tools. In this presentation, EEG and PSG findings of two cases have been discussed under the light of literature information.

**Cases:** Case 1 is a 29 years-old female case followed up with depression diagnosis with psychotic finding. Department of psychiatry has also conducted electroconvulsive treatment with this finding. Right temporal epileptic focus was determined in video EEG PSG records. Case 2 is a 39 years-old male case. Left fronto-temporal epileptic focus was determined in the case having complex partial and secondary generalized tonic-clonic seizures accompanied by oral automatism.

**Result:** Nocturnal paroxysmal events include many disorders with large spectrum and difficult differential diagnosis. Sometimes, comorbid conditions such as associations of parasomnia-nocturnal seizure make the table more complex. In these cases, the need for objective diagnostic tools is inevitable. Video EEG PSG must definitely take place in differential diagnosis of nocturnal paroxysmal events.

**Keywords:** parasomnia, epilepsy, vide EEG PSG

## P524

### A PRELIMINARY STUDY ON RECOGNIZING PSYCHOGENIC NONEPILEPTIC SEIZURES BASED ON SCALP RESTING EEG

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**Purpose:** Diagnosing psychogenic nonepileptic seizures (PNES) remains challenging, and even epilepsy specialists misdiagnose types of seizures in about 25% error rate. In current work, we evaluate the feasibility to classify PNES from the focal epilepsy using the scalp resting EEG.

**Methods:** Fifteen normal subjects, 15 PNES and 10 focal epilepsy patients are involved in current study. The scalp resting EEG of those 40 subjects are recorded with eyes closed and relaxed, each lasting about 2 min. EEGs are recorded using the 60-channel recording system. The 10 s long EEG recordings on the 21 canonical electrodes of 10–20 system were selected from the total 60 electrodes to perform further analysis. The coherence analysis and principal component analysis are performed to extract features for classification between normal subjects and patients (PNES + focal epilepsy), between PNES and focal epilepsy, respectively.

**Results:** The conducted study reveals that the recognition between normal subjects and patients can achieve 90% accuracy, 88% sensitivity, and 93% specificity, while 96% accuracy, 93% sensitivity, and 100% specificity are revealed for the recognition between PNES and focal epilepsy.

**Conclusion:** The preliminary result proves that PNES can be robustly recognized from the normal subject and focal epilepsy based on the scalp resting EEG. The possible limitation of current study is that the subject number is relatively small, but it may provide a new technical tool to help clinical doctors with the diagnosis of PNES.

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## Poster Session: Drug Therapy B Tuesday, 25 June 2013

### P525

#### CLINICAL EFFECTIVENESS OF ZONISAMIDE IN A SAMPLE OF ADULTS WITH EPILEPSY

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**Purpose:** Zonisamide (ZNS) is a relatively new anti epileptic drug in the UK, but has been used in Japan for many years. It was licensed in Europe in 2005, as add on treatment of refractory partial seizures with or without secondary generalisation in adults. Its efficacy has been attributed to several different pharmacodynamic actions on the CNS, mainly affecting sodium and calcium channels. The purpose of this observational study is to investigate the clinical effectiveness of Zonisamide in adults with epilepsy.

**Method:** A retrospective case note review was performed on a cohort of patients with epilepsy who started ZNS at two tertiary epilepsy referral centres in the North West, from April 2008 to February 2011.

**Results:** 193 patients (50% females) were identified, including partial and generalised epilepsy syndromes, which were poorly controlled on current AED. 54% had tried at least five other AED previously, with 74% being on combination AED therapy at time of commencement of ZNS.

Mean maximum dose of ZNS was 417 mg with mean maintenance dose of 410 mg. People who only tolerated lower doses of ZNS often had poorer seizure control. Mean duration rate 2.47 years with 47% remaining on treatment by the end of the study. The retention rate at 3 months was 83%, at 6 months 78% and by 1 year was 67%. Stopping ZNS treatment was predominantly due to poor tolerability or lack of effect. Adverse effects were experienced by 51% of the cohort, most commonly neuropsychiatric.

**Conclusion:** This study shows that in a significant proportion of people with partial and generalised epilepsy syndromes Zonisamide is tolerable and efficacious.

#### P526

### LEVETIRACETAM AS ADD-ON DRUG IN INTRACTABLE EPILEPSY: A TUNISIAN MULTICENTER STUDY

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**Purpose:** Levetiracetam has been authorized for use in Tunisia as an add-on therapy for intractable epilepsy since 2011. The aim of this retrospective study is to document its effectiveness for this indication in a cohort of Tunisian and Libyan patients with intractable epilepsy in two epilepsy centers.

**Method:** The medical files of 38 patients aged 6–82 years (mean, 34.2 years) were reviewed. All received levetiracetam as add-on therapy following a failure to respond to at least two anti-epileptic drugs.

**Results:** 62% of patients had partial epilepsy and the remainder had generalized epilepsy. 57% of epilepsy was symptomatic, 26% idiopathic, and 14% cryptogenic. Average age at first seizure was 14.1 years. In 45% of patients, the number of seizures was reduced by half with levetiracetam treatment; 11.5% of the cohort achieved complete remission. The drug was well tolerated. The most common adverse effects were irritability and impulsiveness, in 20% of patients.

**Conclusion:** Levetiracetam is an effective and tolerable add-on agent for use in most epileptic patients who fail to respond to at least two antiepileptic drugs and should be the treatment of choice in this setting.

#### P527

### EFFECTS OF EZOGABINE/RETIGABINE ON THE PHARMACOKINETICS OF DIGOXIN IN HEALTHY SUBJECTS: RESULTS FROM A DRUG-DRUG INTERACTION STUDY

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**Purpose:** The N-acetyl metabolite of ezogabine (EZG)/retigabine (RTG; NAMR) inhibits P-glycoprotein-mediated digoxin transport in vitro. This study (NCT01583036) assessed the effect on digoxin pharmacokinetics of co-administration with EZG/RTG, at doses across the approved range, in healthy subjects.

**Method:** This was an open-label, single-centre, fixed-sequence study in subjects aged 18–65 years. Following screening, in Session 1, subjects received a single dose of digoxin (0.25 mg) on Day 1. In Session 2 (starting 1 week later), participants entered a 6-week EZG/RTG up-titration phase. Digoxin 0.25 mg was co-administered with EZG/RTG at steady state on Days 10 (EZG/RTG 600 mg/day), 24 (EZG/RTG 900 mg/day) and 38 (EZG/RTG 1050 or 1200 mg/day). After all digoxin doses, samples for pharmacokinetic analysis were collected over 48 h (urine) and 144 h (blood). Subjects were followed up after 7–10 days. No formal hypotheses were tested.

**Results:** Of 30 participants (mean age [standard deviation]: 39.1 [12.2] years; 27% female), 29 were included in the pharmacokinetic analysis. Compared with digoxin alone, co-administration with EZG/RTG led to small increases in the digoxin area under the plasma concentration-time curve (0–120 h) at Days 10, 24 and 38 (geometric mean ratio [90% confidence interval, CI]: 1.08 [1.01, 1.15], 1.18 [1.10, 1.27] and 1.13 [1.05, 1.21], respectively). Digoxin renal clearance was reduced by 17% (geometric mean ratio [90% CI]: 0.83 [0.78, 0.89]) on Day 10 (EZG/RTG 600 mg/day) but not on Day 24 (EZG/RTG 900 mg/day, 0.99 [0.92, 1.06]) or Day 38 (1200 mg/day, 0.93 [0.86, 1.00]). Safety findings were consistent with previous EZG/RTG studies in healthy subjects.

**Conclusion:** This repeat-dose study across the therapeutic range of EZG/RTG resulted in a small increase in digoxin systemic exposure not related to NAMR systemic exposure, suggesting that dose-adjustment is not necessary when digoxin is co-administered with EZG/RTG.

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#### P528

### PHARMACOKINETIC DRUG INTERACTION STUDY BETWEEN ESLICARBAZEPINE ACETATE 1200 MG AND PHENYTOIN 300 MG: A PHASE I, OPEN-LABEL, MULTIPLE DOSE ADMINISTRATION STUDY IN HEALTHY VOLUNTEERS

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**Purpose:** To evaluate the effect of phenytoin (PHT) administration on the pharmacokinetics (PK) of eslicarbazepine acetate (ESL) and its main metabolite eslicarbazepine, and the effect of ESL administration on the PK of PHT, at steady-state.

**Method:** Single centre, multiple doses, open-label, two parallel groups, one-sequence design study. Group A (n = 15) – days (D) 1–2: ESL 600 mg; D3–8: ESL 1200 mg; D9–10: ESL 1200 mg + PHT 100 mg; D11–27: ESL 1200 mg + PHT 300 mg. Group B (n = 13) – D1–2: PHT 100 mg; D3–8: PHT 300 mg; D9–10: PHT 300 mg + ESL 600 mg; D11–27: PHT 300 mg + ESL 1200 mg. All treatments were administered once-daily. Blood samples collected in each group were – D1: pre-first dose; D8 and D27: pre-dose and at pre-determined intervals until 24 h after drug administration (14 samples in each day).

**Results:** Group A – No significant effect of PHT on the ESL PK profile was observed. Geometric mean ratios (GMR) (90% CI) of eslicarbazepine C<sub>max</sub> and AUC (D27/D8) were 69% (65–73%) and 67% (65–70%), respectively; this PK interaction is most likely caused by an induction of glucuronidation by PHT. Group B – GMRs (90% CI) of PHT C<sub>max</sub> and AUC (D27/D8) were 131% (117–146%) and 135% (121–151%), respectively; this PK interaction is most likely caused by an inhibition of CYP2C19 by eslicarbazepine.

**Conclusion:** When given concomitantly and based on individual response, the dose of ESL may need to be increased and the dose of PHT may need to be decreased.

*These studies were sponsored by Bial – Portela & C<sup>a</sup>, S.A.*

#### P529

### EFFECT OF HEMODIALYSIS ON THE PHARMACOKINETICS OF EZOGABINE/RETIGABINE AND ITS N-ACETYL METABOLITE: RESULTS OF AN OPEN-LABEL, SINGLE-DOSE, FIXED-SEQUENCE PHASE I STUDY

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**Purpose:** Ezogabine (EZG)/retigabine (RTG) and its metabolites are mainly eliminated renally. This Phase I study (NCT01480609) evaluated the effect of hemodialysis on the pharmacokinetics of EZG/RTG and its N-acetyl metabolite (NAMR) in subjects with end-stage renal disease (ESRD).

**Methods:** Subjects ( $\geq 18$  years) with ESRD on a stabilized hemodialysis regimen received an EZG/RTG 100-mg tablet 4 h before (Period 1, on-dialysis) or following (Period 2, off-dialysis) routine dialysis sessions separated by  $\geq 7$  days. Blood samples for EZG/RTG and NAMR pharmacokinetic analysis were collected up to 68 h post-dose. In Period 1, samples of pre- and post-dialyser blood and dialysate were also taken. Safety and tolerability were evaluated.

**Results:** Eight subjects completed Period 1; six completed both periods. The area under the plasma concentration-time curve (0–68 h) was 33% lower (geometric mean ratio [90% confidence intervals]: 0.67 [0.61, 0.73]) on-dialysis vs. off-dialysis for EZG/RTG, and 43% lower (0.57 [0.53, 0.62]) for NAMR. EZG/RTG and NAMR peak plasma concentrations were similar for the on-dialysis and off-dialysis periods. Median (range) reductions in plasma concentrations from start to end of dialysis were 52% (17–59%) for EZG/RTG and 51% (27–72%) for NAMR. EZG/RTG 100 mg was well tolerated with no serious adverse events.

**Conclusion:** In subjects with ESRD, hemodialysis initiated 4 h after a single oral 100-mg EZG/RTG dose reduced EZG/RTG and NAMR plasma concentrations by approximately 50%. Compared with the off-dialysis session, the decreased exposure to EZG/RTG and NAMR during dialysis was maintained over the 68 h post-dose period, indicating that dialysis could potentially be of use in cases of EZG/RTG overdose. The impact of dialysis in subjects with normal renal function has not been evaluated.

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### P530

#### IMPACT OF CONCOMITANT SODIUM CHANNEL BLOCKER ANTI-EPILEPTIC DRUGS (AEDs) ON THE EFFICACY OF ADJUNCTIVE PERAMPANEL FOR PARTIAL-ONSET SEIZURES: AN ANALYSIS OF POOLED PHASE III DATA

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**Purpose:** To examine the effect of mechanism of action (concomitant sodium channel blockers [SCBs] vs. non-SCBs) on perampanel efficacy.

**Methods:** In Phase III studies, patients with partial seizures were randomized to once-daily adjunctive placebo or perampanel (2–12 mg). In this analysis, patients were categorized according to whether or not they received a concomitant AED with sodium channel blockade as a primary mechanism of action. Hussein et al. (Neurology 2012; 78[Suppl 1]:P06.127) established that three perampanel enzyme-inducing AEDs (P-EIAEDs; carbamazepine, oxcarbazepine, and phenytoin) reduce perampanel exposure without affecting the exposure-efficacy relationship. Excluding patients on these P-EIAEDs from this analysis avoided confounding effects due

to inducers. This identified sufficient patient numbers for analysis of the effects of both lamotrigine (a non-P-EIAED, SCB) and levetiracetam (a non-P-EIAED, non-SCB) on perampanel efficacy. Valproate (a non-P-EIAED, non-SCB) will be reported in the poster.

**Results:** Median changes in seizure frequency with perampanel 2–12 mg/day were similar regardless of whether patients had received concomitant lamotrigine (–25.2%; n = 332) or not (–24.3%; n = 705), or levetiracetam (–23.7%; n = 310) or not (–24.7%; n = 727). Accordingly, 50% responder rates were also similar regardless of whether patients had received lamotrigine (31.6%) or not (31.5%), or levetiracetam (32.3%) or not (31.2%).

**Conclusions:** Concomitant administration of the non-P-EIAEDs lamotrigine (SCB) and levetiracetam (non-SCB) had no apparent effect on the efficacy of adjunctive perampanel for partial-onset seizures. Therefore SCBs appear to have no effect, unless also a P-EIAED. These non-P-EIAEDs, as well as known P-EIAEDs, all fit the exposure-efficacy relationship previously described by Hussein et al.

Support: Eisai Inc.

### P531

#### ADJUNCTIVE ONCE-DAILY PERAMPANEL REDUCES SEIZURE FREQUENCY AND IMPROVES RESPONDER RATES IN PATIENTS WITH UNCONTROLLED PARTIAL-ONSET SEIZURES, IRRESPECTIVE OF AGE AT EPILEPSY DIAGNOSIS: A POOLED ANALYSIS OF THREE PHASE III TRIALS

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**Purpose:** To explore the impact of age at epilepsy diagnosis (etiology and baseline seizure frequency) on perampanel efficacy in Phase III trials, as risks for developing unprovoked seizures differ in childhood vs. later life (Hesdorffer 2008).

**Methods:** Patients with partial-onset seizures were randomized to once-daily adjunctive placebo or perampanel (2, 4, 8, or 12 mg). Patients were categorized by derived age of epilepsy diagnosis: 0 to <12 years (childhood-onset; 54.0%, n = 796/1478); 12 to <18 years (adolescent-onset; 19.1%, n = 282/1478);  $\geq 18$  years (adult-onset; 26.9%, n = 397/1478). For each category, etiologies and baseline seizure frequencies were summarized, and changes in seizure frequency and 50% responder rates were analyzed.

**Results:** When the most common etiologies (CNS infections, family history, head injury/cranial trauma, other causes, sleep disorders, structural anomalies, vascular anomalies) were analyzed by age at diagnosis, only head injury/cranial trauma demonstrated an age-related effect: 5.8% in childhood-onset, 8.9% in adolescent-onset, and 16.6% in adult-onset patients. Median baseline seizure frequency appeared inversely age-related: 7.5–11.6/28 days in adult-onset, 8.7–14.3/28 days in adolescent-onset, and 10.8–15.8/28 days in childhood-onset patients.

At efficacious perampanel doses (4–12 mg), median percent changes in seizure frequency ranged from –26.2% to –30.9% vs. –13.0% with placebo; –14.5% to –26.2% vs. –13.5%; and –22.1% to –32.8% vs. –11.8% in childhood-onset, adolescent-onset, and adult-onset patients, respectively. Responder rates ranged similarly: 24.2% to 36.5% vs. 18.5%; 29.4% to 38.8% vs. 20.0%; and 30.8% to 39.7% vs. 20.4%.

**Conclusions:** Despite differences in these baseline clinical characteristics, perampanel 4–12 mg demonstrated efficacy without an age relationship.

Support: Eisai Inc.

## P532

## CANADIAN EXPERIENCE WITH EXTENDED USE OF OVER 3 YEARS OF PERAMPANEL IN PARTIAL ONSET SEIZURES IN PATIENTS AGED 12 AND ABOVE

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## P533

## ASSESSMENT OF PHARMACOKINETIC LINEARITY AND RELATIVE BIOAVAILABILITY OF A NASAL DIAZEPAM FORMULATION COMPARED WITH DIAZEPAM RECTAL GEL IN HEALTHY ADULT SUBJECTS

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## P534

## THE AVAILABILITY AND AFFORDABILITY OF SECOND GENERATION ANTI-EPILEPTIC DRUGS IN CHILEAN ADULT'S EPILEPTIC CONTROLLED IN A PUBLIC TERTIARY HOSPITAL IN SANTIAGO, CHILE: RESULTS OF A CHILEAN PROSPECTIVE REGISTER

Galdames DG<sup>1</sup>, Aguilera L<sup>1</sup>, González P<sup>1</sup><sup>1</sup>Department of Neurology, Hospital Sótero del Río, Santiago, Chile**Purpose:** To evaluate the requirement of generic second generation AEDs, used as therapy add-on in the management of Epilepsy in adult patients in a public tertiary Hospital in Santiago, Chile**Method:** We included adults patients suffering epilepsy (by semiology and EEG), with static or unknown etiology (by CT scan and/or MRI), in treatment with AEDs, classified according to the answer to AEDs and the type of drug used. They did not suffer non-epileptic events and all of them have normal hepatic and renal functions. They have follow up at least 1 year in our institution, and they were registered in each visit to the hospital.**Results:** From 1 June 2007 until 31 December 2012, we have registered 600 adults epileptic patients, 400 of them fulfilled the inclusion criteria. Age: 15–80 years old, average 30. Gender: male 175, female 225. Conventional AEDs: 81.5% (mainly Valproic Acid, Phenytoin, and Carbamazepine). Second generation AEDs (all generic drugs, obtained through donation): 18.5% (mainly Levetiracetam, Lamotrigine, and Topiramate).

Efficacy (number and percentage): Without seizures: 240 (60% of total), 11.7% with novel AEDs. Unsatisfactory control: 160 (40% of total) and only 28.7% of them using novel AEDs.

**Conclusion:** The Chilean public health system provides the mayor conventional AEDs, but there is an important gap in the availability and affordability of Second Generation AEDs. These drugs must be included in the national epilepsy program, financed by the state.

Recalcine Laboratory provided without cost all generic second generation AEDs.

### P535

#### PROFILE OF PATIENTS RESPONDING TO LACOSAMIDE TREATMENT IN DRUG-RESISTANT EPILEPSY

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**Purpose:** Lacosamide is approved as an adjunctive therapy in patients with drug-resistant epilepsy. The profile of epileptic patients and seizure subtypes responding to lacosamide is not yet well established.

**Method:** We performed a retrospective analysis of patients with drug-resistant epilepsy who were treated with lacosamide as adjunctive therapy in a tertiary center. Epidemiological and clinical data, tolerability and reduction in seizure frequency was registered. We considered as response a reduction of 50% or more in seizure frequency after a minimum of 3 months of full-dose treatment, and partial response 25% of seizure reduction.

**Results:** From 2010 to 2012 a total of 92 patients received lacosamide. 44.1% were men and 55.9% women, with a mean age 40.6 years. Complete follow up was available in 74 patients.

90.0% (86) had focal epilepsy, being the most frequent type temporal left (44.8%). The 10 other patients (10.0%) had generalized symptomatic or cryptogenic epilepsy. Four (20.0%) had seizures mostly during sleep. In 64.6% a lesion was detected in brain MRI. All patients received other antiepileptic drugs, seven had undergone respective surgery and four associated vagus nerve stimulation.

We obtained a complete response (considered as such no seizures during a minimum of 3 months of treatment, in 15 patients (15.6%) detecting a trend towards higher reduction rate in patients with nocturnal seizures 37.5% compared to the daytime seizure subgroup (18.8%). Also, the reduction was more significant in the focal epilepsy group, especially in temporal or fronto-temporal lobe epilepsy. Only 10 patients with generalised epilepsy were treated with lacosamide, obtaining minimum 50% response in three of the patients (30%).

Twelve patients (13.5%) discontinued the treatment, in 50% due to lack of response. None of those patients had nocturnal seizures.

**Conclusion:** Lacosamide is effective in clinical practice, especially in patients with nocturnal seizures and focal epilepsy.

### P536

#### INITIAL ANTIEPILEPTIC DRUG RESPONSE FOR 6 MONTHS IN PATIENTS WITH NEWLY DIAGNOSED EPILEPSY: SIGNIFICANCE OF AGE OF ONSET

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**Purpose:** In clinical practice, it is important to know that the predicting factors which influence on the response to antiepileptic drugs (AEDs) in the patients with epilepsy. In this study, we tried to find the factors predicting the response to AEDs in the patients with newly diagnosed epilepsy.

**Methods:** This is a prospective study performed in a single tertiary hospital. We studied 176 patients with newly diagnosed epilepsy.

The primary endpoint for this study was seizure free for initial 6 months. We analyzed the relation between duration of epilepsy, pretreatment seizure frequency, seizure density for previous 6 months, age of onset, epileptiform discharges on EEG, abnormal findings of MRI, seizure type, classification of epilepsy syndrome, type of AEDs and initial response to AEDs. We excluded the patients with epileptic encephalopathy, childhood absence epilepsy, juvenile absence epilepsy, juvenile myoclonic epilepsy, and infantile epilepsy.

**Results:** One hundred patients were included in this study, and seizure free for 6 months was achieved in 73 patients. The response to AEDs was significantly lower in the patients with early age of onset ( $\leq 16$  vs.  $>16$ , OR = 4, 95% CI 1.5–12.9, RR = 1.4, 95% CI 1.1–1.8). However, no statistical differences were observed other clinical variables.

**Conclusion:** Early age of onset is an important factor influencing on the response to AEDs in the patients with newly diagnosed epilepsy, suggesting increased disease severity in epilepsy.

### P537

#### NEW ONSET HYPERTENSION AND ATHEROSCLEROSIS IN PATIENTS ON LONG TERM ANTI-EPILEPTIC DRUGS

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**Purpose:** To assess the risk of new onset hypertension and atherosclerosis in patients taking long term anti-epileptic drugs.

**Method:** This study was conducted on patients attending Epilepsy clinic in Madras Institute of Neurology. Forty Epileptic patients (20 male & 20 female) aged between 18 and 30 years and taking Anti-Epileptic Drugs for more than 2 years were studied.

Patients with pre-existent hypertension and/or other atherosclerotic risk factors were excluded.

Age and sex matched healthy population was taken as control.

Blood Pressure was measured and classified as per JNC 7 guidelines. Hypertensive patients were worked up for atherosclerotic markers.

Sub group analysis was done on patients taking different anti-epileptic drugs.

**Results:** The mean systolic BP and Diastolic BP of the patients on long term AEDs are 125.80 and 83.55 mmHg. The healthy population had a mean systolic BP of 120.10 mmHg and mean diastolic BP of 76.80 mmHg.

New onset of hypertension among the patients the patients taking AEDs (32.5%) were found to be significantly higher than the healthy population (5%).

The presence of hypertension in patients taking long term AEDs showed positive correlation with the atherosclerotic markers.

#### Conclusion:

- 1 New onset of Hypertension and Atherosclerosis is high in patients taking long term AEDs compared to age and sex matched healthy adults.
- 2 A larger study is warranted for definite estimation of this risk and insight in to the mechanism behind it.

### P538

#### CHRONIC EFFECT OF LACOSAMIDE ON INTERICTAL EPILEPTIFORM ACTIVITY IN PATIENTS WITH PHARMACORESISTANT FOCAL EPILEPSY

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**Purpose:** To assess the frequency of interictal epileptiform discharges (IEDs) during lacosamide (LCM) adjunctive therapy in adults with intractable focal epilepsy.

**Method:** Inclusion criteria for the study was 50% or greater decrease in seizures frequency during adjunctive LCM treatment. Four patients were selected from the group of 14 patients received LCM. The EEG was analyzed for IED frequency during 25 min video-EEG at baseline period before and after at least 3 months of LCM treatment (range 3–30 months). At baseline all included patients were receiving up to two AEDs. The LCM dose range was 200–600 mg/day. In addition to LCM three patients were treated with oxcarbazepine, topiramate or lamotrigine, and one patient with two drugs oxcarbazepine and topiramate.

**Results:** Three patients had IEDs at baseline, and one had only focal slow waves. One of the patients taking LCM with excellent seizures control defined as rare non-disabling focal seizures only, was converted after 2 months to monotherapy with LCM. In case without IEDs during LCM treatment (400 mg/day), after 30 months focal interictal sharp waves occurred.

Two of patients had increase of IEDs: one treated only with LCM (400 mg/day) and the second patient received oxcarbazepine in addition to LCM (600 mg/day). The last patient was treated with low LCM dose (200 mg/day) with two other AEDs during 3 months. In that case IEDs activation was not detected.

**Conclusion:** Observed increased IEDs frequency in course of LCM therapy was correlated with better seizure control. Further studies are necessary to evaluate possible epileptiform discharges activation during LCM therapy.

#### P539 ARTIFICIAL NEURAL NETWORKS MAY IMPROVE THE PREDICTION OF OUTCOME IN ADULT PATIENTS WITH NEWLY DIAGNOSED LOCALIZATION – RELATED EPILEPSIES

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**Purpose:** To develop and compare the logistic regression (LR) and artificial neural network (ANN) models for prediction efficacy of initial antiepileptic drugs (AED) monotherapy in adult patients with newly diagnosed localization-related epilepsy, using data available at the time of diagnosis.

**Method:** Prospective longitudinal study included consecutive series of adult patients with newly diagnosed localization-related epilepsy. Main inclusion criteria were:

- 1) at least two well documented, unprovoked, clinically evaluated and classified partial seizures within last 12 months,
- 2) EEG within 12 months compatible with localization-related epilepsy,
- 3) Computed tomography (CT) or magnetic resonance imaging (MRI) scan within 12 months,
- 4) No previous use of AED.

Outcome was assessed as 1 year seizure freedom after achieving adequate AED dosage. LR model was developed and fitted using backward procedure. ANN model was developed using the same input and output variables as LR model. We evaluated calibration and discrimination characteristics of the models. Comparison was performed on whole dataset as well as independent test set.

**Results:** Intention to treat analysis included 287 patients on initial AED monotherapy, from which 147 (51.22%) achieved 1 year seizure freedom. Fitted multivariate LR model included:

- 1) age at therapy starts,
- 2) presence of complex partial seizures
- 3) EEG findings
- 4) epilepsy type,
- 5) etiology of epilepsy and
- 6) interaction of age and epilepsy etiology.

In independent test set (n = 57), rate of correctly classified outcome was 77.19% for the LR model and 92.98% for the ANN model. There are significant differences for the area under receiver operating characteristics curve (0.84 for LR vs. 0.952 for ANN, p = 0.0013).

**Conclusion:** Results suggest better potentials of ANN model than LR model for predictions of initial AED efficacy in adult patients with localized-related epilepsy. If validated, our models can serve as additional tool for patient counseling and clinical decisions.

#### P540 THE EFFECTS OF ESLICARBAZEPINE ON TRANSIENT Na<sup>+</sup> CURRENTS IN PILOCARPINE MODEL OF TEMPORAL LOBE EPILEPSY

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**Purpose:** A distinctive loss of carbamazepine (CBZ) effects on the recovery from inactivation is observed in patients with therapy refractory epilepsy and in the pilocarpine model of temporal lobe epilepsy. This study compared the effects of eslicarbazepine, the major active metabolite of eslicarbazepine acetate, on granule cells isolated from brain slices of control animals to those of animals who experienced status epilepticus (SE) following intraperitoneal administration of pilocarpine and who subsequently showed spontaneous seizures.

**Method:** Whole cell patch-clamp recordings were performed on dissociated dentate granule cells (DGCs) from the hippocampus obtained from control and pilocarpine-treated rats under control conditions and after application of CBZ and eslicarbazepine.

**Results:** Eslicarbazepine reduced the maximal conductance of transient Na<sup>+</sup> currents in a concentration-dependent manner without effect on the voltage dependence of activation in both control and SE-experienced rats. CBZ slowed the recovery from inactivation in granule cells from control, but not from SE-experienced rats. When applying 300 μM eslicarbazepine to granule cells from control rats, it slowed the time-course of recovery similar to CBZ. The effects of eslicarbazepine on the time course of recovery were even more pronounced in epileptic rats compared to control rats. Eslicarbazepine was equally effective in inhibiting firing of DGCs in control vs. pilocarpine-treated rats. In contrast, the effects of CBZ on the maximal firing frequency were significantly reduced in chronic experimental epilepsy.

**Conclusion:** Eslicarbazepine exerts use-dependent effects resulting in reduced firing frequencies of excitatory neurons in pharmacoresistant experimental epilepsy and potentially overcomes a cellular resistance mechanism to conventional AEDs.

This study was sponsored by Bial – Portela & C<sup>a</sup>, S.A.

## P541

### ASSOCIATION BETWEEN ABCB1 C3435T POLYMORPHISM AND PHARMACOKINETICS OF CARBAMAZEPINE

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**Purpose:** The C3435T, a major allelic variant of the ABCB1 gene, is proposed to play a crucial role in drug-resistance in epilepsy by limiting gastrointestinal absorption and brain access of antiepileptic drugs (AEDs). In some studies, the C/C genotype carriers reportedly are at higher risk of pharmacoresistance to AEDs. The aim of our study was to investigate the effect of ABCB1 polymorphism (C3435T) on the pharmacokinetics properties of carbamazepine (CBZ) in epileptic patients.

**Method:** Thirty patients with epilepsy were included in the study. As inclusion criteria, constant dose of CBZ in a period of not <4 weeks, age between 15 and 65 years and body mass index 19–25 kg/m<sup>2</sup> were considered, while exclusion criteria included abnormal renal or hepatic function, medical history of cardiovascular, renal and hepatic disorders, thyroid disorders and diabetes mellitus. The blood samples were taken under steady-state conditions, before the morning dose and subsequently after 1, 2, 3, 4, 6 and 8 h. The presence of the ABCB1 C3435T polymorphism was analyzed with TaqMan assay (MxPro 3005P, Strategene). Plasma CBZ concentrations were measured using the fluorescence polarization immunoassay (TDx/FLx system, Abbott Laboratories).

**Results:** The following PK parameters were determined for patients with CC genotype in comparison with CT and TT genotype: Ke(1/h) = 0.034 ± 0.016 (vs. 0.037 and 0.44 respectively); t<sub>1/2</sub> (h) = 25.14 ± 14.46 (vs. 26.152 and 20.519, respectively); Ka(1/h) = 0.466 ± 0.127 (vs. 0.673 and 0.686 respectively); AUC<sub>∞</sub>(μg-hr/ml): 263.9 ± 118.2 (vs. 324.200 and 273.729, respectively); CL<sub>tot</sub>(ml/h/kg): 44.89 ± 18.20 (vs. 35.859 and 79.654, respectively).

**Conclusion:** In conclusion, patients with CC genotype, CBZ was absorbed with lowest rate and extent.

## P542

### LACOSAMIDE TREATMENT – ADDED VALUE OF PLASMA LEVELS?

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**Purpose:** Lacosamide (LCM) has been shown to be an efficacious antiepileptic drug (AED) as add-on treatment in partial seizures.

LCM is a slow acting sodium blocking drug and in daily practice the main problem is adverse effects when used together with fast acting sodium channel AEDs and it is often necessary to taper down the concomitant fast acting sodium channel AED to let LCM be tolerated and increased to sufficient dose.

We wanted to evaluate if LCM plasma determinations added further information to the clinical information established over the time LCM has been used.

**Method:** The dose of LCM was correlated to concomitant AEDs whether these were fast acting sodium channel blockers or not.

The analytical method to determine LCM is a high performance liquid chromatography (HPLC) routine method with UV detection.

**Results:** Ninety-three measurements of LCM in 70 patients with partial seizures were done. Nonparametric statistics (modified Hoffman) was used. A fractile diagram performed and the measurements suggest that there could be a therapeutic interval for LCM from 12 to 35 μmoles/ml when a cut off of 90% was used.

**Conclusion:** A higher number of measurements are needed to confirm these initial findings and to validate the interval.

## P543

### LONG-TERM SAFETY OF PERAMPANEL: ADDITIONAL 10 MONTHS OF DATA FROM STUDY 307, AN EXTENSION OF THREE RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND, PHASE III TRIALS OF PERAMPANEL IN PARTIAL-ONSET SEIZURES IN PATIENTS AGED 12 AND ABOVE

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**Purpose:** To extend previous perampanel long-term safety/tolerability data (Krauss et al. *Epilepsia*, ePub Aug 2012), with an additional 10 months (cut-off Oct 2011).

**Method:** Participants in study 307 (NCT00735397) had completed a Phase III perampanel trial, and were titrated to 12 mg/day (or individual maximum tolerated dose) during blinded titration, followed by open-label maintenance. Data were collected on adverse events (AEs), vital signs, weight, ECG parameters, laboratory values, and seizure frequency/type.

**Results:** Of the 1216 patients, 1122 (92.3%) reached 10 or 12 mg/day; mean maintenance dose was 10.61 mg/day. Median exposure was 1.5 years (1 week–3.3 years), totalling 21,635 patient-months. 59% of patients were ongoing at cut-off. Subject choice or inadequate efficacy drove most discontinuations. AEs occurred in 1,110 patients (91.3%); the majority (80.2%) had mild/moderate events. AEs seen in ≥10% of patients were dizziness (46.8%), somnolence (21.2%), headache (18.3%), fatigue (13.1%), irritability (11.5%) and weight increase (10.9%). Only dizziness and irritability caused discontinuation in >1% (48/1216, 3.9%, and 16/1216, 1.3%, respectively). Two hundred and twenty-seven patients (18.7%) had serious AEs (SAEs). The only individual SAEs seen in >1% of patients were epilepsy-related; others (in >5 patients) were aggression (n = 12, 0.99%; five resolved, seven withdrawn), head injury (11, 0.90%), pneumonia (10, 0.82%), psychotic disorders (6, 0.49%), and suicidal ideation (6, 0.49%). Two patients died since previous cut-off (five total; none study-drug-related). At 122 weeks, mean weight gain was 2.96 ± 6.6 kg (N = 200). No clinically relevant changes in vital signs, ECG parameters, or labs were seen.

**Conclusion:** No new safety signals were identified, with 7,260 additional patient-months.

## P544

### LAMOTRIGINE PHARMACOKINETICS FOLLOWING ORAL AND STABLE-LABELED INTRAVENOUS ADMINISTRATION IN YOUNG AND ELDERLY EPILEPSY PATIENTS

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## Abstracts

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**Purpose:** The objectives of this study were to investigate the effect of age on pharmacokinetic (PK) parameters of lamotrigine (LTG), estimate parameter variability, and ascertain the relationship between patient-specific covariates and PK parameters.

**Methods:** The study was approved by all institutional review boards. Patients (>18 years) who were already on a steady-state dose of LTG either as monotherapy or polytherapy with other non-interacting AEDs were recruited. Patients with significant cardiac disease, severe kidney dysfunction, or moderate to severe liver dysfunction were excluded. 50 mg of a stable-labeled intravenous LTG formulation (SL-LTG) (<sup>13</sup>C<sub>2</sub>, <sup>15</sup>N-LTG: SL-LTG: IND #72,642) replaced 50 mg of a patient's normal daily oral LTG dose. Thirteen blood samples were collected in each person over 96 h. SL-LTG and unlabeled LTG concentrations were measured simultaneously by GCMS. Concentration-time data were analyzed by nonlinear mixed-effects modeling (NONMEM).

**Results:** Twenty-eight patients (384 unlabeled and 352 SL-LTG observations) representing 16 younger (18–48 years old) and 12 elderly (63–87 years) patients were included. A two-compartment model with first order absorption and elimination adequately described the plasma concentration-time data. Bioavailability of oral LTG was 75% and did not differ by age. LTG clearance was 1.37 folds higher in younger than in elderly patients (1.31 L/h for a 70 kg patient). Only body weight and age as a categorical variable remained significant in the final model.

**Conclusions:** LTG clearance was lower in elderly vs. younger patients of comparable body weight. A dose adjustment based on age may be indicated.

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## P545

### A COMPARISON BETWEEN PHARMACOLOGICAL TREATMENT OF EPILEPTIC PATIENTS WITH AND WITHOUT INTELLECTUAL DISABILITY

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**Purpose:** In this study we compare anti-epileptic drug (AED) treatment of intellectually disabled (ID) patients and those with normal intellect (NI).

**Methods:** We reviewed the medical records of 100 epilepsy patients (50 ID and 50 NI and comparatively severe epilepsy), and recorded all current and past AEDs prescribed for epilepsy.

**Results:** Patients with ID were currently taking a greater number of AEDs ( $p = 0.0001$ ) and had been exposed to more AEDs in the past ( $p = 0.005$ ). There were no significant differences between the two groups in terms of past or present exposure to the newer AEDs as a group (lamotrigine, topiramate, levetiracetam, gabapentin, felbamate and tiagabine). Patients with ID were more likely to be currently taking an old AED (phenobarbital, primidone, phenytoin, carbamazepine or valproic acid) ( $p = 0.01$ ). More ID patients were currently taking ( $p = 0.002$ ) and had previously taken ( $p = 0.004$ ) a benzodiazepine (BZD) AED such as clonazepam, nitrazepam and clobazam.

**Conclusion:** Despite the fact that both groups of patients are equally exposed to the old and newer AEDs, their overall pharmacological treatment is different. Patients with ID are more likely to be currently taking at least one old AED and are more commonly treated with BZD. Further investigation should help clarify the reasons for this finding.

## P546

### EFFECT OF ADJUNCTIVE LACOSAMIDE ON SEIZURE-FREE INTERVALS IN ADULTS WITH PARTIAL ONSET SEIZURES: POOLED ANALYSIS OF DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIALS

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**Purpose:** Evaluation of seizure-free days is a widely used secondary endpoint in adjunctive AED clinical trials. This post hoc analysis evaluated change in the maximum seizure-free interval with adjunctive lacosamide vs. placebo.

**Method:** Data were pooled from 3 double-blind, placebo-controlled adjunctive lacosamide trials in adults with uncontrolled partial onset seizures (POS; SP667, NCT00136019, NCT00220415). All patients randomized and treated who had  $\geq 8$  weeks of maintenance data were included in the analysis. A subpopulation with secondarily generalized POS (SGPOS) during Baseline was also analyzed. Maximum seizure-free interval (during the 8-week Baseline and the last 8 weeks on study treatment during Maintenance), percent change in maximum seizure-free interval, and percentage of patients with  $\geq 100\%$  and  $\geq 200\%$  increases in maximum seizure-free interval were evaluated for POS (any subtype) and SGPOS.

**Results:** Overall, 78% of patients had tried  $\geq 4$  lifetime AEDs; 84% were taking two or three concomitant AEDs. Median baseline POS seizure frequency was 11.5/28 days, and 42% had SGPOS at Baseline. The median maximum seizure-free interval during the 8-week Baseline was 7.0–9.0 and 17.5–20.5 days for POS ( $n = 1051$ ) and SGPOS ( $n = 445$ ), respectively. Percent increase from Baseline in maximum seizure-free interval was higher with lacosamide 200, 400 or 600 mg/day (45.8%, 61.3%, 100%, respectively) vs. placebo (40.8%). A higher percentage of patients on lacosamide 200, 400 or 600 mg/day vs placebo experienced a doubling (31.7%, 40.3%, 52.5% vs 29.6%) or tripling (20.2%, 23.6%, 25.8% vs 14.0%) from Baseline in maximum seizure-free interval. Trends were similar for patients with SGPOS.

**Conclusion:** Maximum seizure-free interval increased with lacosamide in adults with difficult-to-treat epilepsy. Seizure-free interval may represent a useful measure when assessing efficacy of AEDs in patients with uncontrolled epilepsy and frequent seizures.

UCB-Funded

## P547

### COMPARISON OF BODY COMPOSITION AND LIPID PROFILE AMONG PERSONS WITH EPILEPSY ON CONVENTIONAL AND NEWER ANTIEPILEPTIC THERAPY

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**Purpose:** Though valproate is known to have side effects like body weight gain, effects of AEDs on the body composition (body fat mass, lean dry mass (LDM), total body water (TBW), intra cellular water, extra



cellular water (ECW) and basal metabolic rate) have not been investigated thoroughly. This study aims to compare the body composition and lipid profile among subjects on newer and conventional AEDs.

**Method:** A total of 109 subjects on different AEDs like conventional AEDs (valproate, carbamazepine and phenytoin) and newer AEDs (levetiracetam, lamotrigine and clobazam) for >6 months were enrolled. Out of them 70 were on monotherapy of AEDs: levetiracetam (12 patients), valproate (16 patients), carbamazepine (20 patients) and phenytoin (22 patients). Their body composition was estimated by Bioelectrical Impedance Analyzer (Quantum X, RJL Systems). Biochemical parameters like lipid profile, blood glucose, liver and renal function assessment were done on all the subjects.

**Results:** Valproate group has lower percentage of fat mass ( $27.5 \pm 8.4$ ) than levetiracetam group ( $33.6 \pm 5.5$ ,  $p = 0.040$ ). LDM and TBW (as% of body weight) were higher in valproate group ( $20.2 \pm 2.7$  and  $52.2 \pm 6.0$ , respectively) than levetiracetam group ( $17.8 \pm 2.4$  and  $48.5 \pm 3.8$ , respectively) ( $p$  value 0.024 and 0.056, respectively). Levetiracetam group has no significant difference with carbamazepine, phenytoin and control group. In comparison with control, valproate group has higher LDM and ECW. There was no significant difference with biochemical parameters except higher triglyceride level in valproate group as compared to other groups.

**Conclusion:** Body composition alteration was not significant with Levetiracetam, but was significant with valproate, which may have effect on patient health and epilepsy treatment response.

#### P548

##### LONG-TERM SAFETY AND EFFICACY OF ZONISAMIDE VS. CARBAMAZEPINE MONOTHERAPY FOR TREATMENT OF PARTIAL SEIZURES IN ADULTS WITH NEWLY DIAGNOSED EPILEPSY: RESULTS OF A PHASE III, MULTINATIONAL, RANDOMISED, DOUBLE-BLIND, ACTIVE-CONTROLLED STUDY

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**Purpose:** To assess the long-term safety and efficacy of zonisamide vs. carbamazepine monotherapy for partial seizures in adults with newly diagnosed epilepsy.

**Method:** Adult patients completing a Phase III, randomised, double-blind, non-inferiority trial comparing zonisamide vs. carbamazepine monotherapy entered a long-term extension study, continuing the same treatment (zonisamide, N = 137; carbamazepine, N = 158). Dose ranges were zonisamide 200–500 mg/day and carbamazepine 400–1200 mg/day. Safety assessments included treatment-emergent adverse events (TEAEs) and clinical laboratory parameters. Efficacy assessments included retention and seizure freedom rates.

**Results:** Overall incidence of TEAEs was similar for zonisamide (52.6%) vs. carbamazepine (46.2%). Most TEAEs (>95%) were of mild or moderate intensity; the most commonly reported being decreased weight (5.8% vs. 0%) and headache (4.4% vs. 6.3%). Incidences of serious treatment-related TEAEs and TEAEs leading to withdrawal were low and similar between groups (0.7% vs. 1.9% and 1.5% vs. 0.6%, respectively). There were small-to-moderate decreases in bicarbonate levels from baseline in the zonisamide group (mean  $-3.4$  mmol/L). Vital signs and physical/neurological examinations identified no safety concerns. Retention rates for zonisamide vs. carbamazepine were generally similar at all time-points (58.4% vs. 61.4%, 27.7% vs. 27.8% and 5.8% vs. 2.5% at 12, 18 and 24 months, respectively; intent-to-treat population). Seizure freedom rates after 24 months of treatment were 32.3% vs. 35.2% (zonisamide vs. carbamazepine; intent-to-treat population).

**Conclusion:** Zonisamide monotherapy demonstrated favourable long-term safety and maintenance of efficacy when used to treat partial seizures in adults with newly diagnosed epilepsy. No new or unexpected safety findings emerged.

*Study supported by Eisai*

#### P549

##### IMPACT OF LONG-TERM TREATMENT WITH ADJUNCTIVE ONCE-DAILY ZONISAMIDE ON MEASURES OF GROWTH AND DEVELOPMENT IN PAEDIATRIC PATIENTS WITH PARTIAL EPILEPSY

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**Purpose:** To investigate potential effects of long-term treatment with adjunctive zonisamide on growth and development in paediatric patients with partial epilepsy.

**Method:** A long-term, open-label extension of a Phase III trial assessed the effects of adjunctive zonisamide (target dose 8 mg/kg/day; administered once daily) on measures of growth and development in 144 paediatric patients (age 6–18 years) with partial epilepsy. Assessments included Tanner stages, skeletal development, Child Behaviour Checklist for Children Aged 6–18 (CBCL 6/18), and Physician and Parent/Guardian Global Impression of Change (GIC). Data are presented for changes from baseline to Open-Label Visit 5 (V5; Weeks 62–71).

**Results:** Median duration of zonisamide exposure was 14.6 months. Median (mean) changes from baseline to V5 were minimal for CBCL 6/18 Total Competence and Total Problems scores ( $-1.0$  [ $-0.7$ ] and  $-2.0$  [ $-3.0$ ], respectively). Results for Tanner staging and skeletal development were as expected for the study population. Most patients were reported as “Much improved”/“Very much improved” at V5 on both the Physician GIC (73.8%) and Parent/Guardian GIC (75.5%), with good correlation between the scales (Pearson's correlation coefficient: 0.8980).

**Conclusion:** Adjunctive zonisamide, administered once daily, was associated with no consistent detrimental effects on growth or development in paediatric patients with partial epilepsy treated for >1 year.

*Study supported by Eisai*

#### P550

##### SEIZURE FREEDOM IN ADULTS WITH PARTIAL-ONSET SEIZURES TREATED WITH ADJUNCTIVE LACOSAMIDE: POOLED ANALYSIS OF THREE OPEN-LABEL EXTENSION TRIALS

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**Purpose:** To evaluate continuous seizure freedom in adults with partial-onset seizures (POS) treated with adjunctive lacosamide in open-label extension trials.

**Method:** Data from three open-label extension trials (up to 8 years; NCT00552305; NCT00522275; NCT00515619) were included in this analysis. To optimize tolerability and seizure control, dose adjustment of lacosamide (100–800 mg/day) and concomitant AED(s) were allowed. The percentage of patients seizure free for  $\geq 3$ ,  $\geq 6$  and  $\geq 12$  months was calculated overall and based on completer cohorts for the open-label population and for the subset of patients exposed to  $\leq 400$  mg/day lacosamide (approved dose range) during the lead-in and open-label extension trials.

**Results:** Patients in the lacosamide open-label extension trials (n = 1054) were difficult-to-treat: 46% had tried  $\geq 7$  AEDs in their lifetime; 84% were taking 2–3 concomitant AEDs at Baseline of the lead-in trial; median Baseline seizure frequency/28 days was 11.5. Overall, 29.5%, 18.2% and 11.1% of patients exposed to open-label lacosamide for  $\geq 3$  (n = 991),  $\geq 6$  (n = 920) and  $\geq 12$  (n = 795) months were seizure free for  $\geq 3$ ,  $\geq 6$  and  $\geq 12$  months, respectively. Of patients in the 1- (n = 793), 3- (n = 554) and 5- (n = 191) year completer cohorts, 11.1%, 15.0% and 23.6% experienced seizure freedom for  $\geq 12$  months. Among patients exposed to  $\leq 400$  mg/day lacosamide during the lead-in and open-label extension trials, 36.2% (n = 315; exposure  $\geq 3$  months), 28.0% (n = 275; exposure  $\geq 6$  months), and 20.2% (n = 233; exposure  $\geq 12$  months) were seizure free for  $\geq 3$ ,  $\geq 6$  and  $\geq 12$  months, respectively. Among 1- (n = 231), 3- (n = 150) and 5- (n = 57) year completer cohorts, 20.3%, 28.0% and 35.1% experienced seizure freedom for  $\geq 12$  months.

**Conclusion:** In adults with difficult-to-treat POS, long-term adjunctive lacosamide resulted in clinically relevant continuous seizure freedom in a meaningful proportion of patients. This analysis further supports the long-term efficacy of adjunctive lacosamide.

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## P551

### VIOLETION OF VASCULAR-PLATELET HEMOSTASIS IN CHILDREN WITH STROKE WITH ANTICONVULSANT THERAPY

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**Purpose:** In recent years in the developed countries has been an increase in childhood stroke, accompanied by convulsions in emergency period. In the intensive care unit used anticonvulsant drugs of different groups, which can lead to disruption of vascular-platelet hemostasis.

**Method:** Examined indicators of vascular-platelet hemostasis in 68 children with convulsions in hemorrhagic stroke who received anticonvulsant therapy.

**Results:** Hospital children's hospital № 1 279 children were hospitalized with a stroke, the period from 1999 to 2008. In 40.2% (68) of the patients had convulsions. To assess vascular-platelet hemostasis determined the number of platelets, their adhesion to collagen, platelet aggregation by adrenaline, collagen.

When comparing before and after the anticonvulsive therapy there was a reduction in platelet count in 85.3% (58), adhesion-aggregation of platelets in 55.9% (38), their adhesion to collagen in 44.1% (30) to adrenaline in 38.2% (26).

After correction of anticonvulsant therapy indicated recovery of vascular-platelet hemostasis.

**Conclusion:** The choice of anticonvulsants and duration of treatment should be determined individually, taking into account the severity of seizures, and the state of the vascular-platelet hemostasis.

## P552

### LONG-TERM SAFETY OF ADJUNCTIVE ONCE-DAILY ZONISAMIDE IN PAEDIATRIC PATIENTS WITH PARTIAL EPILEPSY: RESULTS OF AN OPEN-LABEL EXTENSION STUDY OF A PHASE III, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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**Purpose:** To assess the long-term safety of zonisamide when used as once-daily adjunctive treatment for partial seizures in paediatric patients receiving one or two other antiepileptic drugs.

**Method:** A total of 144 patients (aged 6–18 years) completing a Phase III, randomised, double-blind, placebo-controlled trial entered a long-term extension study, comprising a double-blind transition period (patients previously treated with placebo were up-titrated to a target zonisamide dose of 8 mg/kg/day; patients previously treated with zonisamide continued at the same dose) followed by flexible, open-label dosing. Safety assessments included treatment-emergent adverse events (TEAEs), clinical laboratory parameters, vital signs and electrocardiogram parameters.

**Results:** Overall, 108 (75.0%) patients received zonisamide for  $>1$  year. Median zonisamide dosing during open-label treatment was 7.52 mg/kg/day. Most TEAEs were of mild or moderate intensity. Treatment-related TEAEs were reported by 39 (27.1%) patients; most frequently, decreased weight (6.3%), decreased appetite (4.2%) and headache (2.1%). Serious treatment-related TEAEs were reported by three (2.1%) patients (renal colic, foot fracture, abdominal pain); there were no deaths. Only four (2.8%) patients discontinued due to TEAEs. There were no treatment-emergent laboratory abnormalities, vital signs or electrocardiogram parameters of clinical concern. Decreases in bicarbonate levels  $>3.5$  mmol/L were observed in 64 (44.4%) patients, but no TEAEs of decreased bicarbonate were reported. There were no reports of serious rash or hypersensitivity reactions.

**Conclusion:** Zonisamide displayed an acceptable safety profile in paediatric patients when used as long-term adjunctive treatment for partial seizures. No new or unexpected TEAEs emerged in this population.

Study supported by Eisai

## P553

### EXPERIENCE WITH RETIGABINE TREATMENT IN PHARMACOTHERAPY RESISTANT PARTIAL ONSET EPILEPSY PATIENTS

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**Purpose:** Retigabine (RTG) is a new antiepileptic drug for add-on-treatment of partial epilepsies with and without secondary generalization in adults, that has been available in Slovakia since October 1, 2011. Objective of the study was to monitor pharmacotherapy-resistant patients focusing on RTG efficiency and safety.

**Method:** Fifty-four outpatients with pharmacotherapy-resistant partial-onset seizures with or without secondary generalization receiving RTG add-on therapy were analyzed. The final RTG dose (150–1150 mg/day) was modified according to individual effect, tolerability, and compliance. Variables in the model included demographic data, epilepsy etiology, response to therapy, co-medication, and adverse side-effects of RTG treatment.

**Results:** Thirty men and 24 women of median age 39.5 years (range 20–61) and a median duration of epilepsy of 26 years (range: 2–51) were included. Median seizure frequency 1 month before RTG treatment was 9 (range 3–14). Median RTG final dose was 600 mg/day (range 150–1150 mg/day). Most frequent co-medication: levetiracetam (50%), lamotrigine (37%), valproate (35.2%). Most frequent etiology: 35.2% perinatal injury, 12% cryptogenic, 9% trauma, 5% complex infection. Seizure freedom has been achieved in 14.8% of patients. Responder rate: 42.9% responders reporting 50–99% reduction of seizures (of that, 18.5% reported a 75–99% reduction). 22.2% of patients reported seizure reduction below 50%, 9.26% reported no change, 3.7% reported deterioration,

and 14.8% of patients discontinued their treatment. Side-effects were observed in 20.4% of patients – most frequently fatigue, drowsiness, vertigo and tremor.

**Conclusion:** RTG in our study demonstrated the efficiency and tolerability profile comparable to that in pivotal trials. RTG treatment was efficient and well tolerated in a highly therapy resistant population of partial-onset epilepsy patients.

#### P554

### LONG-TERM SEIZURE OUTCOMES WITH PERAMPANEL IN REFRACTORY PARTIAL-ONSET SEIZURES AND SECONDARILY GENERALIZED PARTIAL SEIZURES: 10-MONTHS ADDITIONAL DATA FROM EXTENSION STUDY 307 FOLLOWING 3 PHASE III CLINICAL TRIALS

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**Purpose:** To examine the impact of time on response to perampanel ( $\leq 12$  mg/day).

**Method:** Study design and interim data from extension study 307 (NCT00735397) are reported in Krauss et al. (*Epilepsia* 2013; 54 (1):126–134). We report 7260 additional patient-months (cut-off Oct 2011). Seizure outcomes were analyzed in 13-week intervals (time from first perampanel exposure) in four subsets of patients, with  $\geq 6$ , 9, 12, and 24 months' perampanel exposure, allowing each subset's seizure outcomes to be examined over time without being confounded by changing patient numbers as the study progresses.

**Results:** Of the 1216 intent to treat patients, 1090 (89.6%), 980 (80.6%), 874 (71.9%) and 337 (27.7%) had perampanel exposure of  $\geq 6$ , 9, 12, and 24 months, respectively. Declining numbers reflected later start-dates and time of data cut-off, as well as drop-outs. The patterns of seizure outcomes were similar for median% change from baseline in seizure frequency, and responder rate (RR;% with  $\geq 50\%$  reduction) and between the four patient subsets based on duration of treatment. Most of the improvement occurred in the first 26 weeks, as perampanel was up-titrated (RR=32–35% at week 1–13 and 42–48% at weeks 14–26). Thereafter, seizure outcomes were stable: RR ranged from 52% (weeks 27–39) to 58% (weeks 92–104) in the subset of patients with  $\geq 24$  months of data. Patterns were similar in secondarily generalized seizures, where RR ranged from 64.7% to 67.4% at 27 to 39 weeks, to 73.0% at 92–104 weeks.

**Conclusion:** Seizure outcomes with adjunctive perampanel, in refractory POS, are stable over time, with data up to 2 years.

#### P555

### AN ASSESSMENT OF CLINICAL PRACTICE TOWARD PHARMACOLOGICAL TREATMENT OF EPILEPSY: A SURVEY OF ADULT NEUROLOGISTS IN R. MACEDONIA

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**Purpose:** The aim of the study was to evaluate clinical practice toward pharmacological treatment of epilepsy among adult neurologists in R. Macedonia.

**Method:** A questionnaire was developed that addressed decisions about when to start and to stop antiepileptic drug (AED) treatment, as well as the choice of the first and alternative drugs about different types of seizures. It was mailed to 30 practicing neurologists from three hospitals in R. Macedonia.

**Results:** Twenty-four neurologists (80%) answered the questionnaire. Half of them would administer antiepileptic drug after first unprovoked seizure considering EEG, MRI and other investigations, while the others will wait for second seizure before introducing treatment. For most of them discontinuation of the treatment should be individualized (taking account the syndrome, etiology), while the others would do that after 3–5 or more than 5 years seizure-free period. Most commonly used first-line drugs for partial seizures were carbamazepine and lamotrigine, while the second choices vary among a number of new generation and older AEDs. For generalized tonic-clonic seizures, absences and myoclonic jerks, valproate was by far the most commonly used AED (surprisingly, carbamazepine was drug of choice for absences for 16.5% of adult neurologists). Valproate is prescribed by almost all of neurologists when patients have several types of seizures. Alternatives for patients with mixed seizures were usually lamotrigine and topiramate. Commonly prescribed doses of AEDs tend to be lower to moderate and almost no one administer maximal tolerate doses.

**Conclusion:** A survey showed that prescription patterns in high percent were in concordance with current evidence about the spectrum of efficacy of individual AEDs in different types of seizures. Yet some of results are a cause of concern and further and continuous education of neurological community on AED treatment of epilepsy is needed.

#### P556

### SAFETY AND EFFICACY OF SUSTAINED RELEASE LAMOTRIGINE AS MONOTHERAPY/ADD ON THERAPY IN THE TREATMENT OF EPILEPSY

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**Purpose:** Lamotrigine (LTG), a phenyltriazine derivative, is an anti-epileptic drug (AED), with beneficial effects against partial and generalized epilepsies. Neurological side effects are normally seen at higher plasma concentrations. LTG<sub>SR</sub> which will produce lower plasma levels and slow plasma concentration escalation, is expected to reduce the incidence of this troublesome side effect. Hence, the present trial (open label, non-comparative, multicentric) was designed & aimed to determine the safety and efficacy of the LTG<sub>SR</sub> in Indian patients of epilepsy.

**Method:** Total 20 patients were enrolled. All patients completed the full (12 weeks) duration of the study. Patients in the age range of 16–70 years with diagnosis of Epilepsy, as defined in ICES were selected. Patient-categories included were: Category-I: Newly diagnosed patients (h/o  $\geq 2$  seizures in last 3 months), Category-II: Patients who did not achieve adequate seizure control ( $\geq 4$  seizures in last 6 weeks) with other AED. Category-III: Patients who were on Lamotrigine Conventional release (IR) formulation, followed by exclusion criteria.

**Results:** LTG<sub>SR</sub> treatment reduced seizure frequency in all patient-categories. Statistically significant reduction in seizure frequency (per 4 weeks) was seen in patient-Category -II. QOLIE-31 total score also significantly improved, in each patient-category. No serious adverse event (AE) was reported during the study.

**Conclusion:** It can be concluded that the LTG<sub>SR</sub> is safe and effective in the Indian patients of Epilepsy. It offers the advantage of a better

tolerability profile as compared to conventional LTG. It also offers a safe switchability from conventional preparation at the same molar dose.

#### P557

### EVALUATION OF INTRANASAL MIDAZOLAM ADMINISTRATION IN PREVENTING CONVULSIVE STATUS EPILEPTICUS DURING PARTIAL ANTI-EPILEPTIC DRUG WITHDRAWAL IN THE EPILEPSY MONITORING UNIT

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**Purpose:** Partial anti-epileptic drug (AED) withdrawal is routinely performed in the Epilepsy Monitoring Unit (EMU) at SEIN during video-EEG seizure monitoring for diagnostic purposes. In 2002 colleagues at SEIN reported that midazolam given via a nasal spray might be useful in the acute treatment of status epilepticus (see <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1874346/>). We performed a retrospective analysis of the efficacy of intranasal midazolam vs. rectal or parenteral benzodiazepine administration in acutely suppressing tonic clonic seizures and preventing occurrence of convulsive status epilepticus in the EMU.

**Method:** AED withdrawal protocols have been in operation for more than 25 years at our EMU with some differences over time in a population of patients with difficult-to-treat epilepsy. We counted the occurrence of status epilepticus resulting to transfer to a Medical Intensive Care Unit (MICU) in the 10 years prior to and after introduction of intranasal midazolam administration at our EMU in 2002.

**Results:** Prior to its use MICU transfer was requested in three of 47 patients who developed secondarily generalized tonic clonic seizures out a total of 376 patients in whom some degree of AED withdrawal was performed during EMU recordings. Since 2002 benzodiazepines other than midazolam were acutely administered to 53 patients while intranasal midazolam was used in another 13 cases out a total of 425 patients on some degree of AED withdrawal in the EMU. MICU transfer was requested in one midazolam-treated patient.

**Conclusion:** Secondarily generalized tonic clonic seizures on partial AED withdrawal leading to convulsive status epilepticus is a recognized hazard. Despite the availability of intranasal midazolam with its proven efficacy and easy application in status epilepticus in the general epilepsy population its use has not significantly changed the overall safety situation in our EMU in those patients in whom some degree of AED withdrawal is required for diagnostic purposes.

#### P558

### PROGESTERONE AND ALLOPREGNANOLONE MAY HAVE DIFFERENT MECHANISMS OF ANTICONVULSANT ACTION

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**Purpose:** To investigate the effects of anticonvulsant drugs and progesterone and its metabolites' effects on kindled seizures and inter ictal discharges (IIDs) in mice.

**Method:** Using a mouse model of hippocampal electrical kindling, we investigated the anticonvulsant efficacy of pregnanes and anticonvulsant drugs against partial and generalized seizures. We also examined the effects of some of these treatments on spontaneous IIDs in fully kindled mice. The compounds tested were progesterone and its metabolites, 5 $\alpha$ -dihydroprogesterone (DHP) and 5 $\alpha$ ,3 $\alpha$ -tetrahydroprogesterone (THP, also called allopregnanolone). The anticonvulsant drugs carbamazepine, fosphenytoin, and midazolam were also tested.

**Results:** Progesterone, THP, carbamazepine and midazolam significantly reduced behavioral seizures. The seizure stage reduction by progesterone, THP or midazolam was associated with diminished EEG afterdischarges. THP suppressed IIDs, and both focal and generalized seizure activities, but progesterone is only effective against generalized seizures.

**Conclusion:** Our data to date suggest GABAergic anticonvulsant drugs mimic the actions of THP on anticonvulsant and IID frequency, but progesterone does not. Given these results, progesterone and THP may exert anticonvulsant actions, at least partly, through different mechanisms. While the anticonvulsant drug therapy is the most widely employed approach to seizure control in clinical practice, the concept of using intrinsic anticonvulsant mechanisms, such as neurosteroid-mediated inhibition, remains an attractive therapeutic option. We are currently investigating the effects of neurosteroids, enzyme inhibitors, and GABA agonists on kindled seizures and IIDs.

#### P559

### MULTICENTER, OPEN-LABEL STUDY EVALUATING TOLERABILITY, SAFETY AND EFFICACY OUTCOMES OF LACOSAMIDE AS ADJUNCTIVE THERAPY FOR PATIENTS WITH PARTIAL-ONSET SEIZURES USING A FLEXIBLE DOSE ESCALATION SCHEDULE AND INDIVIDUALIZED MAINTENANCE DOSES

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**Purpose:** To evaluate the impact of flexible-dose titration on the safety, tolerability and effectiveness of adjunctive lacosamide.

**Method:** During Titration (12 weeks) of this open-label study (NCT01235403), patients received lacosamide 100 mg/day for 1–3 weeks, followed by 200 mg/day. After safety assessments, this could be increased to 300 mg/day and subsequently to 400 mg/day. Patients entering Maintenance (12 weeks) received the dose to which they had been titrated; one dose increase or reduction was allowed. Safety was assessed by treatment-emergent adverse events (TEAEs) and efficacy by median percentage reduction in POS frequency per 28 days,  $\geq 50\%$  response, retention rate and percentage of seizure-free patients.

**Results:** Overall, 100 patients with uncontrolled seizures entered the study; 75 completed Titration and entered Maintenance, and 74 completed the study. Median Baseline partial-onset seizure (POS) frequency per 28 days was 3.1 (range 1–28); 52% had received 1–3 lifetime anti-epileptic drugs. Reasons for discontinuation were AEs (14.0%), consent withdrawal (4.0%), "other" (4.0%), lost to follow-up (2.0%), lack of efficacy (2.0%). Median lacosamide exposure was 169.0 days. Most frequently reported TEAEs were dizziness (42.0%), headache (8.0%), asthenia (5.0%). Incidence of TEAEs was higher during Titration (55.0%) than Maintenance (18.7%). Median percentage reduction in POS frequency per 28 days from Baseline to Maintenance was 69.7%. Among patients who completed Maintenance, 28.4% were seizure-free.

The  $\geq 50\%$  responder rate during Maintenance was 69.3%, and retention rate at end of Maintenance was 73.0%.

**Conclusion:** Tolerability of flexible lacosamide dose titration was generally consistent with that observed in other lacosamide studies that used a forced-titration design, though comparison of these data is limited by other differences in study design and patient population.

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## P560

### ANALYSIS OF EFFICIENCY AND SAFETY OF TOPIRAMATE DEPENDING ON PATIENT'S AGE AND FORMS OF EPILEPSY

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**Purpose:** The aim of the study was analysis of efficiency and safety of topiramate at children and adult epileptic population depending on patient's age and forms of epilepsy.

**Method:** Seven hundred and twenty-two epileptic patients receiving topiramate (male = 374, female = 348) of the age from 3 month till 57 years are observed in dynamics with video-EEG control at the period 2002–2012 in the Department of Neurology, Neurosurgery and Medical Genetic of Russian National Research Medical University and Psycho-Neurological Department N2 of Russian Children Clinical Hospital.

**Results:** Topiramate was effective at 64.4% of patients (n = 465), and among the patient at monotherapy effectiveness (72.2%, at 127 from 176 patients) was higher than in combined therapy (61.9% at 338 of 546 patients). Low efficiency was seen at 27.4% (n = 198) patients. The aggravation effect has been noted at 8.2% (n = 59) of patients. Drug compliance (for >1 year) was 60.7% (n = 438). High efficiency in group <1 year (n = 58) was 55.2% (n = 32), low 34.5% (n = 20), aggravation 10.3% (n = 6); in group 1–3 years (n = 201) high efficiency 54.8% (n = 110), low 31.8% (n = 64), aggravation 13.4% (n = 27); in pediatric population >3 years (n = 385) high efficiency 67.3% (n = 259), low effect in 26.2% (n = 101), and 6.5% aggravation (n = 25), in adult population >18 years (n = 78) the efficiency was 82.1% (n = 64), low effect 16.6% (n = 13) and aggravation in 1.3% (n = 1).

**Conclusion:** Topiramate is highly effective drug in therapy of idiopathic generalized epilepsies without absences and in symptomatic/cryptogenic focal forms of epilepsy. Topiramate also could be useful additional drug in therapy of epileptic encephalopathies. With increasing of patients age the efficiency of topiramate raises, while aggravation risks decrease. Peak of aggravation potential was seen in early childhood population and maximum of effectiveness – in adult population.

## P561

### NOVEL KCNQ2/3 CHANNEL OPENER WITH IMPROVED POTENCY AND CHANNEL SELECTIVITY AS A POTENTIAL NEW TREATMENT FOR PARTIAL-ONSET SEIZURES: PRE-CLINICAL CHARACTERIZATION

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**Purpose:** Potassium channel openers (KCNQ2/3) with improved pharmacological profiles for the treatment of partial-onset seizures are needed. Ezogabine, approved in the U.S. in 2011 must be administered

t.i.d. and carries several warnings, e.g. urinary retention and QT prolongation, that prescribe careful monitoring. A compound that shows improved potency and pharmacokinetics, and addresses the liabilities of ezogabine would be a superior treatment option.

**Method:** We have utilized the strategic incorporation of additional fluorine substitution in ezogabine to discover a novel KCNQ2/3 channel opener, SF0034, and tested it in a series of in vitro and in vivo animal models.

**Results:** The potency for activating KCNQ2/3 is increased approximately fivefold and the selectivity vs. KCNQ4 has also been improved. SF0034 has been assessed in the mouse PTZ model and mouse locomotor activity assays. The increased potency was confirmed in the PTZ model and the locomotor activity results show that the protective index is comparable to ezogabine. SF0034 shows >4 higher IC<sub>50</sub> values for hERG inhibition, which indicates that SF0034 is less likely to cause hERG-inhibition-related, QT-prolongation. Human hepatocyte clearance is also higher than ezogabine, which may indicate a more balanced excretory profile. In addition, an F-18 radiolabeled analog of SF0034 is available to aid in the pre-clinical and potentially clinical development of SF0034 by non-invasive PET imaging.

**Conclusion:** SF0034 demonstrates a favorable pharmacological profile in initial pre-clinical testing. SF0034 also has been submitted to the NINDS Anticonvulsant Screening Program to further characterize its pharmacological profile. The results of these studies will further define the potential of SF0034 as an improved KCNQ2/3 channel opener for use in the treatment of partial-onset seizures.

## P562

### STUDIES ON VITAMIN E IN CYCLOPHOSPHAMIDE AND ITS UTILIZATION FOR THE TREATMENT OF BRAIN METABOLISM: RANDOMIZED CONTROLLED TRIAL

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**Purpose:** The studies were to evaluate the effects of vitamin E upon mRNA synthesis, lipid peroxidation and catalase activities in cerebral cortex, hippocampus and hypothalamus of Albino rats following intraperitoneal administration of cyclophosphamide.

**Method:** Twenty-four male adult white Albino rats aged 12 months old, were divided into three groups of eight rats each: group I (controls), group II which received cyclophosphamide 35 mg/kg body weight for seven consecutive days, group III which received cyclophosphamide and vitamin E for 7 days (12 mg/kg body weight) within 1 h before the administration of Complete Freund's Adjuvant. Cerebral cortex, hippocampus and hypothalamus (3H-uridine), using a Beta Berthold Scintillation Counter. The activities of catalase have been determined in all brain regions. The rate of lipid peroxidation has been determined by Wilbur method expressed in nmol MDA/hour.

**Results:** The data have pointed out immediate and long term effects of chemical stress induced by cyclophosphamide administration upon biochemical and oxidative parameters from brain cortex, hippocampus and hypothalamus. Cyclophosphamide has a negative effect upon mRNA synthesis and catalase activities which significantly decreases in all brain regions under studies. Lipid peroxidant potential is modified following cyclophosphamide treatment, decreasing below the normal limits, especially in cerebral cortex and hippocampus.

**Conclusion:** Vitamin E has a positive effect upon mRNA synthesis, lipid peroxidation rate in brain cortex, and especially in hypothalamus but no effect on hippocampus. The positive effect of vitamin E was noticed also

on catalase, by attenuating the inhibitory effects of cyclophosphamide, especially in hippocampus and brain cortex but not in hypothalamus.

### P563

#### THE ANTICONVULSANT EFFECTS OF OMEGA-3 PUFAs: DATA FROM ANIMAL AND CLINICAL STUDIES

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**Purpose and Methods:** The omega-3 polyunsaturated acids (n-3 PUFA) have antiarrhythmic effects, and might well have anticonvulsant effects as well. The purpose of the present presentation is to review the animal and clinical data related to the anticonvulsant effects of the n-3 PUFAs.

**Results:** The data from both animal and human studies are contradictory.

In animal studies, several groups have reported complete seizure suppression following 2 or 3 weeks i.p. administration of the short- or long-chain n-3 PUFAs. Our own group has consistently failed to replicate these dramatic effects, although we have found increases in seizure latency in the PTZ model, indicating elevations in seizure threshold. Interestingly, these elevations take place within minutes to an hour after s.c. or i.v. administration, but require 3 months or more to occur during p.o. administration.

Clinical studies involving n-3 PUFAs have similarly produced conflicting data. Some studies have reported anti-seizure effects following dietary n-3 supplementation, while other studies have reported none. Of note, the negative studies have involved shorter durations, whereas the positive studies have involved durations of 6 months.

**Conclusions:** The requirement for a long duration of oral administration to produce anticonvulsant effects is in agreement with our p.o. animal data. Future clinical studies of the n-3 PUFAs should involve long durations of administration, possibly as long as 6 months.

### P564

#### THE CLINICAL AND DEMOGRAPHIC SPECTRUM RELATED TO PERCEPTION OF ADVERSE EFFECTS OF ANTIEPILEPTIC DRUGS

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**Purpose:** Approximately 80% of individuals using AEDs will experience adverse reactions. The presence of adverse reactions to AEDs may negatively influence the quality of life of patients with epilepsy.

**Objectives:** We aim to identify, through a standardized questionnaire (Liverpool Adverse Events Profile – LAEP), major adverse effects associated with the use of AEDs, and the clinical and demographic profile associated with adverse effects.

**Methods:** We conducted an observational, cross-sectional study, in patients with epilepsy (n = 100) at the Hospital Oswaldo Cruz (HUOC) between February and October 2012.

**Results:** The mean score obtained in LAEP was 43.8 ± 8.3. The patients were divided in two groups: LAEP > 45 and LAEP < 45. 46% of the individuals had a score of LAEP considered toxic (≥45). The adverse effects most commonly reported were drowsiness (57%), agitation (41%), nervousness (28%), depression (27%) and headache (26%). We did not observe significant differences between gender (X<sup>2</sup>, p = 0.31), treatment regimen (monotherapy vs. polytherapy, X<sup>2</sup>, p = 0.27), marital status (X<sup>2</sup>, p = 0.20), employment status (X<sup>2</sup>, p = 0.80) and schooling (X<sup>2</sup>, p = 0.68) when compared patients with LAEP > 45 vs.

LAEP < 45. We observed a significant correlation (Spearman) between LAEP and quality of life (r = -0.82, 95% CI -0.87 to 0.7402, p < 0.001); LAEP and anxiety (r = 0.28, 95% CI 0.08 -0.45, p < 0.005); LAEP and depression (r = 0.28, 95% CI 0.008–0.45, p < 0.037), and LAEP and stress (r = 0.20, 95% CI 0.007–0.04, p = 0.03). There was no correlation between LAEP with age, with BMI and duration of disease.

**Conclusion:** Patients with higher levels of drug toxicity exhibit a greater impairment in quality of life and greater degree of anxiety, depression and stress.

### P565

#### AN EXTRA DOSE OF ANTIEPILEPTIC DRUG MAY PREVENT EPILEPTIC ATTACK AFTER EXPOSURE TO TRIGGERING FACTORS

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**Purpose:** The effectiveness of one extra dose of antiepileptic drug to prevent a possible epileptic attack after exposure to triggering factors.

**Method:** Twenty-six epileptic patients developing new attacks when they are exposed to precipitating factors such as sleep deprivation or severely stressful conditions. They have been advised to take one extra dose of their antiepileptic drug during or after exposure to a precipitating factor and to register their new attacks

**Results:** Twenty-six epileptic patients have been included. All of them have been well or relatively well controlled on antiepileptic drugs, however they have been developing a new attack when they have been exposed to a precipitating factor. The extra dose that has been given has been preventing a new attack up to 80% as compared with their treatment without extra dose. The JME and secondary generalized temporal lobe epilepsy seem to be more consistently responding to such regimen.

**Conclusion:** An extra dose of antiepileptic drugs may prevent precipitated epileptic attacks. This is a simple and easy to use method and it seems to be effective to prevent recurrent attacks and possibly dramatic complications.

### P566

#### PROSPECTIVE AUDITS WITH NEW ANTIEPILEPTIC DRUGS IN LOCALIZATION-RELATED EPILEPSY: INSIGHTS INTO RESPONSE

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**Purpose:** This paper reviews the results of five consecutive audits with new AEDs using identical methodology.

**Methods:** Prospective audits with topiramate (n = 135; TPM), levetiracetam (n = 136; LEV), zonisamide (n = 141; ZNS), pregabalin (n = 135; PGB) and lacosamide (n = 160; LCM) were undertaken in patients with localization-related epilepsy. Patients were kept under observation until one of the following end-points was reached: seizure freedom for at least 6 months on unchanged dosing; ≥50% reduction (responder) in seizure frequency on the highest tolerated dose; ≤50% seizure frequency reduction (marginal response); or withdrawal due to lack of efficacy, side effects of both.

**Results:** More seizure-free patients were found with LEV (23.5%), LCM (21.9%) and TPM (20.7%) than ZNS (12.8%) and PGB (10.4%). More patients dropped out of treatment due to lack of efficacy or side-effects with ZNS (41.8%) and PGB (50.4%) than with TPM (31.1%), LEV (32.4%) and LCM (22.5%). Most seizure-free patients occurred as first or second add-on for all AEDs (TPM 100%; LEV 97%; ZNS 89%, PGB 86%, LCM 97%) often at modest or moderate dosing (TPM 65%

≤200 mg, LEV 60% ≤1000 mg/day, ZNS 60% ≤100 mg/day, PGB 80% ≤300 mg/day, LCM 80% ≤200 mg/day). Overall, LCM was best tolerated (77% patients remaining on treatment) with PGB being worse tolerated (50% remaining on treatment).

**Conclusions:** Overall, the best tolerated AED produced the greater number of seizure-free patients usually as first or second add-on treatment often at moderate doses. These results suggest that these AEDs have not made a major impact on overall outcomes in this patient population.

## Poster Session: Epilepsy Surgery B Tuesday, 25 June 2013

P567

### TWO YEARS FOLLOW UP AFTER EPILEPSY SURGERY IN PATIENTS WITH A HISTORY OF PRESURGICAL PSYCHOSIS

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**Purpose:** Refractory temporal lobe epilepsy (RTLE) has been associated with a high incidence of psychotic disorders before and after epilepsy surgery. However there are many controversies in the literature; while some patients get better after surgery from their psychiatric condition, others develop de novo depression or psychosis. The aim of this study was to determine the psychiatric outcome after epilepsy surgery in patients with a previous history of psychoses according Axis I criteria of DSM IV.

**Methods:** Patients with RTLE and a positive history of psychoses were included in this study. A follow up during 2 years after surgery was determined. All patients underwent a complete clinical, electrophysiological, and image evaluation to determine surgical procedure. DMS IV Structural Interview for psychiatric disorders for Axis I and II in combination with Ictal classification for psychosis was used to determine psychiatric diagnoses before and after epilepsy surgery. Engel classification was used to determine the epilepsy outcome after surgery.

**Results:** During 2000–2010, 82 patients were admitted to the RMEC (Ramos Mejía Epilepsy Center) program for epilepsy surgery, and completed the psychiatric assessment protocol before surgery. From this population 13p/15% with RTLE had a positive history of psychoses (Axis I of DSM IV). Most common psychosis type before surgery was brief psychotic episode diagnosed in 8p/61.5%. During the first 2 years after surgery, 5 p/38.4% did not developed psychosis and improved from the previous psychiatric condition, 5 p/38.4% developed psychotic symptoms, similar to those presented previous to surgery, and 3p/23% developed other psychiatric condition after surgery (depression). Engel class I-II was determined in 9p/69%.

**Conclusions:** While some patients with a history of psychotic disorders get better from psychoses after epilepsy surgery, others continue having psychotic symptoms, or developed other psychiatric condition such as depression. More research in this area is needed.

P568

### CHANGES IN OPTIC RADIATION INTEGRITY AND VISUAL FIELDS AFTER THREE DIFFERENT TEMPORAL LOBE EPILEPSY SURGERIES

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**Purpose:** The visual field deficits (VFDs) after different approaches of temporal epilepsy surgery are well recognized respectively. But the degrees and visual pathway mechanisms of VFDs of the three approaches, namely transylvian selective amygdalohippocampectomy (Ts-SAH), transcortical selective amygdalohippocampectomy (Tc-SAH), and anterior temporal lobectomy (ATL), have not been compared in one cohort study.

**Method:** A prospective cohort study was conducted, involving the refractory mesial temporal lobe epilepsy patients. All patients underwent preoperative MRI with diffusion imaging at 3 T. With the use of a fiducial-based diffusion tensor tractography (DTT) tool (Slicer 4.2), the entire visual pathways and neighboring tracts were reconstructed within 3-dimensional brain models. All patients underwent preoperative visual fields assessment with Goldmann perimetry. The patients were divided into three groups, i.e. Ts-SAH, Tc-SAH and ATL, and underwent surgery respectively. The postoperative DTT visual pathway reconstruction and VFDs examination were performed 6 months after the surgery.

**Results:** Of 25 patients examined, eight underwent Ts-SAH, seven had Tc-SAH, and 10 had ATL. In the Ts-SAH group, four patients suffered VFDs ranging from 18% to 35% of the contralateral superior quadrant. In the Tc-SAH group, seven patients suffered VFDs ranging from 44% to 79% of the contralateral superior quadrant. In the ATL group, all 10 patients suffered VFDs ranging from 61% to 100% of the contralateral superior quadrant. The reconstructed visual pathways by DTT revealed the disconnections of Meyer's loops covered the superior and lateral wall of the temporal horn in different degrees among the three groups.

**Conclusion:** Ts-SAH in this cohort study was associated with better optic radiation protection and smaller VFD than Tc-SAH and ATL. The mechanism is due to Ts-SAH opening the temporal horn in the smallest extent and avoiding the most of the optic radiation fibers. DTT is a helpful tool for preoperative planning and approach assessment.

P569

### MESIAL TEMPORAL LOBE EPILEPSY AND THE INSULA: POSTSURGICAL EVALUATION

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**Purpose:** Mesial Temporal Lobe Epilepsy (MTLE) is the most frequent epilepsy and refractory to antiepileptic drugs. The anteromesial temporal lobectomy (AMTL) is the surgical technique of election. Even though, the curability could be only achieved in 1/3 of the patients, while in the last decade the involvement of the insular cortex have been proved in some cases. Thus, in this work it was wanted to know how the location of the presurgical symptomatogenic zone (SZ) could affects the postsurgical results.

**Method:** A prospective study was done during 2 years with 22 patients with MTLE whom had undergone to adjusted AMTL. All the collected presurgical data were analyzed, and for a better feedback about the total extraction or not of the Epileptogenic Zone (EZ) the patients were classified post surgically as Cured, Controlled and Uncontrolled.

**Results:** The mean postsurgical evolution time was 4.72 years (range 1–9 years). Only five patients (22.7%) remained Controlled and 17 (77.2%) Uncontrolled. When the epileptogenic network was limited to one cerebral hemisphere and the SZ corresponded with the mesial temporal lobe structures the patients remained Controlled. The Uncontrolled patients were those in which the SZ corresponded with the insular cortex (11 patients of 12, 50.0%), and those with no coincidence between the ictal onset zone (scalp electrodes) and the semiological laterality.

**Conclusion:** These results allow proposing the new Insular Mesial Temporal Lobe Epilepsy Syndrome unlike the true Mesial Temporal Lobe Epilepsy Syndrome, for a differentiated surgical treatment to guarantee the total extraction of the EZ.

#### P570

### EXPERIENCE AND CURRENT STATUS OF VAGUS NERVE STIMULATION THERAPY AT ONE INSTITUTION IN JAPAN

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**Rationale:** Vagus nerve stimulation (VNS) was ultimately approved in 2010 by the Japan Ministry of Health, Labor and Welfare after long-drawn-out expectation more than 10 years. The VNS Committee has been developed and running its business to certify physicians and surgeons to perform VNS therapy. Surgeons who are responsible for implantation must be a dual diplomate by the Japan Neurosurgical Society and the Japan Epilepsy Society. This is particularly the unique requirement as compared to the other countries. Now VNS is expanding all over Japan, even though its approval was far behind. This is a report from one of the leading hospitals in this country, which can provide VNS therapy.

**Methods:** Fifty-three patients underwent implantation of the VNS Therapy System™ from the approval through December 2012. Indications for VNS were multifocal epilepsy (38%), generalized epilepsy (28%), failed cranial surgery (26%), and other reasons (8%).

**Results:** Eight percent of patients became free from seizures. Thirty-five percent of them showed more than 50% seizure reduction. Less than 50% seizure reduction was 36%, and no change in terms of seizure frequency was 21%. All patients well tolerated this treatment and none of them asked discontinuance. Patients did not get any serious complications and surgical site infections in this series.

**Conclusions:** VNS is safe as previously reported, and demonstrated the same effectiveness for patients with intractable epilepsy in Japan. More epileptologists need to join these programs providing VNS therapy, because we believe VNS will be able to prove a great boon to epilepsy patients.

#### P571

### SEIZURE OUTCOME AND COMPLICATIONS AFTER RESECTIVE EPILEPSY SURGERY IN PATIENTS OVER 50 YEARS IN SWEDEN 1990–2009

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**Purpose:** Most epilepsy surgery candidates are young adults. Patients over 50 years only constitute around 7–8% in published series and reports have yielded somewhat varying seizure outcomes and complication rates. The aim of this study was to analyse seizure outcome and complications in a large population based series.

**Method:** We analysed prospectively collected data from the Swedish National Epilepsy Register for 1990–2009 for all patients who were 50 years or more at surgery and had completed 2-year follow-up. Seizure outcome and complication rates were compared with data from all adults 19–49 years who were operated during the period. A minor complication is defined as one which has fully resolved within 3 months, while a major complication persists and affects daily life.

**Results:** Eight hundred and twenty-two patients underwent resective epilepsy surgery 1990–2009 and had 2 years follow-up, 263/822 were children (<19 years). Of the 559 adults 68 were ≥50 years at surgery, constituting 12% of the adult series. The proportion of seizure-free patients at 2-year follow-up did not differ between adults who were above (62%) or below 50 years (61%), neither did the occurrence of major complications (3% both in the group of ≥50 years and in the 19–49 years group).

**Conclusion:** In the Swedish epilepsy surgery series patients over 50 years at surgery constitute 12% of all adults. Seizure outcome was as good for the elder as for the younger adults, and there was no difference in the occurrence of major complications. This constitutes important information in the presurgical counselling process.

#### P572

### LONG TERM FOLLOW-UP AFTER CALLOSOTOMY

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**Purpose:** Callosotomy is a palliative surgical procedure for controlling medically intractable seizures. The most common indication is traumatizing drop attacks (atonic or tonic). Previous long term follow-ups after surgery have showed conflicting results. The aim of this study was to analyze the long-term outcome of callosotomies with regard to seizure types and frequencies, antiepileptic drug treatment and psychosocial situation.

**Method:** This is a longitudinal observational study based on data from the prospective Swedish National Epilepsy Surgery Register. All 32 patients who had undergone callosotomy in Sweden between 1995 and 2007. The patients were followed-up 2 and 5 or 10 years after surgery. Data on these patients' socio-demographic situation, seizure types and frequency, associated impairments and antiepileptic drug use was analyzed.

**Results:** The median total number of seizures per patient and month was reduced from 218 before surgery to 127 2 years after surgery and 90 at the long term follow-up (5 or 10 years). Out of the 19 patients with drop attacks, ten were free from such attacks at the long term follow-up. Four of the remaining nine patients had a reduction by more than 75%.

**Conclusion:** The present study shows that callosotomy reduces seizure frequency effectively and sustainably over the years. Most improvement was seen in drop attacks.

Previous studies have shown that callosotomy at an early age leads to an improvement in daily function and family satisfaction as well as overall quality of life. This, combined with the improvement concerning seizures over time shown in this study, suggests that surgery at an early age may be preferable in children with intractable epilepsy and traumatizing drop attacks.

#### P573

### EFFECTIVENESS AND TOLERABILITY OF VAGAL NERVE STIMULATION WITH INTRACTABLE EPILEPSY: PRACTICAL EXPERIENCE AT CLEMENTINO FRAGA FILHO UNIVERSITY HOSPITAL IN RIO DE JANEIRO

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**Purpose:** Stimulation of peripheral cranial nerves has been shown to exert anticonvulsant effects. The aim of this study is to describe the long-term outcome of vagus nerve stimulation (VNS) in patients with pharmacoresistant epilepsy treated at the Clementino Fraga Filho University Hospital in Rio de Janeiro.

**Method:** Descriptive retrospectively analyze data of eight patients (five male) with mean age of 23.5 years with medically refractory epilepsy.

**Results:** The median age at the time of VNS device implantation was 23.3 years. Median age at onset of epilepsy was 17.6 months old and median duration of epilepsy was 20.5 years. Seventy-five percent had focal seizures. The mean seizure reduction was 26% at 3 months, 30% at 6 months and 48.5% at 1 year. There was no difference in seizure control between generalized and focal epilepsy. Four (50%) patients complained of hoarseness and coughing during when the stimulation parameters were increased that disappeared shorter after stimulation adjustments. We also observed improvement in attention and behavior of the patients independently of seizure reduction.

**Conclusion:** The reduction in seizure severity and frequency and enhancement of behavior and attention had a positive effect in the quality of life. There was no difference in reduction of seizures in focal and generalized epilepsies (Cersósimo et al. *Epileptic Disord* 2011; 13 (4): 382–8). The response rate was higher in patients treated for more than 3 months suggesting a cumulative effect of stimulation as describe by Bao et al. (*Chin Med J* 2011; 124(24):4184–4188). VNS is an important tool for refractory epilepsy.

#### P574

##### THE COMBINATION OF STEREOTACTIC EEG AND STRIP ELECTRODE PLACEMENT

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Stereotactic electroencephalography (SEEG) has become one of the standard invasive procedures for exploring epileptic foci, especially deeper epileptic foci. This methodology is beneficial for three-dimensional mapping of ictal onset and spread; however, this technique can only demonstrate points of the brain and is limited by the location or number of implanted electrodes. This spatial limitation of recordings may cause difficulties in interpretation. The authors describe four cases in which the combined technique of SEEG and strip electrode placement was useful. In Case 1, two different seizure patterns were recorded in the right hemisphere during SEEG evaluation. Then, one strip electrode was inserted in the right basal temporo-occipital area in order to rule out the possibility that these two patterns reflected different seizure propagation patterns from the same basal temporal onset. This additional strip electrode revealed that the patient had multifocal areas of ictal onset zones. The strip electrode was inserted for sensorimotor mapping in Case 2 and for language mapping in Case 3 and 4. In these patients, the strip electrodes provided additional information regarding the following aspects. (i) Precise description of seizure spread, (ii) Identification of seizure onset, (iii) Functional cortical mapping. This technique compensates for the disadvantages of SEEG and provides better information.

#### P575

##### LASER ABLATION SURGERY FOR MESIAL TEMPORAL, LATERAL TEMPORAL, AND EXTRA-TEMPORAL FOCI WITH AND WITHOUT LESION; SUCCESSFUL INTEGRATION OF MSI, fMRI, AND EEG

##### AND BRAINLAB TECHNOLOGY FOR NON-INVASIVE LOCALIZATION AND DESTRUCTION OF EPILEPTIC FOCI USING STEREOTACTIC LASER ABLATION (SLA)

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**Purpose:** To present a less invasive technique for epilepsy surgery treatment combining surface EEG, MSI (magnetic source imaging) and fMRI combined with Brainlab localization to enable minimally invasive MRI guided stereotactic laser ablation (SLA) of epileptogenic foci.

**Method:** Six children and 4-adults with medically refractory focal epilepsy were evaluated with video EEG, 3-Tesla MRI, fMRI, MSI (9-patients) and PET (1-patient). Two adults had mesial temporal sclerosis, three had frontal foci, one had superior non-dominant right superior temporal gyrus focus, one had sub-Wernickes left superior-temporal gyrus, one had deep left cingulate gyrus focus near the posterior body of the corpus callosum, and one each of right and left occipital/temporal/parietal foci.

Three-patients required 2-separate laser probes to be placed, and 1-patient required 3-laser probes. Ten-patients had SLA (Visualase, Inc.) with frameless navigation (Brainlab, Inc.). All had intraoperative EEG monitoring in MRI using plastic electrodes (Ives) placed over ablation region on the cranial surface before MRI guidance of laser ablation, thereby showing pre-ablation and post-ablation spike data. Pre-procedure MSI scans were performed in all patients: 9-patients via UCSF Biomagnetic Imaging Center, CTF Systems, and 1-patient via PET scan, no MSI. Preoperative EEG monitoring and fMRI was done on all patients.

**Results:** All patients showed resolution (8) or diminished number (2) of pre-ablation spikes on intra-procedure EEG taken immediately post-ablation. Seven-patients with single or multiple probe SLA were pain-free, eating, and ambulatory within 6–8 h post-ablation and discharged within 24-h. Three-patients were discharged on post-surgery day 2.

To date, 2/3 frontal, both mesial temporal, both occipital, 1-cingulate, and 1/2 lateral temporal laser ablations remain seizure free. Only 1-mesial temporal patient had a superior quadrantsia. Nine of ten participants have no known permanent undesirable sequelae. Improved EEG and cognitive function was noted after full post-operative recovery, correlating with reduced seizures.

#### P576

##### ACCURACY OF FRAMELESS NAVIGATION FOR DEPTH ELECTRODE IMPLANTATION IN sEEG PATIENTS – TECHNICAL NOTE

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**Purpose:** Frame-based orthogonal stereotactic implantation is the prevalent technique for depth electrode placement in epilepsy surgery candidates. This technique is time consuming and mostly restricted to orthogonal directions only. Robot-assisted oblique implantation affording assumed good accuracy is a very expensive alternative technique. We now report on a technique using an image guided device for depth

electrode positioning. We outline its benefits in pre-planning time, freedom of choice regarding insertion and accuracy of placement.

**Method:** Preplanning of the trajectories was done 1 week before surgery, using strict scan protocols, including MRA data. We adapted the Brainlab VarioGuide system, standardized and protocolized its use, for our specific purpose. We evaluated the accuracy of depth electrode placement in our patients since January 2012, by measuring the distance from planned and true cranial entry point location and targeted ROI. Standardized postoperative CT scans of the head were fused for these measurements with pre-planning CT/MRI imaging containing the planned electrode trajectories.

**Results:** In seven patients undergoing SEEG registration, 89 depth electrodes were planned. The mean OR-time of implantation per electrode was 23.4 min. The majority of the trajectories was oblique. The median  $\pm$  standard deviation entry-entry deviation was  $3.3 \pm 1.4$  mm, the target-target deviation was  $3.7 \pm 1.8$  mm and a depth deviation of  $1.1 \pm 2.3$  mm. The procedure and subsequent SEEG recording was successful in all patients without complications.

**Conclusion:** Our technique is efficient in terms of implantation time, ROI target accuracy and reproducibility of depth electrode placement.

#### P577

##### OPTION GRID' DECISION-SUPPORT INTERVENTION FOR PATIENTS CONSIDERING EPILEPSY SURGERY

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**Purpose:** Patients considering epilepsy surgery face a difficult dilemma: whether to proceed with an intervention that may cure their epilepsy (but may not, and with measurable risk), or to continue without surgery whilst still bearing the risks of seizures, including of death. We designed a decision support intervention, an "option grid", to aid patients' shared decision making.

**Method:** We identified relevant options and answers to frequently-asked questions (FAQs) and developed an evidence document from a literature review. We refined the "option grid" through consultation with local epilepsy clinicians and a patient group.

**Results:** We identified patients' three relevant options as epilepsy surgery, continued current medication without surgery, or new medication without surgery. We chose five FAQs, broadly addressing seizure control, risks (including morbidity and mortality) and lifestyle (including driving). We wrote answers to these FAQs in an Option Grid with an accompanying evidence document.

**Conclusion:** The option grid and evidence document should help patients, with their clinicians to decide their best treatment option regarding epilepsy surgery.

#### P578

##### SURGICAL TREATMENT OF PHARMACORESISTANT EPILEPSY IN THAILAND REDUCES ANTICONVULSANT RELATED TREATMENT COST AFTER TWO YEARS

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**Purpose:** To evaluate antiepileptic (AED)-related treatment costs in patients with pharmacoresistant epilepsy (PRE) before and after evaluation for epilepsy surgery in Thailand.

**Method:** We compared 19 adults who underwent surgery for PRE to 21 adults with PRE who continued on medical treatment. Use and cost of AEDs were evaluated in the 2 years before and after surgery/presurgical evaluation.

**Results:** The surgical and medical groups were similar with regards to gender, age, seizure frequency, and seizure origin. Prior to surgery/evaluation, there were no differences in number or cost of AEDs. In both groups, AED cost increased significantly in the 12 months prior to surgery/evaluation, more so in the surgical group (34.1 vs 23.5%). Following surgery/evaluation, AED cost decreased in the surgical group by 19.1% (1,221 Bht/41 \$), but continued to increase in the medical group by 20.8% (934 Bht/31\$) ( $p = 0.00$ ). This difference became evident in the first 6 months and then largely stabilized. Mean total number of AED at 6 months after surgery/evaluation (2.57 vs 2.11,  $p = 0.037$ ) and number of standard AEDs used at surgery/evaluation (1.57 vs 1.05,  $p = 0.028$ ) were significantly higher in medical group. There were an increase of standard AEDs used in surgical group at 6 months prior to surgery/evaluation (1.53 vs 1.95,  $p = 0.007$ ) and an increase of new AEDs used in medical group at 6 months after surgery/ presurgical evaluation (1.05 vs 1.29,  $p = 0.021$ ).

**Conclusion:** Presurgical evaluation is associated with an increase in AEDs costs. Surgery results in reduced AED costs, while these continue to rise in patients on medical treatment alone.

#### P579

##### SEIZURE OUTCOMES AFTER BITEMPORAL LOBE EPILEPSY SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Purpose:** The role of surgery in the management of bitemporal lobe epilepsy (BTE) remains controversial. BTE is defined as clinical seizures originating independently from each temporal lobe, as documented by ictal intracranial electroencephalography (EEG). Our systematic review is to provide evidence-based quantitative summary estimates of seizure outcomes and predictors of response after resection for intractable BTE.

**Method:** An exhaustive literature search identified articles published since 1980, describing seizure outcomes and predictors of response after resection for intractable BTE. Only studies of at least five patients examining seizure freedom after BTE surgery with postoperative follow-up duration of at least 12 months were included. Two reviewers independently assessed study eligibility and extracted the data. Disagreements were resolved through discussion. Random effects meta-analyses were used after assessing the dataset for heterogeneity.

**Results:** Seven retrospective cohort studies fulfilled eligibility criteria and described outcomes in 86 patients with BTE, the overall rate of post-operative seizure freedom (Engel Class I outcome) was 52.3%. Abnormal preoperative MRI was Significant predictor of seizure freedom (odds ratio [OR] 7.54, 95% CI 1.24–46.01). However, Ictal seizure onset laterality >80% (OR 2.94, 95% CI 0.97–8.96), IAP (intracarotid amobarbital procedure) adequate contralateral memory (OR 1.43, 95% CI 0.03–64.28), age (OR -3.95, 95% CI -11.28–3.38) and duration (OR 4.85, 95% CI 0.10–9.6) were not significant predictors.

**Conclusion:** Based on the currently available evidence, only abnormal preoperative MRI is prognostic factor of seizure freedom in BTE surgery. In addition, there is a trend for correlation between seizure laterality >80% on the side of surgery and seizure freedom. Well-designed cohort studies with large sample size are needed.

## P580

### GAMMA KNIFE RADIOSURGERY FOR TREATMENT OF FAILED ANTERIOR TEMPORAL LOBECTOMY IN MESIAL TEMPORAL LOBE EPILEPSY WITH HIPPOCAMAL SCLEROSIS (MTLE-HS)

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**Purpose:** Gamma knife radiosurgery (GKRS) has proved efficacious in the treatment to drug-resistant mesial temporal lobe epilepsy (MTLE) comparable to conventional resective surgery. Furthermore it can be effective as alternative treatment to surgical reoperation after failed surgery. The purpose of this study was to investigate the efficacy of GKRS as second treatment in unilateral MTLE patients with the incomplete seizure control after anterior temporal lobectomy (ATL).

**Method:** We searched our database in the Epilepsy Center of Asan Medical Center from 1995 to 2009. The target of GKRS included the remnant tissue or adjacent region of previously performed ATL. A marginal dose of 24–25 Gy to the 50% isodose line was administered in all patients. All patients followed up for at least 2 years and post-GKRS outcome for seizures was classified (Engel's modified criteria).

**Results:** We found 12 cases who performed GKRS after ATL (median interval between two procedures; 70.5 months [range 16–169 months]). Pathologic finding of ATL showed hippocampal sclerosis (n = 11) and other combined microscopic abnormality (n = 6). Mean post-GKRS follow up period was 68.2 months (range 42–100 months). Six patients reached to seizure freedom at least two consecutive years finally (IA, IC and ID, n = 6). Among them, three patients showed immediate GKRS response, and never experienced a seizure after GKRS (IA). Two patients showed delayed and incomplete GKRS effect (II and IIIb; 1 ≤ seizure freedom <2 year at final) and remained four patients had no demonstrable reduction in seizures after GKRS (class IV).

**Conclusion:** The main result of this study is that successful outcome obtained after GKRS in half of patients who failed ATL after several years of follow up. These results demonstrate that GKRS is reasonable therapeutic option and alternative to invasive reoperation for patients with incomplete seizure control after ATL with MTLE-HS.

## P581

### VAGUS NERVE STIMULATION IN A PATIENT WITH PROGRESSIVE MYOCLONUS EPILEPSY: A SECOND REPORTED CASE IN THE WORLD

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**Background:** Progressive myoclonus epilepsies (PME) are rare inherited neurodegenerative diseases with great clinical and genetic differences, as well as poor prognosis. The syndrome includes myoclonic seizures and generalized tonic-clonic seizures (GTCS) that are often drug resistant, as well as progressive neurological decline involving cerebellar, pyramidal, extrapyramidal symptoms and dementia. So, vagus nerve stimulation (VNS) is a standard treatment for drug resistant epilepsy, it is surprising that we found only one single case report of VNS implantation in PME – Unverricht-Lundborg disease, 12 years ago.

**Case Presentation:** We report another case of the utility of VNS for PME in a 19-year-old Caucasian male patient. The clinical diagnosis of our patient is probably Lafory body disease. The patient had progressive myoclonus, GTCS, cerebellar and extrapyramidal symptomatology, as well as dementia. After VNS implantation, in the 10-month follow-up period, patient's clinical condition and quality of life improved. There was significant regression of myoclonus, moderate regression of cerebellar symptomatology, and following VNS implantation patient did not experience any more GTCS.

**Conclusion:** VNS therapy may be considered a treatment option for progressive myoclonus epilepsy. Further clinical studies are needed to confirm the clinical effects produced by chronic vagus stimulation in patients with progressive myoclonus epilepsies.

## P582

### SELF-PERCEIVED CHANGES IN PSYCHOSOCIAL FUNCTIONING AND QUALITY OF LIFE IN CHILDREN AFTER RESECTIVE EPILEPSY SURGERY, A LONG-TERM FOLLOW-UP

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**Purpose:** In this follow-up we present long-term outcome (5–21 years), of changes in self-perceived psychosocial functioning and Quality of life (QOL) after resective epilepsy surgery in children at the University Hospital in Lund, Sweden from 1991 to 2007.

**Method:** 44/47 children (two were dead, one had profound mental retardation at follow-up), with a median age at surgery of 8 years (range 0.5–18.7 years) were assessed by a semi-structured interview. Self perceived changes in different aspects of psychosocial functioning were tapped by asking the patients to compare their functioning before/after surgery. Their occupation was described. QOL was assessed by a VAS-scale (1–10). As previously reported, twenty-three children achieved seizure-freedom. Cognitive functional level was preserved, the majority of patients, 34 (76%) followed their expected intellectual trajectory. Those who became seizure-free significantly improved their cognitive processing speed.

**Results:** Regarding aspects of psychosocial functioning, 34% scored better/much better in learning capacity, 16% in short time memory, 14% in long time memory, 27% in concentration, 29% in endurance, 30% in ability to maintain relationship. 11/44 were employed, four unemployed, four had sheltered work, seven went to ordinary schools and 18 went to special schools. Among the 44 patients, 34 scored >5 at the QOL-scale; in the seizure free group 20/23.

**Conclusion:** In this long-term follow-up of 44 children after epilepsy surgery, there was a clinically meaningful change in psychosocial functions. Half of the patients were able to take part in the labor market/ordinary school. Higher QOL was associated with seizure freedom 20/23.

## P583

### EPILEPSY SURGICAL GRADING SCALE (ESGS): UTILIZATION IN EPILEPSY SURGERY COHORTS AT TWO CENTRES IN DIFFERENT COUNTRIES

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**Purpose:** The Epilepsy Surgery Grading Scale (ESGS) was designed to be used by referring neurologists to help predict seizure freedom in patients with treatment-resistant epilepsy, prior to work-up for epilepsy surgery. ESGS uses interictal EEG, MRI, seizure semiology, IQ to stratify patients. Here, we examined the utility of ESGS in a different setting. We applied the scale to cohorts from two epilepsy surgery centres in different countries, comparing ESGS grades prior to resective surgery with post-operative outcome. Seizure freedom was expected to be highest in ESGS Grade 1 and lowest in Grade 3.

**Method:** Inclusion criteria: age  $\geq 18$ , focal epilepsy  $\geq 2$  years, failed  $\geq 1$  medication,  $\geq 1$  seizure 3 months pre-admission. ESGS used in patient monitoring results. Post-operative outcome data had minimum 1 year follow-up.

**Results:** N = 133 at New York University Langone Medical Center, USA and N = 94 at Austin Health, Australia were included. At NYU Medical Center, 78.6% of n = 56 ESGS Grade 1 patients, 65.1% of n = 43 Grade 2, 50.0% of n = 34 Grade 3 patients became seizure-free post-surgery. Grades 1 and 3 were significantly different (p = 0.01). At Austin Health, 72.7% of n = 44 Grade 1, 48.6% of n = 35 Grade 2, 60% of n = 15 Grade 3 patients became seizure-free. Grades 1 and 2 differed significantly (p = 0.04).

**Conclusion:** The ESGS robustly stratifies patients with a higher chance of seizure freedom following epilepsy surgery (Grade 1) from those with a lower chance in centres from different countries and health systems. Both centres showed less differentiation in outcome between Grades 2 and 3 patients.

#### P584

##### EPILEPSY SURGERY IN PATIENTS WITH VASCULAR DESTRUCTIVE LESIONS AND CONGENITAL HEMIPARESIS

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**Purpose:** Vascular destructive lesions associated with congenital hemiparesis (VCH) may be associated with significant morbidity. Epilepsy occurs in 34–60% of patients with CH and is intractable in up to 7%. In this setting, epilepsy surgery is often a consideration because it is potentially curative.

**Method:** The present study examines a surgical series of 12 patients with VCH and intractable epilepsy who underwent neurosurgical resection between March 2002 and July 2010. All of these patients were ambulant and had varying degrees of motor preservation in the paretic hand. The group ranged in age from 5 to 38 years (mean 20 years) at the time of surgery and all had high seizures frequency (mean 20 week). They had noninvasive video-EEG monitoring and MRI. Furthermore, pre- and post-operative fMRI were performed in some patients. Surgical procedures included variable degrees of corticectomy guided by acute electrocorticography (ECoG) and intraoperative cortical stimulation. In some patients, resection included remaining motor cortical areas whose functionality was suggested by fMRI activation and confirmed upon electrical cortical stimulation. Patients were followed for 30–130 months (mean 66 months).

**Results:** Four were completely seizure free, seven had a >90% seizure reduction, and two showed >50% improvement. Motor function in the paretic fingers remained unchanged following surgery in five patients, improved in four and was worse in 2. No patient worsened ambulation.

**Conclusion:** Epilepsy surgery in VCH patients is a safe and effective procedure and significant seizure control can be obtained with focal resections, without the need to resort to complete disconnection. Hemispherectomy should be reserved for patients with very large destructive lesions and very little to be preserved in the affected hemisphere.

#### P585

##### DOES MULTIPLE SUBPIAL TRANSECTION INFLUENCE LONGER TERM OUTCOME IN LANDAU KLEFFNER SYNDROME

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Landau-Kleffner Syndrome (LKS) is a rare paediatric epilepsy characterised by a language-led regression. A form of surgery known as multiple subpial transection (MST) is sometimes considered in cases of intractable LKS. Previous small-scale studies have reported benefits of MST when comparing pre- and post-surgery language measures in patients with LKS. The current study employs a non-surgery group to explore the outcome following MST compared to the natural history of LKS. The surgery group (N = 12) comprised children and young people who underwent MST for intractable LKS. The non-surgery comparison group (N = 21) comprised those with intractable LKS who were considered for MST but did not undergo the procedure. Outcomes were assessed via clinical note review, direct assessment, telephone interviews with parents and parent-report questionnaire measures of behaviour, quality of life, adaptive functioning and communication. There was a wide range of outcomes within each group. At a group level, based on preliminary findings, differences did not tend to reach statistical significance. There were subtle differences with some indication of a positive impact of MST on behavioural outcome. In conclusion, this study does not find evidence for substantial benefits following MST in children with LKS when compared to a non-surgery comparison group; though limitations of the study do need to be considered. It is suggested that MST as an intervention for LKS should continue to be considered an experimental procedure.

P586

### RESECTIVE SURGERY FOR PEDIATRIC INTRACTABLE EPILEPSY ASSOCIATED WITH CORTICAL DYSPLASIA USING 3 TESLA MRI AND MULTIMODAL FUNCTIONAL NEUROIMAGING STUDIES

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**Purpose:** We assess the utility of 3 tesla MRI coupled with multimodal functional neuroimaging studies for localization of the epileptogenic zone in pediatric epilepsy surgery with cortical dysplasia.

**Method:** Fifteen children (3–40 months, mean 13.5) with intractable epilepsy who had undergone epilepsy surgery between 2010 and 2012 were included. We retrospectively analyzed the correlation between surgical outcome and the convergence of findings in multimodal functional neuroimaging studies including fluoroxy-glucose positron emission tomography (FDG-PET), subtraction ictal single photon emission tomography coregistered to MRI (SISCOM), and magnetoencephalography (MEG) to structural lesion on 3 Tesla MRI.

**Results:** Nine patients with findings of all functional neuroimaging studies concordant with a lesion on MRI achieved seizure free postoperatively. Out of six patients with divergent findings between MRI and functional neuroimaging studies, three patients exhibited seizure recurrence. Two patients underwent additional resection. Of these two, one showed scattered MEG spike source around the MRI lesion; the other had metabolic abnormality on FDG-PET involved a larger area beyond the MRI lesion. Cortical dysplasia was also observed in specimens from second operations.

**Conclusion:** Good concordance between structural lesion on 3T MRI and multimodal functional neuroimaging studies suggests favorable seizure outcome in resective surgery for pediatric epilepsy with cortical dysplasia. In some cases, divergent findings may show a larger area of dysplastic cortex extending beyond the MRI lesion.

P587

### EPILEPSY SURGERY IN KFSHRC, RIYADH, SAUDI ARABIA

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**Purpose:** To review the post-operative seizure outcome of patients who underwent surgery for epilepsy in our center.

**Method:** A descriptive retrospective study for patients operated between 1998 and 2012 was conducted using data from the Epilepsy registry in the epilepsy program at KFSHRC, Riyadh.

**Results:** Five hundred and two of pediatric and adults patients were surgically treated for refractory epilepsy. Two hundred and ninety-five Temporal lobe lobotomy and lesionectomy were performed. Fifty-three Frontal lobe surgeries, 16 parietal and occipital lobe surgeries, 64 Functional Hemispherectomy, 26 Two lobes surgeries, 10 Corpus callosotomy, three multiple subpial transaction and one Hypothalamus hamartoma resection.

MRI brain results were 199 mesiotemporal sclerosis/atrophy, 77 primary CNS tumors, 62 Cerebral Cortical Dysgenesis, 38 normal, 36 atrophy, 29 encephalomalacia, 21 cyst, 15 Vascular malformation, seven others.

The 12, 36 and 60 months epilepsy surgery outcome for temporal lobotomy and lesionectomy (Engel class one) is 79.6%, 74.2%, 67.6%. The 12 and 36 months epilepsy surgery outcome for frontal lobe lobotomy and lesionectomy (Engel class one) is 61.8% and 52%.

The 12 and 36 months epilepsy surgery outcome for parietal and occipital lobotomy and lesionectomy (Engel class one) is 67.2%, 66.6%. The 12 and 36 months epilepsy surgery outcome for two lobes surgery (Engel class one) is 65% and 50%. The 12 and 36 months epilepsy surgery outcome for hemispherectomy (Engel class one) is 64% and 63%.

**Conclusion:** Seizure freedom for Saudi epilepsy surgery patients is comparable to other retrospective studies.

P588

### SURGICAL OUTCOME AND PREDICTORS OF TEMPORAL LOBE EPILEPSY SURGERY IN KFSHRC, RIYADH, SAUDI ARABIA

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**Purpose:** To present the epilepsy outcome from epilepsy surgery and to address the predictors that may impact outcome

**Method:** The data was extracted from epilepsy registry in our epilepsy program. 12, 36 and 60 months epilepsy outcome was studied against several predictors' then logistic regression analysis was applied to identify the significant predictors.

**Results:** Two hundred and ninety-five temporal lobe epilepsy surgeries were performed between 1998 and 2012. One hundred and seventy-two patients (58%) were seizure free without aura while 17 (5.7%) had aura and 46 (15.5%) had 1–3 seizures per year, with total of 79.6% Engel class one outcome. At 36 months, 195 patients had 74.2% Engel class 1; divided in 105 (53%) seizure free, 13 (6.6%) had aura and 27 (13.8%) 1–3 seizure per year. At 60 months, 47% were seizure free, 9% had only aura and 11% of 100 patients followed up with 67% Engel Class 1 outcome.

The regression analysis was insignificant for any of the variables tested including febrile convulsion, family history, CNS trauma, CNS infection, histopathology, MRI or PET findings, inter-ictal EEG findings, duration of the epilepsy and history of mental retardation.

**Conclusion:** Temporal lobe epilepsy surgery has rewarding outcome. No predictor can be identified to show direct impact on the epilepsy surgery outcome.

P589

### EPILEPSY SURGERY OUTCOMES IN CHILDREN WITH TUBEROUS SCLEROSIS

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**Purpose:** The aim of this study is to evaluate the surgical outcome of epilepsy surgery in Tuberous sclerosis (TSC) children with medically intractable seizures.

**Method:** We have retrospectively reviewed 19 patients with TSC who underwent epilepsy surgery. Preoperative medical data and the surgical outcome of the patients were collected and analyzed.

**Results:** The age of the patients at time of epilepsy surgery was between 1.1 and 13.9 years (mean: 8.0 years). The mean age at which seizure

onset was 11 months old. Eight patients had infantile spasms and one of them evolved to Lennox-Gastaut syndrome. At postoperative follow-up of average 23.5 months from surgery fourteen patients (73%) showed favorable outcomes (Engel Class I and II). Five of six single tubectomy patients, four of five multiple tubectomy patients showed favorable surgical outcomes. One patient performed functional hemispherotomy due to unilateral diffuse cortical tubers, she had seizure free after operation. In three children, re-operation was carried out. There was one mortality associated with hydrocephalus.

**Conclusion:** These results suggest that epilepsy surgery can improve medically intractable seizures even in the patients with multiple tubers.

#### P590

### LONG TERM OUTCOME IN PERSONS WITH DRUG REFRACTORY EPILEPSY AFTER RESECTION IN UNILATERAL MESIAL TEMPORAL SCLEROSIS

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**Purpose:** Persons with DRE due to MTS have a good seizure outcome after surgery, however their prime concern often remains a medication free life.

**Method:** Prospective study of 284 persons with MTS followed up from 1995 after surgery. The presurgical evaluation protocol included a detailed clinical history, VEEG, interictal EEG, MRI epilepsy protocol, neuropsychological assessments, QOL assesment and fMRI language in dominant hemisphere lesions. In persons where VEEG data was inconclusive or bilateral or contralateral additional tests like PET, ictal interictal SPECTS (SISCOS) was done. All were discussed in the epilepsy surgery case conference. The surgical treatment was anterior temporal lobectomy with tailored hippocampal resections. Postoperative followup was done at 3, 6, 12 months and then six montly for at least 6 years so each patient had a 5 year followup or more (some telephonically). Seizure outcome was recorded by Engel scoring, postoperative QOL scores, neuropsychology scores and age appropriate activity was recorded along with seizure freedom. The protocol followed for AED withdrawal was 1 year following surgery with EEG if EEG was abnormal but patient seizure free medications were reduced gradually from 3 to 2 to 1. If EEG persisted to be abnormal medication was not withdrawn. If EEG was normal and patient seizure free medication was again reduced and withdrawn completely only if EEG was normal at the end of each AED tapering. Some patients decided not to stop and remain on a minimum dose of 1 AED.

**Results:** A mean 7.8 years follow-up post-surgical period 75% were free of disabling seizures (Engel I outcome). At 10.5 years follow-up, 70% patients had similar results. There was a significant improvement in QOL scores and AAA. ( $p < 0.0022$ ).

**Conclusion:** Long term follow up data for MTS are promising with very good seizure outcomes if the medication withdrawal protocols are tailored.

#### P591

### ARE STIMULATION-EVOKED SEIZURES DURING CORTICAL STIMULATION MAPPING DETRIMENTAL TO POSTOPERATIVE LANGUAGE FUNCTION?

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**Purpose:** Electrical cortical stimulation mapping (ESM) is used to identify functional cortex before surgery, with the goal of preserving function postoperatively. Seizures occur frequently during ESM, but their potential effect on functional outcome is unclear. We sought to determine whether stimulation-evoked seizures are associated with postoperative declines in language function.

**Methods:** Clinical documentation was reviewed for 27 patients with refractory focal epilepsy who underwent subdural electrode implantation, ESM, and surgical intervention at Columbia University between 1997 and 2010. Patients were included if they completed the Boston Naming Test (BNT), Auditory Naming Test (ANT), Visual Naming Test (VNT), and WAIS-IV Vocabulary and Verbal IQ subtests pre- and postoperatively. Test scores were compared between patients who had stimulation-evoked seizures and those who did not using repeated measures (group x time) multivariate ANOVA.

**Results:** Ten patients (37%) had stimulation-evoked seizures. These patients demonstrated no significant declines postoperatively (BNT  $p = 0.82$ , ANT  $p = 0.46$ , VNT  $p = 0.80$ , Vocabulary  $p = 0.94$ , Verbal IQ  $p = 0.33$ ). Five patients (18.5%) had seizures that resulted in cessation of mapping. These patients also demonstrated no significant declines (BNT  $p = 0.07$ , ANT  $p = 0.50$ , VNT  $p = 0.57$ , Vocabulary  $p = 0.54$ , Verbal IQ  $p = 0.75$ ).

**Conclusion:** Stimulation-evoked seizures, even when disruptive to ESM, are not associated with diminished language function following epilepsy surgery.

#### P592

### CLINICAL VALIDATION OF AN ONLINE TOOL TO DETERMINE APPROPRIATENESS FOR AN EPILEPSY SURGERY EVALUATION

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**Purpose:** There is still evidence of underutilization of referrals for epilepsy surgery evaluation. To improve this situation, Jette N et al. (Neurology 2012; 79:1084-1093) developed an online tool to determine appropriateness for an epilepsy surgery evaluation. This study aims to evaluate the clinical validity of this tool.

**Method:** All adult outpatients seen in a regularly scheduled epilepsy clinic in the 4th quarter of 2012 were included ( $n = 203$ ). Clinical decision-making was blind to the results of the online tool, current or previous referring to a monitoring unit was coded. Following the consultation, the online tool ([www.epilepsycases.com](http://www.epilepsycases.com)) was used to determine a patient's appropriateness for an epilepsy surgery evaluation by answering eight multiple-choice questions.

**Results:** Thirty-five patients with missing data, generalized seizures, or previous surgery were excluded. 67.5% of the remaining patients were appropriate, 16.6% were uncertain, and 16.0% inappropriate for a surgical evaluation. In 43.9% of the appropriate cases, epilepsy surgery evaluations were recommended by board certified neurologists. In a second analysis, patients with clinically assumable diffuse or global brain damage were excluded ( $n = 49$ ). In 64.9% of the appropriate cases, epilepsy surgery evaluations were recommended. The association between the rating and the clinical decision was highly significant (Chi-Square=22.63,  $p < 0.001$ ). Reasons for mismatch included: favorable seizure frequency, diffuse or complex malformation, psychiatric comorbidity, age above 60 years.

**Conclusion:** The usability of the tool is high and the results are promising. However, there is considerable mismatch between the expert opinions and the tool. One reason for the mismatch could be that the

seizure-frequency item is only loosely related to a clinical rating of burden of epilepsy. Also the score is confounded by the severity of epilepsy or the underlying brain damage, the latter frequently precluding epilepsy surgery.

### P593

#### TIME TO STOP AEDS IN CHILDREN FOLLOWING SURGERY: IS A TRIAL FEASIBLE?

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**Purpose:** There is no consensus about timing of AED withdrawal after pediatric epilepsy surgery. Our previous retrospective study of 766 children suggested that early withdrawal does not affect long-term seizure outcome, unmasks incomplete surgical success sooner, and prevents unnecessary AED use in many. We aim to demonstrate cognitive benefits and confirm safety of early AED discontinuation.

**Methods:** A multicenter randomized trial is needed, with attention as primary and seizure outcome as secondary outcome measure. To reveal significant benefits of early withdrawal 75 children are required for each treatment arm. Important issues to deal with are identification of patients in whom early withdrawal could be unsafe, and ethical concerns with either early or late withdrawal regimens.

**Results:** The "TimeToStop" trial will be an unblinded randomized European trial comparing early (start reduction at 4 m, complete discontinuation <12 m postoperatively) with late withdrawal (start at 12 m, complete <20 m). To be included, children must be able to perform the Connors Continuous Performance test, and doctors and parents must agree with randomization into either arm. Exclusion criteria are previously identified risk factors for poor seizure outcome. Cognitive outcome will be measured after 1 year (one group on-, one off-AEDs) and 2 years (both groups off-AEDs).

**Conclusion:** Safety and benefits of early withdrawal after surgery can be determined from this trial. Feasibility is allowed through the existing collaboration within the European Taskforce of Epilepsy Surgery in Children. Benefits and pitfalls of this prospective study will be discussed on the basis of our retrospective study results.

### P594

#### A REVIEW OF OUR REDO EPILEPSY SURGERY CASES: DOES DOUBLE PATHOLOGY AFFECT EPILEPSY SURGERY OUTCOME?

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**Purpose:** Epilepsy surgery improves the outcome in medical refractory epilepsy in several reports. Despite a comprehensive presurgical evaluation, 30–40% of patients will continue to have disabling seizure. The aim of the study to report the epilepsy surgery outcome of our redo cases and evaluate the prognostic impact of double histopathology (more than one pathology in the resected tissue) on the outcome of epilepsy.

**Method:** Retrospective data analysis of the redo epilepsy surgery patients from our epilepsy registry from 1998 to 2012.

**Results:** Forty-seven patients out of 502 epilepsy surgeries required a redo surgery. The epilepsy redo surgery outcome (Engel class one) for 12 and 36 months is 44.2% and 24% respectively. 38 (7.6%) of the total 502 epilepsy surgery patients had double pathology and 20 (52.6%) out of those 38 cases, required redo surgery. In redo cases heterotopia with sclerosis was the commonest double pathology in eight of 20 patients (40%), followed by tumor and cortical dysplasia/ heterotopia in six patients (30%).

**Conclusion:** The study result showed significant association between double pathology and poor epilepsy surgery outcome.

### P595

#### EPILEPSY SURGERY IN MESIAL TEMPORAL SCLEROSIS WITH ICTAL SCALP VIDEO-EEG TOPOGRAPHICALLY NON-CONCORDANT: THE RELEVANCE OF MINIMALLY INVASIVE RECORDS

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**Purpose:** Surgical results in mesial temporal sclerosis (MTS) decrease when ictal scalp-EEG is topographically discordant from MRI-lesion. In these cases, minimally invasive EEG records (mEEGinv) help to identify the epileptogenic zone (EZ). We describe a case-series of patients with topographically non-concordant electro-imagiological findings evaluated with mEEGinv.

**Methodology:** Review of patient database of our epilepsy surgery program, searching for patients which fulfilled the following criteria: MTS on MRI; ictal scalp-video-EEG non-topographically concordant with the MRI-lesion; undergoing mEEGinv.

**Results:** we identified six patients, four women, mean age 23 years. In the ictal scalp-EEG, four patients had seizures in the frontal region ipsilateral to MTS, two with contralateral temporal onset. In the first four patients, unilateral mEEGinv were used (one foramen ovale, one depth electrode), in the remainder two, bilateral temporal depth electrodes. In 5/6 patients, all recorded seizures started from the MTS region and have been submitted to surgery (amygdalo-hippocampectomy+temporal lobectomy), with 100% Engel I (mean follow-up 40 months); one patient 2/5 seizures arised away from MTS and surgery was refused.

**Conclusions:** In this small series, by using mEEGinv, we demonstrate that in most of the patients with MTS and ictal scalp-EEG topographically non-concordant with the lesions disclosed in MRI, the seizures in fact start from MTS, with the scalp findings resulting from seizure propagation (falsely localized/ lateralized seizures). A minimally invasive study can be considered in the pre-surgical evaluation of patients with MTS and discordant electro-imagiological findings, contributing for the good surgical outcome.

## P596

**TEMPORO-PARIETO-OCCIPITAL DISCONNECTION IN POSTERIOR QUADRANTIC EPILEPSY: A CASE SERIES**

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**Purpose:** Patients with widespread hemispheric foci of epileptogenesis are potential candidates for surgical treatment. Traditionally, hemispheric/subhemispheric epilepsy was treated by resective surgery with removal of large parts of the hemisphere. Similar to the continual evolution of disconnective techniques in hemispherectomy, functional disconnection of the temporal, parietal, and occipital lobes (TPO) was suggested in posterior quadrant epilepsy. However, there are only a few studies that focus on this subgroup of epilepsy. Here, we present our series with respect to patient selection, surgical technique and seizure outcome.

**Methods:** We retrospectively reviewed our prospectively collected data on 10 patients treated for posterior quadrant epilepsy by TPO disconnection between 2005 and 2012.

**Results:** There were three males and seven females (median age 8.7 years; range from 4.2 to 22.1 years). The affected hemisphere was left in 3 and right in 7 patients. The patient median age at seizure onset was 2.4 years (range from 0.2 to 8.3 years). The median duration of epilepsy before surgery was 5.2 years (range from 1.3 to 17.2 years). The underlying pathology was posterior quadrant dysplasia in 5, venous infarction, posterior hemispheric quadrant atrophy, Sturge Weber Syndrome, cortical involvement of a systemic Lupus erythematosus and gliosis after cerebral tumor treatment in 1 each. In six patients a pure TPO disconnection was performed. In two patients the temporal lobe was resected along with parieto-occipital disconnection. The two remaining patients had had previous epilepsy surgery that was extended to a TPO disconnection; disconnection of the occipital lobe (1), resection of the temporal lobe (1). We encountered no complications. 9/10 patients are currently seizure free (class 1a) at a median follow-up time of 2.1 years (range from 4 months to 8.1 years).

**Conclusion:** TPO-disconnection is a safe and effective motor sparing epilepsy surgery procedure in selected patients.

## P597

**RESECTIVE SURGERY FOR INFANTS AND YOUNG CHILDREN WITH REFRACTORY EPILEPSY: DO EARLY SURGICAL INTERVENTIONS RESULT IN GOOD SEIZURE AND DEVELOPMENTAL OUTCOMES?**

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**Purpose:** Infants and young children with drug-resistant epilepsy frequently experience developmental problems as well as recurrent seizures. Early surgical treatment has recently been applied for such patients and may improve seizure and developmental prognosis. This study reviewed seizure and developmental outcomes in patients who underwent resective surgeries before 6 years old.

**Method:** Our pediatric epilepsy surgery program and studies were approved by the institutional review board. Totally 40 patients were included in this study and their medical records were reviewed. Single resective surgery with or without precedent intracranial electroencephalographic monitoring was performed in 19 patients, and stepwise surgeries with a combination of callosotomy and resective surgery was used in 21. Median age at initial surgery was 25.5 months (range, 2–70 months). Median follow-up was 48 months (range, 7–202 months). Seizure outcome was evaluated at final follow-up in all patients. Developmental status (DS) before and after surgery could be measured with developmental quotient (DQ) in 30.

**Results:** Overall, 23 patients (57.5%) showed favorable seizure outcome, including 19 (47.5%) without any seizures by final follow-up. Relatively good DS (DQ >50) was observed in 10 patients (33.3%) before surgery and 11 (35.5%) at final follow-up or 7 years old, respectively. Preoperative DS and postoperative developmental gain (increase in DQ after surgery) trended toward correlations with good postoperative seizure outcomes, and preoperative DS correlated significantly with postoperative DS ( $p < 0.001$ ). Type and number of surgery, etiology, and age at initial surgical treatment did not influence either seizure or developmental outcomes.

**Conclusion:** This study suggests that not simply lower age, but good DS at surgical intervention is more important for good prognosis of the disease. This may imply both the existing fundamental formation of the child brain substrates and less developmental damage consequently caused by recurrent seizures impact greatly on the treatment of epilepsy.

## P598

**BONE MINERAL DENSITY (BMD) IN REFRACTORY EPILEPSY TREATED WITH EPILEPSY SURGERY OUTCOME**

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**Purpose:** Refractory epilepsy and BMD has been widely reported. Few studies were achieved about seizure and BMD. The aim of this study is to investigate the impact of epilepsy surgery on BMD.

**Method:** In the last year, 25 patients with refractory epilepsy were treated in our department, 19 cases were included in this study, all cases were evaluated preoperatively: including, EEG, Video-EEG, MRI, SPECT, Memory test, IQ, and BMD. Reevaluation was performed in six cases after 6 months including the Engle scale outcome and BMD.

**Results:** Surgical treatment included; Temporal lobectomy in nine cases (47.36%), frontal lobectomy in two cases (10.52%) and Vagus nerve stimulator in eight cases (42.10%). Initial BMD, showed, osteopenia were in eight patients (42.10%), Osteoporosis in three cases (15.78%). In the follow-up group (six cases); Temporal lobectomy was performed in three cases, and VNS in three cases, after 6 months: Seizure control concerning Engle scale in three patients with temporal lobe surgery were two grad I and one II, the another cases with VNS surgery, were Engle scale, grad III. Abnormal BMD were presented in five of six cases (83.33%) before surgical treatment; osteoporosis in two cases and osteopenia in three cases, In the follow-up findings, cases with temporal lobectomy had been improved, while in the two cases treated with VNS, had no BMD improvement.



**Conclusion:**

- Osteopenia and osteoporosis are common in refractory epilepsy.
- There is improvement after epilepsy surgery in temporal lobe epilepsy surgery.
- There is a correlation between seizures control after surgery and BMD findings.

**P599**

### LOCALIZED, INTRA-TUBERAL EPILEPTOGENICITY REVEALED BY INTRAOPERATIVE ELECTROCORTICOGRAPHY IN TUBEROUS SCLEROSIS

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**Purpose:** We reported epileptogenicity in tuberous sclerosis (TS) was related to tubers more than perituberal cortex (*Neurology* 2012; 79:2249–57), noting interictal epileptiform discharges (IEDs) and seizure onsets were often confined to intracranial electrode contacts over the center of epileptogenic tubers, where MRI showed a dimpled surface and different signal. We studied this further with intraoperative electrocorticography (ECoG) using surface and depth electrodes.

**Method:** During 2012, four children (age 1–4 years) with TS and unifocal or multifocal seizures underwent five single-stage, epilepsy surgeries. None had epileptic spasms at the time of surgery. Candidate epileptogenic tubers were determined by seizure semiology, scalp-EEG and MRI. Pre-resection ECoG was performed with strip/grid electrodes over the surface of candidate and other tubers, and depth electrodes in candidate tubers.

**Results:** ECoG revealed almost continuous IEDs over candidate tubers in all surgeries, confined to the candidate tuber in two and seen less prominently over other tubers in three. In three surgeries, IEDs were recorded in the center but not the rim of candidate tubers; in one of these surgeries, electrographic seizures and IEDs were recorded in the depth of the candidate tuber but not the tuber surface and surrounding perituberal cortex. HFOs were recorded from candidate tubers in four surgeries, confined to the tuber center in two. Operations performed were resection of candidate and adjacent tubers in one surgery, resection of candidate tubers only in two surgeries, and resection of only the central part of candidate tubers in the two surgeries where localized intratuberal epileptiform activity was recorded. Histopathology revealed prominent cytomegalic neurons in the center of tubers which elsewhere showed disorganization and abundant balloon cells. All patients are free of their preoperative seizures and on reduced medication.

**Conclusion:** Epileptogenicity of tubers may be limited to a dysplastic central core, allowing for more limited surgery than even tuberectomy.

**P600**

### DEVELOPMENT OF FOCAL BRAIN COOLING SYSTEM FOR THE TREATMENT OF INTRACTABLE EPILEPSY

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**Purpose:** Limitations in medication and the neurosurgical indications for epileptic patients have motivated the design of implantable, device-based therapies. Focal brain cooling (FBC) is one of these options, because it has a potential to suppress epileptic seizures. The aim of our study is to establish the FBC system as a promising new neuromodulation therapy for patients with intractable epilepsy.

**Method:** Focal cooling devices with “Peltier” chips or water circulation systems were employed in animal and human studies. The cooling device was placed on the cortical surfaces in rats, cats and non-human primates. Kainic acid (KA) or penicillin G was then injected into the cortex to provoke epileptiform discharges (EDs) and seizures. The cortices of the animals were cooled to varying degrees and the influences of FBC on EDs and seizures were investigated. Focal cooling was also applied in patients with intractable epilepsy. During surgery, cooling was performed on the epileptogenic cortices or hippocampi which had to be resected. Changes in the EDs, cerebral blood flow (CBF) and metabolites during FBC were investigated.

**Results:** The EDs and seizures were suppressed during cooling (15–20°C) in animals. The neurophysiological functions were preserved during cooling above 15°C in rats and non-human primates. Histologically, no apparent damage was observed in the cortices of rats after cooling above 0°C for 1 h. Intraoperative cooling to 15°C invariably showed the suppression of EDs, which was associated with a coupling of the CBF and the metabolism, with a significant reduction in the glutamate level in humans.

**Conclusion:** The FBC has a strong inhibitory effect on epileptic seizures and plays a neuroprotective role for the brain. The present results support the physicochemical and technical feasibility of a cooling device-based therapy for epilepsy.

**P601**

### THE EXPERIENCE OF IMAGE GUIDED OPERATION ORIENTED BY INTRAOPERATIVE MRI IN EPILEPSY SURGERY

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**Purpose:** Image guided operation system (IGOS) based on updated navigation by intraoperative MRI and tractography is useful tool for brain surgery. In epilepsy surgery, usability of IGOS is expected because resection is often wide. We reported efficacy IGOS.

**Method:** We applied intraoperative MRI to four patients with intractable epilepsy caused by parenchymal lesion; two patients with suspected low grade glioma, each one patient tuberous sclerosis and cortical dysplasia. We performed respective surgery after usual presurgical evaluation for epilepsy surgery including the implantation of subdural electrodes.

**Results:** In one of two patients suspected to have low grade glioma, broad right temporal lesion included epileptogenic zone. Tractography indicated MRI lesion adjacent to visual cortex. We first resected MRI lesion close to visual area, and totally resected after update of neuronavigation by intraoperative MRI. Another patient had parenchymal lesion was located in posterior side of temporal lobe and epileptogenic zone

## Abstracts

was close to arcuate fasciculus. After resection of the parenchymal lesion, we removed epileptogenic zone under the guiding of updated navigation. Both patients had seizure free after operation without showing visual field deficit or dysphasia. In patients with tuberous sclerosis and cortical dysplasia, we used intraoperative MRI to make sure the target lesion totally resected.

**Conclusion:** Image guided operation system enables sufficient resection of parenchymal lesion including epileptogenic without impairment of eloquent area.

## P602

### SHORT-TERM HEALTHCARE UTILIZATION IN STEREOTACTIC MRI-GUIDED LASER ABLATION FOR TREATMENT OF MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Compare hospital course of patients treated with MRI-guided laser ablation to patients treated with temporal lobectomy for refractory mesial temporal lobe epilepsy (MTLE).

**Method:** From 8/20/2011 to 11/9/2012, nine patients with MTLE evaluated for epilepsy surgery underwent stereotactic MRI-guided laser ablation. Medical records were reviewed retrospectively for healthcare utilization during the surgical admission. This included immediate post-operative level of care (ICU v. floor), length of stay (LOS), and emergency department (ED) use or readmission within 30 days of discharge.

**Results:** Of the nine patients, three were admitted to the neurointensive care unit (NICU): the initial two patients and a third due to an acute subdural hematoma (SDH) that was treated. Six went to the regular neurosurgery floor after ablation. LOS was 1 day for 6/9 patients, 2 days for the first patient in the series (1 day ICU, 1 day floor), 3 days for two patients including the patient described above with an acute SDH (1 day in NICU, 2 days neurosurgery floor). A second patient had a generalized tonic-clonic seizure on post-op day 1 due to missing his usual seizure medications, and recovered without complications on day 3. In the 30 day period, 2/9 had ED visits due to recurrent seizure, and 1/9 had hospital readmission for nonepileptic events.

**Conclusion:** MRI-guided laser ablation in treatment of TLE was associated with a lower level of care and shorter LOS in 2/3 of our patients, with no difference in 30 days readmission or ED visits compared to our traditional temporal lobectomy patients.

## P603

### IS ADDITIONAL AMYGDALOHIPPAMPECTOMY NECESSARY FOR THE INTRACTABLE LESIONAL TEMPORAL LOBE EPILEPSY?

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**Purpose:** It is controversial whether amygdalo-hippocampectomy (AHT) in addition to lesionectomy result in better outcomes for intractable epilepsy associated with temporal lesions. In this study, we

retrospectively review the surgical outcomes of temporal lobe epilepsy (TLE) cases with temporal lesions.

**Methods:** From 2006 to 2010, 10 intractable epilepsy patients with temporal lobe lesions underwent surgical treatment at our department. Pathologies included two gangliogliomas, five cavernous angiomas, one pilocytic astrocytoma, one DNT and one oligodendroglioma. Four patients had preoperative chronic subdural electrode studies. Lesions were located in the dominant hemisphere in seven cases, and in the non-dominant hemisphere in the other three cases. All cases, only underwent lesionectomy with or without surrounding corticectomy. The hippocampus was preserved, even if FDG-PET or intraoperative electrocorticography (ECoG) suggested secondary epileptogenicity around the hippocampus. Patients were followed for more than 2 years after surgery.

**Results:** All cases resulted in Engel's class Ia, except the dominant hemisphere DNT case that resulted in class Ib.

**Conclusion:** Only lesionectomy and intraoperative ECoG guided corticectomy without AHT resulted in successful outcomes in a vast majority of TLE cases with temporal lesions.

## P604

### THE USE OF MINIMALLY INVASIVE MR-GUIDED LASER INTERSTITIAL THERMAL THERAPY IN THE TREATMENT OF MESIAL TEMPORAL LOBE EPILEPSY OF CHILDREN AND YOUNG ADULTS

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**Purpose:** Mesial temporal lobe epilepsy patients commonly remain refractory to medication, despite optimal treatment, and surgical intervention often offers the best chance of seizure freedom. Common surgical modalities include invasive procedures for resection of seizure foci, where seizure freedom can be achieved in 70–80% of cases. Complications associated with these strategies include visual deficit, cognitive deficit, memory decline, and stroke. Minimally invasive techniques may be adapted and employed for effective treatment of this disabling condition with faster and less painful recovery and similar or improved outcomes. We report a case series describing the use of minimally-invasive MR-guided laser interstitial thermal therapy for the successful treatment of left mesial temporal lobe epilepsy in children and young adults.

**Method:** Complex partial seizure activity was localized to the mesial left temporal lobe in one pediatric (age 16) and two young adult patients (ages 20 and 27) using MRI of the brain, PET analysis, and inpatient video-EEG monitoring. A laser probe was subsequently placed stereotactically into the left amygdalohippocampal complex. We then used MR-guided laser interstitial thermal therapy for minimally-invasive ablation of their seizure foci in the left amygdalohippocampal complex.

**Results:** All patients tolerated the procedure well and were discharged on postoperative day 1 without complication. Two patients are seizure-free (Engel Class I), though one patient continues to have seizures which appear to be contralateral in origin. No permanent complications are evident at 3–7 months follow-up.

**Conclusion:** MR-guided laser interstitial thermal therapy has the potential to provide an effective, minimally-invasive alternative to more conventional techniques for the surgical treatment of medically refractory mesial temporal lobe epilepsy in children and adults.

## P605

### RESULTS OF SURGICAL TREATMENT WITH OR WITHOUT INTRAOPERATIVE ECoG IN PEDIATRIC EPILEPSY WITH SUPRATENTORIAL BRAIN TUMORS

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**Purpose:** Symptomatic epilepsy is common in patients with supratentorial brain tumors. Epileptogenesis depends on several factors including tumor histologic type, location of tumor and also changes in the peritumoral brain parenchyma. The aim of presented research was studying the results of epilepsy surgery in pediatric brain tumors with or without intraoperative ECoG.

**Method:** In the Department of Child Neurology, Neurosurgery and Medical Genetic of Russian National Research Medical University, Neurosurgical Department and Psycho-Neurological Department N2 of Russian Children Clinical Hospital at the period 2006–2012 were treated and operated 75 children with supratentorial brain tumors (42 boys and 33 girls at the age from 5 month up 17 years, medium  $9.6 \pm 5.3$  years) with catamnestic observation for 1–6 years.

**Results:** Among the 75 pediatric patients with supratentorial brain tumors 52 patients had symptomatic epilepsy (69.3%). The most epileptogenic tumors were dysembryoplastic neuroepithelial tumors (DNET), primitive neuroepithelial tumors (PNET), hamartoma, fibrillary astrocytomas, gangliogliomas and atypical meningioma. In 26 patients with surgical intervention without ECoG were observed the following results in Engel epilepsy surgery outcome scale: class I – five patients, class II – seven patients, class III – four patients, class IV – five patients. In 22 patients operated with ECoG: class I – 19 patients, class II – two patients and class III – one girl.

**Conclusion:** Significant difference ( $p < 0.01$ ) between I + II Engel classes in comparison with III + IV Engel classes in these two groups of operated patients demonstrated necessity and effectiveness of ECoG investigation in surgery of supratentorial brain tumors caused epilepsy.

## P606

### MITOCHONDRIAL DISORDERS IN NEOCORTEX OF PATIENTS WITH REFRACTORY EPILEPSY

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**Purpose:** In this study we evaluated the activity of NADH-d, CKmit, VDAC, NOS and NeuN in neocortical of patients with refractory epilepsy.

**Method and Methods:** We studied 31 cases (17 males and 14 females). Ten cases with tumor and 21 cases with temporal lobe epilepsy, all patients were studied according to standardized presurgical protocol and submitted to temporal lobectomy and amigalohippocampectomy. The activity and distribution of the NADH-d, CKmit, VDAC, NOS and NeuN, were studied in (T3 and T4), intraoperative biopsies of temporal cortex, the regions were stained with the NADH-d- technique and Immunohistochemistry.

**Results:** NADH reactive neurons were localized preferentially in layers III and VI and in the subjacent white matter of the temporal cortex, the neurons of the layer VI were larger and significant increased NADH-d reactive. The VDAC and NeuN in the layer VI was observed an enhanced expression, and CKmit and NOS showed a decrease in all cases, Epileptic neurons also showed, hypertrophy, cytomegaly, dysmorphic morphology, hyperchromatic, and balloon cells in three patients. Also we have observed NADH subunits expressed on reactive astrocyte and all components of the neurophil.

**Conclusion:** These results suggest a causal relationship between the activities of respiratory enzymes and metabolic processes that contribute to damage oxidative and /or mitochondrial dysfunction that can be both an important cause and a consequence of the prolonged seizures and could represent change in brain plasticity in these patients.

## P607

### CORRELATION BETWEEN BEHAVIOR PATTERNS OF FOCAL SEIZURES AND LOCALIZATION OF EPILEPTOGENIC LESIONS

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**Purpose:** To correlate behavior patterns of focal seizures (BPFS) (ictal and postictal features) and localization of epileptogenic lesions (EL) in the consecutive group of patients, following long-term video-EEG monitoring (vEEGM) and brain magnetic resonance imaging (MRI).

**Method:** In the period of 01.08.2009–30.04.2012. 331 vEEGM in 310 patients was performed. Epilepsy protocol MRI (thin slices and adequate slice orientation adapted to epileptogenic zone suggested by vEEGM analysis) was obtained in all patients. A total of 91 ictal and 15 postictal semiological signs were investigated. All recorded seizures were studied and unique sequence of semiological signs per patient was further analyzed. Precise anatomical localization of the EL was performed in Automatic Anatomical Labeling module of MRICro software.

**Results:** A total of 180 monitored patients (58.06%) ( $34.2 \pm 10.9$  years of age) had focal seizures (1712 seizures/median 5 seizures per patients/median vEEGM 4 days). Single EL was detected in 124 of patients (68.89%): hippocampal sclerosis (HS) 58; focal cortical dysplasia 28; dual pathology 11; remote infarct 6; DNET 6; cavernoma 4; and other in nine patients. Temporal lobe lesion was seen in 73.39%, frontal and occipital lobe lesion in 8.87%, parietal lobe lesion in 6.45% and insula lesion in 2.42% of patients. Secondary generalized tonic-clonic seizure was detected in 41% of patients (exclusively in 12.7%). Behavior arrest (52.2%), orolalimtar automatisms (OAA) (44.4%), contralateral head version (29.4%), behavior unrest (BU) (26.1%) and unilateral smooth head turn (USHT) (25.6%) were most common ictal features. Unresponsiveness (85.5%), verbal memory (57.2%) and figural memory (54.5%) impairment were most common postictal signs. OAA, BU, USHT and

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epigastric aura were frequent in patients with HS. Visual and somatosensory aura were frequent in extratemporal lobe epilepsy. Strangulation, ictal spitting, hypersalivation, contralateral piloerection were frequent in insular lobe epilepsy.

**Conclusion:** Analysis suggests preference of certain BPFS for particular brain lobes.

## P608

## EPILEPSY SURGERY: 40 YEARS' EXPERIENCE

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From 1972 to 2011 481 surgical procedures for the treatment of pharmacologically resistant epilepsy were performed by the same surgeon at the Osler Clinic in Monterrey Mexico. Out of 5240 patients treated during the last 40 years at such institution, this group represents 9.18%. This report has threefold objectives firstly, to compare our present results with previous report (1993), secondly to review long term results for these four procedures utilized (lesionectomy, callosotomy, amigdalohippocampectomy and hemispherectomy), and thirdly to review the seizure free group following Engel's classification for postoperative outcome (classification used for earlier and present reports). We reviewed 12 indicators purporting good surgical outcome and six of poor surgical results. The procedures comprised 352 lesionectomies from which 289 were Temporal Lobectomies, 21 Frontal Lobectomies, nine Occipital Lobectomies, nine Parietal Lobectomies, 20 Multilobar resections, four Reoperations. Additionally, 99 Callosotomies, 22 Amigdalohippocampectomies and eight Hemispherectomies were done. No fatalities were observed and morbidity was 2.07% (five patients with permanent sequels). In the temporal lobectomy group there were 242 adults and 47 children. Comprising 160 left sided resections and 129 right sided procedures, representing 6.8% of the 4251 patients studied with complex partial seizures from 1972 to 2011. In the lesionectomy series 79.5% improved, 75% were bettered in the callosotomy series, 67% in the amigdalohippocampectomy group improved and only 50% in hemispherectomy series. One hundred and thirty-nine patients either died or were lost for follow up, the rest, 342 patients, had a mean follow up of 24.9 years.

## P609

## EPILEPTIC NETWORK ANALYSIS BASED ON SIMULTANEOUS EEG AND fMRI OF EPILEPSY SURGERY CANDIDATES: A COMPARISON WITH INVASIVE RECORDINGS AND SURGICAL OUTCOME MEASURES

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**Purpose:** EEG correlated functional MRI (EEG-fMRI) is promising as noninvasive method for the delineation of brain regions which are significantly involved when interictal epileptic discharges (IEDs) occur in the EEG. The goal of the present study was to assess whether accurate delineation of these regions is helpful in the preoperative work-up of epilepsy surgery candidates. Furthermore, to deal with the limitation of the relatively low sensitivity of EEG-fMRI we evaluated the usefulness of a data-driven vs. model-driven approach to identify the epileptic network

**Method:** EEG-fMRI data of 21 presurgical candidates were compared to invasive EEG and surgical outcome as gold standards. Five of them were implanted with depth electrodes (SEEG) and sixteen with subdural grids

(ECoG). As a data-driven approach independent component analysis (ICA) was explored. In order to identify the epileptic independent component (ICe) the spatial correlation was determined of this component with the BOLD regions overlapping with the resection area, for periods without and with the occurrence of IEDs in the EEG.

**Results:** For all 21 patients at least one EEG-fMRI area overlapped with active SEEG/ECoG electrodes; some regions were related to the onset of IED activity and others to propagation, suggesting that EEG-fMRI reflects an epileptic network. The EEG-fMRI correlation pattern included the seizure onset zone in 83% and the resection area in 90% of the patients. In addition, ICA of the fMRI of nine of these patients with an Engel score 1 enabled the identification of an ICe, which was similar for periods with and without IEDs occurring in the simultaneously recorded EEG.

**Conclusion:** Together, these results show that EEG-fMRI has predictive value regarding the seizure onset and resection area. In addition, ICA can be helpful to identify this area for those patients in whom no IEDs are seen in the EEG during fMRI acquisition.

## P610

## ROBOTIC-ASSISTED CRANIOTOMY FOR SELECTIVE RESECTION IN EPILEPSY SURGERY: OUR INITIAL EXPERIENCE AT THE MONTREAL NEUROLOGICAL INSTITUTE AND HOSPITAL

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**Purpose:** We present our experience at the Montreal Neurological Hospital and Institute with a stereotactic robotized surgical arm combined to advanced multimodal navigation imaging for resection of epileptogenic foci. We will provide details of our optimized imaging and operative protocol.

**Method:** Thirty-eight patients investigated for intractable epilepsy, underwent craniotomy for focal cortical resection of epileptogenic foci including transcortical selective amigdalohippocampectomy (SeLAH). Prior to the surgical procedure, all patients completed MRI (Philips Sonata 1.5T MR) and CTA (Toshiba Aquilion One). We devised a multimodal imaging protocol: T1W SPGR 3D axial-planar MRI acquisition, CT, 4D-CT arteriography and venography, and BOLD-fMRI, in cases where necessary to localize eloquent brain areas. All acquired images were transferred to our processing server to provide detailed representation of a) the cortical surface, b) cerebral vasculature, c) segmented cortical gyri and sulci. The data were transferred to the image-guided (Medtronic Stealth Cranial) and robotic navigation (Medtech ROSA) systems for further image preparation. For each case, surgical trajectories were created to provide intraoperative localization of anatomy, epileptic foci, or previously implanted SEEG depth electrode positions, based upon the integrated imaging information. For the procedure, the robotic system and neuronavigation reference array were affixed to the patient head clamp (O-Clamp, MNI). Patient-to-image registration was completed using surface and landmark-based registration.

**Results:** We used this framework was used in 38 surgical cases. The patient-to-image registration took on average 27 min to complete and yielded an error of <1.0 mm. There were no complications associated with the use of these systems.

**Conclusion:** The combination of the multimodal navigation imaging and robotic navigation system provided precise intra-operative localization of anatomical regions of interest.

P611

**CORPUS CALLOSOTOMY IN CHILDREN WITH DRAVET SYNDROME AND SCN1A ABNORMALITY**Ritter F<sup>1,2</sup>, Doescher J<sup>1,2</sup>, Wical B<sup>3,4</sup>

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**Purpose:** Dravet Syndrome is a rare epilepsy often associated with abnormal SCN1A. Mortality is high, >10%, with 30–50% of deaths attributed to status epilepticus. Corpus callosotomy may be beneficial for children despite a diffuse underlying channelopathy.

**Method:** We present two children with Dravet Syndrome due to SCN1A abnormalities treated with corpus callosotomy.

**Results:** The first is female, SCN1A abnormality exon 26 gly→val c5174. Seizure onset was with fever at 3 months of age. At 4 years old she had a two-stage corpus callosotomy. Prior to surgery her treatments included 18 different antiepileptic medications (AEM), Ketogenic diet (KD) and vagal nerve stimulator (VNS). The VNS had been used for 2.5 years with no benefit, and turned off due to intolerable dysphagia. Seizures were becoming more frequent and severe. Preoperative/postoperative seizure frequencies respectively were:

- 1 focal secondarily generalized tonic-clonic 24/6 per month (↓75%);
- 2 tonic/atonic/myoclonic >3,000/90 per month (↓97%);
- 3 convulsive status epilepticus unresponsive to rescue medication and emergency department treatment, requiring hospitalization and ventilator support 18/1.5 per year (↓92%).

The second child is male, SCN1A abnormality deletion exons 1–26. At age 3 10/12 he had a 90% anterior corpus callosotomy. Treatments prior to surgery included 7 AEMs and KD. Seizures were progressively more frequent, severe, and longer. Preoperative/postoperative seizure frequencies respectively were: (1) focal secondarily generalized tonic-clonic 30/4 per month (↓87%), (2) tonic/atonic/myoclonic 120/11 per month (↓91%); (3) convulsive status epilepticus requiring hospitalization and ventilator support 2/0 per year (↓100%).

In both children, seizure frequency improved immediately following surgery and has persisted for 9 years and 33 months respectively. Parents report improved function, more alert, and interactive.

**Conclusion:** Despite the diffuse SCN1A channelopathy, two children with Dravet Syndrome have had good response to corpus callosotomy, but additional information is needed to determine who may benefit.

## Poster Session: Genetics A Tuesday, 25 June 2013

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**CLINICAL SPECTRUM OF SCN2A MUTATIONS EXPANDING TO OHTAHARA SYNDROME**

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**Purpose:** SCN2A mutations were responsible for benign familial neonatal-infantile seizures, generalized epilepsy with febrile seizures plus, Dravet syndrome, intractable epilepsies. We examined possible involvement of SCN2A mutations in early-onset epileptic encephalopathies (EOEEs).

**Method:** A total of 328 patients with EOEEs including 67 cases with Ohtahara syndrome (OS) and 150 with West syndrome (WS) were screened for SCN2A mutations by high resolution melt analysis or whole exome sequencing.

**Results:** We detected 14 novel SCN2A missense mutations in 15 patients: nine patients with OS; one with WS; five with unclassified EOEEs. Twelve out of 14 mutations were confirmed as de novo, and all mutations were absent in our 212 control exomes. A de novo mosaic mutation (c.3976G>C) was found in one patient, in which mutant allele frequency was 18%. One mutation (c.634A>G) was detected in the transcript variant 3 which is a neonatal isoform. All the nine mutations with OS were located in the linker regions of SCN2A, and one mutation with WS was in positively charged segments. In seven of nine patients with OS, electroencephalography findings transitioned from suppression-burst pattern to hypsarrhythmia. Zonisamide, valproic acid, phenytoin, benzodiazepines and lamotrigine had relatively good efficacy on seizures. All the patients had severe developmental delay.

**Conclusion:** Our study first elucidated that SCN2A mutations are important causes for OS. Given the wide clinical spectrum caused by SCN2A mutations, genetic testing for SCN2A should be recommended for children with different epileptic conditions.

P613

**THE ROLE OF CYP2C9 POLYMORPHISMS IN PHENYTOIN-RELATED CEREBELLAR ATROPHY**

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**Purpose:** Phenytoin is known to be able to induce cerebellar atrophy in patients with epilepsy. It is also known that a CYP2C9 mutation (\*2 or

\*3) reduces phenytoin metabolism by 25% to 50% and can increase the risk of phenytoin-related side effects. We examined the influence of *CYP2C9* polymorphisms on total cerebellar volume and cerebellar gray and white matter volumes in patients with epilepsy taking phenytoin.

**Method:** For the genotyping, 100 adult patients with documented epilepsy who had been taking phenytoin for >1 year were selected. From this group, we randomly selected 19 mutant individuals (MT group; *CYP2C9*\*2 and \*3) for a whole-brain volume measurement using MRI and 19 wild-type individuals (group WT; *CYP2C9*\*1) with similar clinical and demographic characteristics to those in the MT group for comparison. Total intracranial volume measurements were used to normalize the acquired volumes, which were separated into gray matter volume, white matter volume, and total volume.

**Results:** The MT group exhibited a significant reduction in cerebellar white matter volume ( $p = 0.002$ ) but not in total cerebellar volume.

**Conclusion:** Our study is the first to report evidence linking *CYP2C9* polymorphism and a reduction in cerebellar volume in epileptic users of phenytoin.

#### P614

##### MUTATIONS IN *PRRT2* RESULT IN FAMILIAL INFANTILE SEIZURES WITH HETEROGENEOUS PHENOTYPES INCLUDING FEBRILE CONVULSIONS AND PROBABLE SUDEP

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**Purpose:** Mutations of *PRRT2*, which encodes proline-rich transmembrane protein 2, are associated with heterogeneous phenotypes including benign familial infantile seizures (BFIS) and/or familial paroxysmal kinesiogenic dystonia (PKD).

**Methods:** Here, we performed mutation screening of *PRRT2* in six Italian families with BFIS/PKD phenotypes.

**Results:** The mutation, c.649dupC (p.Arg217ProfsX8), was found in two families with BFIS phenotype. In a third BFIS family, a missense mutation, c.718C/T (R240X), was identified. All these mutations co-segregated with the disease and were not observed in 100 controls of matched ancestry. In one BFIS family that carried the c.649dupC mutation, one affected member developed afebrile focal seizures and died at age of 14 years of probable sudden unexpected death in epilepsy, while his brother also had simple febrile convulsions (FC) and performed poorly on complex psychomotor functioning. In another family carrying the c.718C/T mutation, two of three affected members also had simple FC.

**Conclusion:** This study enlarges the clinical spectrum related to *PRRT2* mutations and underscores the complexity of the phenotypic consequences of mutations in this gene.

#### P615

##### FOCAL SPIKES IN ASYMPTOMATIC MEMBERS OF JUVENILE MYOCLONIC EPILEPSY FAMILIES WITH MUTATED EPILEPSY GENES

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**Purpose:** What is the significance of focal spikes in EEGs of clinically asymptomatic persons?

**Method:** EEGs were prospectively recorded in 380 members of families, ascertained through eighteen patients with JME as defined by the 1989 ILAE classification. Informed consents approved by IRBs at UCLA and participating institutions were obtained. Fourteen families were screened for EFHC1 mutation, four families had whole exome sequencing. Four novel JME genes (Myoclonin 3, 4, 5, 6) were identified.

**Results:** Fifteen index cases had classic JME (cJME) with adolescent myoclonias, GTC seizures and rare absences. Three probands had photosensitive childhood absence epilepsy that evolved into JME (CAE/JME).

**CAE/JME:** In affected family members: Twelve had 3 Hz single spike waves while two others had 3 Hz spike wave complexes and 4–6 Hz polyspike waves. In clinically asymptomatic members: 11 had <1 s fragmented bursts of 3 Hz spike wave complexes; two had centro temporal rolandic spikes; three others had focal spikes in frontal or temporal or parietal areas; one had bifrontal spikes.

**Classic JME:** Clinically affected members can have 3 Hz spike wave or 4–6 Hz polyspike wave. Seven asymptomatic members had posterior temporal spikes (T4-T6 > T3-T5) while two had parieto-occipital spikes. Rarely were focal spikes anteriorly located (1 fronto temporal spikes).

**Conclusion:** Focal spikes in EEGs of clinically asymptomatic persons can be the expression of a JME mutated gene. Location of focal spikes in asymptomatic family members differs between CAE/JME (more anterior- centro temporal rolandic, fronto temporal or bifrontal) and cJME (more posteriorly located, T4 T6 > T3-T5).

#### P616

##### NOVEL MUTATIONS IN PYRIDOXINE DEPENDENT EPILEPSY IN A CHINESE CHILD

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Pyridoxine-dependent epilepsy (PDE) is a rare autosomal recessive disorder with neonates and infants seizures onset. We report one patient with PDE whose seizures were resistant to anti-convulsants. Several times during hospitalization seizures always got control and then the reason was proved to be due to use pyridoxine intravenously. The patient encountered seizure recurrence after pyridoxine withdrawal incidental for three times with the intervals of 13, 14, 38 days respectively. By using pyridoxine monotherapy, seizures were controlled completely accompanied with neurological development improvement. *ALDH7A1* gene mutation analysis revealed two heterozygote mutations: c.410G>A (p.G137E) in exon5 transmitted by the father and IVS11 + 1G>A in intron 11 transmitted by the mother. The two mutations have not been previously reported around the world, and this is the first case of Chinese patient diagnosed with PDE by molecular genetic analysis.

P617

### ASSOCIATION WITH ABCC2 LOCI FOR SEIZURE CONTROL IN WOMEN WITH EPILEPSY ON FIRST-LINE ANTI-EPILEPTIC DRUGS (AEDs)

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**Purpose:** The present study was undertaken to investigate the role of genetic variants from ABC transporters in seizure control with 1st line AEDs.

**Method:** On the basis of gene coverage and functional significance, a total of 98 single nucleotide polymorphisms from ABCB1, ABCC1, and ABCC2 were genotyped in 400 patients from North India. Of these, 216 patients were eligible for therapeutic assessment. Genetic variants were compared between the “no-seizures” and the “recurrent-seizures” groups.

**Results:** Functionally relevant promoter polymorphisms from ABCC2: c. – 1549G>A and c. – 1019A >G either considered alone or in haplotype and diplotypic combinations, were observed for a significant association with seizure control in women (odds ratio > 3.5, p < 10<sup>–3</sup>, power > 95%). Further, low protein-expressing CGT and TGT (c. – 24C > T, c.1249G > A, c.3972C>T) haplotypes were always observed to be present in combination with the AG (c. – 1549G > A, c. – 1019A >G) haplotype that was over-represented in women with “no seizures” group.

**Conclusion:** The distribution of the associated variants supports the involvement of ABCC2 in controlling seizures in women possibly by lowering of its expression. The biological basis of this finding could be an altered interaction of ABCC2 with AEDs and estrogens.

P618

### IDENTIFYING NOVEL PROGRESSIVE MYOCLONUS EPILEPSY GENES BY EXOME SEQUENCING

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**Purpose:** Progressive myoclonus epilepsies (PMEs) are a clinically and genetically heterogeneous group of rare, inherited disorders with action myoclonus, tonic-clonic seizures, and ataxia being the core features. The paradigmatic form is Unverricht-Lundborg disease (ULD), where

cognition is essentially preserved. ULD is caused by mutations in *CSTB*, but there are “ULD-like” phenotypes due to recently discovered (*SCARB2*, *GOSR2*) and other yet to be identified genes. Other PMEs with additional features, particularly dementia, are due to mutations in additional genes. We aim to identify novel genes in unsolved cases of PME, which is a prerequisite for improved diagnostics and understanding of pathogenesis.

**Method:** Through a worldwide collaboration we have collected 83 unrelated patients with PME where mutations in likely known genes have been excluded. We are employing exome sequencing to identify new genes in these unsolved cases. Based on the phenotypic variation seen within the patient cohort we hypothesize they represent several molecular entities. Given that the cases of PME show suggestive recessive inheritance, we select potentially deleterious homozygous or compound heterozygous variants.

**Results:** Exome sequencing and preliminary data analysis has been completed for 38 patients of whom 18 had a ULD-like phenotype. Analysis of known ULD-like and other PME genes revealed two patients with likely causal variants in *CLN6* and *EPM2B*, being known genes for PME due to Kufs disease and Lafora disease respectively; these diagnoses were not suspected clinically. Importantly, potential novel genes with variants in at least two patients have emerged. Sequencing of the remaining cohort of 45 patients is in progress.

**Conclusion:** Exome sequencing shows potential for identification of recessive causes of PME in atypical cases. Variants in novel genes identified in the analysis of the first 38 cases need to be validated by segregation analysis, identification of further cases in the remaining cohort and functional analyses.

P619

### CACNA1A VARIANTS AS A POTENTIAL GENETIC MODIFIER OF DRAVET SYNDROME

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**Purpose:** De novo mutations of *SCN1A*, which encode the Na<sub>v</sub>1.1 neuronal voltage-gated sodium channel, are considered the major cause of Dravet syndrome. In this study, we investigated genetic modifiers of this syndrome.

**Method:** We performed a mutational analysis of all coding exons of *CACNA1A* in 48 subjects with Dravet syndrome. To assess the effects of *CACNA1A* variants on the epileptic phenotypes of Dravet syndrome, we compared clinical features in two genotype groups: (1) subjects harboring *SCN1A* mutations but no *CACNA1A* variants (n = 20) and (2) subjects with *SCN1A* mutations plus *CACNA1A* variants (n = 20). *CACNA1A* variants detected in patients were studied using heterologous expression of recombinant human Ca<sub>v</sub>2.1 in HEK 293 cells and whole-cell patch-clamp recording.

**Results:** Nine *CACNA1A* variants, including six novel ones, were detected in 21 of 48 subjects (43.8%). Based on the incidence of variants in healthy controls, most of the variants seemed to be common polymorphisms. However, the subjects harboring *SCN1A* mutations and *CACNA1A* variants had absence seizures more frequently than patients with only *SCN1A* mutations (8/20 vs. 0/20, p = 0.002). Moreover, the former group of subjects exhibited earlier onset of seizures and more frequent prolonged seizures before 1 year of age, compared to the latter group of subjects. The electrophysiological properties of four of the five novel Ca<sub>v</sub>2.1 variants exhibited biophysical changes consistent with gain-of-function.

**Conclusion:** We conclude that CACNA1A variants in some Dravet syndrome persons may modify the epileptic phenotypes.

#### P620

### ASSOCIATION OF MULTIDRUG RESISTANCE 1 (MDR1) GENE C3435CT POLYMORPHISMS WITH ANTIEPILEPTIC DRUG RESISTANCE IN SOUTH INDIAN EPILEPTIC POPULATION

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**Purpose:** Almost 30% of epileptic patients using antiepileptic drugs are considered to have drug resistance to many drugs. A number of polymorphisms (C3435T and G2677AT) that affect the expression levels of P-glycoprotein have been determined to be associated with poor response to antiepileptic drugs. Polymorphism of this gene results in altered expression levels of P-glycoprotein leading to a range of drug response resistance epilepsy.

**Method:** Two hundred consecutive epilepsy patients who attended epilepsy clinic of Nizam's Institute of medical sciences were included in study and 200 healthy persons who are not suffering with epilepsy were taken as controls. DNA was isolated from 2 ml of venous blood by using the phenol chloroform method. Genotyping of C3435T, single-nucleotide polymorphism was performed by amplification of DNA using polymerase chain reaction (PCR) with forward and reverse primers and subjecting the PCR products by RFLP (MboI enzyme).

**Results:** Statistically significant differences were detected in the allelic frequency and genotype distribution between AED-resistant and AED responsive epileptic patients. The risk of drug resistance was found to be higher in patients with C/T and T/T genotype as compared with C/C genotype. However, no significant association was found between genotypes and epilepsy drug resistance when patients were stratified by type of epilepsy and gender.

**Conclusion:** Our results suggest that SNP C3435T of MDR1 gene might be associated with decreased therapeutic response to AEDs and may represent a possible predictive factor for refractory epilepsy in South Indian Population.

#### P621

### STOP SUDEP PROGRAM: ANALYTICAL ALGORITHM TO ASSESS THE DIAGNOSTIC UTILITY OF ARCHIVED SUDEP SAMPLES

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**Purpose:** The principal goals of the STOP SUDEP Program are

- 1 SUDEP registry,
- 2 tissue biorepository, and
- 3 immediate sample utilization for SUDEP research.

The scope of molecular investigations and validity of results is crucially dependent on the quality of the available tissue. Multiple factors influence sample diagnostic utility and broadly informed qualitative

assessment of the specimen critically dictates investigational and diagnostic value of a specific sample.

**Methods:** STOP SUDEP Program is a national and international collaborative network of families of patients with epilepsy, forensic pathologists, organizations supporting epilepsy research and education, and investigators dedicated to SUDEP research. This Biorepository houses biological specimens that vary in source, conservation methods, collection age, and amount. We performed comprehensive assessment of biospecimens with regards to their integrity, quantity, and quality using traditional analytical methods in parallel with the visual automated fluorescence electrophoresis.

**Results:** We extracted DNA from series of archived tissues and performed the first simultaneous quantitative and qualitative analyses of the genomic DNA on the visual automated fluorescence electrophoresis (VAFE), before and following whole genome amplification (WGA), in parallel with traditional quality control (QC) methods. The VAFE QC data were correlated with subsequent sample performance in PCR, sequencing, and a high-density comparative genome hybridization array. We observed improved standardization of nucleic acid quantity, quality and integrity for high performance in the downstream genomic technologies.

**Conclusions:** STOP SUDEP Program is the first SUDEP registry and tissue repository dedicated to concurrent analysis and research of mechanisms and molecular risk factors of SUDEP that integrates stringent quality control assurance. Our comparative assessment of SUDEP samples establishes that VAFE is cost effective, informative in stratification of biological specimen derived gDNA for investigational and diagnostic applications, and adds to the confidence in the validity of the resultant genetic data.

#### P622

### A NOVEL MUTATION OF M1630V IN CACNA1H IN IDIOPATHIC GENERALIZED EPILEPSIES

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**Purpose:** Idiopathic generalized epilepsies (IGEs) are the most common of epilepsies, classically including childhood absence epilepsy (CAE), juvenile absence epilepsy (JAE), juvenile myoclonic epilepsy (JME), and epilepsy with generalized tonic-clonic seizures (EGTCS). Patients with these IGE sub syndromes have a strong underlying genetic basis. Voltage-dependent T-type calcium channel subunit alpha-1H (CACNA1H) has been reported to contribute to an individual's susceptibility to IGEs (MIM: 607904).

**Method:** We studied a four generation Hispanic family with classic IGEs and 190 IGE probands. Sixty-three family members (eight affected and 55 unaffected) of the four generation Hispanic family participated in this study. Among eight affected members of the large family, three suffered from CAE, two with JAE, two with EGTCS and one with JME.

A pair-end whole exome sequence on six samples including four affected members and two marid-in controls of the large family was performed by Fastrack genetic analysis service of Illumina. Illumina's analysis pipeline, ANNOVAR program, Mendelian inheritance segregation and Sanger sequence were used to annotate, filter, prioritize and confirm the functional DNA variants.

One hundred and ninety Hispanic IGE probands and 226 ethnics-matched population controls were genotyped for the new identified muta-



tion with Roshe SimpleProbe melting curve analysis and Sanger sequence.

**Results:** We identified a novel heterozygous mutation of A4888G/M1630V in CACNA1H for IGEs.

M1630V in CACNA1H was present in two of 190 IGE probands/families, but not in 226 controls.

M1630V in CACNA1H segregated with four epilepsy affected members in the large IGE family and in twin brothers in a small IGE family.

**Conclusion:** Our data suggest M1630V in CACNA1H contribute susceptibility to IGEs, and support CACNA1H as one of genes responsible for classic Idiopathic generalized epilepsies.

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### P623

#### ANALYSIS OF PRRT2 MUTATIONS IN CHINESE FAMILIES WITH BENIGN FAMILIAL INFANTILE EPILEPSY AND INFANTILE CONVULSIONS WITH PAROXYSMAL CHOREOATHETOSIS

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**Purpose:** We aimed to screen the mutations of proline-rich transmembrane protein 2 gene PRRT2 in benign familial infantile epilepsy (BFIE) and infantile convulsions with paroxysmal choreoathetosis (ICCA) in Chinese families.

**Method:** Twenty Chinese families with BFIE and four Chinese families with ICCA were recruited in this study. Clinical data was collected from the families. Genomic DNA was extracted from peripheral blood samples. Mutations of PRRT2 were analyzed using PCR amplification and DNA sequencing.

**Results:** Of the 20 BFIE families, 87 patients were clinically affected. Of the four ICCA families, 16 patients were affected, of which seven individuals with BFIE alone, four individuals with paroxysmal kinesigenic dyskinesias (PKD), and five individuals had infantile convulsions followed by PKD. PRRT2 mutations were detected in 11 of the 20 BFIE families. Mutation c.649dupC (p.R217PfsX8) was found in eight of these 11 families (72.7%), c.649delC (p.R217EfsX12) and c.904dupG (p.D302GfsX39) mutations were identified in two families and one family, respectively. PRRT2 mutations were found in 55% (11/20) of the Chinese BFIE families. PRRT2 mutations were also identified in four ICCA families, including c.649delC (p.R217EfsX12) mutation in two families, c.514-517delTCTG (p.S172RfsX3) mutation in one family, and a novel mutation of c.1023A>T (p.X341C) in another one family.

**Conclusion:** We found PRRT2 mutations are responsible for BFIE, PKD, or ICCA in Chinese families. The truncating mutation c.649dupC is a hotspot mutation of PRRT2 gene. We identified a novel mutation c.1023A>T (p.X341C) in a Chinese ICCA family, which is a terminator codon mutation causing the peptide elongation of amino acids.

### P624

#### GENETIC ANALYSIS IN THE PATIENTS WITH EPILEPSY AND INTELLECTUAL DISABILITY

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**Purpose:** Intellectual disability (ID) affects 1–3% of the population, suggesting that genetic factors may be common in 30–40% of patients. ID affects about 20–30% of patients with epilepsy. Our research group intended to organize a depository system at the National Centre for Neurology and Psychiatry, Tokyo for genetic analysis of patients with ID. In this study, we evaluated the genetic and clinical features of patients with epilepsy and developmental disorders associated with ID.

**Method:** We established the research resource facility and collected samples under informed consent by providing a diagnostic service for known genetic defects or chromosomal abnormalities, such as genes for *FMR1*, *FMR2*, *UBE3*, *ATRX*, *MECP2*, *ARX*, *PQBP1*, *RPS6KA3*, *IL1RAPL1*, *TM4SF2*, *OPHN1*, *PAK3*, *FACL4*, *AGTR2*, *ARHGEF6*, *GDI1*, *SLC6A8*, *FSTS1*, *ZNF41*, *DLG3*, *JARID1C* and copy number aberrations in CGH array analysis.

**Results:** As of the end of December in 2012, 455 ID families consisted of 164 familial and 291 sporadic cases have been registered. In these cases, approximately 44% cases accompanied with epilepsy and 20% cases with developmental disorders, respectively. Sixty-six positive genetic results were documented in 310 examined cases that had analysis of X-linked genes and array CGH, which combined account for approximately 21% of unexplained ID. Thirty cases with epilepsy had *MECP2*, *ARX*, *ATRX*, *ZNF41*, *FSTS1*, *SLC6A8* gene mutations, chromosomal micro-deletions and micro-duplications, and Xq28 duplications including *MECP2*.

**Conclusion:** Approximately 44% of our cohort had ID accompanied by epilepsy. By analysis of X-linked genes and chromosomes including using array CGH, approximately 21% of cases had a genetic diagnosis.

### P625

#### SPECTRUM OF SCN1A MUTATIONS IN CHINESE PATIENTS WITH FEBRILE SEIZURES RELATED EPILEPSY

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**Purpose:** To characterize the clinical and genetic features of febrile seizures related epilepsy in Chinese patients.

**Method:** Total 940 patients were divided into five groups, which included repetitive febrile seizure (FS), FS plus (FS+), generalized epilepsy with febrile seizures plus (GEFS+), partial epilepsy with febrile seizures plus (PEFS+) and Dravet Syndrome (DS). All patients were screened for mutations in *SCN1A* using dHPLC, sequencing and pyrosequencing.

**Results:** A total of 46 mutations in 60 (6.4%, 60/940) patients was detected, and these consisted of 27 missense mutations, 17 truncation (including 1 exons deletion) and two noncoding region variations. All truncating mutations were de novo, found in 71% (12/17) patients with DS and 29% (5/17) PEFS+, but not found in milder patients with FS, FS+ and GEFS+. Missense mutations in the pore region constitute 33% (15/46) and correspond to 63% DS (5/8), 50% PEFS+ (6/12), GEFS+ (3/6) and FS (1/2) patients respectively. Outside of pore region missense mutations were present in 28% (13/46) and correlate with 50% (4/8) milder patients and 33% (4/12) PEFS+ patients. Six of 6 (100%), five of 12 (42%) and four of 21 (19%) mutations were inherited in patients with GEFS+, PEFS+ and DS respectively. It is noted that three of 4 (75%) inherited mutations in DS and two of 5 (40%) in PEFS+ were transmitted by mosaic parents.

**Conclusion:** The results indicate febrile seizures related epilepsy is associated with *SCN1A* and PEFS+ is the intermediate type with regarding to

type and location of mutation, transmitted pattern and phenotype in these patients.

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## P626

### THE *PRRT2*-RELATED DISORDERS: FURTHER PKD AND ICCA CASES AND REVIEW OF THE LITERATURE

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**Purpose:** Recent studies reported mutations in the gene encoding the proline-rich transmembrane protein 2 (*PRRT2*) to be causative for paroxysmal kinesigenic dyskinesia (PKD), PKD combined with infantile seizures (ICCA), and benign familial infantile seizures (BFIS). *PRRT2* is a presynaptic protein which seems to play an important role in exocytosis and neurotransmitter release. PKD is the most common form of paroxysmal movement disorders characterized by recurrent brief involuntary hyperkinesias triggered by sudden movements.

**Method:** Here, we sequenced *PRRT2* in 14 sporadic and eight familial PKD and ICCA cases of Caucasian origin by standard methods including the exon-intron boundaries.

**Results:** The study could identify three novel mutations (c.919C>T/p.Gln307\*, c.388delG/p.Ala130Profs\*46, c.884G>A/p.Arg295Gln) predicting two truncated proteins and one probably damaging point mutation. A review of all published cases is also included. *PRRT2* mutations occur more frequently in familial forms of *PRRT2*-related syndromes (80–100%) than in sporadic cases (33–46%) suggesting further heterogeneity in the latter.

**Conclusion:** *PRRT2* mutations were rarely described in other forms of paroxysmal dyskinesias deviating from classical PKD, as we report here in one ICCA family without kinesigenic triggers. Mutations are exclusively found in two exons of the *PRRT2* gene at a high rate across all syndromes and with one major mutation (c.649dupC) in a mutational hotspot of nine cytosines, which is responsible for 57% of all cases in all phenotypes. We therefore propose that genetic analysis rapidly performed in early stages of the disease is highly cost-effective and can help to avoid further unnecessary diagnostic and therapeutic interventions.

## P627

### PHENOTYPE OF PATIENTS WITH A COMMON C.649\_650C *PRRT2* MUTATION

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**Purpose:** *PRRT2* genes have been identified as causative genes for benign infantile epilepsy (BIE), paroxysmal kinesigenic dyskinesia (PKD), and hemiplegic migraine. Among them, a c.649\_650C mutation has been found in a large majority of such patients. We reviewed the phenotypes of patients with this common *PRRT2* mutation.

**Method:** We explored *PRRT2* mutations in patients with BIE/PKD and other types of infantile epilepsies with favorable outcome. We recruited clinical data using a structured form. This study was approved by the ethics committees of the institution.

**Results:** A common c.649\_650insC mutation was found in 29 of 35 patients with *PRRT2* mutations. Fourteen patients had BIE, three had PKD, and 11 had both. One patient had no neurological symptoms. Twenty-six patients have family history of BIE and/or PKD. The mean age at onset of BIE is 5.1 months (range, 3–14 months) and the mean age at seizure offset was 11.3 months (range, 3–106 months). The mean number of seizures was 7.8 (range, 1–21). The mean age at PKD onset was 9 years (range, 4–16 years). Only one patient had mild mental retardation. Three had febrile seizure and no patient had convulsion with gastroenteritis.

**Conclusion:** Patients with a common c.649\_650insC *PRRT2* mutation had frequent family history and mostly showed typical phenotype. These data will be useful to provide appropriate information to the patients and families.

**Acknowledgement:** We thank all doctors who provided blood samples for this study.

## P628

### X-LINKED PERIVENTRICULAR NODULAR HETEROTOPIA DUE TO *FLNA*-MUTATION INHERITED BY THE FATHER

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**Purpose:** Bilateral periventricular nodular heterotopia (PNH) is a developmental disorder, characterized by heterotopic nodules of cerebral grey matter resulting from disturbed CNS development. A common form of PNH is familial, X-linked dominant, and related to Filamin A gene (*FLNA*) mutation. The classic patient with *FLNA*-associated PNH therefore is female, the main presentation is difficult to treat seizures. Several other clinical findings can be associated, e.g. congenital heart disease. Male offspring is reported as lethal. Here we present familial PNH with paternal transmission of a causal *FLNA* mutation

**Methods:** Clinical histories, MRI, molecular genetics.

**Results:** Index patient was a mentally retarded 31y female with drug-resistant epilepsy. We unraveled a formerly undetected positive family history (father with easily controlled seizures, sister with few seizures and a history of ductus arteriosus Botalli), and PNH in all of them. A c.5686G>A *FLNA* splice mutation was found in father and both daughters with strikingly different clinical manifestation in the family members.

**Conclusion:** Male PNH can be *FLNA*-related. Classic PNH in a female patient might be inherited from the father. This observation stresses the importance to consider the rare genetic constellation of paternal transmission for families with X-linked dominant *FLNA*-associated PNH.

## P629

### ETIOLOGY OF HIPPOCAMPAL SCLEROSIS: FURTHER EVIDENCE FOR A PREDISPOSING FAMILIAL MORPHOLOGICAL ABNORMALITY

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**Purpose:** The etiology of hippocampal sclerosis (HS) is likely to be multifactorial. We sought evidence of a hereditary component by determining if close relatives of probands with temporal lobe epilepsy (TLE) with HS also had asymptomatic HS or subtle variation in hippocampal morphology.

**Methods:** First degree relatives from 15 families where probands had TLE with HS and 32 age and gender matched controls were included in the study. Left and right hippocampal volumes and T2 relaxometry were measured using 3T MRI.

**Results:** Thirty-two asymptomatic first degree relatives and three relatives with a history of seizures or epilepsy were studied. None of the first degree relatives had HS on visual analysis and T2 relaxation times were normal, excluding the presence of HS. Mean hippocampal volume was smaller in asymptomatic relatives ( $2.91 \pm 0.29 \text{ cm}^3$ ) than in controls ( $3.14 \pm 0.22 \text{ cm}^3$ ,  $p < 0.005$ ); the effect was greater in relatives of probands with a positive family history of epilepsy. The relatives also had more asymmetric hippocampi (asymmetric index  $0.92 \pm 0.05$ ) than controls ( $0.96 \pm 0.03$ ,  $p = 0.001$ ).

**Conclusion:** Small asymmetric hippocampi in healthy relatives are likely to represent a familial developmental variant that may predispose to the formation of TLE with HS. The underlying histopathology of these small hippocampi is unknown. This observation may provide an imaging marker for future studies seeking susceptibility genes for HS.

## P630

### SYSTEMS BIOLOGY APPROACH TO JUVENILE MYOCLONIC EPILEPSY: CONTRIBUTION OF THE IONOTROPIC GABAERGIC SYSTEM

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**Purpose:** To review protein mutations reported in family and exome sequencing studies in Juvenile Myoclonic Epilepsy (JME) patients. JME is genetically heterogeneous (OMIM #254770/EJM1-9). Some JME patients require, in addition to valproate or lamotrigine, pharmacotherapy with drugs enhancing ionotropic GABAergic neurotransmission; we postulate that a subset of JME patients have genetically determined abnormalities in this system.

**Method:** Review of presynaptic and postsynaptic proteins found in GABAergic synapses, placed in a cellular and anatomic context (selected mammalian examples of regional localization are given in parentheses) and related to protein mutations in OMIM, or predicted in Heinzen et al 2012, marked\*.

## Results:

#### Presynaptic nerve terminal proteins/protein complexes:

Rate-limiting enzyme of vesicular GABA synthesis: GAD2-R558C\* (eg motor thalamus),  
Vesicular ATPase complex: ATP6V0D2-D12H\*; ATP6V1G2-truncated\* (eg Purkinje cells),  
Sodium channel, voltage-gated, alpha subunit: SCN5A-G833R\* (eg indirect pathway striatal projection neurons),  
Vesicular exocytosis-associated proteins: STXBP5-truncated\*, STX6-W45C\* (eg direct pathway striatal projection neurons).

#### Post-synaptic ionotropic receptor subunits/interactants:

GABRA1-A322D(EJM5), GABRB2-truncated\* and GABRD-R220H(EJM7) (all widely distributed in mammalian CNS, including motor cortex, basal ganglia, cerebellum)  
Scaffolding proteins: RDX-T516I\* (Rdx stabilizes hippocampal Gabra5)  
Trafficking proteins: TRAK2-multiple mutations\*; Trak2 traffics Gabrb2 to the neuronal cell surface  
Developmental proteins modulating cell division and migration of projection neurons and/or GABAergic interneurons in brain motor pathways: EFHC1-multiple mutations (EJM1) and in a JME mouse model, Brd2<sup>+/-</sup>.

An abnormal connectome is found in imaging studies of JME, in the supplementary and primary motor cortex, striatum, and motor nuclei of the thalamus (eg ventral anterior). The Brd2<sup>+/-</sup> knockout mouse model has decreased numbers of GABAergic cells in various nuclei of the direct motor pathway of the basal ganglia.

## Conclusions:

- 1 Multiple proteins interacting in ionotropic GABAergic neurotransmission are mutated in JME.
- 2 JME may be a network disease; various structures in brain motor regions may be affected by different protein mutations, causing network dysfunction.

## P631

### INCREASED CPA6 PROMOTER METHYLATION IN FOCAL EPILEPSY AND IN FEBRILE SEIZURES

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**Purpose:** Focal epilepsy (FE) is one of the most common forms of adult epilepsy. Febrile seizures (FS) often appear during childhood in FE patients. FS are the most frequent human convulsive event associated with fever. We previously showed that *Carboxypeptidase A6* (*CPA6*) gene, which encodes an extracellular exopeptidase, is involved in FS and FE [Salzmann A et al. Hum Mutat. 2012 33:124–35] [Sapio MR et al. J Biol Chem. 2012 287:42900–9]. Genetic evidences for FS and FE have suggested a complex mode of inheritance, where environmental factors might play a role through epigenetic modification. Therefore, we assessed DNA methylation in the promoter of *CPA6*.

**Method:** We measured methylation level in Caucasian cohorts of 186 FE patients, 92 FS patients and 93 healthy controls. Linear regression test was performed to detect the association between levels of methylation and clinical phenotypes.

**Results:** FE ( $3.4\% \pm 3.2\%$ ) and FS ( $4.3\% \pm 3.5\%$ ) patients had significantly higher *CPA6* methylation level than controls ( $0.8\% \pm 2.9\%$ ),  $p = 5.1 \times 10^{-10}$  and  $p = 4.2 \times 10^{-12}$ , respectively. Furthermore, the association evaluating all patients showing FS (FS + FEFS\*) ( $4.0\% \pm 3.5\%$ ) vs. all individuals without FS (FEFS\* + controls) ( $2.2\% \pm 3.2\%$ ) was significant,  $p = 0.001$ . Nevertheless, neither comparisons of FE with

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FS (3.4% ± 3.5%) vs. FE patients without FS (3.3% ± 3.1%) nor FE with HS (3.3% ± 3.4%) vs. FE without HS (3.4% ± 3.1%) were significant.

**Conclusion:** All these results suggest that an epileptic seizure (FE and/or FS) could be a factor which leaves an epigenetic mark on DNA. Consequently, these findings support the growing body of evidence showing the involvement of DNA methylation in epilepsy.

## P632

### TOWARDS A STRATEGY TO UNRAVEL AUTOSOMAL RECESSIVE ENCEPHALOPATHIES

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**Purpose:** Explore different strategies to elucidate the role of homozygous or compound heterozygous variants in families with two or more patients with an epileptic encephalopathy (EE).

**Method:** We collected nine families compatible with autosomal recessive inheritance: two multiplex families with respectively three and four affected individuals in two branches, six families with two affected sibs and one with six affected children. Two families were known inbred families, in one consanguinity was suspected. We performed whole exome sequencing (WES) on all index patients. We also included one additional patient for the largest multiplex family and one of the consanguineous families. Linkage was performed on four families with the highest predicted power: the two multiplex families, the family with six affected sibs and one consanguineous family. All analyses were performed under different models: homozygous, compound heterozygous and mosaic autosomal dominant.

**Result:** None of the families carried a mutation in a known epilepsy gene. After applying our optimized filters, we found (on average) 95 homozygote variants in a single exome and 125 genes with heterozygous double hits. Adding one affected family member to the WES analysis reduced these numbers by 50%. Without reaching conclusive linkage, we identified three to twelve suggestive loci per family. Combining these delineated genomic regions can further reduce the number of candidate variants to validate.

**Conclusion:** To identify recessive inherited genes in families with EE, we explored the possibility of sequencing only one patient per family. We believe that, although this could be sufficient when a variant is present in a known epilepsy gene, the decrease in time and labor intensity for validation is considerable enough to sequence two patients from the start. We furthermore established that combining suggestive linkage with WES can decrease the number of variants to validate, if sufficient family members are available for phasing.

## P633

### ASSOCIATION OF HLA-B\*1502 ALLELE AND LAMOTRIGINE-INDUCED STEVENS-JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS IN HAN CHINESE: A META-ANALYSIS

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**Purpose:** Despite several studies conducting the association research between human leukocyte antigen, HLA-B\*1502 and lamotrigine-induced Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), the association remains unclear. We performed a systematic review and meta-analysis to obtain the association between HLA-B\*1502 allele and lamotrigine-induced SJS and TEN.

**Method:** We searched biomedical literature in databases including MEDLINE, Cochrane Library, EMBASE, the Chinese Biomedical Database (CBM), the Chinese National Knowledge Infrastructure (CNKI) and the Chinese Science and Technique Journals Database (VIP). Only studies investigating association between HLA-B\*1502 and lamotrigine-induced SJS/TEN were included. The Cochrane Collaboration's software RevMan 5.0.24 and Stata software release 12.0 were used for the meta analysis.

**Results:** Four studies (12 SJS/TEN cases and 128 lamotrigine-tolerant control) were identified. HLA-B\*1502 allele was present in 33.3% (4/12) of lamotrigine-induced SJS/TEN cases but in only 9.4% (12/128) lamotrigine-tolerant control. Compared with lamotrigine-tolerant control, SJS/TEN cases were associated with HLA-B\*1502 allele (OR 4.98, 95% CI 1.43–17.28,  $p < 0.05$ ).

**Conclusion:** We found a statistical association between HLA-B\*1502 and lamotrigine-induced SJS/TEN. Future studies with larger sample sizes are suggested to verify the results.

## P634

### SPLICE-SITE MUTATIONS IN SCN1A CAUSE EPILEPSIES WITH FEBRILE SEIZURES: MECHANISMS AND CORRELATIONS WITH CLINICAL SEVERITY

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**Purpose:** The sodium channel  $\alpha 1$  subunit (SCN1A) gene is associated with febrile seizures (FS)-related epilepsies. The mutation types of SCN1A, such as truncation, splice-site and missense mutations, are important determinants of phenotypes. In contrast to truncation or missense mutations in which the resulting protein abnormalities are known, the consequences of splice-site mutations in SCN1A are not studied. It is also considered whether mutations adjacent to splice-site may affect splicing and are associated with epilepsy.

**Method:** Mutations in SCN1A were screened by PCR amplification and denaturing high performance liquid chromatography (DHPLC) analysis and direct sequencing in patients with epilepsy and FS. In vitro minigene splicing assay was applied to investigate the consequences of 11 mutations at or adjacent to splice-sites of SCN1A.

**Results:** Three mutations in invariant splice junction caused exon or partial exon skipping, including mutations c.602 + 1G>A, c.3705 + 1G>T and c.4284 + 2T>C that caused skipping of exon 4, partial skipping of exon 18 (49 bp) and skipping of exon 21, respectively. The associated phenotype was Dravet syndrome. Mutation c.473 + 5G>A generated two aberrant transcripts, partial exon 3 skipping and exon 3 plus partial exon 2 skipping. Two patients with this mutation had FS+ or partial epilepsies and FS+ (PEFS+). Two mutations in introns that are more away from the splice sites, including c.473 + 110A>G and c.4853-25T>A, generated aberrant transcripts as well as normal transcripts. The aberrant transcripts included one with intron 3 retained and another with a 26 bp-intron

sequence retained. The phenotypes associated with these two mutations were PEFS+. In contrast, no aberrant transcripts were detected in mutations that are located in exon and are adjacent to SCN1A splice-sites.

**Conclusion:** This is the first report showing the consequences of SCN1A splice-site mutations in epilepsy patients. The severity of epilepsy is correlated with aberrant splicing level, which depends on the location of mutations.

### P635

#### FAMILIAL CORTICAL MYOCLONIC TREMOR AND EPILEPSY (FCMTE): REFINEMENT OF THE FCMTE2 LOCUS

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**Purpose:** To describe the clinical, neurophysiological and genetic features of a new, large Italian family with Familial Cortical Myoclonic Tremor and Epilepsy (FCMTE) from the province of Naples.

**Methods:** Reliable clinical information was obtained on the 127 members. 31 collaborative individuals were assessed directly. A polygraphic study was conducted in 15 patients, back-averaging analysis and somatosensory evoked potentials with C-reflex study in four. The genetic study investigated 29 subjects with microsatellite markers at three loci on chromosomes 8q (FCMTE1), 2p (FCMTE2) and 5p (FCMTE3).

**Results:** The pedigree included 25 affected members (M/F: 9/16). We studied 16 of the 19 living affected members (M/F:5/11; mean age 47.8 years). Cortical myoclonic tremor (CMT) was associated with generalized seizures in ten patients (62.5%). The mean age at onset of CMT and seizures was 28.1 and 33.8 years, respectively. Four patients (25%) reported a slow progression of CMT with gait impairment in one. Psychiatric disorders occurred in 37.5% of cases. Rhythmic bursts at 7–15 Hz were recorded in all 11 affected members tested. Additional neurophysiological investigations confirmed a cortical origin of myoclonus in all patients tested. Genetic analysis established linkage to the FCMTE2 locus on chromosome 2p11.1-2q12.2 and narrowed the critical interval to a 10.4 Mb segment.

**Conclusion:** This study reduces the number of positional candidate genes in the FCMTE2 locus to 59, thereby contributing to future gene identification by Next Generation Sequencing approaches.

### P636

#### COPY NUMBER VARIANT BURDEN IN A PEDIATRIC POPULATION WITH EPILEPSY

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**Purpose:** Array-comparative genomic hybridization (array-CGH) has allowed the identification of many Copy Number Variants (CNVs) underlying different neurodevelopmental conditions including epilepsy. A systematic evaluation of a pediatric cohort with complex epilepsy has not yet been reported. We aimed to study the occurrence and significance of CNVs in pediatric epilepsy.

**Method:** We used array-CGH on a pediatric population with complex epilepsy phenotypes recruited from Great Ormond Street Hospital for Children, London.

**Results:** Two hundred and ninety-nine patients (172 male) with epilepsy were screened. A total of 26 significant CNVs (11 gains and 15 losses) were identified in 23/299 cases (7.7%); no recurrent significant CNVs were found except for the previously-described 15q13.2-13.3 deletion (two patients: one with atypical absence seizures with intellectual disability and one with infantile spasms and focal epilepsy of structural origin) and 16p13.11 deletion (two patients: one with infantile spasms and one with focal epilepsy of unknown cause). One hundred and eighty-one cases (60%) showed at least one CNV of unknown significance. 40/299 cases (13%) had involvement within the rearrangement of at least one gene previously reported associated with epilepsy.

**Conclusions:** We show that array-CGH is a useful tool to detect pathogenic CNVs in pediatric epilepsies. CNVs of unknown significance are under study as their interpretation is challenging, requiring large numbers of patients, and re-evaluation using evolving bio-informatic tools.

### P637

#### KCNQ2 AND KCNQ3 ABNORMALITIES IN BENIGN NEONATAL EPILEPSY (BNE): A GENETIC ANALYSIS OF BNE IN JAPAN

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**Purpose:** Benign familial or non-familial neonatal epilepsy (BFNE or BNE) is characterized by neonatal onset, focal partial seizures, spontaneous remission and normal mental development without secondary epilepsy. Genetic abnormalities of BFNE or BNE have been reported in KCNQ2 and KCNQ3 which encode potassium channel subunits. Among families or patients with mutations, it has been estimated that above 50% occur in KCNQ2 and <7% in KCNQ3. This study attempts to analyze the proportion of KCNQ2 and KCNQ3 mutations in Japanese BFNE and BNE.

**Methods:** A total 55 patients were recruited: 40 with BFNE; eight with BNE; and seven whose family histories were unclear. The mutations were identified by Sanger sequencing and MLPA.

**Results:** We identified KCNQ2 or KCNQ3 mutations in 16 patients (29.0%) with BFNE or BNE. KCNQ2 mutations were identified in 14 patients (25.5%); KCNQ3 mutations were identified in two patients (3.6%). Among the 14 KCNQ2 mutations, five were SNVs (35.7%) and three small indels (21.4%), both detected by Sanger sequencing. There were 5 micro-deletions (35.7%) and one duplication (7.1%) identified by MLPA. Both of the KCNQ3 mutations were SNVs.

**Conclusion:** The frequency of KCNQ2 and KCNQ3 mutations was lower than previously estimated. While we suspect that an incorrect diagnosis of BFNE or BNE was made, our study suggests that abnormalities in other genes may exist as a cause of BFNE and BNE in Japan. These genes will need to be identified to reveal their molecular pathomechanisms.

## P638

**POLYMORPHISM OF THE MULTIDRUG RESISTANCE 1 GENE MDR1/ABCB1 C3435T AND RESPONSE TO ANTIEPILEPTIC DRUG TREATMENT IN TEMPORAL LOBE EPILEPSY**

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**Purpose:** The efflux transporter P-glycoprotein (P-gp) encoded by the multidrug resistance 1 gene (MDR1), systematic name ATP-binding cassette subfamily B1 gene (ABCB1), may play a role in drug-resistant epilepsy. A synonymous C to T variant at position 3435 (3435C>T) is one common polymorphism of the MDR1/ABCB1 gene. It has been suggested that this polymorphism, and more specifically the 3435CC genotype, may be associated with the response to antiepileptic drug treatment. However, conflicting data have been reported with regard to the functional relevance of MDR1/ABCB1 allelic variant for the response to antiepileptic drugs. Existing literature suggests that the frequency of the synonymous 3435C>T polymorphism has been shown to vary significantly according to ethnicity. Here we wished to examine the role of such candidate variant in a cohort of 175 patients (98 women and 76 men; mean  $\pm$  SD age: 47.90  $\pm$  17.64) with Temporal lobe epilepsy (TLE).

**Method:** Patients were classified according to whether they had drug-responsive (n = 134) or drug-resistant epilepsy (n = 41). We also enrolled 175 healthy controls (93 women and 82 men; mean  $\pm$  SD age: 72.5  $\pm$  6.8), matched for sex and ethnicity. Patients and controls were genotyped for detection of the 3435C>T polymorphism using TaqMan Allelic Discrimination assays, on an Applied Biosystems PCR platform. All patients and controls were Caucasian and were born in Italy.

**Results:** Patients and controls were genotyped for detection of the 3435C>T polymorphism, but the analysis showed no significant association between the CC genotype and the risk of drug-resistant epilepsy.

**Conclusion:** Although our results cannot definitively rule out a role for this gene, they do suggest that 3435C>T polymorphism in our population is unlikely to be a marker for pharmacoresistance in TLE.

## P639

**ROLE OF RARE COPY NUMBER VARIATIONS IN MALFORMATIONS OF HUMAN CEREBRAL CORTEX**

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**Purpose:** Individuals with malformations of cerebral cortex (MCC) often present seizures which are refractory to antiepileptic drugs. Advances in molecular biological led to a better understanding of MCC etiology. However, the genetic defect remains unidentified in the majority of patients with MCC. Recent studies have implicated rare copy number variations (CNVs) in a range of neurodevelopmental disorders. The aim of this study was to identify CNVs which could be associated with MCC.

**Method:** We used a high resolution SNP-array to investigate CNVs in a cohort of 33 patients with MCC, including lissencephaly, nodular periventricular heterotopia and schizencephaly. To assess the

clinical significance of our insertions/deletions findings, we searched the CNVs found in the *Database of Genomic Variants* (DGV) and *The International Standards for Cytogenomic Arrays Consortium* (ISCA). Genes located within rare CNVs were searched at *Gene Ontology Terms* (Go).

**Results:** We detected at least one rare CNV in 13 patients (40%), with a total of 19 rare CNVs identified. Average size of CNVs was 223 kb, ranging from 113 to 456 kb. Each CNV contains approximately two genes. Potentially pathogenic CNVs, according to DGV and ISCA databases, contain genes involved with cell division (*NCAPG2*, *HAUS7*), vesicle mediated transport (*TSNARE1*), cytoskeleton organization (*DAAMI*, *ACTR6*) and axon guidance or neuronal migration (*PLXNA1*, *KIRREL3*, *ARX*, *DCX*).

**Conclusion:** We found a significant number of rare CNVs in patients with MCC. Several genes identified within the CNVs found are related to molecular pathways involved in MCC etiology. Deleterious mutations in genes controlling mitosis, vesicle mediated transport, cytoskeleton organization and neuronal migration, such as *WDR62*, *AFGRF2*, *FLN1* and *LISI* have been reported in patients with MCC. Therefore, we have shown that SNP-arrays can be used successfully to identifying candidate genes involved in the etiology of MCC, as well as an important diagnostic tool in the clinical setting.

## P640

**ASSOCIATION BETWEEN HLA-A\*2402 ALLELE AND LAMOTRIGINE-INDUCED STEVENS-JOHNSON SYNDROME IN HAN CHINESE**

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**Purpose:** Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but severe cutaneous adverse reactions (SCAR) caused by a certain number of medications including antiepileptic carbamazepine (CBZ) and lamotrigine (LTG). Although a strong association between CBZ-SJS/TEN and HLA-B\*1502 has been found in Han Chinese patients, the relationship between LTG induced-SJS/TEN and HLA-B\*1502 was uncertain. Our previous study indicated a potential association between HLA-A\*2402 and CBZ-SJS/TEN. We thus investigated the involvement of HLA-A, B alleles in LTG-SJS Han Chinese patients.

**Methods:** The HLA-A, B genotyping were performed on seven LTG-induced SJS patients and 22 LTG-tolerant subjects who were on the drug for more than 3 months without the adverse reactions.

**Results:** Only one patient with LTG-SJS was positive for HLA-B\*1502. The presence of HLA-B\*1502 in LTG-SJS did not differ significantly from that in LTG-tolerant controls (p = 0.65, OR = 0.44, 95%CI 0.04–4.50). However, we found that HLA-A\*2402 was present in five out of seven (71.4%) LTG-SJS patients, which was significantly higher than that in LTG-tolerant controls (9.1%, 2/22) (p = 0.003, OR = 25, 95%CI 2.79–223.67). No statistical differences were found between the LTG-induced SJS group and the tolerant group in the term of mean age, sex ratio and LTG usage.

**Conclusion:** Our results indicate that HLA-B\*1502 may not be a satisfactory genetic marker of LTG-SJS in Han Chinese. Instead, HLA-A\*2402 is potentially associated with LTG-SJS, and it warrants further study in a larger sample size.

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### NEUROMETABOLIC EFFECT OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION IN THE EPILEPTIC BRAIN: A SHAM-CONTROLLED PROTON MAGNETIC RESONANCE SPECTROSCOPY STUDY

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**Purpose:** The study was designed to evaluate the neurometabolic effect of single and ten sessions of low-frequency repetitive transcranial magnetic stimulation over temporal lobe of epileptogenic hemisphere.

**Method:** Sixteen patients with resistant epilepsy (mean age  $28.1 \pm 2.9$  years) were enrolled in a prospective single-blind, randomized study (sham [n = 7] vs. real [n = 9]). RTMS (1 Hz, 20% MMI intensity of ring coil) was performed during 10 min over the temporal lobe projection with "focusing" over hippocamp. Hippocampal brain regions bilaterally were investigated by single-voxel proton magnetic resonance spectroscopy (1H MRS) before and after rTMS.

**Results:** Our results showed a significant reduction of seizure frequency after real 10 rTMS sessions that lasted for at least 3 months following treatment patients ( $p < 0.05$ ). These clinical changes were correlated with increases in N-acetylaspartate (NAA)/Cholin (Cho)+Creatin (Cr) ratio in the ipsilateral hippocamp region and decreases of that ratio in lateral temporal region after single and ten rTMS sessions ( $p < 0.05$ ). We found a trend for a positive correlation between increases NAA/Cho+Cr ratio levels after rTMS at both hippocampus and remission of epilepsy after complex therapy ( $r = 0.67$ ,  $p = 0.05$ ). For the sham group, there were no any significant changes in NAA/Cho+Cr ratio levels ( $p > 0.1$ ).

**Conclusion:** New technology of low-frequency rTMS delivered into temporal lobe leads to significant antiepileptic effect at patients with resistant epilepsy. That effect correlated with neurometabolic effect in deep brain regions and can predict course of epilepsy after complex therapy with low-intensity rTMS.

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### IN VIVO 4.7 TESLA MRI-BASED MANUAL HIPPOCAMPAL SEGMENTATION IDENTIFIES SUBFIELD-SPECIFIC VOLUME LOSS IN PATIENTS WITH MESIAL TEMPORAL SCLEROSIS: RESULTS FROM A PILOT STUDY

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**Purpose:** Histological literature has demonstrated that classical mesial temporal sclerosis (MTS) selectively involves certain hippocampal subfields (CA1&CA4) and spares others (CA2 ± CA3). Studies have indicated that atypical subtypes of MTS (CA1 predominant & endfolium sclerosis) have different responses to temporal lobectomy. Thus, methods to identify subfield-specific volume loss could assist in predicting surgical outcome preoperatively. Our group has described a method for in-vivo manual segmentation of the human hippocampus in healthy controls. We aimed to determine if this technique identifies subfield-specific volume loss in patients with MTS.

**Method:** Four healthy volunteers aged 23–56 and four unilateral-temporal lobe epilepsy (TLE) patients (based on telemetry) aged 26–45 were studied. TLE patients were classified as MTS (3/4) vs. nonlesional (1/4) based on quantitative-T2-relaxometry. All subjects were scanned at 4.7T using a t2-weighted Fast Spin Echo sequence (spatial resolution  $0.52 \times 0.68 \times 1.0 \text{ mm}^3$ ). Hippocampi were segmented and subfield volumes measured for the: (i) DG (Cornu-Ammonis-4 and Dentate-Gyrus) (ii) SUB (Subiculum) (iii) CA (Cornu-Ammonis-1-3). Patient volumes were compared to the lower limit of normal (calculated as normal controls' mean volume (n = 8) minus two standard-deviations).

**Results:** Volume loss was identified in the DG subfield in 1/3 MTS patients contralateral to the symptomatic hippocampus, while all other subfields were spared. In the symptomatic hippocampus, significant volume loss was demonstrated in 2/3 patients. One patient demonstrated atrophy of CA and DG, while the other manifested volume loss in all three subfields. The single nonlesional patient did not manifest volume loss in either hippocampus.

**Conclusion:** Our preliminary results suggest that hippocampal subfield pathology can be detected with subfield volumetry performed using high resolution MRI at ultrahigh magnetic field strength. These preliminary observations require confirmation with larger sample size. In addition, histological validation of in vivo segmentation protocols is required.

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### PECULIARITIES OF STRUCTURAL WHITE MATTER ABNORMALITIES AND CLINICAL ASPECTS OF EPILEPSY

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**Purpose:** The current study examined patterns of white matter tracts abnormalities and relationships with clinical and neurophysiologic factors in subjects with epilepsy.

**Method:** DTI data with tractography were obtained in 46 epilepsy patients (36 with pharmaco-resistant subjects and 10 at remission stage) and 10 age-matched healthy controls using 1.5-Tesla MR scanner (Philips). Analysis of fractional anisotropy (FA) and mean diffusivity (MD) for anterior and posterior hemispheric quadrants was performed. Correlation analysis for FA and MD with clinical course of disease, neuropsychological state, EEG-mapping and cognitive event potentials parameters was carrying out.

**Results:** Subjects with epilepsy, as compared to healthy controls, demonstrated four patterns of tracts reduce: in frontal lobe, lateral parts of hemisphere mono- or bilaterally, anterior and/or posterior commissure, complex of several tracts changes. Epilepsy subjects have reduced FA, predominately in the epileptogenic cerebral hemisphere ( $p < 0.05$ ). MD increasing and pattern of tracts reduce in frontal lobe typified for pharmaco-resistant course of disease ( $p < 0.05$ ). Pattern of tracts reduce in lateral parts of hemisphere monolaterally correlated with focal onset of epilepsy, bilaterally – with generalized seizure onset ( $R = 0.42$ ,  $p = 0.03$ ). Anterior and/or posterior commissural reducing correlated with prolonged P300 latency ( $R = 0.39$ ,  $p = 0.029$ ). Mean FA and MD was positively correlated with Beck and Spielberg-Hanin scales data ( $R = -0.2$ ,  $p < 0.001$ ) and P300 latency ( $R = 0.23$ ,  $p < 0.001$ ). Epileptic EEG activity presence was correlated with FA reduction ( $R = 0.7$ ,  $p = 0.01$ ).

**Conclusion:** Epilepsy is associated with widespread disturbances in white matter tracts. DTI data can be predictors of clinical course of disease and cognitive disturbances.

## P644

### ADVANCED MRI MORPHOLOGICAL STUDY SHOWS NO ATROPHY IN HEALTHY INDIVIDUALS WITH HIPPOCAMPAL HYPERINTENSITY

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**Purpose:** We already illustrated that brain MRI study of healthy individuals frequently reveals either unilateral or bilateral *Hh* that is considered a hallmark of hippocampal sclerosis. We have carried out a follow-up (5-year interval) clinical and advanced imaging study of these individuals to address whether *Hh* may have masked occult brain atrophies, or contributed to a later onset of epilepsy.

**Methods:** Subjects with *Hh* (n = 13) underwent a detailed clinical-imaging protocol, with a 3 tesla scan and studied with automated hippocampal segmentation (Freesurfer), whole brain voxel-based morphometry (VBM) and shape analysis.

**Results:** All 13 subjects with *Hh* had a normal neurological examination with no cognitive impairment. All multimodal structural neuroimaging methods did not show a clear evidence of significant volumetric changes between subjects with or without *Hh*.

**Conclusion:** We clearly illustrated that *Hh* is not associated with any occult brain atrophies, and furthermore none of the healthy subjects with MRI evidence of *Hh* have developed epilepsy or trouble in cognition.

## P645

### DIFFUSE CORTICAL ATROPHY IN EXTRA-TEMPORAL EPILEPSY WITH NON-DIAGNOSTIC MRI

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**Purpose:** MRI has led to increased rates of focal cortical dysplasia (FCD) detection. Nevertheless, many lesions evade identification even through image processing, although resected specimens may reveal subtle dysplasia. This suggests that patients with non-diagnostic MRI may harbor lesions that fall below MRI detection threshold, and that cryptogenic epilepsy likely exist on a biological continuum with FCD. We aimed at investigating morphological integrity of the neocortex in cryptogenic epilepsy and FCD using whole-brain cortical thickness analysis.

**Method:** We obtained MRI-based cortical thickness in 36 patients with histologically-proven FCD and 37 patients with non-diagnostic MRI (cryptogenic) matched for age, duration of epilepsy and number of generalized seizures. We compared each group to healthy controls (n = 41) using vertex-wise t-tests. We examined longitudinal changes (3.5-years interval) in cryptogenic patients using linear mixed effect models. Results

Cross-sectional group comparisons revealed diffuse bilateral multilobar (fronto-central, parietal, occipital) cortical thinning in both groups, although anomalies were more localized and milder in FCD. Vertex-wise power analysis showed that limited atrophy in FCD was not due to small sample size. Longitudinal analysis revealed faster cortical thickness decline the frontal lobe in patients with pre-central foci compared to those with post-central foci, implying that atrophy may be part of the primary epileptogenic lesion.

**Conclusion:** Despite similar clinical characteristics between the two cohorts, differences in imaging phenotype suggest that factors other than excitotoxic effects of seizures may contribute to the morphological

anomalies observed in cryptogenic epilepsy. Widespread atrophy in patients with non-diagnostic MRI may reflect subtle and diffuse cortical dyslamination.

## P646

### EEG-fMRI OF THE CYCLIC ALTERNATING PATTERN IN HUMAN NREM SLEEP

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**Purpose:** The EEG of NREM sleep in humans is characterized by alternating phases of synchronization and de-synchronization, otherwise known respectively as phases A and B of the cyclic alternating pattern (CAP). By means of EEG-fMRI, this study aimed in determining the brain regions responsible for the accumulation of brain rhythms and waves occurring during every CAP-A phase.

**Method:** Nine patients of various epileptic syndromes achieved NREM sleep of sufficient duration while undergoing resting state EEG-fMRI in the context of their assessment for epilepsy. A GLM with CAP-A blocks (664 in total) was formed and analyzed by means of SPM for every patient.

**Results:** fMRI analysis revealed a basic network involving the insula (in 9/9 patients), the thalamus (7/9) and the cingulate gyrus (8/9), that exhibits maximal BOLD responses during the CAP-A phases, regularly accompanied by cerebellar-pontine signal changes. Secondly, occipital (8/9) and central-precentral (7/9), as well as diffuse frontal (7/9), parietal (6/9, plus 5/9 precuneus), and temporal (6/9) areas, were found to have BOLD changes correlated to the A phases of the CAPs.

**Conclusion:** Our results support the existence of an insular-cingulate-thalamic network that temporally aggregates EEG rhythms-waves produced by the hemispheres, and thereby creates the CAP sequences met during NREM sleep.

## P647

### PET/MRI SURFACE ANALYSIS IN REFRACTORY EPILEPSY: A FEASIBILITY STUDY

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**Purpose:** Malformations of cortical development, especially focal cortical dysplasia (FCD) are the most important causes of refractory epilepsy.

Surgery could be proposed if the epileptogenic lesion is detected by presurgical workup, combining functional and morphologic imaging.

Unfortunately, only 30–70% of patients with focal cortical dysplasia (FCD) show abnormalities on MRI. These morphological features appear to be relatively specific but lack of sensibility.

<sup>18</sup>FDG PET is very sensitive tool and can identify lesions even if MRI is negative. Partial volume effect (PVE) on cortical sulcus induces hypometabolism foci, partially explaining FDG low specificity especially in deep cortical locations.



**Method:** To improve the ability of  $^{18}\text{F}$ FDG PET and MRI to detect epileptogenic lesions, we developed a new FreeSurfer<sup>®</sup> software based approach allowing simultaneous analysis of both cerebral metabolism (corrected for PVE and projected onto cortical surface after PET/MRI coregistration) and morphologic features (as blurring of gray/white matter limit and cortical thickness).

Fourteen patients with refractory epilepsy were enrolled (mean age 27 years). Epileptogenic lesions were confirmed by SEEG and pathology in 10 patients, pathology only for one patient and ictal SPECT for one patient. Pathological study showed FCD for six patients, hippocampal sclerosis associated with FCD for four patients and other lesions for four patients (dysembryoplastic neuroepithelial tumor and/or gliosis).

For each patient, a “vertex based” statistical analysis was performed, compared to a healthy subjects database. Z-score maps for each metabolic and morphologic features were computed.

**Results:** The results of this ongoing work are promising, showing significant hypometabolism encompassing the epileptogenic lesion in 12 patients.

The simultaneous analysis of morphological features provides a gain in specificity by eliminating false positives foci detected by  $^{18}\text{F}$ FDG PET.

Furthermore, this multimodal approach allows a better comprehension of the epileptogenic, irritative and lesional zones.

#### P648

##### THE IMPACT OF GUIDELINES ON THE QUALITY OF MRI DIAGNOSTICS IN ADULT PATIENTS REFERRED TO A TERTIARY EPILEPSY CENTRE

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**Purpose:** To investigate how often guideline-concordant magnetic resonance imaging (MRI) had been performed during the previous 5 years in adult patients who were referred as in-patients to a tertiary Epilepsy Centre due to their difficult-to-treat epilepsy.

**Method:** During 6 months consecutive referrals to three wards of the adult's department of the Kork Epilepsy Centre were systematically investigated. We assessed in how many patients who had been referred due to their difficult-to-treat epilepsy MRI scans had been performed during the previous 5 years and how many of those had been performed according to the Guidelines of the German Societies of Neurology and Epileptology. Patients were excluded if they had severe cognitive and/or behavioural problems that would have required MRI under anaesthesia.

**Results:** Two-hundred-and-eight patients were collected. Eighty-one (29%) had been treated at our Centre previously. In all of them we had performed guideline-concordant MRI scans. Among the remaining 127 patients 114 (90%) had undergone MRI. Thus, in 10% no MRI had been performed at all. If MRI scans had been done, only 34 (30%) fulfilled the criteria of the guidelines.

**Conclusion:** Although official guidelines for MRI in epilepsy were published in 2008, only in a minority of difficult-to-treat adult patients appropriate scans were conducted. Moreover, in a considerable number of cases no MRI had been undertaken at all in spite of ongoing and difficult-to-treat epilepsies. These results indicate an alarming discrepancy between requirement and reality.

#### P649

##### QUANTITATIVE MRI DETECTS ABNORMALITIES IN RELATIVES OF PATIENTS WITH TEMPORAL LOBE EPILEPSY AND MILD FOCAL CORTICAL DYSPLASIA

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**Purpose:** To evaluate temporal lobe cortical surface through quantitative magnetic resonance imaging (MRI) and its relation to postsurgical evolution in patients with temporal lobe epilepsy associated with mild focal cortical dysplasia with MRI negative.

**Method:** Measurements of cortical surface area (SA), cortical thickness (CT), folding index (FI) and volume were generated with FreeSurfer in 19 patient and 20 subject controls. High resolution pre-surgical T1-weighted volume scans 160 contiguous slices were obtained for each subject.

**Results:** The patient group displayed significantly reduced volume in entorhinal cortex, parahippocampus, superior and inferior temporal gyrus; SA was also greater in ipsilateral neocortical epileptogenic zone when compared to the control group. An increase of the CT was also shown in entorhinal cortex and parahippocampus. In addition, the ipsilateral neocortex showed an increase folding index ( $p < 0.0001$  Test Mann-Whitney). Class 1 Engel's patient had greater volume of mesial structures and smaller volume in neocortex. CT was lower in entorhinal cortex and parahippocampus, whereas the SA has a tendency tended to be higher in best evolution patients. ( $p < 0.0008$  Test Mann-Whitney).

**Conclusion:** Patient's with TLE associated with mild FCD showed significant volume reductions and CT increase in entorhinal cortex and parahippocampus. There was also an increase of the SA and a significant volume decrease in ipsilateral temporal lobe epileptogenic zone. Patients who had better clinical evolution showed bigger volume in the mesial structures associated with smaller neocortical volume and SA increase (superior and inferior temporal lobes).

#### P650

##### FDG-PET IN INFANCY PREDICTS LONG-TERM OUTCOME DURING ADOLESCENCE IN CRYPTOGENIC WEST SYNDROME

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**Purpose:** We examined outcome during adolescence in patients with cryptogenic West syndrome to clarify the correlation between FDG-PET findings in infancy and long-term seizure and developmental outcome.

**Method:** In 1991–1999 we prospectively performed FDG-PET from the onset of spasms in 27 patients with cryptogenic West syndrome. PET was performed at the onset and at 10 months of age. In 2012 we evaluated educational status, psychomotor development

and seizure outcome in 23 patients at 13–22 years of age. Correlation between the PET findings and the long-term outcome was evaluated.

**Results:** At the onset, PET showed cortical hypometabolism in 13/23 patients. The second PET after initial treatments revealed cortical hypometabolism in 7/23 patients. At the last follow-up period, seven patients had persisting or recurrent seizures. Eight patients had intellectual impairment and had special-needs education. Findings of the first PET were not correlated with seizure or developmental outcome. Five of seven patients (71%) with hypometabolism on the second PET had persisting or recurrent seizures, and 14 of 16 patients (88%) with normal second PET were free of seizures without medication. Five of seven patients (71%) showing hypometabolism on the second PET had intellectual impairment. Thirteen of 16 patients (81%) with normal findings on the second PET showed normal psychomotor development. There is a significant correlation of the second PET findings and long-term seizure ( $p = 0.01$ ) or developmental outcome ( $p = 0.03$ ).

**Conclusion:** The cortical hypometabolism is not permanent, but changes with clinical symptoms. Persistent hypometabolism after initial treatments predicts poor long-term seizure and developmental outcome.

## P651

### QUANTITATIVE AMYGDALAR MR FLAIR SIGNAL ANALYSIS IN MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** The amygdala is regarded as an independent epileptogenic site in 5% of mesial temporal lobe epilepsy cases. Prolonged amygdalar T2 relaxation times have been suggested as an imaging marker of epileptogenicity. Quantitative magnetic resonance imaging may aid in identifying isolated amygdalar epileptogenicity as part of the presurgical evaluation.

**Method:** We retrospectively reviewed 69 patients who had achieved Engel class Ia outcomes following mesial temporal resection and a control group of 25 nonepileptic subjects. Amygdalar and hippocampal labels were automatically generated on T1-weighted images using multiple-atlas-based segmentation and mapped to FLAIR images using rigid coregistration. Three scatter plots were generated by plotting right: left ratios of FLAIR mean values vs. right: left ratios of FLAIR standard deviations for amygdala and hippocampus and by plotting right vs. left normalized hippocampal volumes. The control group was used to establish a linear boundary domain for each scatter plot; values found in the domain were considered to be nonlateralizing. The boundary domain of amygdalar and hippocampal FLAIR were selected widely enough to declare a distinct laterality.

**Results:** Amygdalar and hippocampal FLAIR metrics identified 25% and 52% of subjects lateralized to the side of epileptogenicity, respectively. Six patients could not be distinguished as harbouring a right- or left-sided epileptogenicity with hippocampal FLAIR imaging metrics. Moreover, two of the six were incorrectly lateralized with hippocampal volumetry, whereas, the remainder were not distinguishable. All six were correctly lateralized with amygdalar FLAIR metrics. Three of these six patients had also required extraoperative electrocorticography in order to correctly lateralize the epileptogenicity.

**Conclusions:** The application of quantitative metrics to both hippocampal and amygdalar magnetic resonance imaging provides an objective means of establishing putative sites of epileptogenicity and allows for a probabilistic assessment in concert with electrographic data.

## P652

### NON-DOMINANT-HAND SENSORY AURA MAY LATERALISE TO EITHER CEREBRAL HEMISPHERE

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**Purpose:** Cerebral laterality of function can be an important consideration in diagnosis and management of epilepsy. However the degree of cerebral laterality of sensory functional representation of the non-dominant side of the body, compared to the dominant side, is still relatively unexplored. We addressed this issue by performing a functional magnetic resonance imaging (fMRI) study of controlled tactile stimulation of the fingertips of the left or right hand of healthy subjects.

**Method:** Normative data from 14 right-handed healthy subjects (Age 23–79 years; seven males) were analysed. Each subject performed a sensory fMRI study for each hand, involving a standardised sensory stimulus via a tactile stimulation device consisting of a plastic texture grating, of set spatial interval, presented to the 2nd, 3rd and 4th digits of the hand (Carey et al. *Neurology* 2002; 59:749–752). Image analysis was performed using SPM8 and iBrain™. An adaptive and largely threshold-independent method of objectively determining laterality (Abbott et al. *NeuroImage* 2010; 50:1446–1455) was adapted for this study to permit statistical comparison of laterality of dominant compared to non-dominant-hand stimuli. Atlas-defined regions-of-interest (ROIs) were used to interrogate laterality of primary somatosensory cortex (SI), secondary somatosensory cortex (SII), thalamus and cerebellum.

**Results:** Laterality of cerebral activity for right (dominant) hand stimuli of individuals

- SI: contralateral to stimulated hand
- SII: contralateral
- Thalamus: contralateral or bilateral or weakly ipsilateral
- Cerebellum: ipsilateral or bilateral except one case contralateral

Laterality of cerebral activity for left (non-dominant) hand stimuli of individuals

- SI: contralateral
- SII: contralateral, bilateral or ipsilateral
- Thalamus: contralateral or bilateral or ipsilateral
- Cerebellum: ipsilateral or bilateral.

The group difference between the left and right-hand laterality of SII was statistically significant ( $p < 0.05$ ).

**Conclusion:** In the clinical context, one should beware of assuming contralateral laterality of SII for sensory function of the non-dominant hand.

## P653

### DIAGNOSTIC VALUE OF DOUBLE INVERSION RECOVERY BRAIN IMAGING AT 3T IN THE DETECTION OF FOCAL CORTICAL DYSPLASIA IN EPILEPSY PATIENTS

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**Purpose:** Focal cortical dysplasia (FCD) has become increasingly recognized as a significant cause of medically refractory epilepsy. The purpose of this study was to compare the sensitivity in the detection of focal cortical dysplasia lesions by using double inversion recovery (DIR), fluid-

attenuated inversion recovery (FLAIR), T1-weighted and T2-weighted imaging at 3T.

**Method:** Seventy patients with probable symptomatic epilepsy were included in this study. Imaging was performed on a 3T MR using DIR, FLAIR, T1-weighted and T2-weighted imaging sequences. The sensitivity at DIR was compared with the corresponding sensitivity at FLAIR, T1-weighted and T2-weighted imaging in detecting thickened cortex, blurring of the grey-white matter interface, increased cortical or subcortical signal and the transmantle sign.

**Results:** Nine out of seventy patients were found focal cortical malformation using DIR sequence compared to six patients using FLAIR, T1-weighted and T2-weighted imaging sequences. Because of higher grey-white matter contrast, the DIR is more sensitive to identify thickened cortex than the FLAIR, T1-weighted and T2-weighted imaging. DIR can also greatly facilitate detection of increased cortical or subcortical signal and the transmantle sign.

**Conclusion:** DIR brain imaging at 3T is more sensitive in the detection of FCD lesions compared to conventional imaging.

#### P654

##### AUTOMATED SHAPE ANALYSIS IMPROVES THE DETECTION OF HIPPOCAMPAL ATROPHY IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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**Purpose:** In patients with mesial temporal lobe epilepsy (MTLE), brain MRI often detects hippocampal sclerosis (HS) that relates to the site of epileptogenicity. Almost half of MTLE patients, especially who are drug-responsive, do not show any hippocampal damage on visual or volumetric assessment. Here, we wished to assess the usefulness of shape analysis (SA) to correctly identify pathological volumes as well as the clinical yield of the method in patients with MTLE.

**Methods:** From March 2010 to March 2012, we prospectively collected 65 patients (41 women; mean age 39 ± 10 years, range 21–69) with non-lesional MTLE. Based on the convergence of electro-clinical and MRI findings of HS, patients were divided in four subgroups: right MRI-negative (nMTLE): 12/65 patients; right MRI-positive with HS (pMTLE): 14/65 patients; left nMTLE: 24/65 patients; and left pMTLE: 15/65 mean. There were no differences among these groups in age, sex, and age at epilepsy onset. All subjects underwent the same 3Tesla MRI protocol. SA of hippocampal formation was conducted comparing each group vs. 44 matched controls.

**Results:** In all groups, SA detected a significant atrophy in the corresponding hippocampus that coincided with the epileptogenic area. The damage was more severe in pMTLE patients (F value 5.00) than in nMTLE subgroups (F value 3.50), mainly corresponded to the CA1 subregion and subiculum.

**Conclusions:** In patients with MTLE, SA detects hippocampal damage that lateralizes with the epileptogenic area. Such damage is most prominent in the CA1 subregion and subiculum that are crucial in the pathogenesis of MTLE.

#### P655

##### INVESTIGATION OF THE BRAIN NETWORKS UNDERLYING EYE CLOSURE SENSITIVITY IN JEAUVONS SYNDROME AND HEALTHY SUBJECTS: AN EEG-fMRI STUDY

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**Purpose:** Eye closure sensitivity (ECS) starts immediately after closing of the eyes and lasts <3 s if the eyes remain closed. In some epilepsies, EEG paroxysms are related to ECS. Eyelid Myoclonia with Absences (EMA or Jeavons Syndrome) is the ideal model for studying ECS. In this work, we aim to investigate the brain networks underlying ECS in patients with EMA by means of an EEG-fMRI study.

**Method:** Ten patients with EMA and 16 healthy volunteers (HV) were selected. fMRI images (180 volumes, TR/TE=3000/50 ms) were acquired using a 3T Philips. The functional study consisted of 10-s epochs of eyes open and eyes closed (EC) conditions. For each EMA and HV subject, two analysis were performed: (i) EC were modelled with stick functions of 0-s duration, named EC-T0; (ii) EC events were modelled as blocks (i.e. duration = 3 s), named EC-length. The EC onset timing was documented by video recorded simultaneously. Data were analysed using SPM8 with a random effect analysis; groups were compared with a two-sample T-test.

**Results:** fMRI results of EC-T0 analysis revealed BOLD increases over the calcarine cortices, subcortical structures (thalamus and brainstem) and precuneus in EMA compared to HV. A positive hemodynamic response at the anterior cingulate cortex and brainstem was detected in EMA vs. HV in relation to the EC-length condition.

**Conclusion:** This study demonstrates, for the first time, that ECS in EMA reflects the pathological hyperexcitability of the occipital cortices which might trigger via subcortical-cortical pathways the paroxysms generation.

#### P656

##### TRANSCRANIAL PARENCHYMAL SONOGRAPHY IN JUVENILE MYOCLONIC EPILEPSY

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**Purpose:** Cognitive and behavioral difficulties in juvenile myoclonic epilepsy (JME) are suggested to involve neuronal processes in basal ganglia (BG) and midbrain structures. Dopamine signaling seems impaired in some regions and related to interictal dysfunction.

**Method:** Thirty-five JME patients (11 male, 24 female, aged from 16.5 to 42 years, mean 28.4) and 30 gender and age-matched control subjects were studied. Ethical authority approval and written informed consent were obtained. Trans-cranial sonography (TCS) study by trans-temporal approach was performed using a color-coded phased array ultrasound system, equipped with a 2.5 MHz transducer, with preauricular position. Influence of clinical parameters on TCS results was analyzed.

**Results:** Substantia nigra was markedly hyperechogenic in five patients with size ranged 0.28–0.37 cm<sup>2</sup>, while its hyper-echogenicity was

moderate and mainly unilateral in additional 8 ( $>0.19 \text{ cm}^2$ ). In all but 3 pts, hyperechogenicity of red nucleus was found. It was marked in eight patients (echogenic size ranged  $0.21\text{--}0.36 \text{ cm}^2$ ), unilateral in six and bilateral in remaining two patients. Echogenic size of red nucleus from  $0.07$  to  $0.20 \text{ cm}^2$  was noted in 24 (bilateral in 19) subjects. Low echogenicity of brainstem raphe (gradus 0) was found in 11 and correlated with depressive mood in six patients. No correlation of hyper-echogenicity of substantia nigra and JME clinical parameters was found. Differently, marked echogenic size of red nucleus in 5/8 was found in patients with incomplete seizure control, short remission and psychiatric disorders. Our findings seem to be independent of the antiepileptic medication.

**Conclusion:** TCS in JME patients suggest additional non-lesional alterations of BG and midbrain structures. Echogenicity of red nucleus was associated with seizure control and mental status. No other clinical parameters are involved.

#### P657

### FDG-PET USING STATISTICAL ANALYSIS PROVIDES RELIABLE SURGICAL DECISION CRITERIA IN TEMPORAL LOBE EPILEPSY

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**Purpose:** FDG-PET is one of the useful evaluations to localize the epileptic areas in patients with epilepsy. However it is not conclusive for definitive detection of the epileptic areas. To increase the ability of FDG-PET to detect epileptic foci and predict therapeutic outcome, statistical analysis considered indicated.

**Method:** Thirty-three patients with temporal lobe epilepsy were presurgically evaluated interictal glucose metabolism with  $18\text{F}$ -FDG-PET and analyzed statistically by 3D-SSP comparing to normal database. We put region of interest (ROI) as follows: hippocampus, amygdala, uncus, parahippocampal gyrus, fusiform gyrus, T1, T2, and T3 gyri. Significant hypometabolic areas were defined as voxels giving more than 1.69 in Z-score. We analyzed the relation between the ratio of significant voxel (% voxel) and surgical outcome by Engel classification I vs. II-IV in each ROI. We also detected the correlation among %voxel in the hippocampus, frequency and amplitude of spikes of intraoperative EEG on the hippocampus, and pathological damage in hippocampus by Watson's grading.

**Results:** With 3D-SSP, the diagnostic value of focus detection with FDG-PET increased in good surgical outcome group. The %voxel in all ROI except fusiform gyrus was significantly higher in good outcome group. We found correlation between %voxel in the hippocampus and pathological grading, however no correlation between %voxel and intraoperative EEG was found.

**Conclusion:** FDG-PET with statistical analysis can enhance the detection of epileptic areas. Hypometabolism in mesial temporal lobe especially hippocampus and amygdala is a reliable predictor of good surgical outcome. The hypometabolism in hippocampus indicates pathological damages rather than epileptic discharges.

#### P658

### ALTERED SPONTANEOUS LOW-FREQUENCY BOLD FLUCTUATIONS IN MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** The purpose of the present study is to evaluate the spontaneous low-frequency blood oxygenation level dependent (BOLD) fluctuations in patients with mesial temporal epilepsy and hippocampus sclerosis (mTLE).

**Method:** Twelve left mTLE patients and 12 healthy volunteers were recruited and performed resting state functional magnetic resonance imaging (fMRI) scanning. The regional homogeneity (ReHo) and amplitude of low-frequency fluctuation (ALFF) of BOLD signal were examined for each subject. The RoHo map and ALFF map were compared between groups respectively.

**Results:** In the left mTLE group compared to controls, we found that significantly increased ReHo at bilateral fusiform, middle cingulate gyrus, and left middle frontal gyrus, as well as significantly decreased ReHo at medial frontal gyrus, posterior cingulate cortex, and thalamus. The patients group also showed increases in ALFF in left parahippocampal gyrus, hippocampus, amygdala, temporal pole, and bilateral cingulate cortex. And the regions showing decreased ALFF included medial frontal gyrus and the precuneus.

**Conclusion:** Consistent with the previous study, the decreased ReHo and ALFF in default mode network (DMN) might reflect that DMN was widely affected with impaired hippocampus in left mTLE. Furthermore, the ALFF might be contributed to indicate the localization of left mTLE. This study demonstrated the features of the spontaneous low-frequency BOLD fluctuations is effective to understand the neuropathophysiology of mTLE.

**Keywords:** fMRI, temporal lobe epilepsy, Low frequency fluctuation, regional homogeneity

#### P659

### RESTING STATE CINGULATE NETWORK IN IDIOPATHIC GENERALIZED EPILEPSY

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**Purpose:** The cingulate cortex, a nexus of information processing and regulation in human brain, is implicated in the propagation of generalized spike in patients with idiopathic generalized epilepsy (IGE). We hypothesize that the functional connectivity of cingulate cortex should be altered in IGE, especial the abnormal association between cingulate cortex and subcortical nuclei, which may related to the spike propagation.

**Method:** Twenty-four patients with IGE and twenty-four healthy controls were included. According to the high resolution T1 imaging, nine regions of interesting (ROIs) were identified. Using seed-based correlation analysis, nine resting-state functional networks were acquired in both groups. Then, the compared analysis was performed between groups.

**Results:** Compared with controls, significantly increased functional connectivity to the ROIs (ROI2 and ROI3) in anterior cingulate cortex (ACC) were revealed in the caudate head, insula and putamen, and decreased functional connectivity to ACC in the precuneus, insula, hippocampus and parahippocampal gyrus were found in IGE patients ( $p < 0.05$ , FDR-corrected). Furthermore, the results of the ROI7, ROI8 and ROI9 (located in the posterior cingulate cortex) revealed the significantly decreased functional connectivity in the precuneus, insula, hippocampus and parahippocampal gyrus, and the increased in the cuneus ( $p < 0.05$ , FDR-corrected).

**Conclusion:** The findings implicated the abnormal increased functional connectivity between the cingulate and basal ganglia. The abnormality may take part in the modulation of the generalized spike in IGE. Furthermore, the aberrant functional connectivity of cingulate cortex may contribute to the impairment of default mode network in IGE.

**Keywords:** fMRI, functional connectivity, cingulate cortex, idiopathic generalized epilepsy

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## P660

### THE ROLE OF <sup>11</sup>C-METHIONINE POSITRON EMISSION TOMOGRAPHY IN EVALUATING THE EPILEPTOGENIC REGION

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**Purpose:** <sup>18</sup>F-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) is an important tool to detect epileptogenic region. Amino acid tracer, <sup>11</sup>C-Methionine (MET) PET is useful in diagnosis with glioneural tumor and low grade tumor which cause epilepsy. However, the role of MET PET is not clear in evaluation for epileptogenic region. We evaluate the role of MET PET for presurgical assessment of the patients with intractable epilepsy.

**Method:** We examined 13 patients with cerebral lesion (three male and 10 female, from 1 to 38 years old: median 24.0 years old). The patients had MET PET in addition to usual evaluation for epileptogenic area. We assessed two patients had epileptogenic region in frontal lobe in, seven in temporal, each one in frontal/temporal, parietal, occipital lobe. All patients had resective surgery. We made tracer distribution image according to standardized uptake value (SUV) and evaluated the uptake in vision. We also evaluated tracer uptake by the lesion-to-contralateral ratio (L/C ratio).

**Results:** Twelve of 13 patients showed lower uptake around cerebral lesions in FDG PET. In the four patients with migration disorder, MET PET had higher uptake in MRI lesion. In two patients with multiple cortical tubers, MET PET showed higher uptake in the tuber related with epileptogenic lesion, nevertheless all tuber had lower uptake in FDG PET. Two patients with cavernous angioma had lower accumulation in MET PET. Two patients with ganglioglioma and a patient with low grade glioma revealed higher uptake, and each one patient with ulegyria, epidermoid did not show uptake change in MET PET. One patient with focal cortical dysplasia remained seizure after surgery.

**Conclusion:** Higher uptake of <sup>11</sup>C-Methionine in PET might indicate epileptogenic lesion. This would help to detect epileptogenic region in the patients with multiple or broad brain lesion.

## P661

### WHITE MATTER FIBER DIAMETER BASED OPTIMAL MAGNETIC RESONANCE DIFFUSION WEIGHTED SEQUENCE

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**Purpose:** In order to investigate diseases caused by structural changes of white matter fibers, this research focused on optimizing imaging sequences based on different fibers sizes by using Monte Carlo simulations.

**Method:** According to Gaussian diffusion within white matter fiber, Monte Carlo simulations were designed with pulsed-gradient spin-echo sequence.  $2 \times 10^5$  particles were evenly placed in the space of simulated fibers with fixed length 70  $\mu$ m and variety diameters ranged from 5 to 20  $\mu$ m to simulate the spin motions. The probability distribution of particles' average distances between initial and final position with variable diameters and motion time were calculated. The optimization purpose is to obtain the largest ratio between signals perpendicular and parallel to the fiber, optimization parameters are fiber diameters, length, field gradient strength and duration time. Combined with the analytic relationship between signal and spin displacement distribution, sequence parameters can be confirmed. DTI and 4th order DTI (DT4) were also performed to compare the effects of optimized sequences and non-optimized ones.

**Results:** With limited range of gradient strength and duration time, the optimized sequence has direct relation with fiber diameter. Results of DTI and DT4 show that ellipsoids generated by the optimized data are of larger aspect ratio and main eigenvalues. Fractional Anisotropy and Generalized Eigenvalues have also increased, however, differences in Trace and Generalized Trace are neglectable.

**Conclusion:** This research can better detect diffusion in white fibers, make it possible to select fibers of a certain range of diameters for researching, thus may provide a new way to investigate white matter fiber related brain diseases.

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**Keywords:** Monte Carlo simulation, diffusion tensor imaging (DTI), optimal imaging sequences, white matter fiber, fiber size.

## P662

### ARTERIAL SPIN LABELLING PERFUSION MRI IN EPILEPSY SURGERY EVALUATION

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**Purpose:** Perfusion sequences used in Magnetic Resonance Imaging (MRI) can give quantitative data on cerebral blood flow in specific regions of interest. Application in the investigation of refractory epilepsy is emerging. We investigated the use of pseudo-Continuous Arterial spin-labelling (pCASL) as a potential tool in the pre-surgical evaluation of patients with epilepsy, as a method of lateralisation and localisation of epileptogenic areas.

**Method:** We studied 11 patients with refractory epilepsy undergoing pre-surgical evaluation; 6 with mesial temporal sclerosis. Perfusion images, using a pseudo-continuous arterial spin labelling (pCASL) sequence, and high-resolution volume scan were acquired on a GE 3T HDx MRI scanner. Regional perfusion values were calculated using quantitative analysis of perfusion images, for lobar, subcortical and hippocampal regions of interest after application of a grey matter mask. Laterality of perfusion values was determined for each of the regions of interest.

**Results:** Acceptable perfusion images were obtained in all subjects. Hippocampal asymmetry in perfusion was seen seven in of 11 cases concordant with electro-clinical epilepsy lateralisation. Of these, two patients have undergone planned surgery, confirming hippocampal sclerosis and remain seizure free. Two patients have undergone FDG PET, one of whom showed PET hypometabolism, co-localising with perfusion asym-

metry. Lateralised perfusion changes were also seen in ipsi-lateral thalamus, caudate and insula.

**Conclusion:** We found lateralised regional cerebral perfusion changes, affecting hippocampus and related structures in patients with refractory epilepsy being evaluated for epilepsy surgery. pCASL has potential to add further complimentary information to epilepsy surgery evaluation and may also contribute to the definition of networks involved in epileptic seizures. Distinct advantages are the short acquisition scan (5 min), absence of radiation and accessibility, particularly when compared to PET imaging.

#### P663

### PATTERNS OF LARGE-SCALE BRAIN NETWORKS ORGANIZATION IN LESIONAL AND NON-LESIONAL EXTRA-TEMPORAL EPILEPSY

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**Purpose:** The impact of a focal epileptogenic lesion on structural brain connectivity is yet to be defined. We aimed at investigating large-scale organizational patterns of structural networks in patients with focal cortical dysplasia (FCD) and those with extra-temporal epilepsy and non-diagnostic MRI using graph-theoretical analysis, a powerful formalism to quantitatively describe the topological organization of connectivity.

**Method:** We studied 36 patients with histologically proven FCD and 37 with non-diagnostic MRI (cryptogenic). The control group consisted of 41 age- and sex-matched healthy subjects. Networks were constructed from correlation matrices of cortical thickness in 78 regions and analyzed using graph-theory. Differences in clustering coefficients, path length, robustness against random failures and targeted attacks were assessed separately between each patient group and controls at various network densities using non-parametric permutation tests with repetitions.

**Results:** Compared to controls, both patient groups showed abnormal small-world architecture, characterized by high path length and clustering, suggesting altered whole-brain organization. On the other hand, brain networks in patients with cryptogenic epilepsy were more vulnerable to random failure and targeted attack than those with FCD.

**Conclusion:** Although our graph-theoretical analysis showed large-scale alterations of structural network organization in both cohorts, network robustness tests revealed reduced resilience in patients with cryptogenic epilepsy compared to those with FCD. Reduced network tolerance against failure and attacks likely stem from a lack of alternative backup routes, which suggest severe impairment of parallel organization of information transfer, supporting the hypothesis of distributed cortical structural pathology in cryptogenic epilepsy.

#### P664

### ALTERED STRUCTURAL AND FUNCTIONAL CONNECTIVITY OF THALAMOCORTICAL NETWORK IN IDIOPATHIC GENERALIZED EPILEPSY

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**Purpose:** While many studies using resting-state fMRI (rs-fMRI) uncovered abnormalities in resting-state networks including default-mode network in IGE patients, only a few studies addressed the issue of changes in functional connectivity (FC) of thalamocortical network. We investi-

gated alterations in both structural and functional connectivity of thalamocortical network in IGE.

**Method:** Forty-nine patients with IGE and 42 controls were studied. Volumetric T1-weighted and 240 volumes of resting-state BOLD images were acquired for voxel-based morphometry (VBM) and FC analyses, respectively. VBM was applied to identify regional volume change within the thalamus, and rs-fMRI was utilized for seed-based FC analysis of thalamocortical network. Group comparisons between patients and controls were performed (corrected  $p < 0.05$ ). Correlation analyses were performed to delineate relationships between FC strength of thalamocortical network and clinical variables in patients ( $p < 0.05$ ).

**Results:** VBM showed grey matter volume reductions in bilateral anterior-medial thalamus in patients compared to controls. Using anterior-medial thalamus seed, rs-fMRI analysis showed decreased FC in bilateral medial frontal and cingulate cortex in patients compared to controls. FC strength between thalamic seed and both medial frontal and cingulate gyri was negatively correlated with epilepsy duration.

**Conclusion:** The present results confirm that patients with IGE have structural abnormality of the anterior-medial thalamus and decreased FC between thalamus and medial frontal and cingulate cortex. Negative correlations between disease duration and FC of frontal and cingulate gyri suggest that recurrent seizures may have a consequence on thalamocortical network. Collectively, IGE is associated with alterations in structural and functional connectivity of anterior thalamus and medial frontal lobe, which supports the hypothesis of thalamocortical network changes in IGE.

#### P665

### FUNCTIONAL CONNECTIVITY CHANGES IN ABSENCE EPILEPSY STUDIED BY RESTING-STATE FUNCTIONAL MAGNETIC RESONANCE IMAGING

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**Purpose:** Functional connectivity has been correlated with a patient's level of consciousness and has been found to be altered in several mental disorders. Absence epilepsy patients, who experience a loss of consciousness, are assumed to suffer from alterations in thalamo-cortical networks; however, previous studies have not explored the functional connectivity between different brain modules in this mental disorder.

**Method:** We used resting-state functional magnetic resonance imaging to examine the alteration in functional connectivity that occurs in absence epilepsy patients. By parcellating the brain into 90 brain regions/nodes, as was performed in previous small-world network studies, we uncovered an altered functional connectivity within and between functional modules.

**Results:** Some brain regions had a greater number of altered connections and therefore behaved as key nodes in the changed network pattern; these regions included the superior frontal gyrus, the amygdala and the putamen. The within/between module functional connectivity in absence epilepsy patients showed a tendency of divergence from the pattern in control subjects that included an increase in the value of positive connections and a decrease in the value of the negative connections. In particular, the superior frontal gyrus demonstrated both an increased value of connections with other nodes of the frontal default mode network and a decreased value of connections with the limbic system. This divergence is positively correlated with epilepsy duration.

**Conclusion:** These findings provide a new perspective and shed light on how functional connectivity and the balance of within/between module connections may contribute to both the state of consciousness and the development of absence epilepsy.

P666

### IN VIVO MYELIN CONTENT ALTERATION IN ABSENCE EPILEPSY REVEALED BY T1- AND T2-WEIGHTED MRI

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**Purpose:** Absence epilepsy (AE) patients show abnormal anatomical structures in several subcortical and cortical areas revealed by diffusion parameters and volumetry. These changes, especially those in the fractional anisotropy (FA) of diffusion-weighted images, are often assumed to be related to myelination in the brain. However, the diffusion-based measurement of myelin content is indirect, and direct measurements such as immunohistofluorescence and electron microscopy are not feasible in vivo for human subjects. We try to measure the myelin concentrations in vivo through MRI techniques.

**Method:** In the current study, taking advantage of the recent progress of MRI, we measured in vivo myelin concentrations by T1- and T2-weighted MRI in absence patients and normal control subjects.

**Results:** We found that several frontal and parietal brain regions showed a decrease in myelin content in AE patients, whereas some subcortical structures showed an increase in myelin content. We found that myelin content was also altered in the corpus callosum, located in the ventral portion of the first 2/5 of the corpus callosum. The results also revealed that the myelin concentrations in the left postcentral gyrus and the left supramarginal gyrus were positively correlated with epilepsy onset, whereas the right superior occipital gyrus showed a negative correlation between myelin content and epilepsy onset.

**Conclusion:** Our finding show the complementary role of the current T1w and T2w based MRI measurement of myelin on the diffusion tensor imaging-based analysis of structural changes related to mental disorders. The results are consistent with previous findings that the corpus callosum has a decreased FA due to an increase in perpendicular diffusivity. Our results imply that the increased perpendicular diffusivity could be explained by an increase in myelination, resulting in thicker fibers and faster transmission between two hemispheres, which could lead to synchronized activity of the spike-and-wave discharges (SWD).

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### NIFTE – A NOVEL METHOD OF MULTIMODAL FUSION OF EEG SIGNAL – fMRI IMAGE TO STUDY NEUROHAEMODYNAMIC ACTIVITY IN EPILEPSY AND ITS CLINICAL APPLICATIONS

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**Purpose:** Neurobiology of epilepsy is yet to be understood. Different imaging modalities such as EEG/MEG source imaging, SPECT, PET, fMRI have been used to represent the different physiological variables associated with epilepsy. However a common consensus can be achieved with a fusion algorithm which allows a common visual and statistical platform for all these modalities.

**Material and methods:** Different combination of our simple and customized fusion technique algorithm (NIFTE an abbreviation for Neuro Image Fusion TEchnique) can be used to represent the different hypothesis developed in epilepsy using simultaneous EEG fMRI.

**Results:** Different variables were represented using EEG source imaging (ESI) and later this image was fused with EEG convolved fMRI.

- (a) different sets of interictal discharge
- (b) pre IED, IED and post IED segment of ESI fused with fMRI
- (c) Negative and positive neuronal activity ESI with positive and negative BOLD of fMRI.
- (d) beta /alpha / gamma activity ESI with fMRI
- (e) Fusion correlation of first and second rising phase of the Global Field Power using ESI with fMRI.
- (f) Scale-free functional organization in the brain using EEG microstate on ESI with fMRI
- (g) Cognitive studies using ERP such as P300 using ESI with various fmri paradigms.
- (h) Fusion of SPECT with EEG convolved fMRI during interictal period.

**Conclusion:** Future Applications that can be developed using our algorithm

- (a) wavelet transformation based ESI with fMRI.
- (b) Gamma frequency represented on ESI fused with GABA- PET
- (c) MEG and EEG with fMRI.

Hence we conclude that the our fusion algorithm will help spatio temporal mapping as well statistical degree of neuro-metabolic-haemodynamic coupling occurring in pathological conditions such as epilepsy.

P668

### ASSESSMENT OF DYNAMIC EFFECTIVE CONNECTIVITY OF EPILEPTIC NETWORKS IN TEMPORAL LOBE EPILEPSY USING SCALP EEG

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**Purpose:** We aimed to analyze the dynamic behavior of epileptic networks through the study of effective connectivity using scalp EEG signals, in order to improve the understanding of pathologic neural activity in particular spikes, seizures, and their electro-clinical and cognitive manifestations.

**Method:** In 10 patients with temporal lobe epilepsy, we assessed the connectivity of large-scale cortical networks during interictal spikes at high temporal resolution, using high density (96–256 channels) EEG recordings. The cortical electric source activity was obtained for 82 cortical regions of interest (ROI) using an individual head model and a distributed linear inverse solution. A multivariate, time-varying (millisecond resolution), and frequency-resolved (1–50 Hz) Granger causality analysis (Partial Directed Coherence) was applied to the source signal of all ROIs. In all patients, the results were validated by subsequent intracranial recordings or post-surgical outcome.

**Results:** The key driving structures were located in the anterior and medial temporal regions. Peak information transfer occurred before the spike maximum, sometimes with a different structure being the key driver at the time of spike maximum and the following slow wave. In three patients with a multifocal irritative zone, we found evidence of connectivity from the main anterior temporal driver towards the secondary spike focus remote from the epileptogenic zone, as validated by post-operative seizure freedom.

**Conclusion:** EEG-based time-varying effective connectivity of epileptic spikes was able to identify the major contributors to interictal

epileptic activity. This was concordant with invasive electro-clinical findings and supports the fact that the key drivers should be identified before the spike maximum. This enhanced characterization of the epileptic networks could have major clinical implications for tailoring resective, disconnective and functional surgery.

Study funded by Swiss National Foundation (SNF) grants 33CM30-140332, 141165, 144529, 122073.

#### P669

### COMPARISON OF 3T AND 1.5T BRAIN MAGNETIC RESONANCE IMAGING IN THE EVALUATION PATIENTS WITH DRUG-RESISTANT FOCAL EPILEPSY

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**Purpose:** To evaluate the value of re-imaging patients with drug-resistant focal epilepsy using 3T magnetic resonance imaging (MRI).

**Method:** Thirty patients with drug-resistant focal epilepsy and negative or non-consistent 1.5T-MRI were re-scanned with 1.5T and 3T. The epilepsy protocol was the following: T1-weighted 3D, FLAIR-3D, T2-weighted 3D, T2 coronal, T1 inversion recovery coronal and DWI-ADC axial. Two neuro-radiologists, blinded for prior imaging results and patient information randomly reviewed the MRIs. Kappa score was used to assess the inter-observer and intra-observer reliability. Findings were compared with reports from radiologists from general hospitals.

**Results:** Mean age of patients was  $30.1 \pm 11.3$ , seizure frequency per month was  $25.2 \pm 56.6$ , 87% had focal onset seizures in the frontal or the temporal region. The intra-observer agreement for the first radiologist was 0.74 for 1.5T and 0.77 for 3T (kappa value). In the second radiologist was 0.81 and 0.66 respectively. The inter-observer agreement was 0.76 for 1.5T and 0.77 for 3T. Three lesions (10%) were identified by regional hospitals using 1.5T with a standard protocol. In our center were identified 10 lesions (33%) using 1.5T-MRI and 11 lesions (36%) using 3T-MRI.

**Conclusion:** A similar number of lesions were identified with 1.5 and 3T-MRI. The most important difference was found from the reports of MRIs performed in not specialized hospitals vs. our center. The last finding supports the notion of having MRI protocols and specialized radiologists to do the interpretation of scans in patients with drug-resistant epilepsy.

#### P670

### MRI PROFILING OF THE TRANSMANTLE SIGN

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**Purpose:** The transmantele sign (TM), a funnel-shaped signal abnormality extending towards the ventricular wall may be found on MRI in a sub-

set of patients with focal cortical dysplasia (FCD). Our purpose was to systematically characterize the TM in relation to lesion size, sulcal location and histology.

**Method:** We studied 57 patients with FCD-related drug-resistant epilepsy. In 37 (65%) patients, lesions initially overlooked on routine MRI assessment were subsequently identified using image-processing. According to ILAE classification, two had FCD-1, eight FCD-2a and 22 FCD-2b. Lesions were segmented on co-registered T1, T2 and FLAIR images, and categorized according to size (small  $\leq 3.093 \text{ mm}^3$ ) and sulcal location (bottom/crown).

**Results:** A TM was observed in 27/57 (47%) of FCD lesions, the majority in those initially overlooked (21/27 = 78%). The TM sign was most prevalent in FCD-2b (55%), whereas it was found in only 28% of FCD-2a and absent in FCD-1. The TM was more frequent in small (23/34 = 68%) than large lesions (4/23 = 17%;  $p < 0.0005$ ), and in lesions located at the sulcal bottom (22/31 = 71%;  $p < 0.0001$ ).

**Conclusion:** The TM occurs in almost half of FCD cases. Evidence that TM is preferentially associated with small lesions located at the sulcal bottom may direct the search for developmental abnormalities, particularly in patients in whom large-scale MRI features are only mildly abnormal or absent.

#### P671

### ALTERED RESTING-STATE CONNECTIVITY OF THE INSULA DURING INTERICTAL GENERALIZED SPIKE-WAVE DISCHARGES IN DRUG-NAIVE CHILDHOOD ABSENCE EPILEPSY

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**Purpose:** To investigate the intrinsic brain connections of insula at the time of interictal generalized spike-wave discharges (GSWDs) in order to understand their mechanism of effect on brain function in untreated childhood absence epilepsy (CAE).

**Method:** The EEG-functional MRI (fMRI) was used to measure the resting state functional connectivity during interictal GSWDs in drug-naive CAE. Functional connectivity were assessed from resting state fMRI scans using seed regions of interest in the bilateral anterior, middle, and posterior insula with cross-correlation functional connectivity analysis.

**Results:** Decreased connectivity were detected during interictal GSWDs between anterior insula and bilateral dorsolateral prefrontal cortex (DLPFC), middle cingulate cortices, and left Supplementary\_Motor\_Area(SMA), as well as right middle insula and bilateral DLPFC, which are primarily located in the networks of central executive network(CEN) and salience network. Moreover, decreased connectivity were also found between middle-posterior insula and superior temporal gyrus, SMA. Increase in connectivity was found mainly between middle-posterior insula and bilateral thalamus, right Postcentral cortex, Cerebellum, Periaqueductal Gray. These areas are mainly involved in Sensorimotor system.

**Conclusion:** The current findings demonstrate significant alterations of resting-state functional connectivity of insula in drug naïve CAE subjects during interictal GSWDs and interictal GSWDs can cause dysfunction in insula related networks important for psychosocial function. The change of insula related networks may be implicated in the underlying pathophysiology of CAE. Our study may contribute to the understanding of neuro-pathophysiological mechanism of psychosocial function impairments in patients with CAE.



P672

### EXTRA-TEMPORAL MEMORY ENCODING NETWORKS IN TEMPORAL LOBE EPILEPSY- AN fMRI STUDY

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**Purpose:** Functional magnetic resonance imaging has demonstrated reorganisation of memory encoding networks within the temporal lobe with varied results on their efficiency. Less is known of the extra-temporal networks in these patients. We investigated the neural correlates of successful temporal and extra-temporal subsequent memory networks in refractory temporal lobe epilepsy.

**Methods:** We studied 44 patients with unilateral temporal lobe epilepsy and hippocampal sclerosis (24 left) and 26 healthy controls. All participants performed a functional magnetic resonance imaging memory encoding paradigm of faces and words with subsequent out of scanner recognition assessments. Neural correlates of subsequent memory were investigated using an event related analysis. Event related activations were then correlated with out-of-scanner verbal and visual memory scores.

**Results:** Controls displayed subsequent verbal memory effects within left parahippocampal gyrus, left orbitofrontal cortex and fusiform gyrus whilst left hippocampal sclerosis patients activated only right posterior hippocampus, parahippocampus and fusiform gyrus. Correlational analysis showed that left hippocampal sclerosis patients with better verbal memory additionally activated left orbitofrontal cortex, anterior cingulate cortex and left posterior hippocampus.

Controls showed subsequent visual memory effects within right amygdala, hippocampus, fusiform gyrus and orbitofrontal cortex. Right hippocampal sclerosis patients showed subsequent visual memory effects within right posterior hippocampus, parahippocampal and fusiform gyri, and predominantly left hemisphere extra-temporal activations within the insula and orbitofrontal cortex. Correlational analysis showed that right hippocampal sclerosis patients with better visual memory activated the amygdala bilaterally, right anterior parahippocampal gyrus and left insula.

**Conclusion:** Reorganisation of verbal and visual subsequent memory networks within the medial temporal lobe is an efficient process. The orbitofrontal cortex is critical to subsequent memory formation in controls and patients. Verbal subsequent memory activations within anterior cingulum and visual subsequent memory activations within left insula represent effective extra-temporal recruitment in left and right hippocampal sclerosis patients respectively.

P673

### ALTERED DEFAULT-MODE NETWORK IN BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES

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**Purpose:** Benign epilepsy with centrotemporal spikes(BECTS) is associated with language difficulties and impairment in attention, memory and executive function in clinical practice. The altered functional connectivity in default mode network(DMN) was observed related to the

cognitive impairment in some neuropsychologic syndromes. In this study we aim to assess the functional connectivity of DMN in BECTS.

**Method:** Resting state functional magnetic resonance images (fMRI) data sets were acquired in 12 patients with BECTs group and 12 health controls group. Then group independent component analysis(ICA) was used to identify the DMN in two groups. Furthermore, the difference of functional connectivity between groups was assessed.

**Results:** In contrast to controls, patients group demonstrated the significantly decreased functional connectivity( $p < 0.001$ , cluster $>20$  voxels)in dorsal medial prefrontal cortex, right superior frontal gyrus, left superior parietal lobe, right posterior cingulate cortex and right precuneus cortex.

**Conclusion:** This study demonstrated the decreased functional connectivity in BECTS. Although there is no direct evidence to show that the DMN was related to the spike in BECTS, The decreased functional connectivity in DMN might reflect cognitive disturbance, including attention, language deficit.

**Keywords:** Default mode, ICA, Benign epilepsy with centrotemporal spikes,fMRI

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P674

### FUNCTIONAL CONNECTIVITY ANALYSIS IN LANGUAGE NETWORK IN BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES

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**Purpose:** The impair language function was common observed in patients with benign childhood epilepsy with centrotemporal spikes (BECTS) in clinical practice. In this study we aim to assess the resting state functional connectivity in language network in patients with BECTS.

**Method:** Resting state functional magnetic resonance images (fMRI) and high resolution T1 data sets were acquired in 10 patients with BECTS group and 10 health controls group. The left inferior frontal gyrus(Broca area) and its contralateral homologous cortex were identified in T1 image for every subjects. The seed-based functional connectivity analysis was used to image the language network, and then the functional connectivity was compared.

**Results:** In contrast to controls, no significantly altered functional connectivity to Broca area was found. However, significantly increased functional connectivity was found between the contralateral homologous cortex and right Insula, right anterior cingulate gyrus, right Rolandic region and right superior temporal gyrus( $p < 0.001$ , Cluster $>10$  voxels).

**Conclusion:** Although the pilot study showed that the resting state functional connectivity to Broca area is not difference between two groups, the increased functional connectivity to right homologous region was observed in patients with BECTS. The finding may provide a potential evidence to support the contralateral compensation for the language deficits in BECTS. It is valuable to study in large cohort in the future.

**Key words:** Resting State, functional connectivity, BECTS, Language dominance

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#### P675

### IMAGING EPILEPTIC NETWORKS USING LOCAL CANONICAL CORRELATION ANALYSIS: A SIMULTANEOUS EEG-fMRI STUDY

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**Purpose:** Simultaneous electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) recordings are common used to delineate the patterns of metabolic changes response to interictal epileptic discharges (IEDs), and the local canonical correlation analysis (CCA) are proposed and demonstrated in a partial epilepsy EEG-fMRI study to more favorably identify the epileptic network.

**Method:** First, IEDs events identified on the simultaneously recorded EEG are convolved with hemodynamic response functions (HRFs) with variable shapes (different delay peak time). Using the local CCA, the linear combinations of local voxel time courses (27 adjacent voxels) and temporal IEDs convolution matrix (the correlation between both quantities is maximum) are solved. And then, the activation of center voxel (statistical significance of maximal canonical correlation coefficient) is quantified by F statistic.

**Results:** In a thirteen-year-old male patient with left temporal lobe epilepsy, the estimated activations mainly lied in left inferior temporal gyrus, middle temporal gyrus and bilateral temporal poles ( $p < 0.05$ , FDR corrected,  $k = 20$  voxels) using local CCA. And using conventional regression model, few and questionable activations in posterior cingulate gyrus and precuneus were obtained ( $p < 0.001$ , uncorrected,  $k = 20$  voxels).

**Conclusion:** These results perhaps indicated that the local CCA was favorable to identifying the epileptic networks related to focal IEDs, and might lead to a more appropriate representation of pathological epileptic discharges than conventional regression model. It perhaps also provided new opportunities for investigating epileptic networks to some degree.

**Keywords:** EEG-fMRI; local CCA; IEDs; epilepsy.

**Acknowledgements:** The work is supported by the National Basic Research 973 Program (2011CB707803), National Natural Science Foundation of China (81271547) and the 111 Project (B12027).

#### P676

### IS THERE LOSS OF VOLUME IN EXTRAHIPPOCAMPAL STRUCTURES IN PURE MTLE WITH HS NOT DISCERNIBLE BY HIGH RESOLUTION STRUCTURAL MRI?

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**Purpose:** Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) is now considered as a prototypic syndrome of drug resistant epilepsy. After anterior temporal lobectomy (ATL), majority of these patients become seizure-free; however, few do not. We studied through voxel based morphometry (VBM), if this could be due to volume loss of extrahippocampal structures in them not discernible by MRI.

**Method:** We selected 30 consecutive patients operated for drug-resistant pure MTLE-HS from 2009–2010 who did not have any involvement of structures outside the mesial temporal lobe in a high resolution 1.5T MRI done under epilepsy protocol. Their extrahippocampal structures were analysed by VBM through normalization, segmentation, modulation and smoothing. The volume of extrahippocampal structures, of both hemispheres were computed by multiplying and summing voxel-by-voxel volume. Chi-square test/Fisher exact test and students t test were used for comparing variables between left and right MTLE-HS patients. The volume of various structures over the hippocampal sclerosis (HS) side and non-HS side were compared using paired sample t-test. p value of  $< 0.05$  was considered significant.

**Results:** Mean age =  $32.9 \pm 8.9$  years (57% males). 17 patients had left MTLE-HS; 13 had right MTLE-HS. Mean hippocampal volume of HS side = 3.93 ml, non-HS = 4.50 ml ( $p < 0.001$ ). Parahippocampal volume was lesser on HS side compared to normal side (5.04 ml vs. 5.50 ml;  $p = 0.017$ ). Mean volume of inferior temporal gyrus on ipsilateral = 14.5, contralateral side = 15.8 ml ( $p = 0.01$ ) temporal polar volume = 0.9 ml and 21.5 ml ( $p = 0.49$ ) on pathological and non-pathological side respectively.

**Conclusion:** VBM of extrahippocampal structures showed that even in patients with the classic MTLE-HS syndrome, there is volume loss of extrahippocampal structures, especially the adjoining structures on the side of HS compared to contralateral side. VBM can be used as a sensitive tool to prognosticate patients before ATL and it also gives insight into the pathogenesis of seizure recurrence in pure MTLE-HS after focal resection.

#### P677

### FOCUS DIAGNOSIS OF MESIAL TEMPORAL LOBE SPONTANEOUS SEIZURES BY OPTICAL TOPOGRAPHY

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**Purpose:** In epileptic patients whom must be treated surgically, it is essential to localize accurately the epileptic focus. Although invasive intracranial EEG methods are useful to lateralize the epileptic focus, this comports risks as any invasive procedure. We evaluate the usefulness of long-term monitoring optical topography (OT) that measure noninvasively in lateralizing the epileptic focus of mesial temporal lobe epileptic (MTLE) patients during spontaneous ictal periods for presurgical evaluation.

**Method:** This study included six MTLE patients who were candidates for epilepsy surgery underwent long-term video-EEG and OT monitoring as part of their presurgical evaluation.

During recording, patients did not perform any task. All recorded seizures were spontaneous without any provocation or stimulus. Cerebral hemodynamic changes during spontaneous seizures were estimated by using OT after obtaining informed consent. Epileptic focus then lateralized.

**Results:** Four complex partial seizures were successfully recorded during EEG-OT monitoring from four out of the six patients with intractable mesial temporal lobe epilepsy. All of these four patients revealed high increase of Oxy-Hb on epileptic focus side during spontaneous seizure compare to non-focus side. Although our study was limited by a lack of corresponding data, these results are extremely significant since recording of spontaneous seizure by optical topography is rare.

**Conclusion:** Cerebral hemodynamic changes recorded by optical topography suggest us location of seizure focus. In findings the focus diagnosis of epileptic patients noninvasively, combination of video-EEG monitoring and optical topography is one useful reliable technique.

P678

### BOLD RESPONSES RELATED TO FOCAL FRONTAL SPIKES AND WIDESPREAD BILATERAL SYNCHRONOUS DISCHARGES

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**Purpose:** To investigate whether the generators of focal frontal spikes and widespread bilateral synchronous discharges (WBSD) are region specific in the frontal lobe and assess relationships between these discharges and BOLD changes.

**Method:** Thirty-three patients with interictal epileptic discharges (IEDs) with fronto-central predominance underwent EEG-fMRI at 3T. Only responses related to focal frontal, fronto-central, or hemispheric spikes, or to WBSD with fronto-central predominance were studied. Patients were divided into a focal (17 patients) and a WBSD group (16 patients).

**Results:** Each patient had one IED type meeting inclusion criteria with significant BOLD responses. A focal BOLD response was more frequent (14/17) in the focal group than in the WBSD group (4/16). Diffuse/multifocal responses were less frequent (3/17) in the focal group than in the WBSD group (12/16). Maximum BOLD responses were common in both groups in the following regions: dorsolateral prefrontal, mesial prefrontal, anterior cingulate and premotor cortices. In the focal group, maxima could also locate in precentral gyrus, frontal operculum, fronto-polar and orbito-frontal regions. In the WBSD group, maxima also occurred in thalamus, supplementary motor and postcentral cortex. A thalamus response was less common (4/17) in the focal group than in the WBSD group (10/16).

**Conclusion:** The spatial distribution and extent of BOLD responses correlates well with electrophysiological changes: widespread EEG changes indicate a widespread epileptogenic network. The generator of focal and WBSD is not region specific in frontal lobe. The same frontal region can generate focal and generalized spikes. Thalamus plays an important role in bilateral synchronization.

P679

### TEMPORAL CORTEX SURFACE MORPHOMETRY IN MESIAL TEMPORAL LOBE EPILEPSY PATIENTS AND THEIR UNAFFECTED SIBLINGS

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**Purpose:** To investigate the morphometric features of the ipsilateral temporal cortex in patients with mesial temporal lobe epilepsy and hippocampal sclerosis (MTLE+HS) and their unaffected siblings.

**Methods:** Fifty patients with unilateral MTLE+HS (left/right: 27/23), 50 of their unaffected siblings and 40 healthy controls underwent high-resolution T1 weighted brain MR imaging. In each subject, surface-based morphometry (SBM) was applied to quantify the degree of metric distortion required to register cortical surfaces to an average template. Regions of altered surface geometry within the ipsilateral temporal cortex in patients relative to controls were defined as regions of interests (ROIs), which were subsequently mapped to each subject. Within each ROI, cortical geometric measures (including volume, surface area, and thickness) were determined to compare patients and their siblings to the healthy subjects.

**Results:** In MTLE+HS patients, regions of increased metric distortion were detected within the ipsilateral mesial and anterior temporal cortex,

including the entorhinal cortex, parahippocampal gyrus, and temporal pole. Analysis of geometric measures within these ROIs in patients revealed volume loss relating mainly to a contraction in surface area but not cortical thickness. In the unaffected siblings, volume loss was also detected within the same ROIs but appeared to relate to a combination of surface area contraction and cortical thinning.

**Conclusion:** Altered surface morphometry of the ipsilateral mesial and anterior temporal cortex is common to MTLE+HS patients and their unaffected siblings. This may be indicative of genetic predisposition to temporal cortex surface abnormalities in MTLE+HS.

P680

### DECREASING SCANNING TIME AND INCREASING SENSITIVITY IN EEG-fMRI STUDIES OF EPILEPTIC PATIENTS USING A NEW FAST MRI SEQUENCE

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**Purpose:** Recently, magnetic resonance encephalography (MREG), a 100-ms resolution fMRI sequence was shown to increase the sensitivity in BOLD response detection in EEG-fMRI studies of epileptic patients. This study aims at comparing spike-related BOLD responses obtained with the standard EPI (2-s resolution) and MREG, and at assessing whether MREG can reduce the scan time of EEG-fMRI studies.

**Method:** Four epileptic patients were investigated with EEG-EPI and a 2.5 times shorter EEG-MREG. Functional images from EPI and MREG were analyzed and significant regions of activation and deactivation ( $p < 0.05$ , corrected) were compared. Common regions were compared based on their statistical t-values, while exclusive regions were assessed based on the goodness-of-fit of their hemodynamic response function (HRF).

**Results:** Six EEG spike types were marked for the four patients. The spiking rate for all four patients was similar during EPI and MREG, with therefore 2.5 times more spikes recorded in EPI. In total, 19 common activated and deactivated regions were identified; MREG had a larger t-value in 63% of regions. In addition to common regions, eight were exclusive to EPI, 25% having plausible HRFs. MREG detected 23 exclusive regions, 69.5% having plausible HRFs.

**Conclusion:** With an MREG scanning time 2.5 times shorter than EPI, EEG-MREG detected more regions of activation and deactivation, most of which had plausible HRFs. These results suggest that scanning time using MREG can be reduced by two – threefold compared to EPI to obtain BOLD responses, while bringing new information in the analysis of EEG-fMRI studies in epilepsy.

## Poster session: Neuropsychology A Tuesday, 25 June 2013

P681

### COMPUTER-ASSISTED TEST BATTERY FOR NEUROPSYCHOLOGICAL EVALUATION IN EPILEPSY: NORMATIVE DATA

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**Purpose:** We have created a computer-assisted test battery that provides a comprehensive neuropsychological evaluation for epilepsy. It contains

15 tasks that in our clinical practice are sensitive to cognitive dysfunction in epilepsy patients and that include tests of learning/ memory, mental flexibility, attention, vigilance /reaction time, visual perception, comprehension and naming. The battery provides three versions of every test, allowing re-evaluations with minimal practice effects, and is in English and French. We will present a sample of results from our normative database.

**Method:** Current N is 200 subjects aged 20–45, distributed equally across age groups and by sex; education ranges from 9 to 15 years, appropriate for our patient population. We will present results from two verbal and two nonverbal tasks: auditory naming, story learning (three measures), visual perception and face learning. We compare test versions, languages, sexes and age.

**Results:** Auditory naming results did not differ across test versions in English or French, but francophone mean score was one point lower than anglophone. Scores did not differ between the sexes or across age. On story learning, Version 2 was slightly more difficult than the other two on two measures, and francophones differed from anglophones on one measure. There were no differences among versions, between languages or by sex or age on the visual perception or face learning tasks.

**Conclusion:** Equivalence across test versions is excellent, as the few differences we found are minor. These results confirm that the different versions can be used interchangeably and used in retest with confidence. Only a few small differences were observed in French vs. English language tests, allowing comparisons across languages when needed. The lack of differences across ages probably reflects the current narrow range in our sample, but this range covers the ages typically encountered in our epilepsy population.

## P682

### POSTOPERATIVE NEUROPSYCHOLOGICAL CHANGES IN PATIENTS WITH NON-DOMINANT POSTERIOR CORTEX EPILEPSY

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**Purpose:** We studied the neuropsychological changes in patients with non-dominant posterior cortex epilepsy (PCE) before and after surgery.

**Method:** The subjects included four consecutive patients (three men, one woman; mean age at surgery, 18 years) with right PCE who were language non-dominant as shown by the Wada test and had undergone surgical resection at our hospitals two or more years ago since 2007. As on October 2012, Engel's surgical outcomes were I for three patients and II for one patient. The control subjects were six patients with right temporal lobe epilepsy (TLE) who were determined to be language non-dominant and had underwent surgical resection in the same period 2 or more years ago. Wechsler Adult Intelligence Scale-Revised (WAIS-R), Wechsler Memory Scale-Revised (WMS-R), and Benton visual retention test (BVRT) were the neuropsychological tests conducted before and after surgery, and we obtained the pre-to-postoperative neuropsychological ratios (PPNR) by dividing the postoperative means at 2 years by preoperative means.

**Results:** The PPNR in patients with non-dominant TLE and non-dominant PCE were as follows: WAIS-R; full-scale intelligence quotient (IQ) 1.01 and 0.92, verbal IQ 1.03 and 1.21, and performance IQ 1.00 and 0.86, WMS-R; Verbal 1.08 and 0.97, Visual 1.04 and 0.85, and General 1.00 and 0.93, and BVRT; correct response 0.93 and 0.73 and error response 1.13 and 3.08, respectively.

**Conclusion:** Patients with non-dominant PCE tend to have decreased postoperative neuropsychological changes, particularly in index numbers concerning visual memories.

## P683

### COGNITIVE DEVELOPMENT OF BENIGN EPILEPSY WITH CENTROTEMPORAL SPIKES (BECTS): DOES THE EPILEPTIC SIDE MAKE ANY COGNITIVE DIFFERENCE?

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**Purpose:** BECTS is the most common form of childhood epilepsy. It occurs, caused by the hyperexcitability of a system of neurons in only one hemisphere without apparent brain injury or cerebral structural abnormalities (Capovilla et al., 2009), it is usually well controlled by medication and seizures disappear by adolescence. Although BECTS is still officially considered as a benign syndrome without cognitive impairments (Berg et Scheffer, 2011), a growing body of literature highlights the existence of a wide range of cognitive deficits (Sarco et al., 2011; Baglietto et al., 2001; Metz-Lutz et Filippini, 2006; Weglage, Demsky, Pietsch, et Kurlmann, 1997). The aim of this systematic literature review was to investigate a link between the hemisphere encompassing the epileptic focus and a specific pattern of cognitive deficits.

**Method:** Abstracts of 815 articles and manuscripts (Medline 1945 – now, Eric, PsycINFO, Web of Science, Proquest Dissertations and Thesis) were carefully read. 17 articles and manuscripts were selected since they reported cognitive functioning according to seizure focus.

**Results:** In 17 articles reviewed here, the hypothesis of a specific cognitive profile according to the hemisphere of epileptic focus was confirmed, specifically according to the functional specialization of the brain.

**Conclusion:** We found specific cognitive deficits linked to the epileptic focus localization in BECTS. We propose that the epileptic activity possibly inhibits specific functions that are supported predominantly by certain cerebral areas and we conclude that those children are suffering from a “not so benign” disease (Perkins et al., 2008).

## P684

### COGNITION, BEHAVIOUR AND QUALITY OF LIFE FIVE TO TEN YEARS AFTER CHILDHOOD EPILEPSY SURGERY

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**Purpose:** Neuropsychological and psychosocial outcomes following epilepsy surgery have been argued to depend on post-operative duration. Few prospective studies have been done after pediatric surgery, and have largely focused on cognitive outcomes, yielding contradictory results about whether improvements eventually occur. In this study, IQ, behaviour, and quality of life (QOL) were examined prior to and five to ten years following surgery in patients with intractable epilepsy and in a

comparison group of nonsurgical patients with a history of childhood-onset intractable epilepsy assessed at comparable times.

**Method:** Fifty participants (23 male; mean age 20.3 years) were tested; 32 had undergone surgery on average 7 years ago. 36 participants (22 surgical, 14 non-surgical) completed both a standardized IQ test and questionnaires of behaviour and QOL; the remainder completed only the questionnaires. The two groups did not differ on age at baseline, age at seizure onset, current age, sex, handedness, or number of anti-epileptic drugs.

**Results:** IQ and behaviour were similar for surgical and nonsurgical patients at baseline and at long term follow-up, with no significant changes found over time. Seizure status at follow-up was not related to IQ. Those who were seizure free at follow-up had lower levels of externalizing, but not internalizing, behaviour problems. QOL did not differ between groups at follow-up, although significantly higher QOL was reported by those who were seizure free, irrespective of whether patients had or had not undergone surgery.

**Conclusion:** These results show a similar pattern of outcomes for both surgical and non-surgical patients with a childhood history of intractable epilepsy. Changes in IQ and internalizing and externalizing behaviours were not specific to the surgical group. Seizure outcome was the strongest predictor, with lower externalizing behaviour problems and better QOL in those participants in both groups who were seizure free. *Funded by the Ontario Brain Institute*

## P685

### ANALYSIS OF COGNITIVE IMPAIRMENT AND CORRELATION WITH SEIZURES VARIABLES

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**Purpose:** Investigate cognitive impairments and understand its correlation to seizure variables using standard neuropsychological tests conducted in 120 patients with epilepsy.

**Method:** Comprehensive neuropsychological test were conducted on 120 patients with epilepsy and the statistical data was matched against 40 healthy volunteers. 20 parameters defining memory and cognition in patients were recorded. Cognitive parameters were analyzed as a percentage of the total memory score. Neuropsychological data was tabulated across four age groups and seven seizure types with normal and subnormal IQ. Neuropsychological tests administered were Bhatia, Binet Kamath, Wechsler Memory Scale, Bender Gestalt, Benton Visual Retention Test & Mixed Group Intelligence Test.

**Results:** Demographic data indicated 70 Males, 50 Females. There were 44 patients with IQ < 79 and 76 patients with IQ > 79. Group I (6–15 years) patients who had generalised tonic clonic seizures (GTCS) revealed 31.8% of total memory impairment. Coupled with a low IQ there was 59.4% impairment. Group II (16–25 years) patients with complex partial seizures with generalization with IQ < 79 had 48.78% memory impairment. Group III (26–35 years): patients with simple partial seizures with generalization and IQ < 79 developed 64.42% memory impairment. Group IV (Above 36 years): patients with complex partial seizures with generalization with normal IQ had 72.72% memory impairment. In 120 patients visuo-constructive memory affected in 73.3% of patients, verbal paired associate affected in 68.3% of patients, immediate memory in 63.34% of patients, working memory in 57.5% of patients. Percentages also account for decline in multiple cognitive parameters in each patient. Decline in other cognitive parameters such as numerical memory, delayed memory, attention, concentration, reasoning, analogy and conceptual thinking was not commensurate. On the whole cognitive scores were worst in patients in age group II (16–25 years).

**Conclusion:** Cognitive impairment was present in all patients and worst in those with IQ < 79. Cluster of three memory parameters visuo-constructive, working and immediate was common to 46 patients, majority of sample set (38.34%). Maximum cognitive decline in the entire demographic was attributed to GTCS seizure subtype.

## P686

### FLUENT LANGUAGE DISORDERS IN ADULTS WITH TEMPORAL LOBE EPILEPSY

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**Purpose:** To discuss quantitatively and qualitatively the underlying language problems of fluently speaking adults with temporal lobe epilepsy (TLE).

**Method:** Three patients with TLE participated. Case 1: 22 years, male, left TLE, undergraduate student; Trail Making Test (TMT): normal; Wechsler Memory Scale-Revised (WMSR): normal. Case 2: 50 years, male, right TLE, employee; TMT: normal; WMSR: impaired. Case 3: 56 years, female, left or bilateral TLE, unemployed; TMT: normal; WMSR: impaired verbal memory. Word, sentence, and discourse production examinations were administered: the Western Aphasia Battery, the Test of Lexical Processing in Aphasia (naming of 100 high familiarity words and 100 low familiarity words (LFW)), the Sentence Forming Test (composing sentences using two presented nouns, verbs, conjunctions, etc.), and the four frame cartoon of the Standard Language Test of Aphasia (SLTA).

**Results:** Case 1 showed impaired naming of LFW (79/100) and a lack of necessary words in sentence and discourse productions (SLTA level 4/6). Case 2 showed problems with sentence production (26/33), owing to a lack of necessary words, and with discourse production (SLTA level 5/6), owing to error of aspect. Case 3 showed impaired naming of LFW (65/100), sentence production problems (25/33), and a lack of necessary words in sentence and discourse productions (SLTA level 4/6).

**Conclusion:** The quantitative and qualitative language examination results suggested that some fluently speaking individuals with TLE had difficulty naming LFW and failed to use some necessary words. These problems might negatively affect the quality of their communication, characterized by imprecise, strange sentences and verbosity.

## P687

### PRE- AND POST-OPERATIVE NEUROPSYCHOLOGICAL FUNCTION IN EPILEPTIC PATIENTS UNDERGOING PARTIAL INSULECTOMY

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**Purpose:** Partial or complete insulectomy in patients with drug-refractory insular cortex epilepsy has long been neglected because of the risk of injury to neighboring brain structures and arteries and due to the fear of inducing permanent deficits in patients. Indeed, the insula is involved in multiple functional systems and its role in neuropsychological function has remained enigmatic until recently. Since the advent of microsurgical

techniques, the neurosurgical option is more frequently considered and has been associated with efficient seizure control, but its consequences for neuropsychological function still remain poorly documented.

**Method:** We conducted pre- and post-operative neuropsychological assessments in nine patients (seven women; age range: 20–49 years; all right-handed) undergoing insular surgery in the right ( $n = 6$ ) or left ( $n = 3$ ) hemisphere for treatment of their refractory epilepsy. Post-operative testing was conducted at least six months after surgery. Domains assessed included attention and executive function, working memory, verbal and visual episodic memory, language, and visuo-constructive abilities.

**Results:** Cognitive impairments were relatively frequent before surgery. At the post-operative assessment, both decline and improvements occurred on a variety of outcomes, although new deficits were relatively infrequent among patients who had obtained normal performance at baseline. No significant mean difference between the two assessments was found on any outcome. However, a non-significant trend suggesting greater decline in letter fluency was observed following surgery.

**Conclusion:** These preliminary findings suggest that partial or complete resection of the insular cortex in refractory epileptic patients can be conducted without producing permanent neuropsychological impairments in the domains that were assessed in this particular study.

#### P688

##### BLURRING OF THE GRAY AND WHITE MATTER BOUNDARY AND COGNITION IN FOCAL CORTICAL DYSPLASIA

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**Purpose:** The presence of focal cortical dysplasia (FCD) is a contributing factor to cognitive dysfunction in epilepsy. Dysplastic tissue is often detectable on MRI by focal blurring of the gray and white matter boundary. Decreased gray-white contrast (GWC) in left hemisphere perisylvian regions is associated with reduced verbal abilities in healthy adults. This study aimed to determine whether decreased GWC is associated with disruption of language networks in patients with FCD.

**Method:** A group of 25 patients with histopathologically verified FCD and 23 age- and sex-matched controls underwent a T1-weighted structural MRI at 3T and a standardized index of verbal abilities from the Wechsler Adult Intelligence Scale-III. GWC was estimated by calculating the non-normalized T1 image intensity contrast above and below the cortical gray/white matter interface. Spherical averaging and whole-brain correlational analyses were performed to test the hypothesis that decreased GWC in fronto-temporal language regions would be associated with reduced verbal abilities in patients with FCD.

**Results:** Verbal abilities were significantly reduced in patients relative to controls [ $F(1,47) = 24.16; p < .001$ ]. Lower verbal abilities in patients were associated with blurring of the gray and white matter boundary in inferior temporal and inferior frontal regions, bilaterally.

**Conclusions:** The regional specificity of our results in classic temporal and frontal language regions suggests that focal blurring of the gray and white matter boundary may be an indicator of decreased neuronal efficiency. Results were similar to prior findings of a relationship between GWC and verbal abilities in healthy adults, with the exception of bilateral, rather than left-lateralized

findings. In sum, this study supports the use of GWC to probe the neuroanatomical substrates of cognitive performance impairment in patients with FCD.

#### P689

##### NEUROCOGNITIVE PROFILING OF DEPRESSION IN EPILEPSY

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**Purpose:** Depression is a common comorbidity of epilepsy and often involves cognitive symptoms. Although seizures propagate along neuro-cognitive pathways, little is known about the cognition of depressed epilepsy patients. We aimed to broadly characterize the neurocognition of epilepsy patients with and without depression.

**Method:** Participants comprised 47 adult focal epilepsy patients (27 female) and 40 controls (27 female). Patients had a mean age of 37 years ( $SD = 12$ ) and a mean FSIQ of 101 ( $SD = 13$ ). Controls had a mean age of 50 years ( $SD = 14; p < 0.05$ ) and a mean FSIQ of 105 ( $SD = 14; p > 0.05$ ). Well-established psychometric measures assessed psychiatric status, autobiographic memory, auditory-verbal and visual recall, and working memory.

**Results:** Fifty-three percent of patients had a lifetime history of unipolar depression compared to 15% of controls ( $p < 0.001$ ). There was no difference between patients with and without a lifetime history across epileptological or demographic factors ( $p > 0.05$ ). Epilepsy patients with lifetime depression exhibited high levels of impaired episodic autobiographic (60%) and visual memory (63%), and less impaired semantic autobiographic (12%), auditory-verbal (39%), and working memory (0%). Epilepsy patients who had never been depressed exhibited high levels of impaired episodic autobiographic (60%) and auditory-verbal memory (50%), and less impaired semantic (25%), visual (23%), and working memory (0%). Depressed epilepsy patients evidenced worse visual memory than never-depressed patients ( $p = 0.05; p > 0.05$  for all other comparisons). Results were equivalent whether patients with a lifetime history were currently depressed ( $n = 16$ ) or not.

**Conclusion:** Our study reveals that the cognitive profile of depression in epilepsy is fundamentally different to that captured in psychiatric populations, with little evidence of distinct impairments that differentiate between people with and without a vulnerability to depression. The finding that visual memory was worse in depressed patients suggests that relationships between the cognitive sequelae of seizures and mood are complex and require further delineation.

#### P690

##### A MORE REALISTIC APPROACH, USING DYNAMIC STIMULI, TO TEST FACIAL EMOTION RECOGNITION IMPAIRMENT IN TEMPORAL LOBE EPILEPSY

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**Purpose:** To explore the possible factors leading to impaired social functioning due to epilepsy, we evaluated facial emotion recognition (FER)

in patients with mesial temporal lobe epilepsy (MTLE) using moving facial stimuli.

**Method:** We evaluated FER in 88 MTLE patients, including 25 post-temporal lobectomy (PTL) patients, after the subjects were made to watch videos of actors expressing the six basic emotions: happiness, sadness, anger, fear, surprise, and disgust. Thirty-two healthy subjects were examined as controls. The relationships between task performance and clinical, neurophysiological, and radiological variables potentially affecting the ability to recognize the emotions of moving faces were examined by multivariate analysis.

**Results:** Both the MTLE patients and the PTL subset demonstrated significantly impaired FER compared with healthy controls (control: 93% correct, MTLR: 86% correct, PTL: 86% correct;  $p = 0.05$ ). Both MTLE and PTL groups showed impaired recognition of sadness, fear, and disgust. There was no difference in task performance between patients with right- or left-sided epileptic foci, while MTLE patients with bilateral foci showed more severe FER impairments.

**Conclusion:** FER is impaired in patients with chronic MTLE, particularly those with bilateral damage. Failure to recognize emotional expressions, particularly fear, disgust, and sadness, may contribute to difficulties in social functioning and relationship building.

## P691

### A PROTOCOL FOR THE ASSESSMENT OF LANGUAGE NETWORKS USING FMRI: APPLICATION OF DIFFERENT METHODS OF DATA ANALYSIS AND RELATION TO WADA TEST RESULTS

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**Purpose:** Using fMRI to study language networks in patients referred for epilepsy surgery has become a standard. However, compared to the Wada test fMRI assessment of language lateralization may be less sensitive, especially in patients with bilateral or atypical language representations. Our aim was to compare different methods of analyzing fMRI data and to correlate their results with the Wada test.

**Method:** Our study included 12 patients with drug-resistant epilepsy, with a mean age of 33.1 years (SD = 8.78 years). As part of a preoperative language assessment the patients completed an fMRI verbal fluency and verb generation tasks. Six patients also underwent a Wada test. The lateralization of language function by fMRI tasks was assessed by visual inspection of activation, by a lateralization index and by analysis of co-activation of language areas.

**Results:** Using fMRI the anterior language networks were localized to the left in seven patients, were bilateral in four and were found on the right in one patient. Lateralization of posterior and anterior language networks was mostly concordant with the exception of two patients, who had bilateral posterior and left anterior language representations. Two patients had insufficient activation to localize the posterior networks. The fMRI data and Wada test were concordant, but for one adolescent patient with intellectual disability.

**Conclusion:** Although our fMRI protocol for the lateralization of language function seems promising and valid in relation to the Wada test, further refinements are required to help more clearly elucidate posterior language areas and assess patients with intellectual disability.

## P692

### PROFILING MUSICAL FUNCTION IN FOCAL EPILEPSY: A CASE SERIES

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**Purpose:** Multiple networks of the brain are activated during music perception and production, including regions that are routinely considered for resection in the treatment of medically intractable seizures. Despite this, there is limited understanding of cortical reorganisation of music functions in epilepsy. This study examined the musical profiles of a series of patients with focal epilepsy to investigate the effects of seizures and pathology on the organisation of music networks in the brain.

**Method:** Eleven patients (six temporal, five extra-temporal; five male; nine right-handed) were recruited from the Austin Health Comprehensive Epilepsy Program (mean age = 33.3 years, mean education = 13.5 years, mean music training = 5.0 years). Patients underwent a comprehensive music assessment of pitch, melodic, rhythmic, and metre discrimination, pitch working memory, and melodic learning. Individual performance profiles were constructed relative to published normative data.

**Results:** Relative to normative data, temporal patients were generally impaired on melodic and rhythmic discrimination, and melodic learning, while extra-temporal patients exhibited more difficulties on metre and pitch discrimination. Compared to the extra-temporal group, temporal patients were significantly impaired on recognition of previously heard melodies ( $F_{(1,9)} = 13.30$ ,  $p = 0.005$ ). There was a trend toward diminished short-term memory for pitch in the extra-temporal compared to the temporal group ( $F_{(1,9)} = 3.98$ ,  $p = 0.077$ ). Strikingly, two patients with bilateral temporal lobe seizures and extensive musical training (9–10 years) were able to successfully learn new melodies.

**Conclusion:** These preliminary findings suggest that temporal lobe epilepsy impairs melodic discrimination, learning and recognition, however in the presence of extensive musical training, melodic learning may be preserved. This points to the possibility that training may promote reorganisation of music networks in patients with intractable seizures, which has important clinical implications for pre-surgical planning, particularly for musicians.

## P693

### MEMORY OUTCOME AFTER TEMPORAL LOBE RESECTION IN CHILDHOOD

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**Purpose:** Temporal lobectomy is a successful surgical treatment for intractable temporal lobe epilepsy. However, little is known about long-term memory outcome after this procedure in children.

**Method:** Fifty-three children who underwent assessment for the surgical treatment of epilepsy were re-evaluated a minimum of 5 years later, aged  $\geq 16$  years. Analyses were carried out on 39 individuals with available pre-surgical memory evaluations (11 excluded) and post-surgical IQ  $\geq 60$  (three additional exclusions). Eleven subjects underwent right (RTL) and 21 underwent left temporal lobectomy (L-TL), the remainder were treated pharmacologically. Surgical participants were diagnosed with developmental tumours (N = 13) or hippocampal sclerosis

(N = 19), underwent surgery at a mean age of 14.1 years, and were reassessed on average 9.3 years later. Memory functions were evaluated preoperatively and at follow-up using Wechsler Memory Scale-Revised (visual and verbal episodic memory) and age-appropriate Wechsler Intelligence Scales (semantic memory composite from Information, Vocabulary and Comprehension subtests).

**Results:** Pre- to post-surgical change in verbal episodic memory (prose recall) was influenced by side of surgery ( $p = 0.03$ ). Improvements were seen in the R-TL group alone, with little change seen in L-TL and control groups. Side of surgery predicted change in visual episodic memory (recall of line drawings:  $p = 0.021$ ), with post-surgical gains seen in L-TL only, and no changes in R-TL and control subjects. Semantic memory function improved across time ( $p = 0.026$ ), but with no effects of laterality. No effects of pathology were seen for any measures.

**Conclusion:** Temporal lobectomy resulted in improved memory functions in children followed into late adolescence and adulthood. Whilst semantic memory measures showed no effects of surgical laterality, episodic memory measures which are presumed to be subserved by the unoperated temporal lobe improved after temporal lobe surgery.

#### P694

##### THE ASSESSMENT OF LONG-TERM MEMORY IN TEMPORAL LOBE EPILEPSY (TLE): THE CONTRIBUTION OF STANDARD AND EXTENDED DELAYS OF RECALL

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**Purpose:** Assessment of memory functions is usually restricted to one testing session and retention of newly learned material can only be evaluated over that short period of time. In some patients with epilepsy such assessment can reveal normal memory performance although the individual has serious problems in everyday functioning due to memory difficulties.

**Method:** We explored the validity of a modified version of a widely used list-learning test in which we additionally assessed the retention of information over a period of seven days. In addition to ten healthy participants, our study included a 52-year-old patient suffering from non-lesional drug-resistant right TLE.

**Results:** The patient and his family members reported that he had difficulties retaining memories for events that happened weeks or months ago. By contrast, standard neuropsychological tests revealed no obvious cognitive deficits. Recall of newly learned words after a 30 min delay was unimpaired. Unlike the healthy participants, the patient could not recall any of the test stimuli seven days later, neither spontaneously, nor with the help of semantic cues. His recognition of the stimuli was at chance level.

**Conclusion:** In patients with TLE the assessment of long-term memory is often insufficient although the ability to retain memory over longer periods of time is a crucial aspect of normal everyday functioning. Slight adjustments of standard memory tests may improve the sensitivity of neuropsychological evaluation of potential deficits in long-term memory consolidation.

#### P695

##### SUBJECTIVE MEMORY EVALUATION BEFORE AND AFTER TEMPORAL LOBE EPILEPSY SURGERY

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**Purpose:** Subjective memory (SM), a self-evaluation of memory, is an important determinant of epilepsy management that, in contrast to objective memory (OM), is less well studied in epilepsy patients. We used a straightforward and easy-to-use measure to evaluate SM before and after temporal lobectomy.

**Method:** The Frequency of Forgetting 10 scale (FOF-10), developed to evaluate SM in dementia, was assessed in intractable epilepsy patients before and one year after temporal lobectomy. Reliability was tested using internal consistency (Cronbach's alpha and ICC). Validity was tested using Pearson correlation with the memory assessment clinics self rating scale (MAC-S). The CES-D for depression, PANAS for neuroticism and OM were done both preoperatively and one year postoperatively. Analyses of overall score change and reliable change index of SM, as well as subgroup analyses were done.

**Results:** In 48 patients who completed the evaluation, the FOF-10 showed high internal consistency (alpha >0.82) and high reproducibility (ICC: 0.67–0.93,  $p < 0.01$ ). It correlated with the MAC-S ( $r: 0.44–0.71$ ,  $p < 0.01$ ). FOF-10 scores improved postoperatively by more than 10% in 21 patients (44%) and worsened in 15 (31%). The FOF-10 did not correlate with OM but did correlate with perceived word finding difficulty ( $p < 0.001$ ) and postoperative CES-D ( $p < 0.05$ ). Further, a reduction in antiepileptic drug (AED)s after surgery appeared to distinguish those with improved postoperative SM. Of five seizure free patients who would not go through surgery again, four had postoperative SM impairment. No differences were found in SM after left vs. right temporal lobectomy.

**Conclusion:** The FOF-10 is a brief and reliable measure of SM in epilepsy patients. Perceived memory impairment reflects more emotional state, language problems and quantity of AEDs than actual defects in memory function. These results may be useful in presurgical counselling and management of memory issues in patients after epilepsy surgery.

#### P696

##### NEW METHODS FOR EXAMINING FAMILY FUNCTIONING IN EPILEPSY

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**Purpose:** Research has indicated that chronic epilepsy can place a burden on families and disrupt family relationships. However, few measures exist to capture the complexity of these effects, and none are specific to epilepsy. We purpose-built a computer program to interactively capture information about the patient's psychosocial functioning and adjustment to epilepsy, including a "family map" that graphically depicts family cohesion and closeness.

**Method:** Participants comprised 43 (24 female) adult focal epilepsy patients (18 mesial temporal focus) and 44 family caregivers (data not reported here). Patients had a mean age of 37 years (SD = 12), a mean FSIQ of 101 (SD = 13), and 25 (58%) had a partner or spouse. At the time of participating, 16 lived with parents, 20 with a partner, four in shared accommodation, and three lived alone. We used the Family Adaptability and Cohesion Evaluation Scale (FACES-IV) to assess the convergent validity of the program.

**Results:** Inspection of the family maps showed three broad family types: "Well-adjusted" (43%), "Enmeshed" (33%), and "Fractured" (24%). Distance on the map between the patient and daily caregiver (i.e. perceived closeness) was significantly smaller for enmeshed families (mean = 1.7 mm) compared to well-adjusted (mean = 5.9 mm,



$p = 0.01$ ) or fractured families (mean = 7.6 mm,  $p = 0.002$ ). However, patients in enmeshed families (57%) felt less able to talk about their epilepsy compared to those in well-adjusted (22%) or fractured (10%) families ( $p = 0.008$ ). There was good agreement between the nature of the maps and ratings on the FACES-IV.

**Conclusion:** Our study demonstrates the utility of a computer-based measure to capture the complex effects of intractable seizures on family dynamics. It shows that the majority of families living with chronic epilepsy (56%) are affected by enmeshment or fracturing of relationships, which impacts the patient's experience of family closeness and satisfaction, and being able to talk about epilepsy.

#### P697

### CONTRIBUTION OF HIPPOCAMPAL SUBFIELDS TO MEMORY PROCESSES IN HUMANS: THE ROLE OF CA1 AND THE DENTATE GYRUS

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**Purpose:** Decoding the anatomical organization of memory is a major challenge in clinical neuroscience. As memory impairment is a characteristic feature of mesial temporal lobe epilepsy (mTLE), epilepsy surgery offers the unique possibility to study the contribution of specific hippocampal subfields to memory processes in humans.

**Method:** We studied hippocampal subfield specialization in 100 consecutive mTLE patients submitted to epilepsy surgery. Memory z-scores were obtained from Intracarotid Amobarbital Testing (IAT) and non-invasive verbal memory assessment prior to surgery and correlated with histopathologically quantified cell loss pattern in hippocampal subfields, using an established classification scheme for hippocampal sclerosis (HS).

**Results:** Patients with cell loss selectively restricted to CA1 (HS type 2;  $n = 13$ ) did not show memory impairment and were indistinguishable from patients without any hippocampal cell loss (no-HS,  $n = 19$ ). In contrast, patients with neuronal loss affecting all hippocampal subfields (CA1, CA3, CA4 and dentate gyrus (DG); HS Type 1;  $n = 62$ ), or sparing selectively CA1 (HS Type 3,  $n = 5$ ) showed significantly reduced memory capacities (IAT:  $p < 0.001$ ; verbal memory:  $p < 0.05$ ). Furthermore, Multiple Regression Analysis confirmed that memory function is sustained even in the presence of most severe cell loss in CA1 ( $>6$  SD), while DG granule cell loss exceeding 62% ( $>3.5$  SD) results in a failure of memory function ( $R = 0.71$ ,  $p < 0.001$ ).

**Conclusion:** Our results confirm a differential contribution of hippocampal subfields to declarative memory formation, with CA1 pyramidal cells being less critically involved while the dentate granule cell layer plays a crucial role.

#### P698

### VISUAL NOVELTY PROCESSING IN PATIENTS WITH UNILATERAL TEMPORAL LOBE RESECTION

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**Purpose:** The (mesio) temporal regions play an essential role in novelty processing. Damage to these regions causes abnormalities of the N2 and P3a, Event Related Potential (ERP) components associated with novelty processing. Whether novelty processing is bilaterally processed equally remains unclear. We investigated the contribution of the left and right hippocampus in novelty processing in patients who underwent medial temporal lobectomy.

**Method:** Patients with a left ( $N = 9$ ) or right ( $N = 8$ ) MTL resection (eight females, mean age 41.5) completed a visual novelty-oddball task during EEG-recordings in which frequent standards, infrequent targets (requiring reaction time) and equally infrequent novels were presented both ipsilateral or contralateral to the resected hemisphere.

**Results:** Processing stimuli only differed between the non-resected MTL and the resected MTL for L- MTL patients, measured on Fz; novelty N2 was more negative when a novel stimulus was presented to the non-resected R-MTL compared to a novel stimulus presented to the resected left MTL,  $t(8) = -2.48$ ,  $p = 0.04$ . Although it was expected that the more positive novelty P3a peak would be observed when a novel was presented to the non-resected right MTL, compared to the resected left MTL, a reversed result was found,  $t(8) = -2.51$ ,  $p = 0.04$ . Furthermore, target P3b components were elicited by target presentation to both the non-resected and the resected MTL.

**Conclusion:** We conclude that visual novelty processing is more exclusively lateralized to the right MTL. The absence of the P3a peak is because: 1) patients did not allocate their attention to the deviant, novel stimuli after being distracted from their primary task (i.e. responding to the target). 2) flaws in average referencing led to weak observed novelty P3a. Finally, the hippocampus is not involved in processing target stimuli as no differences were found between processing target stimuli at the non-resected or resected hemisphere.

#### P699

### DEVELOPMENT OF AN ABSTRACT WORD-LEARNING TEST FOR TEMPORAL LOBE EPILEPSY: ENGLISH-FRENCH EQUIVALENCE AND CLINICAL FINDINGS

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**Purpose:** Neuropsychological diagnosis of temporal lobe epilepsy (TLE) remains challenging because clinical tests do not lateralize dysfunction with adequate sensitivity. Most verbal tests use concrete words, often remembered more easily than abstract words because they can be evoked using verbal or visual cues. Abstract words are less open to visualization, providing a more accurate measure of pure verbal memory and integrity of dominant medial-temporal structures. An added problem in bilingual Canadian settings is the extent to which it is appropriate to measure French speakers' performance with translations of English tests. We used the *Nicole* Abstract Verbal Learning Test (nAVLT), developed in English and French, with a known nonverbal analog, the Aggie Figures Learning Test (AFLT), to examine whether a) multiple forms of the same language test are equivalent, b) performance across language groups is comparable, and c) analogous verbal and nonverbal memory tests can detect dysfunction in TLE.

**Method:** Three forms of the nAVLT were constructed in each language and matched for imagery, concreteness, and word frequency. The nAVLT and the AFLT were administered to 202 healthy undergraduate subjects and 25 patients with TLE.

**Results:** The three forms of nAVLT were shown to be equivalent for each language. No significant difference in performance was observed across English and French tests. In TLE patients, the learning and memory profiles obtained using nAVLT and AFLT correlated with side of surgical resection.

**Conclusion:** The nAVLT, in conjunction with the AFLT, is an effective tool for lateralization of seizure focus in TLE.

### P700

#### NEUROPSYCHOLOGICAL PROFILES IN FAMILIAL PERIVENTRICULAR NODULAR HETEROTOPIA

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**Purpose:** Periventricular nodular heterotopia (PNH) is a developmental cerebral malformation caused by neural migration failure and often accompanied by epilepsy. Knowledge about cognitive functioning of these patients remains incomplete and is generally described as normal, except for reading impairment. In this study, neuropsychological profiles and anatomical features of an exceptional family with paternal transmission of PNH are reported.

**Method:** Three family members with PNH due to FLNA-mutation and seizures, the father (62), daughter I (31) and daughter II (30), were studied with extensive neuropsychological assessment of intelligence, memory, language, attention and executive functions, as well as structural magnetic resonance imaging (MRI) and volumetrics.

**Results:** Neuropsychological assessment revealed interesting individual cognitive profiles and significant differences between family members. The father showed above-average intelligence and overall intact cognitive functions; MRI displayed scattered heterotopic nodules. Daughter I showed normal intelligence and specific deficits in working memory and reading; MRI demonstrated mild bilateral PNH. Daughter II showed mental retardation (IQ<60) as well as significant cognitive impairment concerning working memory, attention and language; MRI showed more extensive bilateral PNH. Fractional PNH volumes were 0.68%, 1.18% and 1.97%.

**Conclusion:** Our data illustrated a remarkable variation of cognitive functions within the family and showed a graduation from the unimpaired father to daughter II with significant impairment, contrasting findings about PNH patients being normal or mildly impaired. Cognitive profiles correlated roughly to the degree of PNH, but whether differences are explained by extent of PNH, epilepsy severity, antiepileptic drugs or other factors remains to be clarified. A more systematic approach to neuropsychological testing in patients with PNH is of high importance.

### P701

#### DOES POLYOTHERAPY OR CORTICAL RESECTION INFLUENCE THE ABILITY OF PEOPLE WITH EPILEPSY TO BENEFIT FROM A MEMORY REHABILITATION PROGRAM?

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**Purpose:** To determine whether benefits from a memory training program are different for those on polytherapy (vs. monotherapy) and for those who have had a resection for control of seizures (vs. unoperated patients).

**Method:** Forty-seven patients with epilepsy and memory complaints (26 on polytherapy and 12 with a resection) completed a 6-week memory training program as well as assessments on a new Face-Name-Profession

association-learning task. Randomised alternative versions of the task were completed before and after the program. The score comprised the number of individual elements plus associations recalled immediately after studying a six-item display for 2 min. The manualised training program (Radford et al., ASSBI Resources, 2010) involved a group-based weekly meeting (with homework) in which mental and compensatory strategies were taught and patients were educated about neurological and lifestyle factors that influence memory. (The Face-Name-Profession task was not practiced.) Two-way (Group x Test-time) repeated measure analyses of variance (ANOVAs) were used to look for differences between

- (1) those on 1 vs. >1 anticonvulsant drug (AED) and
- (2) those with a history of resection vs. those without.

**Results:** Training resulted in significant improvement over the two test times ( $p < 0.02$ ), and ANOVAs revealed no main effects or interactions involving Group. Furthermore, number of AEDs was not correlated with change in task score.

**Conclusion:** This study yielded new evidence from an association-learning task that patients with epilepsy can benefit from a group-based memory training program. Furthermore, the benefits are not influenced by number of AEDs or history of resection.

### P702

#### ACCELERATED LONG-TERM FORGETTING (ALF) FOR NEW AUTOBIOGRAPHICAL EXPERIENCES OCCURS IN TEMPORAL LOBE EPILEPSY (TLE) BUT DOES NOT EXPLAIN RETROGRADE AUTOBIOGRAPHICAL MEMORY IMPAIRMENTS

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**Purpose:** To determine the relationship between ALF for recent experiences and remote autobiographical memory in patients with focal epilepsy.

**Method:** We compared 12 patients with RTLE, seven with LTLE, and 12 with extra-temporal epilepsy (ETE) with 30 normal controls (NC). The testing session served as an autobiographical experience (AE) about which the subjects were questioned after 30-min, 24-h and 4-day delays. Autobiographical fluency (AF) (names and events from different life periods) and word fluency were also measured. The Test of Premorbid Functioning was used to estimate IQ.

**Results:** The groups were well matched for age, IQ, gender, illness duration and number of AEDs. The RTLE group had a relatively high proportion with hippocampal lesions. On the AE task, a Group by Delay interaction ( $p < 0.05$ ) resulted. Post-hoc analyses revealed no between-group differences at 30 min, but RTLE and LTLE groups recalled less than NCs at 24 h ( $p$ 's  $< 0.001$ ) and 4 days ( $p$ 's  $< 0.01$ ). On AF, the RTLE group recollected fewer names ( $p < 0.02$ ) and events ( $p < 0.005$ ) than NCs, but LTLE and ETE groups were unimpaired. No significant correlations were found between AE and AF and neither measure correlated with IQ or word fluency.

**Conclusion:** ALF for autobiographical experience is evident in patients with temporal, but not extratemporal epileptic foci. However, ALF does not fully explain deficits in retrograde autobiographical memory. Instead, the right temporal lobe seems to be crucial for the recall of remote autobiographical material. Further research into the hippocampal contribution to these processes is needed.

P703

### SEIZURES (BUT NOT INTERICTAL DISCHARGES) WITHIN 24 H CAUSE ACCELERATED LONG-TERM FORGETTING (ALF) OF AUTOBIOGRAPHICAL EXPERIENCES IN PATIENTS WITH TEMPORAL LOBE EPILEPSY (TLE)

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**Purpose:** To examine effects of epileptiform discharges and/or seizures on 24 h recall of autobiographical experiences (AEs) vs. semantic details (story) in TLE patients.

**Method:** We enrolled 17 patients with TLE and 30 normal controls (NC). Recall of details from an AE (the testing session with additional staged events) and a story (read once) was tested after 30 min and 24 h. Based on ambulatory EEG data acquired over the same day, patients were divided into three groups: No Discharges (seven Right TLE); Discharges (four Right, one Bilateral TLE) and Discharges+Seizures (four Right, one Left TLE). One-way ANOVA was used to compare groups for change in percent recall between 30 min and 24 h.

**Results:** Groups were well matched in terms of age, education and gender distribution. The Discharges and Discharges+Seizures groups did not differ in the number of discharges (mean = 43.6). Subjects in the Discharges+Seizures group experienced 1–3 seizures. On AE, the Discharges+Seizures group lost more information (26%) than NCs (5%,  $p = 0.001$ ), but no differences involving the Discharges (12%) or No-Discharges groups (11%) were found. On story recall, the groups did not show significant differences in information lost (range = 1–6%).

**Conclusion:** Seizures caused ALF for incidental memory of autobiographical experiences over 24 h, but the same pattern was not evident for verbal material presented once in a directed learning task. Further work is needed to clarify the importance of lateralization of epileptic discharges/seizures and the influence of the differences in learning condition/material.

P704

### CHILDREN (10–12 YEARS AGE) OF MOTHERS WITH EPILEPSY HAVE LOWER INTELLIGENCE AND VISUAL ATTENTION

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**Purpose:** To compare the intelligence quotient (IQ) of children of mothers with epilepsy (CME) with that of children of mothers without epilepsy (CMO).

**Method:** CME (10–12 years) under follow up in this registry ( $n = 195$ ) were evaluated with WISC-IV, Trail making test (TMT), Rey Auditory Verbal Learning Test (RAVLT) and compared with age and sex matched CMO ( $n = 145$ ) drawn from schools in the same region.

**Results:** Maternal epilepsy syndrome was Generalized Epilepsy (94), Localization Related Epilepsy (87), and Unclassified (14) for the study group. Antenatal AED exposure: monotherapy for 109 (Phenobarbitone 21, phenytoin 11, carbamazepine 38, valproate 36, others 3), polytherapy for 72, and no AEDs for 14. Maternal IQ was comparable for the two groups. The Full Scale IQ of CME ( $78.1 \pm 14.5$ ) was significantly lower

than that of CMO ( $86.9 \pm 13.5$ ). CME (compared to CMO) had significantly lower Verbal Comprehension Index ( $80.4 \pm 14.0$  vs.  $87.1 \pm 12.7$ ), Perceptual Reasoning Index ( $77.7 \pm 14.5$  vs.  $84.4 \pm 12.5$ ), Working Memory Index ( $89.4 \pm 13.8$  vs.  $97.4 \pm 14.0$ ). They performed poorer on TMT Part A ( $107.8 + 67.5$  vs.  $80.5 + 25.4$  s) and TMT part B ( $320.3 \pm 147.0$  vs.  $249.1 \pm 101.3$  s). The RAVLT also showed lower scores ( $80.8 \pm 11.6$  vs.  $85.0 \pm 12.6$ ). The FSIQ (monotherapy only) for those exposed to phenobarbitone ( $76.1 \pm 12.6$ ) was significantly lower than that of others ( $82.7 \pm 13.2$ ). The FSIQ for other AED monotherapy exposures were not significantly different. AED polytherapy had significantly lower FSIQ ( $72.3 \pm 14.7$ ) than monotherapy ( $81.5 \pm 13.3$ ).

**Conclusion:** The IQ and visual attention were significantly lower for Children of mothers with epilepsy particularly those with antenatal exposure to phenobarbitone or polytherapy.

P705

### DECISION MAKING IN ROLANDIC EPILEPSY

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**Purpose:** The aim of this study was to evaluate the decision-making style in children with rolandic epilepsy (RE) and compare their performance with healthy children taking into account clinical variables of epilepsy.

**Method:** We evaluated 42 children, 17 with RE (RE Group) and 25 healthy controls (Control Group). All children were assessed with the Iowa Gambling Task (IGT), the most used instrument to evaluate the decision-making style, and the Wechsler Intelligence Scale for Children (WISC-III) to investigate the intellectual level (estimated IQ). The clinical variables of epilepsy were: age of seizure onset and remission, type of seizure (partial vs. generalized), use of AED (none, monotherapy or polytherapy), and seizure lateralization (right, left, and bilateral).

**Results:** No significant differences were found between the two groups. However, when analysing the RE group, we observed that the later the onset of epilepsy, the best style of decision making presented ( $p = 0.04$ ). The same was true when comparing the intellectual level of the RE group: the higher the IQ, the better the decision-making style ( $p = 0.02$ ).

**Conclusion:** We conclude that although RE is known as a benign entity, difficulty in decision-making ability may be observed. More studies are necessary to corroborate our findings.

P706

### WISC-III-TAKING FATIGUE IN CHILDREN WITH EPILEPSY: NO MAJOR ISSUE

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**Purpose:** To examine whether the 12 Wechsler Intelligence Scales for Children (WISC-III) subtests lead to lowering of scores as testing progresses. Wechsler test developers counter testing fatigue alternating verbal and performance subtests. Clinicians maintain ex-

aminees' alertness at an optimal level providing breaks. However, in epilepsy, fatigue can be of concern in prolonged (2- h) testing.

**Method:** Participants: 131 children with epilepsy (44% girls) from tertiary epilepsy settings (47 clinic; 84 school). Mean age = 10.1 years; AOE = 6.0 years; 82.7% on AEDs = 1.3 (maximal 1, 60%; minimal 2, 40%); mean FS-IQ = 85.8 (range 47–119); seizure type: 57% focal, 25% generalized, 18% uncertain/unknown. All had taken the complete WISC-III.

Analyses: Repeated measures ANOVA with polynomial (linear, quadratic, higher order) contrasts wherein standardized order of the 12 subtests formed the within-subjects variable. Pair-wise comparisons with Bonferroni corrections.

**Results:** A significant effect for subtests arises, suggesting differences between levels of proficiency across subtests. Importantly, no linear or quadratic trend could be identified. Significant "sixth" and "ninth-order" models ( $p < 0.001$ ) suggest patterns of peaks and troughs unrelated to test order. Separate analyses according to source (clinic/school), number of AEDs ( $\leq 1$ ;  $\geq 2$ ) or scale (Verbal; Performance) yielded similar results. Pair-wise comparisons show relative strengths on two verbal subtests (Similarities and Comprehension) and weaknesses on two performance (Coding, Picture Arrangement) and one verbal subtest (Arithmetic).

**Conclusion:** Given optimized testing conditions, testing fatigue need not be an issue of concern in WISC-III-taking. The subtest pattern found in a child with epilepsy is likely to reflect its "true" profile.

#### P707

##### EMPATHY ABILITY AND EMOTION RECOGNITION IN TEMPORAL LOBE EPILEPSY AND IDIOPATHIC GENERALIZED EPILEPSY

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**Purpose:** To investigate social cognition disorders in idiopathic generalized epilepsy (IGE) patients and compare their performances with temporal lobe epilepsy ones (TLE).

**Method:** We recruited thirty-five patients (17 TLE, 18 IGE) and 18 healthy controls (HC) matched for age. General exclusion criteria were history of other neuropsychiatric disorders, learning and intelligence deficits, age <18 years. All patients and controls underwent standardized neuropsychological battery. Social cognition abilities were assessed with a single non-verbal cartoon test assessing emotion and intention attribution (story-based empathy task-SET) and emotion recognition with Ekman-60-Faces Test. Nonparametric tests were used to analyze group differences.

**Results:** The three groups did not differ in age at testing, gender and education ( $p > 0.05$ ). Compared to HC, TLE patients were significantly impaired both on SET global score ( $28.6 \pm 5.6$  vs.  $33.7 \pm 1.9$ ;  $p < 0.001$ ) and single scores (emotion and intention attribution, causal inferences). Mean Ekman score was significant lower in both TLE ( $47.4 \pm 4.7$ ) and IGE ( $47.4 \pm 5.4$ ) compared with HC ( $51.7 \pm 3.9$ ;  $p = 0.02$ ). Compared to HC, TLE showed significantly worse scores in fear and disgust recognition, while recognition of fear and anger were worse in IGE ( $p < 0.05$ ).

**Conclusion:** We confirmed previous findings showing deficits in social cognition and global facial emotion recognition in TLE, with a prevalent impairment of negative emotions. We also demonstrated poor facial emotion recognition in IGE. Our data provide evidence of neurobehavioral impairment and difficulties in social functioning

in chronic epileptic patients. Specific deficits are associated with TLE and IGE subtypes, related to disruption of a pathway involving frontal, temporal and limbic regions.

#### P708

##### EPISODIC AND SEMANTIC MEMORY IN CHILDREN WITH TEMPORAL LOBE EPILEPSY: ARE THEY RELATED TO LITERACY SKILLS?

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**Purpose:** Children with temporal lobe epilepsy (TLE) are at risk of academic underachievement and memory deficits. While difficulties with episodic memory (new learning / recall of information) have long been recognised, semantic memory deficits (knowledge of word meaning / object naming) have been documented in these patients only recently. Although memory is critical for acquisition of knowledge, the relationship between memory and academic skill has not been examined in children with TLE, which is the aim of the current study.

**Method:** Fifty-seven children with unilateral TLE completed tests of episodic and semantic memory, and literacy (reading accuracy, reading comprehension and spelling). Relationships between memory and literacy skills were examined at the group and individual level.

**Results:** As a group, the children performed significantly below normative means on all tests. Regression analyses revealed that semantic memory made significant, unique, large contributions to all literacy skills (explained over 30% of the variance in each). Episodic memory played a significant (albeit small role) in reading and spelling accuracy (explained <10% of the variance in each), but not in reading comprehension. Together, semantic and episodic memory accounted for significant and large proportions of the variance in literacy skills (41–54%). Individual patient analyses showed that children with impaired semantic (but intact episodic) memory performed significantly below children with impaired episodic (but intact semantic) memory, children who had intact semantic and episodic memory, as well as significantly below the normative means.

**Conclusion:** Semantic memory plays a critical role in literacy skills in children with TLE. As semantic memory precedes development of literacy skills, semantic memory impairments may be early markers of future literacy deficits. Thus early screening of semantic memory may allow for identification and treatment of children with TLE at risk of academic difficulties.

#### P709

##### HIPPOCAMPAL NAA AS AN EVALUATIVE METHOD FOR MEMORY FUNCTION: JAPANESE NORMATIVE DATABASE

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**Purpose:** The aim of the study is to evaluate whether the hippocampal memory functional ability can be evaluated quantitatively with a proton

magnetic resonance spectroscopy (1H-MRS), and to establish a 1H-MRS normative database to exam memory dysfunction.

**Method:** One-hundred healthy normal volunteers aged between 16 and 74 years old were undertaken to 1H-MRS and Wechsler memory scale-revised (WMS-R) study. Toshiba 1.5T MRI system was used to take 1H-MRS. The regions of interests (ROIs) were placed on both hippocampi. The quantities of N-acetyl aspartate (NAA), choline-containing compounds (Cho) and creatine/phosphocreatine (Cr) in the ROIs were statistically obtained to fit LC-Model analysis. The people who had abnormality in conventional MRI or scored under 85 point in WMS-R were eliminated. 87 were finally taken into account.

**Results:** The hippocampal NAA values gradually decreased with the age and their correlation coefficient were  $-0.46$  in left and  $-0.40$  in right hippocampus. The WMS-R score did not show any correlation to the MRS values. In raw scores before weighted, the correlation coefficient of NAA and verbal and visual memories showed a little correlations (0.23–0.37).

In the scatter diagrams plotted WMS-R subtest scores and MRS value, heterogeneity or discontinuous patterns were observed in score distribution. It is suggested that WMS-R has limited sensitivity for the person with high memory performances in normal adults.

**Conclusion:** There was a possibility that 1H-MRS could detect memory function according to the age and not related to WMS-R score.

## Poster session: Pediatric epileptology B Tuesday, 25 June 2013

### P710

#### DELAYS TO EPILEPSY DIAGNOSIS IN CHILDREN WITH EARLY-ONSET EPILEPSY: A COMMUNITY-BASED EXPERIENCE

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**Purpose:** Determine the frequency of delayed diagnosis in children with early-onset epilepsy and factors associated with delay.

**Methods:** Children with early-onset (<3 year) epilepsy were recruited in a community-based cohort of epilepsy ( $\geq 2$  unprovoked seizures) in Connecticut (1993–1997). Time from second unprovoked seizure to epilepsy diagnosis was categorized: <1 m, 1–3 m, 4–11 m,  $\geq 12$  m. Factors associated with  $\geq 1$  m delay were grouped: parental, pediatrician, neurologist, scheduling, insurance/social, medically complicated child. A child could have  $\geq 1$  factor. Initial seizure types and other features of the child's presentation were considered. Institutional ethics committees approved all methods.

**Results:** 191/613 (31%) children in the cohort had a first unprovoked seizure before their 3rd birthday. Time to epilepsy diagnosis was <1 m in 113 (59%) including 51 (27%) who were diagnosed at the 2nd unprovoked seizure; 1–3 m, N = 28 (20%), 4–11 m, N = 14 (7%), and  $\geq 12$  m, 26 (14%). Children who initially presented with a first vs. recurrent seizures ( $p < 0.0001$ ), had a history of neonatal or febrile seizures ( $p = 0.01$ ), convulsive seizures ( $p = 0.004$ ) and a college-educated parent ( $p = 0.02$ ) were more likely to have a <1 m diagnostic interval. Behavioral seizures (absence, dyscognitive, other staring spells) vs. all other seizure types combined were associated with a higher chance of a  $\geq 1$  m diagnostic interval ("delay"). Factors associated with delays included parents not recognizing events as seizures (N = 52), pediatrician missing diagnosis (N = 16), neurologists deferring diagnosis (N = 11), scheduling (N = 12) insurance or social issues (N = 4), and medically complex child (N = 15).

**Conclusion:** Diagnostic delays  $\geq 1$  m affect a substantial proportion (41%) of children with early-onset epilepsy. Several factors influence the delay and represent potential opportunities for intervention and improved pediatric epilepsy care.

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### P711

#### CLINICAL CHARACTERISTICS OF POST-TRAUMATIC SEIZURES IN CHILDREN

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**Purpose:** Post-traumatic seizures (PTS) are well-recognized complications of head injury and they are particularly more vulnerable to pediatric populations. The authors conduct a study to investigate the clinical characteristics of PTS in children and to determine the utility of several diagnostic tools as well as the role of prophylactic anticonvulsants.

**Method:** We retrospectively reviewed the medical records of patient under 18 years of age who presented with seizures after traumatic brain injury. Data analyzed included patient's demographics, clinical presentation, radiological and electroencephalographic findings, management and follow-up.

**Results:** Thirty one patients with PTS were included in the study and consisted of 13 males and 18 females. A mean age of accident was 3.2 years (4 months – 6.8 years) and a mean duration of follow-up was 26.0 months (12 months – 54 months). Twenty one patients (67.7%) developed seizure within 24 h after injury. Focal radiological findings were observed in 83.8% and described as intracranial hemorrhage (45.1%) and intraparenchymal lesions (51.6%). Electroencephalographic findings were background abnormalities in 32.2% and interictal epileptiform discharges in 45.1%. All patients were administered transient anticonvulsants and a mean duration of treatment was 12.5 weeks (4–40 weeks). Eight patients (25.8%) developed subsequent seizures during follow-up period and two patients (6.5%) were diagnosed afterward with post-traumatic epilepsy.

**Conclusion:** PTS generally have benign clinical course but in minor proportion, subsequent seizures including epileptic seizures can occur. In this case, radiological and electroencephalographic findings are helpful in prediction of clinical course of PTS and transient anticonvulsants application is recommended.

### P712

#### RESISTANT FORMS OF EPILEPSY IN CHILDREN OF EARLY AGE

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**Purpose:** The problem debut of different forms of epilepsy and cognitive disorders in patients is one of the most acute problems in the pediatric neurology.

**Method:** In the St. Petersburg Academy of Pediatrics we have examined a 257 patients, who applied for the epileptic seizures, disorders of development and behaviour of identified epileptic changes in the EEG. All of the patients examined by a neurologist, EEG, MRI. Has been tested by a psychologist.

**Results:** Epileptic encephalopathies diagnosed in 23 patients (8.9%). Epileptic encephalopathy with early debut presented in our study Ohtahara syndrome. We examined the patient at the age of 3 months with resistant epileptic seizures and significant lag in the development. Attacks

debuted in the neonatal period and were presented serial tonic spasms. In neuroimaging revealed gross structural changes of the brain. Registered «suppression-burst» pattern of the EEG. In the future there has been an evolution of the state in West syndrome. West syndrome diagnosed with us have six children of the first year of life (26% of the total number of epileptic encephalopathy and 2.3% of all children with epilepsy). All the children in the attacks made their debut at the age from 4 to 7 months, were observed infantile spasms. The attacks were characterized by a high frequency. There was violation of development of different degree of intensity, prior to the opening of attacks or developed subsequently. Identified pattern hypsarrhythmia and modified hypsarrhythmia. Observation allowed us to note, that the full clinical-EEG remission in these patients achieve failed. Have three children outcome was a partial epilepsy, the 1 the syndrome Lennox-Gastaut.

**Conclusion:** Epileptic encephalopathy diagnosed with 8.9% of children with epilepsy.

### P713

#### SLEEP DISTURBANCES IN SCHOOL-AGED CHILDREN WITH AND WITHOUT EPILEPSY: PREVALENCE AND ITS EFFECT ON HEALTH-RELATED QUALITY OF LIFE

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**Purpose:** To explore the prevalence of sleep disturbances in school-aged children with partial epilepsy compared to normal children and to find the relation between sleep disturbances and health related quality of life (HRQoL).

**Methods:** In this study, in children with and without epilepsy, the questionnaires Sleep Disturbances Scale for Children (SDSC), Medical Outcomes Study-Sleep Scale (MOS-SS), Groninger Sleep Quality Scale (GSQS) and Kidscreen-27 were used to measure respectively sleep (over several time units) and quality of life. The Hague Scales were used to measure the severity of epilepsy. The returned questionnaires of 130 children, 4–10 years of age, treated in Dutch epilepsy outpatient clinics, and of 161 normal children, of the same age were compared. Additional a comparison of HRQoL was performed in children with and without sleep disturbances, this in both study groups.

**Results:** The sleep was scored worse in children with than without epilepsy. Pathological scores on SDSC (past half year) ( $T > 70$ ) were seen 12 times more often in children with epilepsy (36.92% vs. 3.01%,  $p < 0.001$ ). HRQoL was scored significantly lower in children with than without epilepsy. Comparison of HRQoL in subgroups children with and without sleep disturbances, resulted in scores below norm in those with epilepsy and also sleep disturbances, significantly lower than those without sleep disturbances.

**Conclusion:** This study confirms the high prevalence of sleep disturbances in children with partial epilepsy compared to children without epilepsy. Quality of life is already lower in children with than without epilepsy, sleep disturbances lead to further worsening.

### P714

#### LIFE QUALITY AND HEALTH OF ADOLESCENTS AND EMERGING ADULTS WITH EPILEPSY DURING THEIR YEARS OF TRANSITION: A SCOPING REVIEW

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**Purpose:** To explore and classify the issues and challenges that adolescents with epilepsy face in their transition into adulthood using the International Classification of Functioning Disability and Health (ICF 2001) and a theoretical model of health related quality of life (HRQL).

**Methods:** We searched PsychINFO, Ovid MEDLINE and web of science for the past 20 years for studies that reported on HRQL and health issues identified by adolescents and emerging adults aged 12–29. Studies were limited to those in English and those from the patients' own perspectives. Data were extracted and charted using a descriptive analytical method. The identified issues were classified according to the aforementioned frameworks.

**Results:** Sixty-four studies were identified for inclusion. The studies highlight a broad range of issues faced by adolescents with epilepsy. Adolescents emphasized issues surrounding peer acceptance and social situations leading to feelings of anxiety, fear and sadness. Maintaining dignity and control over one's life, fear of injury and SUDEP and worries about passing on the epilepsy to their own children were not easily classified with the ICF or HRQL framework.

**Conclusions:** The ICF and HRQL frameworks help classify many of the challenges faced by adolescents with epilepsy and cover mental and body functions; activity and participation; attitudes of peers and family; relationships; feeling embarrassment and guilt; and concealment of epilepsy. Further progress is needed how to fully classify and later utilize these issues to advance the life quality of adolescents and emerging adults.

### P715

#### THE EFFICACY OF INTRAVENOUS VALPROATE COMPARED TO INTRAVENOUS PHENOBARBITAL IN CONTROLLING SEIZURES AMONG PEDIATRIC PATIENTS WITH BENZODIAZEPINE-REFRACTORY STATUS EPILEPTICUS: A RANDOMIZED CONTROLLED TRIAL

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**Purpose:** To determine the efficacy and safety of intravenous valproate compared to intravenous Phenobarbital in controlling seizures among pediatric patients with benzodiazepine-refractory status epilepticus.

**Method:** Status epilepticus patients 2–18 years old admitted at the emergency department, intensive care unit, service and pay wards of a tertiary pediatric government hospital were randomly divided into groups A and B and received intravenous Phenobarbital in doses of 20 mg/kg as loading dose at a rate of 1 mg/kg/min and intravenous valproic acid in doses of 20 mg/kg as loading dose at a rate of 6 mg/kg/min, respectively. The patients were blinded as to the drug they received. They were followed up for 24 h and were switched over to the other group if seizures were not controlled within 1 h or there was seizure recurrence within 12 h of treatment.

**Results:** The duration of the status epilepticus at the time of presentation was  $< 2$  h in all patients in Group A and in 82% of patients in Group B. All subjects in the two groups had good outcomes of treatment: seizure was controlled, no one left against medical advice and there was no mortality. Seizure recurrence was mainly seen during the first 12 h in both study groups. There was no recurrence noted after 12 h. Intravenous valproic acid and phenobarbital infusions were well tolerated. Elevation of SGPT was the most common adverse effect seen but the difference in proportion was not statistically significant between the two groups.

**Conclusion:** Intravenous valproic acid is as effective and just as safe as intravenous phenobarbital as a second line non-sedative anti-convulsant

for pediatric patients with status epilepticus who failed to respond to bolus doses of diazepam.

#### P716

### ASSESSING THE CONCEPTUAL CONTENT IN HEALTH STATUS AND QUALITY OF LIFE MEASURES IN PEDIATRIC EPILEPSY USING WORLD HEALTH ORGANIZATION DEFINITIONS

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**Purpose:** The impact of epilepsy on children's lives includes health status-, health-related quality of life- (HRQL) and quality of life- (QOL) dimensions. Frameworks to assess the impact of illness on the child's life can be conceptualized in differentiating HRQL/QOL from the health-status or functioning approach. Firstly, we distinguish the perspectives of health, HRQL, or QOL found in commonly used measures. Secondly, we determine the health content for epilepsy-specific measures.

**Method:** We searched MEDLINE, EMBASE and PsycINFO from 2001–2011, for biopsychosocial health, HRQL and QOL measures in pediatric epilepsy literature. To identify the measures' perspectives we analyzed two generic- and 13 epilepsy-specific measures on an item-by-item basis according to World Health Organization definitions of health, QOL and the International Classification of Functioning, Disability, and Health (ICF). For content we coded each individual item according to ICF-CY classification for its components.

**Results:** Eight of 13 epilepsy-specific measures utilized a health status-dominant perspective (>82%) as opposed to HRQL/QOL to measure the impact of epilepsy on children's lives. The dominant contents (in %) of the measures were found to be *body function* in 7 (19–57%), *activity and participation* in 10 (21–60%), and *(social) environment* in five measures (19–30%).

**Conclusion:** Most measures in childhood epilepsy measure the impact of epilepsy on the lives of children using health-status rather than HRQL/QOL perspectives and contain content of body functions and daily activities and participation in life roles. Awareness of these concepts and contents is important in selecting the best measure of outcomes for research or clinical purposes.

#### P717

### NEUROCOGNITIVE FUNCTION IN CHILDREN WITH NEWLY DIAGNOSED EPILEPSY

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**Purpose:** Neurocognitive problems in patients with childhood epilepsy have long been recognized. The present study aims to identify the neurocognitive function in children with newly diagnosed epilepsy, and find out the factors that affect it.

**Method:** We retrospectively reviewed the records of 54 children with newly diagnosed epilepsy, in whom Korean Wechsler Intelligence Scale for Children-III, Stroop Color and Word Test, Children's Color Trail Test (CCTT), Attention-Deficit Hyperactivity Disorder (ADHD) Rating Scale, ADHD Diagnosis System (ADS), Children's Depression Inventory, and State-Trait Anxiety Inventory for Children, were performed.

**Results:** The mean age of the patients was  $9.7 \pm 4.0$  years (29 male and 25 female). The patients with abnormal background activity of electroen-

cephalography (EEG) ( $n = 8$ , 14.8%), five of whom revealed normal brain MRI findings, showed lower verbal IQ ( $79.4 \pm 23.5$  vs.  $95.3 \pm 17.3$ ,  $p = 0.04$ ), lower score in CCTT and Stroop Color and Word Test, and higher score in ADHD Rating Scale and ADS, compared to the patients with normal EEG background ( $n = 46$ , 85.2%). Location and frequency of epileptiform discharges on EEG, etiology of epilepsy, presence of abnormality on brain MRI, duration between seizure onset and diagnosis, and seizure frequency, did not influence the results of psychocognitive tests. Patients with benign Rolandic epilepsy showed higher full scale IQ score than the patients with idiopathic generalized epilepsy, and localization-related epilepsy other than benign Rolandic epilepsy ( $101.9 \pm 10.5$  vs.  $87.1 \pm 20.1$  vs.  $90.4 \pm 18.3$ ,  $p = 0.049$ ).

**Conclusion:** In patients with abnormal EEG background in newly diagnosed childhood epilepsy, it may be necessary to identify the presence of cognitive problems and ADHD.

#### P718

### CLINICAL FEATURES OF BENIGN INFANTILE CONVULSIONS WITH MILD GASTROENTERITIS: A RETROSPECTIVE STUDY OF 34 CASES IN A SINGLE CENTER

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**Purpose:** The aim of this study was to analyze the clinical characteristics in patients who presented with convulsion with mild gastroenteritis (CwG).

**Method:** We reviewed the medical records of 34 children with CwG hospitalized in Kyung Hee University Hospital, Seoul, Korea, between March 2001 and January 2013. Patients with meningitis, encephalitis/encephalopathy or history of epilepsy were excluded.

**Results:** Age at onset ranged from 3 to 44 months (mean; 17.9 months). Twelve were males and 22 were females. Seizures were focal in four patients (11.8%), focal to generalization in 2(5.9%), generalized in 27 (79.4%) and atonic in one patient (2.9%). The duration of seizures were <5 min in 31 patients (91.2%). Twenty three patients (67.6%) had  $\geq 2$  seizures, 12 of them (35.2%) experienced  $\geq 3$  seizures. The median interval between first and second seizure were 3 h. Even in patients with  $\geq 3$  seizures, seizures did not occur beyond 24 h. Antiepileptic drugs were administered for five patients. One patient experienced a recurrence of CwG, and one experienced febrile seizure. All patients exhibited normal psychomotor development at the last follow-up.

**Conclusion:** CwG is characterized by brief generalized seizures in cluster occurring within 24 h. Recognition of this condition will help pediatricians to avoid long term antiepileptic drug therapy.

#### P719

### EPILEPSY EVOLUTION IN FOCAL CORTICAL DYSPLASIA AND TUBEROUS SCLEROSIS COMPLEX

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**Purpose:** FCD and TSC are the commonest malformations of cortical development causing intractable epilepsy. Natural history of epilepsy in these disorders and outcomes is not fully elucidated. This study aims to address that.

**Method:** Ten-year retrospective chart-review of FCD and TSC cases at Montreal Children's Hospital (major referral centre for neurological disorders). We included all cases involved neurosurgery, neurology and neuroradiology.

**Results:** Thus far, we reviewed 32 charts (24 FCD, 8 TSC). Presentation age ranged from birth to 13-year. In FCD Group, all but one had epilepsy (75% intractable). The prevalent potential risk factors: febrile seizures and family history. One third had a developmental delay. Fifteen patients (63%) required surgery, mainly lesionectomies. Of the six patients who had well-documented follow-up more than one year, three were completely seizure-free. The commonest pathology was FCD type 3. In TSC group, five -of eight- patients had epilepsy (four intractable). No significant risk factors were found. Genetic testing was confirmatory in three cases only. Two patients had developmental delay. Two required surgery.

**Conclusion:** This work helps in a better understanding of the natural history of epilepsy in these disorders, and success of medical/surgical interventions. Further work would help to address variability in these two disorders in epilepsy development and control.

#### P720

##### THE RISK OF POST-TRAUMATIC EPILEPSY IN CHILDREN AFTER TRAUMATIC BRAIN INJURY

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**Purpose:** The aim of this study is to evaluate the risk of post-traumatic epilepsy in children with traumatic brain injury.

**Method:** We used a group of 102 children evaluated in our clinic or in emergency room, in 2007–2012, with brain injury with clinical signs of commotion syndrome arising immediately after head trauma. Causes of traumatic brain injury were road traffic accidents (63.72% cases), falls (23.53% cases), struck by objects (10.78% cases), sports and recreation (1.97% cases). Injuries were classified as mild (loss of consciousness or amnesia less than 30 min), moderate (Glasgow Coma Scale score = 8 or skull fracture) or severe (Glasgow Coma Scale score <8, subdural hematoma or brain contusion).

**Results:** In our study 11 (10.78%) cases had early post-traumatic seizures with onset in the first 7 days after head trauma. During the follow-up period 13 (12.74%) children had developed post-traumatic epilepsy from 3 month to 5 years after traumatic brain injury. Of these 13 patients diagnosed with post-traumatic epilepsy, 46.15% had immediate seizures after traumatic brain injury and 38.46% had previous seizure predisposition (three children had febrile seizures and two children had family history positive for epilepsy).

**Conclusion:** Significant risk factors of post-traumatic epilepsy were brain contusion with subdural hematoma, skull fracture, Glasgow Coma Scale score <8. Also early onset of seizures is associated with an increased risk of developing post-traumatic epilepsy.

**Key words:** head trauma, child, post-traumatic epilepsy.

#### P721

##### A RARE COMBINATION OF THE NEUROCUTANEOUS MELANOSIS AND DANDY-WALKER VARIANT WITH DRUG-RESISTANT EPILEPSY: CASE REPORT

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Neurocutaneous melanosis is a rare congenital neurocutaneous disorder that was first described by Rokitsansky in 1861, characterized by congenital melanocytic nevi in association with leptomeningeal melanosis. Approximately 8–10% of patients with neurocutaneous melanosis

present with a variant of the Dandy-Walker complex. We present a rare case that overcomes existing definition. The 8-month-old girl was admitted because of frequent generalized seizures which started 2 month before admission, physical and mental retardation. The frequency of seizures was about 6–7 per day. At the time of clinical examination several congenital nevi were observed on her scalp, trunk, and extremities, including a giant hairy nevus over her lumbosacral area. MR scan showed vermian hypoplasia, fourth ventricle was enlarged and seemed to be continuous with the cisterna magna, suggesting a Dandy-Walker variant. The brain MR scan without contrast also revealed in T1 weighted images characteristic hyperintensive brainstem and intraparenchymal (especially in anterior temporal region) lesions in the absence of meningeal involvement. The EEG shows attenuation and desorganisation, diffuse slowing of background with multifocal spikes. With valproate sodium 400 mg/day and phenobarbital 20 mg/day (started since she was 3 month-old) seizures were still occurring 2–3 times in day. Taking into account of inefficiency valproate sodium and phenobarbital were cancelled. Levetiracetam in dose 400 mg/day (50 mg/kg/day) was started instead and frequency of seizures were reduced by 50%. We increased levetiracetam to the target dosage rapidly at 2 weeks interval, by increasing 5 mg/kg per day once every 3 days. The girl has now been seizure free for 3 month.

#### P722

##### ANALYSIS OF COMPLIANCE AND SAFETY OF KETOGENIC DIET TREATMENT OF CHILDREN WITH INTRACTABLE EPILEPSY

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**Purpose:** To evaluate the compliance and security of the ketogenic diet (KD) in the children with intractable epilepsy.

**Method:** This was a prospective, open-label study of intractable epilepsy patients treated with the classic KD with a lipid-to-nonlipid ratio 4:1. 83 children (49 males and 34 females) were managed and followed-up through multidisciplinary KD team from May 2011 to December 2012. The variables related to the compliance and security was also analyzed.

**Results:** 1. At 5 days, 3 and 6 months after initiation, 92.8% (77/83), 70.7% (53/75), and 57.1% (32/56) patients remained on the diet.

2. The main causes to stop the treatment of 26 cases included poor efficacy accounts for 27% (7/26), the children's rejection for KD accounts for 19% (5/26), a poor compliance of parents accounts for 15% (4/26), the infection and accidental death were 12% (3/26). The cause of treatment discontinued was the noncompliance of the patients or the parents in the early days; inefficiency and the infection were the main causes to stop the therapy in the near future; the stopping of treatment according to abnormal nutrition indicators in long-term.

3. The side effect was drowsiness, fatigue, intolerance of Gastrointestinal tract and abnormal blood lipids in the early days. The tolerance of gastrointestinal tract got better in the near future, and the main side effect was the abnormal blood lipids in this period. There dead cases were not relative with KD.

**Conclusion:** The KD is a safe and effective alternative therapy for intractable childhood epilepsy. Multidisciplinary KD team is profit for children with KD treatment.

#### P723

##### CLINICAL FEATURES AND THERAPEUTIC EFFECT OF 30 PATIENTS WITH LANDAU-KLEFFNER SYNDROME

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**Purpose:** To study the clinical features, therapeutic effect and prognostic factors in children with Landau-Kleffner syndrome (LKS).

**Method:** Thirty patients with LKS were enrolled in our Hospital from 2005 to 2012. All patients were given Corticosteroids treatment for 6 months and some of them AEDs based on their epilepsy seizure type.

**Results:** (1) General data: Thirty patients were enrolled including 13 male and 17 female. The onset age of aphasia was from 14 to 168 months. 2. Clinical features: There were eight cases (26.7%) presenting acute onset and 22 cases presenting chronic onset (73.3%). 11 (36.7%) had expressive aphasia, and 19(63.3%) had both receptive and expressive aphasia. (2)20 patients had epileptic seizure (66.7%). (3) Moderate abnormal cognitive function accounted for 64%. (4)17 patients (63%) had normal and 10 patients had mild slow background activity. 18 patients had epileptiform discharges and seven children had ESES (23.3%). 3. Prognosis: (1) There were 15 patients (57.7%) totally recovered and 11 patients (42.3%) partially recovery. The onset time of treatment was within 3 months in 89.3% patients. The effectual time was within 6 months in 77.3% patients. There were 80% children recovered totally within 1 year. Three patients relapsed. (2)Twenty patients had epileptic seizure. Eighteen of them (90%) were controlled for seizure and the other two (10%) improved. (3) Two thirds of all patients had cognitive dysfunction. 4) Ten patients had slower background initially and returned to normal totally later. 28 patients had discharges. All ESES disappeared within 3 weeks, while three patients had recurrent ESES. 4. The data showed the patients who had longer course of disease, presenting aphasia at a younger age and having ESES probably had poor outcomes.

**Conclusion:** LKS is rare. Corticosteroids treatment is effective. The course of disease, onset age of aphasia and ESES might have important impact on long-term outcome.

## P724

### EFFICACY OF LOW GLYCEMIC INDEX DIET THERAPY IN CHILDREN WITH REFRACTORY EPILEPSY: A RANDOMIZED CONTROLLED TRIAL

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**Purpose:** To determine the efficacy and safety of low glycemic index diet therapy (LGIT) in children with drug refractory epilepsy.

**Methods:** This was a open label randomized controlled trial with two parallel groups. Children with drug refractory epilepsy were randomized into LGIT and control groups. Variable block size randomization was used. Serially numbered opaque envelopes were used for concealing the allocation. Carbohydrates of only low glycemic index were allowed in the diet in LGIT group were encouraged to take large amounts of fatty and carbohydrate free food items. Carbohydrate intake was restricted to 40–60 g per day or 10% of the daily caloric intake whichever was lower. Patients in control group were continued on AED treatment without any dietary intervention. Daily seizure diary was maintained by parents. Patients were followed up monthly for at least three months. Institute ethics committee approved this study. This trial was registered with www.clinicaltrials.gov (identifier NCT01645072).

**Results:** Forty patients (20 patients in LGIT group and 20 patients in control group) were enrolled. Patients were aged between two to eight years. The compliance to LGIT was 88.5%. Six out of twenty patients (33%) in the LGIT group had more than 50% seizure reduction from the baseline at the end of three months including one patient who was seizure

free. None of the 20 patients in the control group achieved more than 50% seizure reduction ( $p = 0.02$ ). Number needed to treat for more than 50% seizure reduction at three months was three. Two patients developed lethargy and one patient had vomiting during the study period. Five patients continued on LGIT on last follow up (median duration: eight months). One patient had withdrawn due to poor palatability of the diet.

**Conclusion:** Low glycemic index diet therapy is feasible, effective and safe in children with drug refractory epilepsy.

## P725

### A GENETIC BASIS FOR TREATMENT RESPONSE TO THE KETOGENIC DIET

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**Purpose:** The Ketogenic diet (KD) is an alternative treatment option for children with drug-resistant epilepsy. It may reduce seizures by >50% in approximately 40% of patients, but it is a resource-intensive treatment and may cause adverse side effects. Predictors of response – which, in the absence of specific metabolic disorders, are currently unknown – would improve patient selection and may enhance our understanding of its underlying anticonvulsant mechanisms. Looking for genetic predictors of response, we selected KCNJ11 and BAD as candidate genes. Variation in these genes is associated with altered glucose metabolism. BAD modification increases mitochondrial utilisation of beta-hydroxybutyrate and decreases utilisation of glucose in neurons and astrocytes, reminiscent of the response to the KD. These metabolic changes cause an increase the activity of  $K_{ATP}$  channels.

**Method:** After informed consent, blood was taken for DNA extraction from KD patients at our study sites. Sanger sequencing of KCNJ11 and BAD was completed. Cases were divided into non-responders (with no change or an increase in seizure frequency) and responders (partial responders: 25–75% seizure reduction, and extreme responders: >75% seizure reduction), at 3-month and 6-month follow-up.

**Results:** One hundred and ninety-one cases have been sequenced. Ten SNPs were found in KCNJ11 and 8 SNPs in BAD. All SNPs in each gene were in full linkage disequilibrium. By logistic regression, the strongest association of KCNJ11 variation with diet response was at 6 months ( $p = 0.0175$ ). For BAD, the strongest association was at 6 months ( $p = 0.106$ ).  $p$ -values are uncorrected.

**Conclusion:** There may be a possible association of KD response with variation in KCNJ11. Currently, there seems to be no impact of BAD on KD response. Analyses are ongoing.

## P726

### ROLE OF EMERGENCY CT SCAN AS AN INVESTIGATIVE TOOL IN CHILDREN WITH FIRST AFEBRILE SEIZURE

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**Purpose:** In the previous studies radiologists were not blinded to the clinical information.

1. To determine how often the CT scan influences acute management of children presenting to the emergency room (ER) with first afebrile seizure.
2. To calculate the rate of abnormal CT scan in children with first afebrile seizure when the radiologists are blinded to the clinical information, and
3. To identify the clinical factors predictive of abnormal CT findings.

**Method:** Design: Historical prospective study.

**Inclusion criteria:** 1. Children (1 mo-17 years) presented to the McMaster Children's Hospital ER with first afebrile seizure between 01/01/2005–31/12/2010. 2. Had CT scan ordered in the ER. Control subjects: Children who had CT for reason other than first afebrile seizure. (control to study subjects 2: 1). Two radiologists blinded to the clinical information reported the study and control CTs independently. A *prospective management algorithm* was constructed for the study subjects by showing the CT report & images to two ER physicians. ER physicians consulted neurologists and or neurosurgeons (two each), if needed. Management decisions were recorded on a standardized form. Only the age of the child was provided to the physicians.

**Results:** 150 (of 292) children presented to ER with first afebrile seizure had CT. 36/150 (24%) had abnormal findings. 22 (15%) had at least one acute management decision based on CT. Focal neurological finding was a strong predictor (OR-6.06, 95% CI: 1.84–19.96,  $p = 0.003$ ) of abnormal CT scan (binary logistic regression), others being focal seizure and altered level of consciousness (LOC).

**Conclusion:** This is the first study where radiologists were blinded to the clinical information. Urgent CT scan should be considered in children with first afebrile seizure in the presence of focal neurological finding, focal onset of seizure, or altered LOC.

#### P727

### VARIABILITY IN THE DIAGNOSIS AND MANAGEMENT OF ELECTRICAL STATUS EPILEPTICUS OF SLEEP

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**Purpose:** To understand the variability of the criteria for definition of Electrical Status Epilepticus of Sleep (ESES) and the treatment methods used by Canadian pediatric neurologists for this condition.

**Method:** Participants: Pediatric Neurologists working at the 16 academic centers in Canada. A 27 item draft questionnaire was prepared (seven members of the Canadian Pediatric Epilepsy Network- CPEN). Questions on expertise, experience, criteria, EEG and management were included.

**Results:** Sixty of the 82 (73%) surveys were returned. 46 (76.7%) identified themselves as capable of providing an opinion on the diagnostic criteria or treatment options. Ten opined the diagnosis of ESES should be based only on EEG criteria, 36 considered the diagnosis based on EEG and clinical findings. 86% (30/36) considered behavioral/cognitive deterioration reported by the caregivers as sufficient to meet the clinical criteria. 27 (27/37) recommended EEG diagnosis should be based on the visual impression of near continuous spike and wave activation during sleep. 10 (10/37) recommended calculating the spike and wave index during sleep (SWI) manually or using software. 97% (42/43) recommended a sleep SWI of at least 50% to make an EEG diagnosis of ESES.

**Management:** 72% (33/46) aimed pharmacological management towards sleep EEG abnormality as well as clinical seizures. 26% (12/46) targeted the sleep EEG abnormality alone. 85% (39/46) initiated treatment of sleep EEG abnormality when the caregiver/health professional reported deterioration in behavior/cognitive status. 61% (28/46) treated ESES to improve the clinical seizures as well as cognitive status.

**Conclusion:** There is reasonable agreement on the diagnostic criteria of ESES. A systematic review on the therapeutic efficacy of various treatment methods needs to be studied using defined diagnostic criteria and monitoring methods, preferably in a prospective manner.

#### P728

### LONG TERM OUTCOME OF LENNOX-GASTAUT SYNDROME

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**Purpose:** Lennox-Gastaut syndrome (LGS) is a severe childhood onset epileptic encephalopathy, usually intractable to medical treatment. Although clinical and electrographic features of LGS are well documented, few studies about long term outcome of LGS have been reported.

**Method:** Medical records were retrospectively reviewed for 32 patients, diagnosed as Lennox-Gastaut syndrome in the Severance Children's Hospital and older than 18 years old in January, 2013. Age of seizure onset, seizure type, etiology, EEG characteristics, intelligence quotient, treatment and seizure outcome were evaluated.

**Results:** The mean age of the 32 LGS patients was 22 years (ranged from 18 to 34 years) with 21 male patients and 11 female patients. Mean age of seizure onset was 50 months (ranges from 1 month to 12 years). Twenty three patients were performed surgery including vagus nerve stimulation, corpus callosotomy, hemispherotomy and resective surgery. Despite aggressive management for seizure control, overall outcome was poor. Although nine patients (28%) were almost seizure free, 15 patients (47%) remained without improvement of seizure. Prior history of infantile spasm or age of seizure onset were not associated with seizure outcome. Cognitive impairment and gait disturbance were also common. Therefore independent daily activities were possible only in seven patients (22%).

**Conclusion:** Long term outcome of LGS, in terms of seizure control and intellectual development is poor.

#### P729

### EFFICACY OF REPEATED ADRENOCORTICOTROPIC HORMONE THERAPY IN PATIENTS WITH INTRACTABLE EPILEPTIC SPASMS

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**Purpose:** We examined the effectiveness of repeated adrenocorticotrophic hormone (ACTH) therapy in short-term and long-term seizure control in patients with intractable epileptic spasms.

**Method:** Twenty-five patients with intractable spasms, in whom epileptic seizures were not controlled or relapsed after the first ACTH therapy, were given repeated ACTH therapy. The short-term effect (seizure control longer than two months) of repeated ACTH therapy was analyzed, and the long-term effect was estimated by Kaplan-Meier method.

**Results:** Short-term seizure control by repeated ACTH therapy was achieved in 13 of 25 patients (52.0%), and in five of 13 patients, seizures were controlled by ACTH therapy at higher doses compared with the first ACTH therapy. Short-term effectiveness was obtained in 76.5% of patients who had epileptic spasms alone at the time of the second ACTH therapy, but was ineffective in all eight patients who had multiple types of seizures, with relapses within 2 months. Short-term effectiveness was not associated with clinical factors such as onset age, age of repeated ACTH treatment, and EEG findings. Regarding the long-term effect of

repeated ACTH therapy, the period until seizure relapse was significantly longer in patients with epileptic spasms alone compared to patients with multiple seizure types. Spasms were controlled in five of 25 cases (20.0%) at the final observation. In patients with multiple seizure types and patients with onset age older than eight months, seizure control was not obtained. Long-term outcome was good in patients with treatment lag within 2 months.

**Conclusion:** In repeated ACTH therapy, seizure type seems to be one of the major determinants for short- and long-term seizure outcome.

### P730

#### INCREASED INFLAMMATORY CYTOKINES IN SERA OF CHILDREN WITH ACUTE-ONSET FEBRILE SEIZURES

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**Purpose:** Febrile seizure is common in childhood and the pathogenic mechanism includes the inflammatory processes as well as genetic factors. This study is focused on the cytokine expressions in sera of the children with seizure.

**Method:** Study subjects were classified as four groups. Group 1 is the children with febrile seizure whose sera were obtained within the 24 h of febrile seizure. Group 2 includes the children with febrile seizure, but the sera were obtained after the 24 h of seizure onset. Group 3 is the children with afebrile seizure and the sera were obtained within 24 h of seizure onset. Group 4 includes the children with epilepsy whose sera were obtained after 24 h of seizure development. The authors measured several cytokine levels in sera of each group using Luminex multiple bead technology (Milliplex; Human Adipokine assay kit, Millipore Corporation, Billerica, MA, Bio-plex; Human Cytokine assay kit, Bio-Rad laboratories, Hercules, CA). IL-1b, IL-6, IL-10, visfatin, resistin, PAI-1 and TNF $\alpha$  were assayed. Independent t-test and Kruskal Wallis test were used using IBM SPSS Statistics 20.0 for the statistical analysis.

**Results:** Total 31 samples were assayed for the cytokines and they include 18 samples from group 1, 2 from group 2, 4 from group 3, and 7 from group 4. IL-6, IL-10, resistin and visfatin levels were significantly elevated in the sera of patients with febrile seizure which developed within 24 h.

**Conclusion:** Elevated levels of inflammatory cytokines such as IL-6, IL-10, resistin and visfatin were noted in the sera of children with febrile seizure which were obtained within 24 h of seizure onset. Further study about the pathogenic mechanism or clinical outcomes will be required with large study subjects.

### P731

#### CHARACTERIZATION OF EPILEPTIC SEIZURES IN THE FIRST 3 YEARS OF LIFE OF NEWBORNS AT RISK. CUBA

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**Purpose:** Studying the incidence of clinical types of seizures, and their behavior

**Method:** Retrospective study of 520 newborns followed of neurodevelopment by risk of functional and/or structural damage of the Central Nervous System (severe asphyxia at birth, neonatal seizures, ventilated, <1500 g) that were admitted in Neonatology Service to "América Arias" Gynecologic and Obstetric Hospital during the period 2004–2012. All the patients were checked through a neurological exam with techniques

the Amiel-Tison, Fenichel, Precht, polysomnography studies and the fontanel ultra sonogram. Also were performed periodical evaluations of the mental and motor development using the Bayley test. Epileptic seizures were classified as occasional crises (CO), epileptic syndromes (SE) and febrile convulsions (CF).

**Results:** Of the 520 newborns studied had seizures 98 cases (18.8%) of this amount 68 cases (69.3%) the first crisis occurred in the neonatal period, 5 (5.1%) occurred in the first year of life (excluding the neonatal period), 11 (12.1%) occurred in the second year of life and in 14 of them came up in the third year of life. To investigate evolution and etiology found that 91.6% of neonatal seizures proved to be the result of a perinatal brain insult and the remaining 8.4% were classified as epileptic syndromes of the newborn. There were seven cases of febrile convulsions, of which 75% was occurred in the second year of life. The 35.1% of epileptic syndromes occurred in the neonatal period, in the first year of life excluding the neonatal period was the higher incidence of, one case as partial epilepsy symptomatic and 74% as encephalopathy. Epileptic them seven cases with West syndrome and two patient with Aicardi Syndrome.

**Conclusion:** The highest incidence of crisis was in the neonatal period, which demonstrates the selective vulnerability of the immature brain.

### P732

#### CLINICAL, COGNITIVE AND BEHAVIORAL OUTCOME IN FEMALES WITH PCDH19 GENE – RELATED EPILEPSY

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**Purpose:** Evaluating long-term epilepsy and neurocognitive outcome of girls affected by PCDH19 gene related epilepsy.

**Method:** We retrospectively selected all the patients with PCDH19 gene-related epilepsy and a minimum follow-up of 12 months. Medical records have been carefully examined in order to review age at onset, seizures semiology at onset and during follow-up, and neurocognitive development. Cognitive level was regularly evaluated during follow-up with standardized tests according to the age and the specific ability of every single patient.

**Results:** We selected 10 girls; seizure onset ranged from 3 to 38 months, usually with seizures in clusters, mostly febrile. 4/10 girls are seizure free; in the remaining patients seizure frequency significantly decreased over time. Seizures appeared to be mostly focal and characterized by staring, eyes and head deviation, focal jerks; hypomotor seizures are common at the onset of epilepsy, becoming less frequent with the patients growing up. Affective symptoms were common, but not constant. Ictal EEG during clusters was available for all the patients. Normal intelligence was present in 4/10 girls, with different degrees of mental retardation in the remaining patients. Autistic features have been detected in four cases; behavioral problems such as hyperactivity, challenging behavior and emotional lability, appeared to be common.

**Conclusion:** Seizures in PCDH19 gene related epilepsy appear to be mostly focal and grouped into clusters, which usually become less frequent over time. Mental retardation and autistic traits are common, but apparently not strictly related with age at seizure onset, seizure frequency and the recurrence of status epilepticus.

### P733

#### HIGH-DOSE ORAL PREDNISOLONE IN WEST SYNDROME – A VIABLE ALTERNATIVE TO ACTH

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**Purpose:** West Syndrome is one of the catastrophic epileptic encephalopathies of childhood. Current guidelines recommend ACTH as the first line treatment in this condition. Cost of natural ACTH, intramuscular route of administration, side effect profile and limitations on treatment duration make it less attractive. Synacthen is often substituted but shares many of the same limitations except cost. High-dose oral prednisolone has been used clinically and in trials. We studied the outcome of patients treated with prednisolone in the local population.

**Method:** Retrospective cohort study of children diagnosed with West syndrome between May 2002 and May 2012 and treated with oral prednisolone.

**Results:** Of 67 patients with West Syndrome, 22 were treated with high-dose prednisolone. Maximum dose was 60 mg/day. Duration of treatment ranged from 10 to 131 days (median 45 days). 11 (50.0%) had clinical resolution of spasms and 10 (45.5%) had EEG resolution.

**Conclusion:** High-dose prednisolone is a viable alternative to ACTH and results are comparable to other evidence-based treatments.

### P734

#### UNDERSTANDING THE RELATIONSHIP BETWEEN INFANTILE SPASMS AND AUTISM

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**Purpose:** Infantile spasms (IS) are a catastrophic childhood epilepsy frequently associated with severe developmental outcomes, including autism spectrum disorders (ASDs) in (9–35)% of cases. The objective of this multicenter study was to determine whether rapid diagnostic and early spasm control could limit the incidence of ASDs, while identifying clinical risk factors involved in developing ASDs within our population.

**Method:** Patients with IS were treated with a standardized protocol with Vigabatrin as first line therapy followed by sACTH and Topiramate in refractory patients. Using our protocol, 96% of children became spasm free within 8 weeks of diagnosis and none recurred. Autism assessments were conducted with the Checklist for Autism in Toddlers (CHAT) and the Autism Diagnostic Observation Schedule (ADOS) at the 24 and 30-months follow-up respectively.

**Results:** Of the 69 patients enrolled, autism evaluations were available for 44, 10 (23%) of which had an ASD confirmed with ADOS. Earlier diagnosis and cessation of spasms did not correlate with a reduced rate of ASD ( $p = 0.53$  and  $p = 0.79$ ). Significant risk factors for developing ASD were Tuberous sclerosis (TS) as the underlying etiology and chronically epileptiform EEGs ( $p = 0.03$  and  $p = 0.001$ ). Other risk factors included post-IS seizures ( $p = 0.07$ ) and symptomatic etiologies at large ( $p = 0.09$ ).

**Conclusion:** Earlier IS diagnosis and treatment did not correlate with a reduction of ASD outcome. TS and the persistence of epileptiform EEGs are the major predictive factors of ASD outcome which could be used as markers for preventative therapeutic trials for ASD.

### P735

#### CLINICAL CHARACTERISTIC AND TREATMENT OF EPILEPSY FOR CHILDREN WITH TUBEROUS SCLEROSIS

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**Purpose:** The aim of this study is to estimate the clinical characteristic and treatment of epileptic seizures in children with tuberous sclerosis.

**Method:** The medical data of 11 children diagnosed with tuberous sclerosis and epileptic seizures were retrospectively studied. The study protocol included: general physical and neurological examination, seizures characterization, electroencephalography (EEG) findings, brain imaging studies, psychological examination. Therapeutic efficacy was estimated by percentage of patients who had been achieved significant clinical response.

**Results:** The age of onset of epileptic seizures was 4 month – 3 year. Seven children have epileptic seizures before being diagnosed as having tuberous sclerosis and three children showed epileptic seizures after being diagnosed with tuberous sclerosis. Two of these patients were first diagnosed with cardiac rhabdomyoma in the neonatal period. The EEG was abnormal for all children: generalized or focal spikes and diffuse or focal slowing in four cases, hypsarrhythmia in five cases, generalized spike-wave discharges in two cases. Brain imaging was performed in all 11 patients (7IRM, 4CT) and revealed cortical tubers varying in number and location and/or intracranial calcifications. Among these children 5 (45.45%) had infantile spasms, 2 (18.18%) had tonic-clonic seizures, 1 (9.09%) had complex partial seizures, 3 (27.27%) had different types of seizures (focal seizures, atonic seizures, atypical absence seizures). The children were treated employing ACTH, vigabatrin, sodium valproate, lamotrigine, topiramate, clonazepam single or add-on. Partial seizure control was achieved in 36.36% patients.

**Conclusion:** Refractory epilepsy is common in children with tuberous sclerosis, these patients can develop multiple seizures type. Therapeutic efficacy was variable depending on type of seizures and antiepileptic drugs used.

### P736

#### DRAVET SYNDROME IN SWEDEN: A POPULATION BASED STUDY

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**Purpose:** We assessed prevalence and incidence in Sweden, of children diagnosed with Dravet syndrome (DS) between 2007 and 2012. We describe geographical presentation, electro-clinical features, gene-abnormalities and treatment-effects.

**Method:** All university- and county-hospitals and neuro-pediatricians in Sweden were approached, asking for patients with the electro-clinical profile of DS. Genetic laboratories in Sweden were approached according genetic analyses of the SCN1A-gene and the referral clinicians. Approval by the ethics committee and informed consent was obtained and clinical data was collected. We identified 47 (1–22 years) patients. Five were >17 years and excluded.

**Result:** Incidence in a 5-year birth-cohort 2007–2011 was one in approximately 33000 live births. Prevalence December 31, 2012 was one in 46810 children. In the 42 children (18 boys/24 girls) median age was 7 (1–17) years, median age at seizure onset was 6(0–12) months and median age at diagnosis was 3(1–14) years. 37/42 (88%) had a mutation in the SCN1A-gene. Four were familiar. 15/30 (12 not specified) had autism, 28/39 mental retardation (three not specified) and 30/42 neurological deficits. 18/42 had Stiripentol as add-on, 7/18 were seizure-free, 6/18 had >50% seizure reduction and 5/18 < 50% seizure-reduction or had recently started Stiripentol and were not possible to evaluate.

**Conclusion:** This is the first population based study of Dravet syndrome in Sweden. Our data confirms international data. Sweden is well set for obtaining information about population. All citizens are included in an official census at birth. The medical-care system is transparent and available for information-exchange and pediatric epilepsy is centralised to pediatric neurologists.

P737

### TRANSITION FROM PEDIATRIC TO ADULT HEALTH CARE FOR YOUNG ADULTS WITH SIGNIFICANT COGNITIVE IMPAIRMENTS AND EPILEPSY: PARENTAL PERSPECTIVES

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**Purpose:** The movement towards adult health care services is an expected and desired outcome of pediatric care. When the young adult has a cognitive impairment in addition to a complex chronic neurological condition, including epilepsy, parental involvement is critical in the transition process. The objective of this study was to identify salient issues confronting these parents.

**Method:** A qualitative interpretive design was used to gain an in-depth understanding of parents' perceptions of their young adults' transition process from a pediatric to an adult epilepsy setting. Purposive sampling was used to interview 17 parents of 11 young adults who had transitioned to an adult epilepsy setting

**Results:** The young adults were between the ages of 18 and 21 years of age, had severe symptomatic epilepsies and an IQ of less than 80. Five of the young adults were non-ambulatory, did not speak, were enterally fed, and two had tracheostomies. Findings suggest that parents' perceived a tremendous sense of abandonment, a sense of loss, and fear and uncertainty as they navigated the transition of their young adult. What hindered transition was a lack of sufficient coordination within the health care system, the vulnerability of the young adult, the lack of appropriate resources in the adult health care system given the multifaceted needs of the young adult, and the parents own tenuous health status. The transition process was felt to be facilitated by the parent's resourcefulness and ability to establish new relationships within the adult setting.

**Conclusion:** The emotional toll of the parent is tremendous and requires thoughtful consideration planning the transition process for young adults' with complex chronic neurological disorders and who have a cognitive impairment. In light of these findings several initiatives have occurred. These initiatives include transition clinics, formal parental information sessions in collaboration with community organizations and improved information transmission.

P738

### TREATMENT OUTCOME OF LENNOX-GASTAUT SYNDROME

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**Purpose:** To evaluate the long-term treatment outcome of various treatment options including antiepileptic drugs (AEDs), ketogenic diet (KD), and surgery in patients suffering from Lennox-Gastaut syndrome (LGS) with various treatment options.

**Method:** We The hospital retrospectively reviewed 322 children and adolescents who were treated diagnosed with LGS within the between and a minimum follow-up period of at least 1 year. They had multiple mixed seizure types and electroencephalographic features of LGS. All patients were treated with one or several AEDs, 289 patients were treated with either KD and/or (144 patients) and or surgery (145 patients), or even both (55 patients).

**Results:** The mean seizure onset age was 26.3 months and the mean age at last follow-up date was 10.3 years. Patients showed multiple mixed seizure types including tonic (71.1%), atypical absence (59.0%), and atonic (42.9%) seizures. Twenty-eight patients (8.7%) of 322 patients achieved seizure free by using only AEDs, while 26 patients (18.1%) out of 144. patients who have tried KD achieved seizure freedom. twenty-six patients (18.1%) experienced seizure free Surgery was performed in 1450 patients, were performed epilepsy surgery including resective specific surgical cases, and 57 (39.3%) patients reported seizure freedom at last follow-up. were Out of the 59F patients who went through were performed resective surgery, almost and half of them achieved seizure free outcome were without any seizures at their last visit. Overall, 34.5% patients in Lennox-Gastaut syndrome became seizure free ed from seizure with AEDs by using, KD, and surgery. Developmental outcome was better in seizure free cases than the others.

**Conclusion:** To be cured, Intensive treatment option actively treatments including KD and surgery are needed to control seizures in LGS for better outcome. when seizures are not stopped by using antiepileptic medications.

P739

### LATE-ONSET EPILEPSY IN CHILDREN AFTER ACUTE FEBRILE ENCEPHALOPATHY WITH PROLONGED CONVULSIONS

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**Purpose:** To analyze the characteristics of epilepsies as the sequelae of acute febrile encephalopathy with prolonged convulsions during childhood.

**Methods:** Sixteen patients aged 2–13 years with history of febrile acute encephalopathy were retrospectively reviewed. These patients experienced febrile encephalopathy at the age of 11 months to 4 years, with 11 individuals presenting with findings of a biphasic clinical course (n = 5), frontal predominant (n = 8) lesions, and/or reduced diffusivity in the cerebral white matter on magnetic resonance imaging (MRI; n = 3). The remaining five patients had hemiconvulsion-hemiplegia-epilepsy syndrome (HHES).

**Results:** Epilepsy emerged with a latent period of 2 months to 2 years after the acute phase of febrile encephalopathy. Head nodding or spasm with subsequent motion arrest and brief tonic seizures were the main seizure phenotypes. Ictal records of epileptic seizures were available in nine patients. Epileptiform discharges with a focal or uneven distribution appeared at the seizure onset and lasted less than 1 s in all patients; these were followed by either generalized attenuation or fast activity in eight patients with head nodding, spasm, or brief tonic seizures, and by localized fast activity in one patient with versive tonic seizures. Notably, the seizure onset area was often located outside the severe lesions on MRI, i.e., in the parietal areas

in patients with frontal predominant lesions, and in the spared hemisphere of HHES. Although phenobarbital, zonisamide, carbamazepine, clobazam, clonazepam, and clorazepate were partially effective in some patients, daily seizures persisted in 11 patients. Callosotomy was performed in two patients, and beneficial effects were observed in both.

**Conclusion:** These characteristics suggested a broad distribution of augmented excitability in these patients, resulting in the rapid propagation of epileptic activity in the initial phase of ictal phenomena.

#### P740

##### CLINICAL CHARACTERISTICS OF EPILEPTIC SEIZURES IN A CASE OF DIHYDROPTERIDINE REDUCTASE DEFICIENCY

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**Purpose:** To assess the clinical characteristics and efficacy of neurotransmitters and levetiracetam in a patient with hyperphenylalaninemia due to dihydropteridine reductase (DHPR) deficiency who developed epileptic seizures.

**Method:** A boy with DHPR deficiency, who had been successfully treated with tetrahydrobiopterin (BH4), levodopa and 5-HTP since he was 2 months old, started having monthly episodes of blurred vision, loss of consciousness, and fall at the age of 12. He was taking BH4 510 mg/day, levodopa 670 mg/day, 5-HTP 670 mg/day, and entacapone 300 mg/day. We evaluated the seizure semiology, EEG findings, and efficacy of levodopa, 5-hydroxytryptophan (5-HTP), and levetiracetam.

**Results:** His seizures comprised of abrupt loss of awareness and eyes deviation to right. Ictal EEG showed seizure pattern starting at left temporal region, and interictal EEG showed multiregional independent spikes in bilateral hemispheres. Brain MRI showed diffuse signal increase of deep white matter on T2-weighted and FLAIR images. Dose increase of levodopa to 1340 mg/day or 5-HTP to 1500 mg/day did not suppress seizures. Levetiracetam 2000 mg/day markedly reduced seizures without any adverse events.

**Conclusion:** Epileptic seizures in patients with DHPR deficiency can be successfully treated by levetiracetam in safe.

#### P741

##### MENKES DISEASE: AN IMPORTANT CAUSE OF EARLY ONSET REFRACTORY SEIZURES

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**Purpose:** Menkes disease is an X-linked multisystem disorder characterized by early onset cerebral and cerebellar neurodegeneration, fair skin, hypopigmented sparse hair and connective tissue abnormalities. We aimed to evaluate the clinical, electrophysiological and radiological features of children with Menkes disease seen at our institute.

**Method:** The medical records of children diagnosed with Menkes disease admitted in the pediatric neurology ward or attending the special pediatric neurology clinic at a tertiary care and a referral hospital in North India from January 2010 to December 2012, were retrospectively reviewed. The clinical data of each case was subsequently summarized and reported.

**Results:** During the study period, 1174 children were seen. Out of these, six cases were diagnosed as Menkes disease on the basis of clinical phenotype, low serum copper and ceruloplasmin and supportive neuroimaging. All the children were males and had disease onset within 3 months of age with four children presenting in the neonatal period. Global developmental delay and refractory seizures were the predominant clinical symptoms. Two children had symptomatic West syndrome. Other seizure semiologies included tonic-clonic (4), myoclonic (2) and tonic seizures (1). The electroencephalographic abnormalities included dysrhythmia (2) and multifocal epileptiform discharges (3). The salient radiological features included white matter changes, temporal lobe abnormalities, global atrophy, subdural hygromas and tortuous cerebral blood vessels.

**Conclusion:** Menkes disease should be suspected in a case of refractory early onset seizures especially in the presence of subtle clinical clues. The neuroimaging findings may further support the diagnosis. Early copper treatment and gene therapy coupled with supportive management may be beneficial.

#### P742

##### EPIDEMIOLOGIC, CLINICAL AND ETIOLOGICAL ASPECTS OF EPILEPTIC ENCEPHALOPATHY IN SENEGAL

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**Purpose:** Epileptic encephalopathy are conditions in which the neurological deterioration is secondary in the epileptic demonstrations. This could either be related to the severity of the epileptic seizure or the duration of the seizure. Our objective is to describe the epidemiology, associated signs, and the frequency of the various types of encephalopathy.

**Method:** We led a retrospective study from July 2003 to December 2011. The folders of 197 children of the neuropaediatric consultation clinical of Fann University Teaching hospital and Albert Royer Children hospital were reviewed. Data analysis was made by SPSS.16.0.

**Results:** We collected 113 folders of patients. The average age was 3 years 2 months with a range of 1 month to 14 years; the sex ratio was 2.3/1 in favor of males. The mean age of onset was 11 months. Asphyxia was found in 17.7%, parental consanguinity was 15%. Among our patients, 49.5% had only one type of seizures. A partial motor seizure was found in 42.4%. Initial psychomotor development was abnormal in 61.1%. Motor disorder 48.6%, with axial hypotonia in 23.8%. Cognitive abnormalities seen in 62%, while 49.5% had mental disorders that were dominated by hyperactivity in 23.8%. West syndrome was found in 23% of the POCS syndrome in 7.1%, while Dravet syndrome accounted for 4% of our patients. Medical imaging was normal in 18.6%, with 16.8% of cortico subcortical atrophy. Regarding therapy, 73.45% were boarded on VPA, 81% had necessitated a triple therapy which was predominated by the association of VPA, carbamazepine, and clonazepam. Were noted drug resistance in 44.2% while in 31% seizures were controlled. Academic pursuit was disrupted in all our patients.

**Conclusion:** Epileptic encephalopathy have a problem of drug resistance, and poor prognosis both cognitive, social and motor disorders. Hence the need for a multidisciplinary approach.

P743

### FOCAL CORTICAL DYSPLASIA AND EPILEPSY IN INFANCY: FOCAL SEIZURES VS. EPILEPTIC SPASMS

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**Purpose:** Focal cortical dysplasia (FCD) has been recognized as one of the most frequent causes of drug resistant epilepsy, especially in children. In infancy, onset of FCD-related epilepsy is alternatively characterized by epileptic spasms or focal seizures. Which elements pertaining to the FCD are responsible for the onset of one type of seizure over the other is still unclear. Purpose of our study was to compare the characteristics of FCD in terms of lateralization and site in patients with epileptic spasms vs. patients with focal seizures.

**Method:** We retrospectively reviewed data from 42 patients with FCD related epilepsy with onset during the first 14 months of life. Seizure semiology and drug resistance were analyzed, as were age at onset and FCD site and lateralization.

**Results:** Nineteen children presented with focal seizures, 18 with epileptic spasms and four presented both. Mean age at onset was respectively 8.3, 4.9 and 1.5 months. Drug resistance was present in respectively 8 (42%), 14 (78%) and 4 (100%) children. The patients whose FCD involved the frontal lobes were respectively 9 (47%), 14 (78%) and 1 (25%). Out of 14 patients with epileptic spasms and frontal lobe involvement, 11 (79%) had a right lateralization of the FCD. Seizure semiology of focal seizures was heterogeneous and included psychomotor arrest, perioral cyanosis and focal hypertonia.

**Conclusion:** Right frontal lobe localization of FCDs seems more closely associated with onset of epileptic spasms, as is early onset. Also, FCD-related epileptic spasms seem to be more drug resistant than focal seizures.

P744

### CLINICAL FEATURES AND LONG-TERM SURGICAL OUTCOME OF CHILDREN WITH EPILEPSY DUE TO FOCAL CORTICAL DYSPLASIA

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**Purpose:** Focal cortical dysplasia (FCD) is a specific malformation of cortical development characterized by the disorganization of the cerebral cortex associated with early onset intractable epilepsy. We studied the electroclinical characteristics and surgical outcome in children with intractable epilepsy due to FCD.

**Method:** The medical records of 19 children (M:F = 13:6) diagnosed as epilepsy with pathologically proven FCD at Asan Medical Center between 1997 and 2012, were reviewed. FCD was classified according to the new three-tiered ILAE classification system.

**Results:** Median age at seizure onset was 18 (0–134) months, median age at surgery was 7.0 (0–15) years and median duration of follow-up was 7.0 (0–15) years. Initially, 13 (68.4%) children presented with partial seizures and 6 (31.6%) with generalized seizures. Localization was possible in 14 (73.7%) children by the presence of focal interictal epileptiform

discharges (IED) on preoperative EEG, while others showed focal and generalized, multifocal or generalized IED only. Brain MRI revealed typical FCD findings in 9 (47.4%) children. Corticectomy was performed in 6 (31.6%) children, temporal lobectomy in 6 (31.6%), hemispherectomy in 4 (21.1%) and combined or second operation in 3 (15.8%). Complete seizure-freedom after surgery was achieved in 12 (63.2%) children. Pathology revealed type I FCD in 5 (26.3%), type IIa in 2 (10.5%), type IIb in 7 (36.8%), type IIIa in 1 (5.3%), type IIIb in 1 (5.3%) and dual pathology in 3 (15.8%) children. Older age at seizure onset (58.0 ± 47.9 vs. 12.9 ± 21.7, p = 0.01) and absence of mental retardation (22.2% vs. 100%, p = 0.02) were associated with favorable outcome. FCD type II also showed more favorable outcome compared to other FCD types, which, however, was statistically insignificant.

**Conclusion:** FCD is an important cause of medically intractable epilepsy in children. However, appropriate surgical treatment may be curative in many cases and prompt management is necessary in the suspicion of FCD.

P745

### INTRAVENOUS LEVETIRACETAM IN CHILDREN WITH ACUTE REPETITIVE OR PROLONGED SEIZURES

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**Purpose:** Acute repetitive seizures and status epilepticus constitute one of the major medical emergencies in children. The effectiveness and safety of intravenous (IV) levetiracetam in children with these acute prolonged seizures were evaluated.

**Method:** We evaluated the medical records of patients who received IV levetiracetam to treat acute repetitive seizures or status epilepticus from 2010 to 2012. Patients were classified according to their epilepsy syndrome, underlying etiology, seizure types, previous antiepileptic medication, and febrile conditions at the time of seizure. The effectiveness and safety of IV levetiracetam was evaluated.

**Results:** Forty patients (age range, 53 day – 15 years) were treated with 30–40 mg/kg of IV levetiracetam. Twenty three of the 40 (57.5%) patients became and remained seizure-free. IV levetiracetam was more effective in patients with generalized tonic clonic seizures than those with other seizure types (p = 0.017). No other clinical factors affected the efficacy of IV levetiracetam. Irritability and aggressive behavior occurred in four children during maintenance, two of whom needed reduction or discontinuation of levetiracetam.

**Conclusion:** This study showed that IV levetiracetam therapy is effective and safe in children with acute prolonged seizures, especially with generalized tonic clonic seizures. Further randomized controlled studies are needed to determine the efficacy and safety of levetiracetam over the conventional IV antiepileptic drugs.

P746

### THE ETIOLOGICAL PROFILE OF NEONATAL SEIZURES AND NEURODEVELOPMENTAL OUTCOME

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**Purpose:** The purpose of this trial is to obtain etiological profile and prognosis of neonatal seizures.

**Method:** Fifty one patients who were interned in Dr. Behçet Uz Children's Hospital with the diagnosis of neonatal seizure, were followed up prospectively. All the patients in the trial were assessed with Bayley-2 developmental test.

**Results:** Patients between 12–36 months old were included in the trial. 22 (43.1%) of them were girl and 29 (56.9%) were boys 58.8% were term and 41.2% were preterm infants. According to the tests made for searching the etiology of seizures; hypoglycemia (seven patients), central nervous system infections (two patients), cerebral hemorrhage (six patients), asphyxia (22 patients), cerebral anomaly (one patient), cerebral infarct (one patient) were blamed as etiological factors. 12 patients whose tests obtained normal, assumed as idiopathic neonatal seizures. Most common seizure type was subtle seizures with persantage of 45.1. 29.4% were tonic, 19.6% clonic, 5.9% were clonic seizures. Thirteen patients had cerebral hemorrhage, four had cerebral edema, one had cerebral anomaly and four had periventricular leukomalacia. Eleven (84%) of the 13 patients who had cerebral hemorrhage were prematures. There was a significant correlation between cerebral hemorrhage and prematurity ( $p < 0.001$ ). Seizures due to asphyxia were 31.8% tonic and 31.8% subtle type equally. Seizured due to cerebral hemorrhage were 82% subtle type. There was a significant correlation between cerebral hemorrhage and subtle seizures ( $p = 0.02$ ). Following examination in paediatric neurologia polyclinic showed that, 29 (56.9%) patient had no sequelae formation. Spasticity was the most common sequelae with a percentage of 43.1%, and epilepsy formed in 27.5%. As a consequence; the risk factors that has influence on the prognosis of the patients with neonatal seizures are; etiological diagnosis, time of the seizure, birth weight, abnormal EEG acitivity, status epilepticus and having reanimation procedures.

#### P747

##### EVALUATION OF EFFICACY OF VAGUS NERVE STIMULATION IN 62 CHILDREN WITH UP TO 4 YEARS FOLLOW-UP IN A SINGLE CENTER IN LEBANON

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**Purpose:** Vagus nerve stimulation (VNS) is an established treatment modality for patients with medically refractory epilepsy. The purpose of this study was to evaluate the efficacy of VNS in a consecutive cohort of children implanted over a four years period at a single Medical Center in Lebanon.

**Method:** Children with refractory epilepsy not candidates for epilepsy surgery and implanted with a VNS were prospectively evaluated. All children had a full evaluation, including CCTV/EEG monitoring, epilepsy protocol MRI, and metabolic and genetic testing when indicated. The responder rate (>50% reduction in seizure frequency) was assessed

at 6, 12, 24, 36 and 48 months following implantation. In addition, the quality of life and usefulness of the magnet were assessed.

**Results:** Sixty-two children (range 6 months–18 years) were implanted. The responder rates were 61%, 66%, 64%, 82% and 75% at 6, 12, 24, 36 and 48 months following implantation, respectively. In addition, 56% of children had amelioration in seizure severity, shorter seizure duration in 36% and shorter post-ictal state in 38%. 73% of children had an improvement in the quality of life with an improvement in alertness and in the level of social interactions. The magnet was reported to be useful by 47% and the number of AEDs was reduced in 14% of those children.

**Conclusion:** VNS is a good treatment option for children with refractory epilepsy when conventional therapy fails. Prospective studies are needed to better delineate the characteristics of children most likely to benefit from VNS implantation.

#### P748

##### HOW MANY ANTIEPILEPTIC DRUGS SHOULD BE TRIED TO DIAGNOSE INTRACTABLE PARTIAL EPILEPSIES IN CHILDREN OR YOUNG ADULTS?

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**Purpose:** Two-drug definition for intractability (Kwan P, 2000, N Engl J Med) has been widely accepted, however, this has been developed in newly diagnosed epilepsies mainly in adults including the elderly. We studied whether this definition can be applied to children or young adults with non-idiopathic partial epilepsies (NIPE).

**Method:** Two hundred and forty-four referral cases of intractable NIPE, aged 1–38 years, mainly  $\leq 18$  years, which had not responded to two or more antiepileptic drugs (AEDs) prior to referral, were treated with further AEDs over 1 year or more by the author (KS). They consisted of 198 cases of frontal lobe epilepsy, 26 cases of temporal lobe epilepsy, and 20 cases of parietal or occipital lobe epilepsy. Further AEDs were selected based on the precise seizure symptoms, and added or switched to the previous AEDs.

**Results:** At the last evaluation, 1 year or more seizure-freedom was obtained in 138/244 cases (57%). Seizure-freedom was obtained in 46/55 cases by the 3rd AED, 34/49 cases by the 4th AED, 23/38 cases by the 5th AED, 21/41 cases by the 6th AED, 7/22 cases by the 7th AED, 5/11 cases by the 8th AED, 1/13 cases by the 9th AED, 0/5 cases by 10th AED, 1/5 cases by the 11th AED, and 0/6 cases by the 12th to 14th AED. More than half of the cases (84–51%) achieved seizure freedom among 3rd to 6th AED, and cumulative seizure-free rate by 3rd to 6th AED was 51% of all subjects.

**Conclusion:** Two-drug definition for intractability is not always applicable to NIPE in children or young adults. This may be because it has developed in newly diagnosed epilepsies consisted of all kinds mainly in adults including the elderly. Up to 6th AED should be tried to NIPE in children or young adults.

#### P749

##### EUROPEAN RANDOMIZED CONTROLLED TRIAL IN CHILDREN WITH ELECTRICAL STATUS EPILEPTICUS IN SLEEP (ESES)

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**Purpose:** Epileptic encephalopathy with ESES is a rare pediatric epilepsy syndrome with abundant interictal epileptiform discharges in sleep and impairment of cognition or behavior. Treatment with conventional anti-epileptic drugs yields limited effects. Observational data have suggested that clobazam and steroid treatment may be beneficial. Evidence from randomized controlled trials (RCT) to prove efficacy of both treatment options, or superiority of one over the other, is mandatory and still lacking.

**Methods:** This is a European randomized open clinical trial in 140 patients aged 2–12 years with recent onset epileptic encephalopathy with ESES, to compare the effects of steroid vs. clobazam on cognition. Clobazam treatment will be increased to 0.5–1.2 mg/kg/day if tolerated. Steroids will be given either intravenously (pulsed methylprednisolone 20 mg/kg/day for 3 days, once monthly) or orally (prednisolone 2 mg/kg/day for one month, followed by tapering in 20 weeks). Primary outcome is cognitive functioning after six months. Secondary outcomes include cognitive functioning at 18 months, spike wave index in sleep, seizure frequency, safety and tolerability.

**Expected results:** This is the first randomized controlled trial in patients with ESES. We hypothesize that treatment with steroids leads to a 25% increase in favorable outcome as compared to clobazam and is relatively safe.

**Conclusion:** Since current treatment of epileptic encephalopathy with ESES is only based on expert opinion, this RCT is needed to prove superiority of either steroids or clobazam in terms of efficacy and tolerability.

## P750

### WHITE MATTER DEVELOPMENT IN CHILDREN WITH IDIOPATHIC LOCALIZATION-RELATED EPILEPSY

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**Purpose:** Only few studies, focused on rather mixed syndromes, reported changes in white matter architecture in children with recent onset epilepsies (Hutchinson E et al. *Epilepsy Res* 2010;88: 208–214,2; Widjaja E et al. *Epilepsy Res*; *in press*). Conversely, there are no studies examining childhood localization-related epilepsies early in its course and the neurodevelopmental course is not adequately defined. However, abnormalities at the cellular level affecting the neuronal microstructure may be associated with these syndromes, particularly in one of the most common forms of epilepsy in children – benign epilepsy with centro-temporal spikes (BECTS).

**Method:** In this study, we explored the white matter in 24 children suffering from BECTS and in 25 age- and sex matched controls. The EEG focus (left, right, or bilateral fronto-centrotemporal) was established from EEG reports and 14 patients were classified with left sided focus, one with right sided, nine with bilateral foci. We used a region-of-interest

approach as well as voxel-based analysis to detect regions with significant group difference (FSL and SPM8).

**Results:** Significant differences of DTI-derived parameters were observed between BECTS and healthy groups mainly within the areas that surround left central sulcus.

**Conclusion:** Though undetectable with conventional MRI, white matter integrity is compromised in BECTS.

## P751

### INITIAL EEG FINDINGS IN CHILDREN PRESENTING WITH NEW-ONSET EPILEPSY

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**Purpose:** Electroencephalography (EEG) is part of the standard workup for new-onset epilepsy. This study seeks to establish prognostic clues from initial EEG findings in a population-based cohort of children with new-onset epilepsy.

**Method:** Children with new-onset epilepsy between 1980–2009 while resident in Olmsted County, MN were identified through the Rochester Epidemiology Project database and subsequent medical record review. The initial EEG of each patient was classified according to the presence and type of background abnormalities and epileptiform discharges and these were then correlated with long-term epilepsy outcome.

**Results:** Four hundred and sixty-eight pediatric patients with newly-diagnosed epilepsy were identified, all of whom had at least one EEG. Of these, 175 (38%) had background abnormalities and 73% had epileptiform discharges on initial EEG. Eighteen of 42 patients with severe background slowing on their initial EEG (42.9%) still had severe background slowing on the last EEG in their chart. Of children without epileptiform discharges on initial EEG, 68% showed epileptiform abnormalities within the first 2 years. Fourteen percent of patients with no initial background slowing were later classified as intractable or required surgery, vs. 50% of those with severe background slowing ( $p < 0.001$ ). The presence of epileptiform discharges on initial EEG was predictive of lack of seizure freedom or need for surgery (OR 2.07; 95% CI 1.16–3.71).

**Conclusion:** Although many patients with epilepsy require serial EEGs over time, characteristics of the initial EEG can provide important prognostic as well as diagnostic clues.

## Poster session: Adult epileptology C Wednesday, 26 June 2013

### P752

#### POINTS TO KEEP IN MIND FOR PRIMARY CARE DOCTORS IN TREATING EPILEPSY PATIENTS

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**Purpose:** Because we have recognized some trends in consultations of epilepsy patients from primary care doctors, we would like to offer some helpful suggestions.

**Method:** During the past year, we retrospectively reviewed the charts of patients in our neurosurgery department. There were 20 cases (9 women and 11 men; mean age, 50 years; partial epilepsy, 18; generalized epilepsy, 1; reflex epilepsy, 1; mean number of medications, 1.7) referred from primary care doctors.

**Results:** Fourteen patients did not need a change in medication (partial epilepsy, 13; generalized epilepsy, 1). Six patients needed an additional medication (partial epilepsy, 5; reflex epilepsy, 1). Between the two groups of patients, there were no significant differences in age, gender, and number of anticonvulsants. In the latter group, four patients had myoclonic-like episodes, one patient had complex partial seizures without motor seizure episodes (all five patients had partial epilepsy). We added levetiracetam in all five cases, and the subsequent clinical courses were good. The last patient was diagnosed with a psychosomatic disorder by a primary care doctor, but this patient had diffuse spikes on 6 Hz photo stimulation. Because this patient was already prescribed valproate, we added lamotrigine; the subsequent clinical course was seizure-free.

**Conclusion:** We suggest that primary care doctors should pay attention to myoclonic motion episodes and complex partial seizure without motor seizures in partial epilepsy patients. They also should consider reflex epilepsy in hysteria-like episodes.

### P753

#### POSTICTAL EXTREME ELEVATION OF SERUM CREATINE KINASE IN COMBINATION WITH INCREASED LIVER TRANSAMINASES

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**Purpose:** Raise awareness of the possibility of extreme postictal serum level increases of creatine kinase and liver transaminases.

**Method:** Case report and review of the literature.

**Results:** We report on a patient with extreme elevation of serum creatine phosphokinase (CK) combined with increased liver transaminases. A 40-year-old Eritrean was admitted to a local hospital after recurrent generalized tonic-clonic seizures (GTCS; 4 in total) and transferred to our Center on day 2 after phenytoin loading. He had not been on a chronic antiepileptic medication before. His personal history was unremarkable with the exception of war injuries (shrapnel) of the head and spine about 20 years ago. Posttraumatically he suffered from personality changes. In 2009 he experienced a first epileptic seizure and was treated with phenobarbital for some months. He remained seizure free after phenobarbital withdrawal in the following years until three months before the acute episode. On admission he was found postictally confused and somnolent. The laboratory tests showed increased values of leukocytes, CRP and an alcohol level of 0.7 mm. CT scan revealed multiple metallic intracranial fragments and a right frontal elderly scar with a gun-projectile still present. Laboratory investigations showed an extreme high CK value (80.778 U/l). In addition, the liver transaminase (alanine-, aspartate- and gamma glutamyl transaminase) were increased. In the following days the abnormal lab values were regressive and CK was normal again on day 12. Only the gamma glutamyl transaminase increased continuously until day 12. Renal parameters were controlled periodically and were at all times in the normal range. Levetiracetam was started and phenytoin withdrawn; no further seizures occurred.

**Conclusion:** Postictally increased CK values have to be considered and controlled to prevent renal complications. The peak level may be delayed up to several days. Alcohol withdrawal seizures predispose to high serum CK levels.

### P754

#### VIDEO-TELEMETRY IS ASSOCIATED WITH REDUCED HEALTH RESOURCE UTILISATION

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**Purpose:** To examine the cost-effectiveness of Video-EEG telemetry for the investigation of epilepsy. Previously, VEM resulted in changes in diagnoses in 58% and in management in 73% of 131 patients. This study follows this cohort's socio-economic status, health resource utilization and quality of life (QOL) changes comparing before and after VEM.

**Method:** Patients were sent a questionnaire to assess their overall medical, social, educational, work and financial aspects in the year before VEM and over the most recent 12 months. Current Quality of life (via QOLIE-89) in the four weeks immediately prior to filling in the questionnaire was also assessed.

**Results:** 45 (34%) of the original cohort returned questionnaires. Compared to before VEM, the per patient per year declines recorded were: number of visits to the GP by 1.8 (~50% reduction); Emergency Room attendances, by 1.1 (~70%); ambulance trips by 0.5 (~70% reduction); EEGs requested fell by 0.5 (~70% reduction); CT brain scans undertaken fell by 0.5 (~80% reduction); MR scans of brain dropped by 0.6 (~70% reduction); blood tests for seizures fell by 1.2 (~60% reduction). Anti-epileptic medications used was not significantly different (2.1 vs. 1.9). Sixteen patients (36%) had undergone epilepsy surgery: with 15 of these having at least improvement in their seizure control and eight of these – a reduction in anti-epileptic medications. Income, social relationships and educational aspirations did not change compared to prior to VEM. The cost of each health service used was documented in two ways: the Australian Medical Association (AMA) rates and the Medicare rates. Direct savings ranged from \$2,000–7,800 per patient per year.

**Conclusion:** VEM in this cohort was associated with reduced use of health-related resources in the following 12 months and cost savings. The reasons for lack of change in the social, educational and income outcomes require further evaluation.

### P755

#### WALKING PLEDS: A CASE REPORT OF "ICTAL" PERIODIC LATERALIZED EPILEPTIFORM DISCHARGES

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**Case report:** Controversy exists about whether or not periodic lateralized epileptiform discharges (PLEDs) represent an ictal phenomenon.<sup>1</sup> Case reports show that SPECT imaging in an infarcted area with PLEDs shows increased cerebral blood flow (CBF) in the affected region. After treatment with antiepileptic drugs, repeat SPECT shows decreased CBF in the same region.<sup>2</sup> This pattern is consistent with reversible cortical hyperactivity and suggests the possibility that PLEDs may be on the ictal spectrum. We present a case of a 69-year-old gentleman who suffered a mild left MCA stroke in November 2011 that left him with no residual deficit. Six months later, he presented to a local hospital after waking up with a non-fluent aphasia. MRI with diffusion weighted imaging was negative for acute stroke. EEG at the time of presentation showed periodic L hemispheric sharp waves and sharp-and-slow wave complexes (Fig. 1). Valproic acid was quickly titrated to 2 g daily with prompt resolution of symptoms. On outpatient followup, the patient was continuing to have disabling aphasic episodes, albeit fewer than previously. Low dose lamotrigine was started, and since that time the patient has not had further recurrence. Repeat EEG after the addition of lamotrigine showed mild focal slowing in the left temporal electrode chain with rare sharp

wave discharges (Fig. 2). The clinical and electrographic findings in this case imply that PLEDs may be an ictal rather than inter-ictal phenomenon. In patients with PLEDs and clinical manifestations, a trial of anti-epileptic therapy may be warranted.

#### P756

##### SEIZURES AFTER STROKE IN 12 YOUNG PATIENTS IN FANN TEACHING HOSPITAL

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**Purpose:** Vascular epilepsy is defined by repeated seizures on the effects of a stroke. We report the cases of vascular epilepsy occurred in young subjects in the neurology department at Fann Teaching Hospital.

**Method:** We conducted a prospective study from 1 January 2011 to 31 October 2012, concerning cases of epilepsy after stroke in patients aged 25–45 years, hospitalized in the neurology department of Fann Teaching Hospital

**Results:** Twelve patients were recruited, the average age was 31.67 years with a sex ratio of 1.4. In our sample, seven of our patients were male and five were female. Of the 12 cases, 48.1% were motor focal seizures, 29.7% of focal seizures secondarily generalized and 22.2% of generalized tonic-clonic seizures. We had three cases of vascular epilepsy secondary to a hemorrhagic stroke (25%) and nine cases of vascular epilepsy secondary to an ischemic stroke (75%). The evolution of our patients was favorable with classic anti epileptics drugs: carbamazepine, phenobarbital or valproate.

**Conclusion:** Seizures occurring after stroke are common, they occur most often (but not exclusively) in cortical lesions, the ischemic stroke is the more frequent etiology.

#### P757

##### LONG TERM EVOLUTION OF UNVERRICHT LUNDBURG DISEASE IN TUNISIAN PATIENTS

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**Purpose:** Unverricht Lundborg disease (ULD) is the most common form of progressive myoclonic epilepsies; it is a genetic degenerative progressive disease with a severe outcome however with the advances of genetics the rate of deterioration seems to be variable.

We aimed to assess the long-term evolution of ULD based on clinical and electrophysiological features in Tunisian patients.

**Method:** In a prospective study in neurological department of Razi Hospital between 2003 and 2012, we included all the patients with genetically confirmed ULD evolving at least since 15 years. We analyzed clinical and electrophysiological features (EEG, EMG, visual and somatosensory evoked potentials). We separated electrophysiological exam into two groups: group 1: patients with stabilized epilepsy and group 2: non stabilized.

**Results:** 20/24 patients belonging to eight Tunisian families were included. Dodecamer expansion was found in all patients. Mean age at onset was 11.5 years. Mean duration of the disease was 26.5 year (16–31 years). All patients had myoclonus. Generalized tonic-clonic seizures were observed in only 18/20. Cerebellar signs were observed in 8. None had mental retardation. Mainly used antiepileptic drugs were Valproate (14/20) and Clonazepam (18/20). In group 1: 17/40 EEG and 12/18 EMG were normal and there was no giant

response on evoked potential (12/20). In group 2: 23/40 EEG showed slow background activity and spikes, C reflex and positive myoclonus was found in 6/6 EMG, and giant potential in 4/8 evoked potential.

**Conclusion:** We reported the large series with an outcome of 26 years (more longer in literature). In stabilized patient even after this long term evolution, EEG showed no Spikes and waves disappear with normal background, disappearing of C reflex on EMG and Giant evoked potentials Electrophysiological profile of ULD is based on EEG and EMG depends on stabilization of the disease.

#### P758

##### SERDAS: A EW DISABILITY SCALE FOR EPILEPSY PATIENTS

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**Purpose:** To develop an epilepsy disability scale called SERDAS (Seizure Related Disability Assessment Scale). It is based on a validated migraine scale.

**Method:** We tested the scale in two groups. One group was patients recruited during an inpatient epilepsy admission (EMU). The second was patients enrolled in the outpatient setting (Outpatients). We assumed that the EMU group would be more disabled than the Outpatients and used a daily disability diary as the gold standard. The QOLIE-31 and BDI were administered at baseline and the SERDAS at one month. SERDAS queries disability during the most recent month, and includes a separate self-disability report. We compared the daily disability diaries to SERDAS scores for both the EMU and the Outpatient groups.

**Results:** 44/85 patients completed. Between groups there were no significant differences in any of the epidemiological variables, the BDI, or the QOLIE-31. Contrary to assumption, EMU patients trended towards having less disability than Outpatients (EMU 25%, Outpatient 40%). The SERDAS scores correlated well for both groups (EMU Pearson = 0.86 and Outpatient Pearson = 0.67). In contrast the self disability report did not correlate well for either group (0.44 EMU vs. 0.54 Outpatient). For both groups combined, the SERDAS (Pearson = 0.74) was superior to the self disability report (Pearson = 0.49).

**Conclusion:** The SERDAS scores did not differ between the two groups, though the scores correlated better with disability diaries for the EMU group. The overall correlation of SERDAS to disability was reasonably good (0.74). This promising scale should be tested again in a different epilepsy population.

#### P759

##### CLINICAL MANAGEMENT OF EPILEPSY ASSOCIATED WITH CAVERNOUS HEMANGIOMAS AND ARTERIOVENOUS MALFORMATIONS

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**Purpose:** The aim is to present the seizure outcome in epilepsy associated with cavernous hemangiomas (CH) and arteriovenous malformations (AVM) with respect to pharmacological or surgical treatment.

**Method:** Four patients with epilepsy associated with CH (four females) and four with AVM

(three females and one male) on age 16–50 years were analyzed, clinically, with electrophysiological (EEG) and imaging (MRI, MRA, angiography) methods.

**Results:** Lesionectomy was done in three patients with epilepsy associated with CH. Right sided motor deficit which gradually improved happened in one of the surgically treated patients, with seizure control of complex partial seizures after surgery in follow up period of one year. There are no neurological deficits in the other two surgically treated patients, with seizure control in one and with secondary generalized tonic-clonic seizures (GTCS) in the other until topiramate was added as additional antiepileptic drug (AED) to the ongoing carbamazepine. One patient with multiple CH and rare focal motor seizures was only on pharmacological treatment with carbamazepine and acetazolamide. During her pregnancy acetazolamide was withdrawn, without seizure worsening. In the long follow up period afterwards she has rare simple partial seizures. Three patients with epilepsy associated with AVM were treated surgically with embolisation. Seizure control is achieved in one, worsening in one with respect to the right sided motor neurological deficit and right sided focal motor seizures and no significant changes in one. Only pharmacological treatment was used in one patient with rare secondary GTCS and right sided motor deficit.

**Conclusion:** Clinical, electrophysiological and imaging evaluation of patients with epilepsy associated with CH and AVM is important for planning the optimal treatment of epilepsy and underlying causes.

#### P760

##### BENIGN MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** We describe the clinical feature of a benign form of temporal lobe epilepsy.

**Method:** Retrospective review of 24 patients (six Males), with history of TLE, the mean age 35.3 years (range 28–80 years). Who were followed for longer than 2 years. Neurological examinations were performed at every follow up visit (4–12 months). All patients had at least 2 EEG and one MRI studies done.

**Results:** All had simple partial seizures and nine had complex partial seizures that were controlled on monotherapy in 20 or 2 drugs in four patients. The mean age of epilepsy onset was 28.9 years. Attempts to stop medication in three patients resulted in recurrence of seizures. Only one had subjective short term memory complaints. All were able to drive. EEGs were normal in 4, showed temporal slowing in 17 and temporal spikes in 3. Mesial temporal sclerosis (MTS) on MRI was seen in 16 (67%). Aetiology was viral encephalitis in one and unknown in 23. And two had a family history of seizures.

**Conclusion:** Not all temporal lobe epilepsy even with MTS is refractory to medication. The findings support later age of onset as a favourable prognostic indicator. Lifelong treatment is advocated.

#### P761

##### NOCTURNAL SEIZURES MASQUERADING AS CATATHRENIA: A CASE REPORT

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A 28 year old man was admitted to our epilepsy monitoring unit (EMU) due to frequent nocturnal spells. His spells, predominately nocturnal, consisted of cold “chills” in the right shoulder moving across his chest associated with groaning sounds lasting 2–3 s without loss of awareness. They occurred up to 15 times per day on a daily basis. His neurological examination and cranial MRI were normal. His background EEG was normal. During sleep, there were right hemispheric epileptic spikes maximal in the right temporal-frontal regions. Several typical spells were captured that were consistent with right hemispheric seizures. His sleep study was noncontributory despite the clinical suspicion of catathrenia. Catathrenia is a rare parasomnia in the International Classification of Sleep Disorders Diagnostic and Coding Manual (ICSD-2) from the American Academy of Sleep Medicine (AASM) with less than 50 documented cases. Patients themselves do not have any complaints of sleep disturbances or excessive daytime sleepiness. The referral to a sleep clinic is generally made by family or bed partners due to the groaning sounds. Catathrenia begins with a deep inspiration followed by a short expiratory phase and a prolonged expiratory period where breathing signals are reduced signaling a hypopneic event. These events last approximately 10 s and usually do not produce significant night time arousals. These occur during both NREM and REM sleep. Nocturnal seizures are on the differential diagnosis of catathrenia although true seizures mimicking catathrenia has not been described. Our case is unique in that the seizure semiology closely resembled the breathing patterns seen in catathrenia and his grunting responded well to AEDs.

#### P762

##### CHILDHOOD-ONSET EPILEPSY PREDICTS PROLONGED STAY IN THE SHADOWS

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**Purpose:** The relationship between Age of Onset of epilepsy and Lead Time to Treatment (LTT) and how the latter modifies the effects of the former on epilepsy outcome were investigated.

**Method:** Ninety-seven adults (56 males) with epilepsy supplied data on their age of onset of seizures, LTT and other demographic and disease-specific variables. They were then divided into childhood-onset epilepsy (COE) (51.5%) and adult-onset epilepsy (AOE) (48.5%) groups. LTT was categorized into  $\leq 5$  years and  $> 5$  years. Clinical and psychosocial outcomes were also assessed using standard measures.

**Results:** Fifty (51.5%) of the participants had COE and 47 (48.5%) AOE. The childhood-onset group was younger ( $27.2 \pm 10.2$  years vs.  $41.2 \pm 14.6$  years,  $p < 0.001$ ), less likely to be married (14.3% vs. 52.3%,  $p < 0.001$ ), and more likely to be on AED polytherapy (39.1% vs. 7.5%,  $p < 0.01$ ) to achieve the same level of seizure control ( $p = 0.286$ ). LTT was  $> 5$  years in 47% of the participants, COE accounting for 70.6% ( $p < 0.05$ ) of these. LTT  $> 5$  years was associated with an earlier onset of epilepsy ( $13.1 \pm 11.3$  years vs.  $23.7 \pm 17.4$  years,  $p < 0.01$ ). The childhood-onset group had a lower quality of life score ( $p < 0.05$ ) and a higher level of stigma perception ( $p < 0.001$ ). Logistic regression analysis revealed LTT  $> 5$  years and higher number of AEDs as independent predictors of stigma perception.

**Conclusion:** A significant percentage of our patients stayed long in the shadows before treatment. Childhood-onset epilepsy predicts prolonged stay in the shadows. Lead time to treatment may be more important in predicting outcome compared to age of onset.

P763

### MEASURES FOR IMPROVING TREATMENT OUTCOMES FOR PATIENTS WITH EPILEPSY: RESULTS FROM A LARGE MULTINATIONAL PHYSICIAN-PATIENT SURVEY

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**Purpose:** To identify measures for changing physician and patient behavior and physician-patient interaction to improve treatment outcomes for patients with epilepsy.

**Method:** Epileptologists, neurologists and general practitioners from France, Germany and US were randomly selected from a physician database to complete an online survey. The first section related to general epilepsy management, while the second related specifically to the next five patients with epilepsy seen in consultations. Immediately following consultation, these patients, all aged  $\geq 18$  years, completed a paper-based questionnaire comprising questions similar to those in the physician survey.

**Results:** Overall, 337 physicians and 1150 patients with epilepsy completed the survey (France 113 and 414; Germany 110 and 472; US 114 and 264, respectively). 50% of patients were female, mean age was 46 years and mean time since diagnosis 17 years. Based on physician records, 16% of patients were initially misdiagnosed. Treatment non-adherence was common; 43% reported by patients and 47% by physicians. The most frequent patient-reported reason for non-adherence was forgetfulness, whereas physicians identified complacency as the main reason. Physicians reported 26% of patients had no treatment change for 2 years, despite experiencing side effects, seizures or compromised quality of life. 58% of these were seen  $< 4$  times a year.

**Conclusion:** Results of this survey suggest disparity in physician-patient understanding regarding quality and frequency of follow-up and reasons for non-adherence. Education on diagnosis of epilepsy and protocolled disease status monitoring for physicians, and on importance of treatment adherence for patients could improve patient outcomes.

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P764

### HIGH PREVALENCE OF SINGLE SMALL CT LESIONS AMONG PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY: DIAGNOSTIC AND TREATMENT IMPLICATIONS

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**Purpose:** Most Indian patients presenting with a first seizure to community physicians, are investigated with CT scans. Single small CT lesions (SSCTL) are a common finding, possibly leading to diagnostic consideration of focal epilepsy. This may also lead to erroneous misdiagnosis of juvenile myoclonic epilepsy (JME) and other generalized epilepsies as focal. Our anecdotal observations in the clinic setting suggest that this finding is commonly seen among patients with JME. The purpose of this study was to objectively assess whether patients with JME, have a higher prevalence of SSCTL, as compared to another distinct epilepsy population i.e. temporal lobe epilepsy (TLE) and to non-epilepsy controls.

**Method:** Two groups of consecutive patients with a definitive diagnosis of epilepsy syndromes (Group 1 – JME, Group 2 – TLE), who came with

CT scans, over a 3 year period; were compared with age and gender matched controls (subjects with headache), for the CT finding of an SSCTL.

**Results:** Thirty-seven out of 116 JME patients seen during the study period (16 F, mean age  $21.8 \pm 7.6$ ) and 30 out of 168 TLE patients (7 F, mean age  $22.4 \pm 12.6$ ) met inclusion criteria. A total of 58 subjects (24 F, mean age  $26.6 \pm 13.4$ ) formed the control group. A significantly higher percentage of JME patients showed an SSCTL on CT scans, compared with TLE patients and controls (14/37 [38%] v/s 4/30 [13%] v/s 6/58 [10%];  $p = 0.003$ ) [Odds ratio 5.27 (CI 1.8–15.4)].

**Conclusion:** CT finding of single lesions is significantly high among Indian patients with JME. This finding has much treatment related implication, since false diagnosis of focal epilepsy in these patients, based on CT scans, may result in wrong choice of AEDs and treatment failure.

P765

### IS CLASSIFICATION OF PSYCHOGENIC NONEPILEPTIC SEIZURES FEASIBLE IN AN OUTPATIENT SHORT-TERM VIDEO EEG COHORT?

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**Purpose:** Several studies have identified distinct semiologic subgroups of psychogenic nonepileptic seizures (PNES). A recent PNES classification was proposed (Seneviratne, *Epilepsia* 2010). We aimed to (i) analyze the semiology of PNES in a population with suspected PNES undergoing short-term outpatient video EEGs and (ii) assess the feasibility of the above classification.

**Method:** Retrospective review of short-term outpatient video EEG findings in all patients diagnosed with PNES from 2007–2013 at a tertiary centre. Patients were selected if at least one typical event was captured on video with normal corresponding EEG. Each PNES was categorized into one of six stereotypic classifications.

**Results:** One hundred and ninety-six PNES were recorded from 68 patients. The mean age of patients was 37 (range 15–80); 30 (44.1%) were males. There were 39 (57.4%) Chinese, 17 (25%) Indians and 12 (17.6%) Malays; 30 (44.1%) patients were on anti-epileptic drugs, and 17 (25%) on anti-depressants. There were 109 (55.6%) rhythmic motor, 42 (21.4%) complex motor, 18 (9.2%) dialeptic, 15 (7.7%) nonepileptic auras, 3 (1.5%) hypermotor, and 9 (4.6%) mixed PNES. Few patients (5.9%) had more than 1 type of PNES.

**Conclusion:** PNES carry stereotypic homogeneity and it is feasible to categorize PNES according to the above semiologic classification, even in short-term outpatient VEEGs. The frequency of each subtype may vary across populations – nonepileptic auras were uncommon in our cohort when compared with other studies. Trance behaviour, being deeply rooted in our cultural history, may perhaps influence the semiology of PNES.

P766

### CLINICAL, ELECTROENCEPHALOGRAPHIC AND IMAGING CORRELATES OF PRIMARY AND SECONDARY DYKE DAVIDOFF MASSON SYNDROME IN ADULTS WITH INTRACTABLE EPILEPSY

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**Purpose:** Dyke Davidoff Masson Syndrome (DDMS) involves cerebral hemiatrophy and compensatory skull hypertrophy. DDMS is a rare cause of medically refractory epilepsy. We describe two cases of adults with refractory seizures and DDMS and illustrate both primary and secondary DDMS.

**Method:** Case report.

**Results:** Patient 1 (age 29 years): Developed encephalitis at age eight with subsequent seizures and mental retardation. MRI demonstrated right sided cerebral and cerebellar hemiatrophy, right calvarial hypertrophy and pneumatization of the frontal paranasal sinus. Seizures average between 1–10 per year. EEG demonstrated multiple seizures with right frontal onset (F8), semiology of hyperactivity. Medications: topiramate, lamotrigine, levetiracetam and clobazam plus Vagal Nerve Stimulator. Patient 2 (age 39 years): Perinatal complications with difficult forceps delivery, with long history of refractory epilepsy. Neurological examination reveals profound intellectual developmental delay and left hemiplegia. MRI: Right sided cerebral and cerebellar atrophy, cystic changes and right skull hemihypertrophy. EEG: Multiple seizures with non localizable onset, convulsive. Medications include lobazam, phenytoin, levetiracetam, lacosamide and zonisgran.

**Conclusion:** DDMS, defined in 1933, was originally described as a clinical triad of hemiplegia, seizures and mental retardation with a radiological correlate of brain hemihypertrophy, ipsilateral skull thickening and hyperpneumatization of the paranasal sinus. In our cases one patient had all three radiological findings but only two clinical findings; the other all three clinical findings and two radiological findings. Two etiologies are described, the primary etiology is congenital with cerebral hypoplasia. Patient 2 is characteristic for this condition while secondary cases may follow stroke, infection or trauma and patient 1 represents this etiology with no hypoplasia on MRI. DDMS is an important though rare cause of epilepsy, easily identified on clinical examination and by radiological examination, either with CT or MRI.

## P767

### EPILEPSY IN ADULT PATIENTS WITH DOWN SYNDROME

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**Purpose:** Patients with Down syndrome (DS) have an increased risk to suffer from epilepsy. The aim of this study was to assess the extent of intellectual impairment and severity of epilepsy in DS patients.

**Method:** Patients with DS were compared with age- and sex-matched control patients with intellectual disability of other causes regarding the extent of intellectual impairment, emergency admittances, total time of inpatient treatment, and number of anticonvulsant drugs in medical history and at discharge.

**Results:** Out of 2,024 patients with intellectual disability and epilepsy (1999–2012), we identified 35 subjects with DS (1.7%). Compared to 35 CS, DS patients did not differ regarding sex distribution and age at first admittance (DS, 47 ± 13 year; CS, 43 ± 10 year). However, patients with DS were less likely to suffer from mild forms of intellectual disability (6% vs. 29% in CS,  $p = 0.023$ ). So far, DS patients had been treated with fewer antiepileptic drugs ( $2.2 \pm 2$ ) compared to CS ( $4.5 \pm 3.4$ ;  $p < 0.001$ ). At discharge, the number of antiepileptic drugs did not differ between groups (DS,  $1.6 \pm 0.7$ ; CS,  $1.7 \pm 0.8$ ). The total number of admittances was significantly lower in patients with DS ( $1.5 \pm 0.9$ ) than in CS ( $2.2 \pm 1.5$ ;  $p = 0.033$ ). Emergency admittances were not different between groups (DS, 23%; CS, 26%). There was a trend for a shorter length of inpatient treatment in DS patients ( $39 \pm 33$  days) compared to CS ( $54 \pm 50$  days), but differences were not significant.

**Conclusion:** In patients with DS, the degree of intellectual disability was more severe than in age- and sex-matched controls, lower number of

hospital admittances and lower number of prior antiepileptic drugs point to less severe epilepsy. These findings argue against a simple correlation between extent of intellectual disability and severity of epilepsy. The pathophysiological mechanisms of epilepsy in patients with DS may differ from those in patients with other causes of intellectual disability.

## P768

### ICTAL AND POSTICTAL MRI FOR THE LOCALIZATION OF SEIZURE ONSET

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**Purpose:** Presurgical localization of seizure onset zone in intractable focal epilepsy frequently relies on ictal SPECT, but the technetium tracer is becoming difficult to acquire. Breakdown of the blood-brain barrier might be a component of seizure physiology (Alvarez, V., P. Maeder et al, 2010), suggesting that gadolinium enhanced MRI might be useful in seizure onset zone localization. We sought to determine the feasibility of ictal contrast-enhanced MRI to localize seizure onset zone.

**Method:** Subjects with intractable focal epilepsy undergoing VEEG monitoring received gadolinium within 30 s of seizure onset, followed by MRI (MPRAGE, DWI, FLAIR and T2W) within 2 h. Each subject also underwent inter-ictal contrast-enhanced MRI at least 24 h after ictal MRI. We examined inter-session differences in individuals. Using SPM5, ictal images underwent a 3D affine-only alignment to the inter-ictal images. Next the images were smoothed with a 3 mm FWHM Gaussian filter. The ictal images were then subtracted from the inter-ictal images, and the resulting data were visually inspected for focal differences with regard to location of seizure onset based on EEG.

**Results:** Four subjects completed the study. It was feasible to inject gadolinium ictally and perform MRI within 2 h of the seizure. We found no focal difference in MRI signal in any sequence between the sessions.

**Conclusion:** Ictal contrast-enhanced MRI does not appear to be useful in localizing seizure focus and is not an alternative to ictal SPECT. Breakdown of the blood brain barrier during single seizures might not be consistently sufficient to lead to changes in MRI imaging.

## P769

### IDENTIFYING SCN1A MUTATIONS AND TREATMENT OPTIONS IN ADULT PATIENTS

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**Purpose:** Severe myoclonic epilepsy of infancy (SMEI), associated with mutations of SCN1A gene, can be the underlying cause of intractable epilepsy. Treatment is based on preventing seizures and immediate introduction of anti epileptic treatment, avoiding myoclonic attack inducing agents (NICE 2012). Identifying patients having SCN1A mutations may lead to different treatment options.

**Method:** In this study from 2003 to 2012, we identified 19 adult patients in our Epilepsy Centre having SMEI. In these patients we tried to change treatment, avoiding myoclonic attacks inducing agents and administrating medication advised in patients having SMEI. Treatment effects on seizure frequency (SF), motor ability and behaviour are described.

**Results:** All 19 patients (mean age 33, male 10, female 9) had a mutation of SCN1A gene. Seizure frequency (SF) ranged from 0 to >50 weekly. 14 Patients showed autistic behaviour of which 8 Patients showed acting out behaviour which indicates administration of antipsychotics. Five Patients lost their ability to walk. In 12 patients we changed therapeutic regimen.

In five patients parents did not agree changing medication. Two patients died. SF decreased in five patients, increased in three patients and did not change in four patients with changed treatment. Motor ability improved in four treated Patients. Improvement of behaviour was observed in two of treated patients. Two patients showed more acting out behaviour. In all patients with unchanged treatment we saw unchanged SF.

**Conclusion:** Careful investigation of underlying cause of epilepsy in adult patients with intractable epilepsy is important to identify epilepsy syndromes that indicate to adapt treatment. In SMEI this may lead to improved seizure control and regain of lost functions. Behaviour can improve or patients can become more restless because of the improved awareness.

#### P770

##### A CASE OF MUSICOGENIC EPILEPSY

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**Purpose:** To report a patient with musicogenic epilepsy and discuss the potential dichotomous effect of music.

**Method:** We report a patient in whom a certain music triggered focal seizures, while some other pieces inhibited interictal epileptic discharges.

**Results:** A 31-year-old right handed male patient started having seizures at 27 years when he suffered from encephalitis. He likes listening to a variety of music, although he has neither received special musical training nor played any musical instruments. Spontaneous focal seizures consist of headache-like cephalic sensation followed by impairment of consciousness, sometimes developing generalized convulsion. MRI shows residual high intensity along the surface of right temporoparietal cortex. He noticed at 28 years that some of his seizures were triggered by nonmusical sounds such as warning sound at a railway station or ringtone of a cellular phone. When he was 31 years old, he realized that listening to a specific piece, "Rydeen" performed by Yellow Magic Orchestra, could trigger his seizures. Not only listening to it, but also thinking it could trigger his seizures. He remarks that he has never been touched by listening to it. Loading various pieces of music during EEG monitoring was performed under the patient's agreement and cooperation. Soon after playing "Rydeen", sharp waves at F8 frequently appeared on EEG, and some 3 min later, rhythmic discharges at F7 appeared, being associated with impaired responsiveness suggesting focal seizure. On the other hand, interictal epileptic discharges disappeared when listening to some pieces of music that he felt innocuous or neutral. No significant reduction of interictal discharge was seen during listening to Mozart K448.

**Conclusion:** Our experience confirms the hitherto described characteristics of musicogenic epilepsy and potential dichotomous effect of music, i.e. facilitating or inhibiting epileptic activity. A certain kind of music may work on demand for cessation of seizure.

#### P771

##### EVALUATION OF PATIENTS WITH ICTAL KISSING AUTOMATISM

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**Purpose:** Automatisms are repetitive motor activities that occur during or after a seizure that are followed by amnesia. While several different automatisms showing complex or simple characteristics have been described, ictal kissing (IK) automatism remains a rarely seen phenomenon. The aims of this study are to investigate the semiological and electrographical features of this complex ictal behavior, and demographical, neuroimaging findings of the patient with IK.

**Method:** Twelve patient (five male) presenting IK automatism during the seizures were included in this study. The mean age of patients was 30 ± 6.65 years. Ictal EEG and video recordings were studied in detail. Cranial MRI according to standard epilepsy protocols, PET scan and neuropsychiatric evaluations were performed.

**Results:** The seizures recorded were primarily characterized by ictal speech, kissing and gestural automatisms in all patients. Ictal EEG demonstrated temporal region. Seizures were related to the non-dominant temporal lobe in nine (eight right, one left) and the dominant temporal in three patient (two right, one left). The MRI showed mesial temporal sclerosis in eight of the patients (six right, two left), right occipital ulegria in one, right parietal neuronal migration in one, whereas it was normal in two.

**Conclusion:** IK is a complex behavior that may occur as a result of release phenomena rather than a cortical stimulation related to mainly but not exclusively to temporal lobe.

#### P772

##### SOME CLINICAL FEATURES OF POST-TRAUMATIC EPILEPSY PATIENTS IN KHAN UUL DISTRICT OF ULAANBAATAR

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**Purpose:** To study reasons of post-traumatic epilepsy, identify specific features of its clinical manifestations.

**Method:** Thirty-six patients with epilepsy were included in our study, of which 28 are male (77.8%), and eight female (22.2%). The study was conducted through retrospective studies of the patients' history and clinical notes among post-traumatic epilepsy patients treated at the neurology department of the Khan Uul district hospital in Ulaanbaatar during April-August 2012.

**Results:** Among all injury-related epilepsy patients included in the study, 43% of traumas were related to impact from fights, 36% car accidents, 11% falling from heights, and 10% falling from a horse. 75% of patients in the study suffered brain contusion, 25% suffered brain compression. At the time of the injury, 44.5% of injuries were assessed as severe head injuries, and 55.5% as significant head injuries. Commonly seizures were induced by physical labour, dyssomnia, watching TV, suddenly change of weather, alcohol consumption. In terms of clinical manifestations, 58.3% of patients suffered partial epilepsy, 41.7% suffered partial epilepsy with secondary generalization. In 50% of all studied cases patients suffered epileptic auras, 42% suffered autonomic seizures, and 5.5% of patients suffered psychomotor seizures. 55.6% of epilepsy cases began with vegetative auras, 22.2% percent visual auras, and 5.6% of cases began with aura smells.

**Conclusion:** The study result demonstrates that post-traumatic epilepsy is commonly caused by impact from fights, car accidents, with seizures starting in the first year of the brain injury in most cases, and manifesting through partial seizures with auras.

P773

### POSTICTAL GENERALIZED EEG SUPPRESSION IS NOT A CONSISTENT FINDING IN PEOPLE WITH MULTIPLE CONVULSIVE SEIZURES

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**Purpose:** Postictal generalized EEG suppression (PGES) of >20 s after convulsive seizures (CS) may be associated with increased risk of sudden unexpected death in epilepsy (SUDEP) (Lhatoo SD et al. *Ann Neurol* 2010; 68: 787–796). To determine its reliability as predictor of SUDEP risk, we analyzed whether PGES is a consistent finding in people with multiple CS. We also aimed to elucidate which co-factors facilitate onset of PGES.

**Method:** We retrospectively reviewed video-EEG data of people with ≥2 CS recorded. Presence and duration of PGES were assessed by two independent observers blinded to patient status. Intraindividual consistency of PGES >20 s was determined and correlations with clinical characteristics analyzed after correction for patient effects and the varying number of seizures.

**Results:** One hundred and fifty-four seizures in 59 people were analyzed. PGES >20 s was found in 37 (63%) individuals and 57 (37%) CS. Occurrence of PGES >20 s in all seizures within an individual critically depended on the number of seizures recorded: PGES reliably occurred in 45% (9/20) of people with two CS, in 33% (3/9) with three CS, and in 0% (0/8) with four CS. PGES of >20 s was more frequent in seizures arising from sleep (OR 3.29, 95% CI [1.21–8.96]), and when antiepileptic medication was tapered (OR 4.80, 95% CI [1.27–18.14]).

**Conclusion:** Apparent PGES consistency strongly depended on the number of recorded seizures, suggesting that PGES >20 s is not a reliable predictor of SUDEP. Sleep and antiepileptic drug reduction appear to facilitate onset of PGES, maybe via effects on perictal hypoxemia or neuronal network excitability.

P774

### CONTRIBUTION OF HISTORY AND ADDITIONAL INVESTIGATIONS IN DIAGNOSTIC ALLOCATION OF NEW ONSET EPILEPTIC SEIZURES AND EPILEPSIES

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**Purpose:** To evaluate the contribution of history and further investigations for early diagnostic allocation of seizures and epilepsies in a retrospective study.

**Method:** We performed a database search for patients ≥18 years admitted to our neurological department for new onset seizures and epilepsies between 01/2008 and 12/2010. Based on information on semiology and history, together with EEG and neuroimaging results, cases were allocated to one of six groups: acute symptomatic and isolated unprovoked seizures, partial, generalized and undetermined epilepsy, and uncertain diagnosis. Furthermore, antiepileptic treatment strategies were assessed.

**Results:** A total of 296 patients were included (59.5% male, mean age 56.6 ± 19.1 years). In 272 patients (91.9%), history alone sufficed to diagnose a definite epileptic seizure, while the remaining

patients required additional investigations. For group allocation, pathological findings in standard or sleep deprivation EEG were helpful in 18.2% or 4.7%, respectively. Imaging studies were performed in 98% of patients: 26.9% had MRI only, 34.1% CT scan only, and 39% both modes. For group allocation, neuroimaging results were helpful in 48.6%. Most frequent pathological MRI findings were cerebrovascular (30.4%) or neoplastic (6.8%) lesions. Eventually, group allocation was as follows: acute symptomatic seizures 12.5%, isolated unprovoked seizures 20.6%, partial epilepsy 53.4%, generalized epilepsy 1.7%, undetermined epilepsy 2.4%, and uncertain diagnosis 9.5%. Treatment was initiated in 21.3% of patients with isolated seizures and in 84.9% of patients with partial epilepsy ( $p < 0.001$ ). In both groups, levetiracetam was the most frequently used AED (53.8% and 50.7%, respectively).

**Conclusion:** The majority of new onset seizures can be diagnosed by history alone. For correct group allocation, neuroimaging is more helpful than EEG ( $p < 0.001$ ). To determine prognosis of new onset seizures and epilepsies and to follow treatment decisions, prospective long-term studies are required.

P775

### INCREASED PREVALENCE OF ELECTROCARDIOGRAM MARKERS FOR SUDDEN CARDIAC ARREST IN EPILEPSY

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**Purpose:** We have shown in a recent community-based study that people with epilepsy may be at increased risk for sudden cardiac arrest (SCA) due to ventricular fibrillation/ tachycardia (VF/VT). We aimed to determine whether electrocardiogram (ECG) markers of increased VF/VT risk were more prevalent in those with epilepsy.

**Method:** In a cross-sectional, retrospective study, we evaluated the ECGs of 188 people with chronic epilepsy and 178 controls without epilepsy. Data on epilepsy characteristics, cardiac comorbidity, and medication use were collected. We analyzed ECGs for presence/absence of three markers of increased VF/VT risk: QTc prolongation (male >450 ms, female >470 ms), Brugada pattern, and early repolarization potentials (ERP). General ECG variables were also studied: heart rate, PQ/RS intervals, and QRS axis. Multivariate regression models were used to analyze differences between groups and to determine which clinical and epilepsy-related characteristics were associated with these ECG markers.

**Results:** Except for heart rate, which was increased in cases (71 vs. 62 bpm,  $p < 0.001$ ), general ECG variables did not differ. ERP and QTc prolongation were more prevalent in people with epilepsy (34% vs. 13%,  $p < 0.001$ ) and (5% vs. 0%,  $p = 0.002$ ), while the frequency of the Brugada pattern was similar in both groups: 2% vs. 1%,  $p = NS$ . The association between epilepsy and ERP remained significant after adjustment for gender, heart rate, cardiac comorbidity, and use of sodium channel blocking drugs: OR 2.5; 95% CI 1.2–5.1. Due to insufficient numbers advanced analysis of QTc prolongation was not performed.

**Conclusion:** ERP and QTc prolongation are more prevalent in people with chronic epilepsy. Future studies must resolve whether this contributes to the increased risk for VF/VT in epilepsy.



P776

**SUDDEN CARDIAC ARREST IN EPILEPSY: CIRCUMSTANCES AND RISK FACTORS***Lamberts R<sup>1</sup>, Blom MT<sup>2</sup>, Wassenaar M<sup>1</sup>, Bardai A<sup>2</sup>, De Haan G-J<sup>1</sup>, Leijten FSS<sup>3</sup>, Sander JW<sup>1,4,5</sup>, Thijs RD<sup>1,4,6</sup>, Tan HL<sup>2</sup>**<sup>1</sup>Epilepsy Institute in the Netherlands Foundation – SEIN, Heemstede, Netherlands, <sup>2</sup>Academic Medical Center, Amsterdam, Netherlands, <sup>3</sup>University Medical Center Utrecht, Utrecht, Netherlands, <sup>4</sup>UCL Institute of Neurology, London, UK, <sup>5</sup>Epilepsy Society, Chalfont St Peter, UK, <sup>6</sup>LUMC Leiden University Medical Center, Leiden, Netherlands*

**Purpose:** We recently have shown in a prospective, community-based study that people with epilepsy may be at increased risk for sudden cardiac arrest (SCA) due to ventricular tachycardia/fibrillation (VT/VF). We aimed to determine circumstances and risk factors for SCA in epilepsy.

**Method:** Eighteen people with SCA and active epilepsy from the population-based Amsterdam Resuscitation Studies (ARREST) database were compared with 54 age- and sex-matched controls with epilepsy and no SCA from a pharmacy-based cohort. Data on epilepsy characteristics, cardiac risk factors and comorbidity, and medication use were collected. The diagnosis of active epilepsy was confirmed by a panel of neurologists. A multivariate logistic regression model was used to analyze differences between groups and determine clinical and epilepsy-related risk factors for SCA.

**Results:** SCA in epilepsy was mostly witnessed (n = 13; 72%) and diurnal (07:00–23:00) (n = 16; 89%). In two cases (11%) preceding seizure-like movements were reported. Three people (17%) survived. Underlying causes of SCA were acute myocardial infarction (n = 8; 50%), cardiomyopathy (n = 1; 6%) and aspiration/pneumonia (n = 1; 6%). Compared to those with no SCA, cases more frequently had concomitant heart disease: OR 5.8; 95% CI 1.7–18.9. Refractoriness and use of polytherapy did not differ between groups.

**Conclusion:** Circumstances and risk factors for SCA in epilepsy differ from those seen in SUDEP. Concomitant heart disease appears to be the main determinant of SCA in people with epilepsy.

P777

**PILOMOTOR SEIZURES OF AUTOIMMUNE ORIGIN***Rocamora R<sup>1</sup>, Vivanco-Hidalgo R<sup>1</sup>, Becerra JL<sup>2</sup>, Fossas P<sup>3</sup>, Mauri JA<sup>4</sup>, Albert M<sup>5</sup>**<sup>1</sup>Hospital del Mar, Neurology, Barcelona, Spain, <sup>2</sup>Hospital Germans Trias i Pujol, Neurology, Barcelona, Spain, <sup>3</sup>Hospital de Mataró, Neurology, Mataró, Spain, <sup>4</sup>Hospital Clínic Universitario, Neurology, Zaragoza, Spain, <sup>5</sup>Hospital Dr. Josep Trueta, Neurology, Girona, Spain*

**Purpose:** Ictal piloerection is an infrequent epileptic semiology classified as a subtype of autonomic seizures. Due to its lack of specificity, pilomotor seizures are commonly overlooked as ictal epileptic manifestation. The described etiology in the literature includes a wide variety of structural causes.

**Method:** We retrospectively reviewed the incidence of ictal piloerection in the clinical files of patients who underwent VEEG monitoring between 2007 and 2012. All patients presented with pharmacoresistant epilepsies and were examined routinely with a protocol that included brain 1.5 or 3T MRI, a neuropsychological evaluation and VEEG monitoring.

**Results:** A total of 511 patients were evaluated. Four patients were detected that presented piloerection as main manifestation of their seizure semiology (prevalence 0.78%). Three patients were additionally exam-

ined with FDG-PET and or SISCOM. All of them presented temporal lobe epilepsy. Two were right-sided and two left-sided. Due to suspicion of an autoimmune etiology of the epilepsy a lumbar puncture was done. The etiology detected in all cases was limbic encephalitis. Two showed positive antibodies for LGI1, one anti-Hu and other anti-Ma2. In the last case a testicular intratubular germ cell tumor was identified.

**Conclusion:** In our case series, pilomotor seizures seem to be highly indicative for limbic encephalitis. Also we report here on two patients with ILG1 limbic encephalitis with piloerection as main clinical manifestation. In the non-paraneoplastic cases the prognosis was favorable after the immunotherapy but seizures remained uncontrolled in the paraneoplastic cases.

P778

**MAJOR OBSTACLES IN THE MANAGEMENT OF ADULT EPILEPTICS IN A TERTIARY REFERRAL HOSPITAL IN NORTHEAST NIGERIA***Salawu FK<sup>1</sup>, Olokoba AB<sup>2</sup>, Martins OF<sup>3</sup>, Machunga D<sup>1</sup>, Isa BM<sup>1</sup>, Danburam A<sup>1</sup>**<sup>1</sup>Federal Medical Centre, Department of Medicine, Yola, Nigeria, <sup>2</sup>University of Ilorin Teaching Hospital, Medicine, Ilorin, Nigeria, <sup>3</sup>Federal Medical Centre, Medicine and Public Health, Yola, Nigeria*

**Purpose:** Epilepsy is a chronic neurological disease that is common in the developing world, including Nigeria where it affects hundreds of thousands of people with only a few neurologists available. We set out to assess the present state of epilepsy care in a district tertiary care hospital in northeast Nigeria, and to compare with modern management of patients with epilepsy.

**Method:** This was a retrospective study of hospital records of 200 adults with established epilepsy over the previous 4 years. We used a questionnaire to collect relevant data relating to diagnosis and management of epilepsy.

**Results:** There were 150 (75%) males and 50 (25%) females with mean age of 30.2 years (SD 5.8 years). The main aetiology was post traumatic (37%), cerebrovascular disease (22.5%), partially treated meningitis (17.5%), encephalitis (12%), and alcohol (10%). The majority of cases (85%) were generalized tonic clonic seizures. Less than a fifth had EEG and neuroimaging before commencement of AEDs. Patients referred had to travel long distances for EEG, CT and MRI brain and most could not afford the high cost of these investigations. There was no neurosurgeon. Majority of the patients (75%) were on phenytoin capsules, followed by phenobarbitone (10%), carbamazepine (7.5%), sodium valproate (5%), and ethosuximide (2.5%). There were no facilities to monitor blood concentrations of AEDs. No patient had surgical intervention, even among eligible cases. There was lack of knowledge regarding causes and treatment.

**Conclusion:** There is paucity of older AEDs and unavailability of newer generation AEDs and most of them are not aware of the possibility neuroimaging or do not have money to travel to places where they are available. Cultural beliefs and preference for traditional healers delay treatment. Raising public awareness with addressing of discrimination, measures to prevent neurological disease, and strengthening partnerships are all important to lower the treatment gap.

P779

**NOCTURNAL FOCAL EPILEPSY: CLINICAL, NEUROPHYSIOLOGICAL AND RADIOLOGICAL ANALYSIS***Delil S<sup>1</sup>, Yavuz Demiray D<sup>1</sup>, Benbir G<sup>1</sup>, Yeni N<sup>1</sup>, Karaağaç N<sup>1</sup>, Uzan M<sup>1</sup>, Ozkara C<sup>1</sup>**<sup>1</sup>Istanbul University Cerrahpasa Faculty of Medicine, Istanbul, Turkey*

**Purpose:** We aimed to evaluate demographic, clinical, electrophysiological and neuroradiologic variables in patients with nocturnal focal epilepsy.

**Method:** Patients with nocturnal focal epilepsy diagnosed on the basis of their past medical history confirming seizures while asleep at night exclusively or predominantly were enrolled. Any abnormalities were noted and classified as non-epileptiform or epileptiform abnormalities. We classified seizure types as focal seizures, with or without evolving into generalized tonic and clonic seizures or cognitive impairment. Drug resistance was defined as the persistence of seizures after adequate trials with at least three antiepileptic drugs used at the maximally tolerated dosage. Categorical variables were compared by chi-square test, and quantitative variables were compared by student's t-test. Threshold for significant p level was accepted as 0.05.

**Results:** A total of 143 patients were investigated with a mean follow-up of  $30.2 \pm 41.2$  months; 65 of them were men (45.5%) and 78 patients were women (54.5%). The mean age of the study population was  $32.2 \pm 13.4$  years (ranging between 5 and 84 years). Cranial magnetic resonance imaging was normal in 59 (41.2%) patients, while others had lesions such as dysplasia, tumor, post-traumatic lesions and developmental lesions. Fifty-six patients (39.2%) had frontal epileptiform discharges, while 63 patients (44%) had epileptiform discharges in temporal regions. Remaining patients had either occipital or undetermined focus. Patients with temporal epilepsy had higher risk for lesions in MR images ( $p = 0.36$ ). Thirty-one patients (21.6%) had drug-resistant seizures, which were mostly of those with frontal seizures ( $p = 0.001$ ).

**Conclusion:** In this study, we sought to determine characteristic features of nocturnal focal epilepsy. Detailed long-term researches are necessary to determine factors that govern the nocturnal or diurnal occurrence of focal seizures.

#### P780

### CAVUM SEPTUM PELLUCIDUM: ASSOCIATION WITH MENTAL RETARDATION, EPILEPSY, MACROCEPHALY AND HYPOGONADISM IN A 19-YEAR OLD NIGERIAN FEMALE: A CASE REPORT

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**Purpose:** Cavum septum pellucidum (CSP) persisting postnatally have been shown to be a putative marker of disturbance in early brain development and has been associated with some neuropsychiatric disorders including; epilepsy, schizophrenia, mental retardation, psychosis etc. Recent report has documented the association of macrocephaly, epilepsy and mental retardation with CSP in two male monozygotic twins.

**Method:** We report a case of a 19 years old female who presented to our neurology clinic with recurrent seizures of 3 years. The seizures were secondary generalized tonic clonic seizures preceded by aura of headache. She had febrile convulsion in infancy and childhood seizures as a toddler which stopped at age 4. Her menarche was delayed till age 16 when she had an episode of scanty menstrual flow for three days. Subsequently she has remained amenorrhoeic till date. Her school performance was noted to be very poor.

**Results:** Physical examination showed a large head size with an occipitofrontal circumference of 59 cm. She had underdeveloped secondary sex characteristic (Tanner stage II). Brain CT scan and MRI showed the presence of cavum septum pellucidum. The pituitary gland was unremarkable. The hormonal assay done showed low progesterone and markedly elevated Follicle stimulating hormone (FSH) and Luteinizing hormone (LH) suggestive of premature ovarian failure. Her seizures have been brought under control with carbamazepine 200 mg bd. She has been referred to the gynaecologist for further review.

**Conclusion:** The presence of CSP may not just be a normal variant but may represent a marker of neurodevelopmental anomaly with a spectrum of neuropsychiatric and possibly endocrine associations.

#### P781

### IS IT HEAD BOBBING OR HEAD NODDING SEIZURES?

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**Purpose:** Head nodding or bobbing was described as epileptic negative myoclonus. However the same clinical manifestation was reported as an epidemic epilepsy in Africa associated with encephalopathy characterized by atonic seizures. The term is used interchangeably and may have different etiologies which can cause confusion and lead to misdiagnosis. The purpose of this study is to describe two patients with paroxysmal head bobbing events evaluated at our institution.

**Method:** We described two patients with head bobbing events, who were admitted for continuous video-EEG monitoring (cVideo-EEG) for characterization of their events and seizure classification. The first patient is a 27 year old woman with history of childhood generalized tonic clonic seizures. She was recently noted to have a different type of events all triggered by stress. These were characterized by head bobbing without alteration of awareness and were thought to be non-epileptic psychogenic in etiology. The second patient is a 14 year old woman with history of global developmental delay and absence seizures, who presented with clusters of head bobbing.

**Results:** During cVideo-EEG monitoring, the patients' typical events were captured. For the first patient, these episodes were associated with bursts of generalized 4–5 Hz spike and wave discharges lasting up to 9 s. In the second case, these episodes were associated with generalized 1–2 Hz spike and wave discharges lasting up to 25 s. In both cases the head bobbing corresponded to single generalized spike and wave discharges indicative of generalized epilepsy with myoclonic seizures.

**Conclusion:** Head nodding or bobbing can be observed in both children and adults. In our patients these events were consistent with myoclonic seizures. Continuous Video-EEG monitoring remains the gold standard for identify paroxysmal events and classifying seizures. A standardized ictal phenomenology and terminology would be very useful for clinical and research purposes.

#### P782

### THE ETIOLOGIC ROLE OF CALCIFIED CYSTICERCOTIC LESION IN DRUG-RESISTANT EPILEPSY: A SYSTEMATIC REVIEW

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**Purpose:** It is unclear the role of calcified cysticercotic lesion (CCL) as an epileptogenic lesion and its contribution in drug-resistant epilepsy (DRE).

**Method:** MEDLINE, EMBASE, Scopus and LILACS were interrogated, since their inception until September of 2012, searching for case reports and case series of patients with CCL and DRE. We included all cases where the ictal-onset zone was determined with standard pre-surgical evaluation in an epilepsy center. Cases in which there was discordance between the anatomical location of CCL and the ictal-onset zone were excluded. Abstracted data included semiology of seizures, presence

of other lesions in imaging, type of pre-surgical investigations, surgical treatment, seizure outcomes and histological reports.

**Results:** A total of 2500 references were identified using terms related to cysticercosis and epilepsy. After the first screening, 56 documents were read and critically reviewed. Five final articles were selected. They included 13 patients. Nine (69.2%) of the patients had CCL in the temporal lobe. Hippocampal sclerosis (HS) was detected using MRI imaging in four (30.8%) patients (three had a CCL in the temporal lobe and one in the parietal lobe). One patient with frontal CCL had recurrent perilesional edema. Four patients (30.8%) required extensive pre-surgical investigation (one with invasive recording and three with PET scan). Eleven patients had epilepsy surgery, and became seizure free. Details about histological description were available only in two patients, both demonstrated perilesional gliosis.

**Conclusion:** CLL rarely represents the ictal-onset zone in patients with DRE. There is a need of prospective studies to clarify the association between CCL and HS, the role of perilesional gliosis in CCL, and the role of CCL in DRE.

### P783 CONTINUOUS EEG MONITORING IN CRITICAL CARE

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**Introduction:** Continuous electroencephalographic monitoring (cEEGm) is the main tool for diagnosis in subclinical seizures and non-convulsive status epilepticus (NCSE), in the intensive care units (ICU).

**Methods:** We prospectively evaluated the cEEGm conducted between April 2012 and January 2013 in the Adult and Pediatric ICU.

**Results:** We analyzed 38 cEEGm, corresponding to 36 patients (19 men). Mean age was 50 years (range 5 months to 88 years). The most common indication for monitoring was impaired consciousness (53%), seconded by, the presence of seizures observed by an ICU staff (42%). On average, monitoring lasted 85 h (range 4–479 h). We found NCSE in 13 patients (34%) and subclinical seizures in 10 (26%). The mean duration of NCSE was 79 h (range 11–400 h). Eight patients met criteria for super-refractory NCSE (62% of all NCSE). The treatment of choice was anesthetics in 13 patients and the association of three antiepileptic drugs was commonly used (range 0–10 drugs). In 79% of the patients, cEEGm motivated a change in the treatment plan. Overall mortality was 18%, and severe neurological sequelae were observed in 40% of patients.

**Conclusions:** The cEEGm is a fundamental tool in the management of ICU patients; it allows accurate diagnosis of NCSE and subclinical epileptic activity, especially in patients with impaired consciousness and no clear evidence of seizures. These findings are associated with significant mortality and future neurologic sequelae.

### P784 REVERSIBLE POST PARTUM CARBAMAZEPINE INDUCED ENCEPHALOPATHY

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**Purpose:** To enhance the awareness of Carbamazepine side effects in pregnant women.

**Method:** Study the case of a woman with temporal lobe epilepsy with transient clinical and electro-encephalography findings consistent with encephalopathy. We present the case of 39 year old lady who is known case of temporal lobe epilepsy for many years treated with Carbamazepine. She got pregnant and her epilepsy has been controlled on Carbamazepine. Her pregnancy has been with no events. Immediately after her delivery she developed higher mental dysfunction with higher

mental dysfunction. She had no motor or sensory deficit. Cranial nerves examination was unremarkable. Her brain CT scan and MRI did not reveal abnormalities. Her EEG showed diffuse slowing with minimal changes on stimulations. Her lab investigations including CBC, ESR, urea/electrolytes, LFT, TFT were unremarkable. She started to improve 3 day after onset and became normal 5th days after delivery. She had similar presentation after her previous delivery that was not documented.

**Conclusion:** Carbamazepine was the most likely cause of the transient encephalopathy. The pathophysiology of such rare setting is not clear.

### P785 PROFILE OF PATIENTS WITH EPILEPSY AT MOHAMED VI UNIVERSITY HOSPITAL OF MARRAKECH

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**Introduction, Purpose:** Epilepsy is a frequent chronic disorder, with a prevalence of 1.1%. It is the second cause of consultation in neurology after migraine. The purpose of this study is to analyse the epidemiological, clinical, aetiological, therapeutic and evolutionary profile of epileptic patients in the 3rd level University Hospital of Marrakech.

**Method:** This first study in Marrakech is retrospective, from January 2009 to January 2011. Patients collected were 454

**Results:** Among this series of 454 patients, 249 (54.8%) were male, with a mean age of 23.1 ± 16.9 years. The urban origin was found in 61.8% of cases and the patients were low socio-economic level in almost half of cases (49.6%). The mean age of seizure onset in our patients was 13.3 years. Seizures' type was simple partial seizures in 5.4% of cases, partial seizures with secondary generalization in 42.7%; and generalized seizures in 19.4%. Cryptogenic epilepsies were the most dominant etiology. The use of maraboutage was found in 46% of cases (herbal ingestion, amulets or holy incantations...). Monotherapy was used in 59.5% of cases, bitherapy in 37.8% and polytherapy in 2.7% of cases. Side effects were encountered in 28.7% of cases. The evolution was a total recovery in 68.6% of cases, stabilization in 21.4% of cases and worsening of seizures in 10% of cases.

**Discussion and Conclusion:** As in Morocco, three quarters of affected people in developing countries do not get adequate treatment they need. In this study percentage of patients improved with medical treatment is closer to the one found in literature. The long delay of consultation and the high rate of use of traditional practices (46%) points out the importance of efforts needed for education and awareness of epileptic patients not only in Marrakech, but all over Morocco and a good training of general practitioners.

### Poster session: Basic sciences C Wednesday, 26 June 2013

#### P786 IMPACT OF NAV1.1 KNOCKDOWN ON CA1 IN HIPPOCAMPAL FUNCTION

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Mutations of the *SCN1A* gene, which codes for voltage-gated sodium channel Nav1.1 is of particular relevance for neurological disease: loss of function mutations cause Dravet Syndrome (DS), a severe childhood epileptic disorder associated with profound cognitive impairment. *SCN1A* mutations have also been described in autism and reduced levels of Nav1.1 are observed in various models of Alzheimer disease (AD). The aim of this study is to investigate the neural mechanisms by which Nav1.1 reduction induces cognitive impairments. Using ShRNA interference approach, we induced a local Nav1.1 down regulation in the CA1 area in adult rats.

*In-vitro* experiments show that Nav1.1 deficits in CA1 affect neuronal coding of interneurons. *In-vivo* single-unit recording in the same area reveals that the relationships between place cell firing and hippocampal theta rhythm has been altered. This impairment is associated with an increase of exploratory activity related to spatial memory deficits.

### P787

#### EFFECTS OF DC ELECTRIC FIELD ON SYNAPTIC PLASTICITY AND SEIZURE-LIKE ACTIVITY IN THALAMOCINGULATE CIRCUITRY

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**Purpose:** Field stimulation could modulate synaptic plasticity as well as influence epileptiform activities in various brain regions. However, seldom research focus on the field effect on synaptic transmission within thalamocortical system, which is an important circuitry in sensory processing and in generating epileptiform activities. The medial dorsal thalamic nucleus (MD) is heavily connected to anterior cingulate cortex (ACC) and medial prefrontal cortex (mPFC) and could regulate seizure activities in cortical regions. Seizures generated in mPFC and ACC are often drug-resistant and alternative treatment such as field stimulation needs to be evaluated. Therefore, the current study is aimed to investigate the effect of DC field stimulation on the changes of thalamocingulate synaptic plasticity and seizure-like activities within this circuitry.

**Method:** Male C57BL/6J mice were used in this study. Brain slice preserves the pathway between MD and ACC was used in this study. The local field potentials were recorded with multielectrode array. Uniform electric fields were generated by passing constant current between two parallel AgCl-coated silver wires.

**Results:** Application of anodal DC stimulation for 15 min could potentiate the synaptic transmission in the MD-ACC pathway. While cathodal DC stimulation depress synaptic transmission in the MD-ACC pathway. The potentiation/depression effect was mediated by the volume changes of extracellular space. Using furosemide to stabilize the extracellular space could block DC mediated potentiation or depression. The DC mediated potentiation/ depression is NMDA dependent. Application of APV could block potentiation/ depression. Seizure-like activities was induced by perfusion brain slice with 4-aminopyridine and bicuculline. Prior application of cathodal DC could elevate the seizure threshold thus prevent seizure initiate.

**Conclusion:** DC mediated potentiation is caused by increasing concentration of neurotransmitter because application of furosemide and APV could prevent potentiation. Cathodal DC could prevent the initiation of seizure-like activities.

### P788

#### STRUCTURE BASED DRUG DESIGN, SYNTHESIS AND SCREENING OF ADENOSINE A2A ANTAGONISTS AS NOVEL ANTI-EPILEPTIC DRUGS

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**Purpose:** Adenosine receptors (AR) play an important role in chemical signaling in both, peripheral and central nervous systems. Four subtypes of Adenosine Receptors have been identified: designated A1, A2A, A2B, and A3. A2A ARs are found in high density in certain brain regions, such as Striatum, Nucleus accumbens, and Olfactory tubercle. Adenosine exhibits high affinity to A2A ARs, which appear to be tonically activated under physiological conditions. A2A AR antagonists have been proposed as novel therapeutics for Epilepsy and Parkinson's disease.

**Method:** Human A2A AR bound to ZM241385 with IC<sub>50</sub> 0.22 nM (PDB ID: 3EML) crystal coordinates were downloaded from protein data bank. Energy-optimized pharmacophore was prepared using Schrodinger software. The resulting pharmacophore model contains one hydrogen bond Acceptor (A), one hydrogen bond Donor (D) and three Ring systems (R). Using these features, screened against the public library of compounds (Asinex) to find potential lead compounds.

**Results:** The compounds which yielded fitness score of more than 1.0 the pharmacophore model were further subjected to Glide HTVS, SP and XP. Glide docking results revealed 33 hits were identified as potential lead molecules.

**Conclusion:** This study demonstrates that a pharmacophore search using a model based on A2A AR inhibition, and the enzyme's structural features can be used to screen for new candidates for antiepileptic therapy. The lead with highest docking score and more number of hydrogen bonds with Glu169, Asn253 amino acids selected for synthesis. Furthermore, derivatives are synthesized to develop SAR. These have to be validated by using *In vitro* inhibitory activity.

### P789

#### PRENATAL PREVENTION OF EPILEPSY: MATERNAL TUBACIN TREATMENT PREVENTS EMBRYONIC NEURONAL MIGRATION DEFECTS AND EPILEPTIC ACTIVITY CAUSED BY RAT *SRPX2* SILENCING IN UTERO

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**Purpose:** Altered development of the human cerebral cortex can cause severe malformations with often intractable focal epileptic seizures and may participate in common pathologies, notably epilepsy. This raises important conceptual and therapeutic issues. Ideally the patients would benefit from as early intervention as possible, before the long-term epileptic consequences appear later in life – hence the need to test the feasibility of such preventive strategies in the appropriate animal models.

**Method:** We had previously reported on the detection of two missense *SRPX2* (Sushi-Repeat Protein, X-linked 2) mutations in two related epileptic disorders of the speech cortex. Using an *in utero* *Srpx2* silencing approach, we have now created a rat model of altered development of the cerebral cortex, that was analyzed using a large combination of complementary approaches, including morphological analyzes, time-lapse videomicroscopy and electrophysiology recordings.

**Results:** We demonstrate that *Srpx2* influences neuronal migration in the developing rat cerebral cortex, and that it increases alpha-tubulin acetylation. Following *in utero* *Srpx2* silencing, spontaneous epileptiform activity was recorded postnatally. The neuronal migration defects and the postnatal epileptic consequences were prevented early in embryos by transient maternal administration of tubacin, which is a tubulin deacetylase inhibitor.

**Conclusion:** Early prevention of the neuronal migration defects and of the postnatal epileptic consequences as obtained here, could be of broad interest given the known convergence of multiple neuronal migration pathways and disorders on alpha-tubulins, and as future progress in developmental neuroimaging and in prenatal genetic diagnosis can be anticipated.

#### P790

### SEVERE HYPOGLYCEMIA IN THE HIPPOCAMPAL CA3 CIRCUITRY INDUCES NMDA RECEPTOR DEPENDENT SEIZURES AND CA1 SYNAPTIC FAILURE IN VITRO

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Seizures are the most common clinical presentation of severe hypoglycemia, usually as side effect of insulin treatment for diabetes type 1, juvenile onset diabetes mellitus, and advanced diabetes type 2. We characterized a new *in vitro* model for the study of hypoglycemia-induced seizures, using the mouse hippocampal thick slice suitable for all developmental stages, and evaluated the effects exerted by severe glucose depletion on the hippocampal rhythmic activity.

**Methods and Results:** Dropping the glucose concentration from the standard 10–1 mM produced epileptiform activity in 88% of the slices tested. Analyses of these events revealed that seizures originated in the CA3 region, then spreading into the CA1 region. Following the seizure-like event (SLE), spreading depression (SD)-like events with frequent irreversible synaptic failure occurred in the CA1 region (8/12 slices). SD-like events also occurred in the CA3 region (3/12) ~30 s after the SD-like event in the CA1 region. Additionally, prior to the onset of SLE in CA3 area, there was a quantifiable decrease in the activity of interneuronal network while there was an increase in the frequency and power of activity originated by pyramidal cells, which was correlated with progressive depolarization and increased synchrony of this neuronal population. The initiation of hypoglycemic seizures required glutamatergic synaptic activity in the hippocampus and NMDA receptor blockade prevented the hypoglycemia-induced SLEs and SD in the hippocampal formation.

**Conclusions:** Severe glucose depletion induces fast changes in the CA3 circuitry of the hippocampus which may underlie the mechanisms of seizure generation under this condition. Hypoglycemic seizures can induce failure of neighbor areas of the brain using NMDA receptor activation as main mechanism.

#### P791

### EXPRESSION CHANGE OF SEMAPHORIN 3F IN THE HIPPOCAMPUS OF THE LITHIUM CHLORIDE-PILOCARPINE EPILEPSY MOUSE MODEL AND ITS RELATION WITH MOSSY FIBER SPROUTING

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**Purpose:** Several studies suggest that mossy fiber sprouting is crucial for repeated convulsions. However, the key factor causing mossy fiber sprouting is not clear. This study aimed to investigate the correlation of semaphorin 3f with mossy fiber sprouting in lithium chloride-pilocarpine epilepsy mouse model.

**Method:** The mossy fiber sprouting was observed in hippocampuses by Timm staining, and expression level of semaphorin 3f were detected in hippocampuses by western blot and immunohistochemistry methods at 1 day, 14 days and 45 days after lithium chloride-pilocarpine induced status epilepticus (PISE).

**Results:** The expression level of semaphorin 3f began to be down-regulated in granular cells of dentate gyrus and pyramidal cells of hilar region of CA3 region at 14 days after PISE in PISE mice, and the down-regulation was also present at 45 days after PISE. However, there was no such change in other regions of the hippocampus. Meanwhile, the mossy fiber sprouting in the superficial layer of CA3 region and inner layer of dentate gyrus began to increase at 14 days after PISE and grew obviously at 45 days after PISE.

**Conclusion:** The expression change of semaphorin 3f was in accordance with time and site of the mossy fiber sprouting, which suggests that semaphorin 3f might be the reason of mossy fiber sprouting and even be an important reason of repeated seizures.

#### P792

### STE20/SPS1-RELATED PROLINE/ALANINE-RICH KINASE IS INVOLVED IN PLASTICITY OF GABA SIGNALING FUNCTION IN MOUSE ACQUIRED EPILEPSY

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**Purpose:** To explore the role of STE20 (sterile 20)/SPS1-related proline/alanine-rich kinase (SPAK) in epileptogenesis and the relation between SPAK and NKCC1, KCC2.

**Method:** Co-expression of SPAK and NeuN, NKCC1, KCC2 in the hippocampus of PISE was observed via immunofluorescence, and the expression change of SPAK was detected by immunohistochemical, western blotting analysis and RT-PCR. The cultured neurons are infected with pGC-FU-Stk39-GFP *in vitro*. Oxygen-deprivation was introduced to simulate the pathophysiological process of SE. The interaction between SPAK and NKCC1, KCC2 was detected by immunoprecipitation.  $[Cl^-]_i$  was estimated by fluorometric measurement of N-(6-methoxyquinolyl) acetoethyl ester (MQAE).

**Results:** The expression of SPAK significantly increased at 1 day after SE, and further increased at 14 day compared to the control ( $p < 0.01$ ) *in vivo*, and downward trend in SPAK expression was observed at 45 day, but still higher than the control ( $p < 0.05$ ). *In vitro*, hypoxia enhanced SPAK, NKCC1 expression and decreased KCC2 expression in hippocampal neurons, ( $p < 0.01$ ). SPAK over-expression failed to influence the expression of NKCC1 or KCC2, but enhanced NKCC1 immunoprecipitation. As the amount of SPAK precipitation increased, more NKCC1 could be detected in the pGC-FU-Stk39-GFP-infected group than the others, but KCC2 could only be detected via co-IP together with pGC-FU-Stk39-GFP in oxygen-deprived neurons. The fluorescence detected increased in the pGC-FU-Stk39-GFP neurons compared to the control ( $p < 0.05$ ), which suggest  $[Cl^-]_i$  decreased in neurons over-expressing SPAK. Moreover, after hypoxic conditioning, the fluorescence intensity further weakened in the pGC-FU-Stk39-GFP group compared to the control groups ( $p < 0.05$ ).

**Conclusion:** SPAK may contribute in plasticity of GABA signaling function by mediated NKCC1, KCC2 and adjusting  $[Cl^-]_i$ .

**Keywords:** STE20/SPS1-related proline/alanine-rich kinase; epilepsy; epileptogenesis;  $Na^+$ - $K^+$ -2 $Cl^-$  co-transporters;  $K^+$ - $Cl^-$  co-transporters

### P793

#### GENDER DIFFERENCES IN FEBRILE SEIZURE OUTCOME AND SEXUAL DIMORPHISM TO EARLY-LIFE STRESS

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**Purpose:** Understanding the factors that lead to atypical febrile seizures (FS) in early life could enable their potential prevention as well as the development of temporal lobe epilepsy later in life. Clinical and experimental data suggest that early life stress could predispose to atypical FS.

**Methods:** Induction of early postnatal stress on Sprague Dawley rats consisted of daily postnatal injections of corticosterone in pups followed by hyperthermia-induced seizures (HS) at P10 using warm dry air (45–48°C). Consequences of stress on HS were studied in males and females at P10 looking at generalized convulsion (GC) behaviors, body temperature and EEG monitoring using matlab approaches. To assess longitudinal anatomo-functional effects on the hippocampus, neuronal counts using the optical fractionator approach and patch-clamp recordings of CA1 pyramidal cells on acute brain sections in vitro were performed on P20 males.

**Results:** Our data show that high levels of corticosterone in early life significantly accelerates GC occurrence during hyperthermia in both genders. Using a thermographic camera, we found that the critical body temperature was lower in the treated male pups only. Higher corticosterone plasma levels were found in males as compared to females. Performing EEGs, we saw a significant increase in burst-like activities, seizure duration and frequency. Interestingly, ten days later in males, EPSP amplitudes were greater and EGABA tended to be depolarized in CA1 pyramidal cells. Finally, the P20 dual pathology males also revealed specific alterations in the inhibitory interneuron subpopulations expressing Parvalbumin or Somatostatin in the CA1.

**Conclusions:** Our results support the two-hit hypothesis of epileptogenesis and suggest a pathophysiological link between early-life stress and atypical febrile seizures, conditions that have a high prevalence in children with temporal lobe epilepsy. On the bedside it may imply to be extremely careful when using dexamethasone or corticosteroid regimens in preterm and young children.

### P794

#### EPILEPTIFORM ACTIVITY IN A MOUSE MODEL OF THE FETAL ALCOHOL SYNDROME

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**Purpose:** Chronic prenatal alcohol exposure can injure the developing brain, and is associated with a variety of physiological and behavioural postnatal anomalies, collectively referred to as the Fetal Alcohol Spectrum Disorder (FASD). Included among the anomalies is a markedly increased prevalence of seizures. To date, there exists limited information regarding the underlying mechanisms. The hippocampus is a structure implicated in the FASD and is a source of seizure activity in a variety of epileptic conditions. The purpose of the present study was to investigate the effects of prenatal alcohol exposure in mice on the physiology and seizure susceptibility of the hippocampus.

**Method:** Pregnant mice received 10% v/v ethanol for the first trimester of gestation by voluntary consumption. Extracellular field potentials were recorded from the CA3 and CA1 hippocampal regions using acute brain slices prepared from control and ethanol-exposed pups of age PD 15 to PD 21.

**Results:** Prenatal alcohol exposure for the first trimester resulted in an increase of spontaneous field activity in both the CA3 and CA1 hippocampal regions. These spontaneous discharges consist of depolarizing shifts of 0.2–1 mV in amplitude and 30–150 ms in duration, which were blocked by the addition of the gap junctional communication antagonist, carbenoxolone. Furthermore, prenatal alcohol exposure resulted in an increase in spontaneous and recurrent seizures in the CA3 and CA1 hippocampal regions. Along with the physiological changes we observed molecular changes in FASD mice, including up-regulation of connexin 30 mRNA and connexin 30 protein compared to age-matched controls.

**Conclusion:** These findings demonstrate that exposure of the developing brain to alcohol results in abnormal physiological and molecular changes and an increase in seizure susceptibility in the hippocampus.

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### P795

#### THE ROLE OF GAP JUNCTIONAL COMMUNICATION IN HYPOGLYCEMIC AND GLUCOSE REPERFUSION SEIZURES

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Severe brain hypoglycemia, as the result of an insulin overdose in diabetic patients, can cause serious clinical complications such as seizures and coma. However, the mechanisms of hypoglycemic seizure generation and propagation remain unclear. Moreover, preliminary studies have shown that reperfusion with normal glucose after a period of severe hypoglycemia can cause neuronal hyperexcitability that can have further damaging effects. Gap-junctional communication plays a critical role in the genesis of hypoglycemia related injury by engaging astrocytic networks in metabolic compensation under low glucose conditions. We found that mouse brain slices perfused with low-glucose (0.5 mM) artificial cerebral spinal fluid (aCSF) typically displayed one seizure-like event (SLE), after which they experienced an irreversible loss of evoked potentials within 30 min unless they were immediately rescued by normal glucose aCSF. When gap junction blockers were added to the hypoglycemic perfusate, the slices had several SLEs before evoked potentials were lost. We found that 100% (n = 7) of the brain slices that showed SLEs during hypoglycemia also showed subsequent SLEs during glucose reperfusion if the rescue was immediate. The addition of gap junction blockers into the aCSF during glucose reperfusion resulted in the cessation of SLEs and normal evoked responses. These data suggest that blockade of gap junctional communication plays a neuroprotective role, both during hypoglycemic conditions, where it maintains evoked potentials for a

longer period of time, and during glucose reperfusion, where it reduces the incidence of SLEs.

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## P796

### TEMPORAL LOBE EPILEPSY – A GLIAL DISORDER?

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Glial cells are now recognized as active communication partners in the CNS, and this new perspective has rekindled the question of their role in pathology. We observe unusual immunohistochemical and functional phenotypes of glial cells surviving in the sclerotic hippocampus (HS) of patients with temporal lobe epilepsy (TLE), including a complete loss of gap junction coupling. It is, however, unclear whether these changes reflect the cause, effect or adaptive response in the progression of epilepsy. To investigate temporal aspects of glial dysfunction during epileptogenesis we established a mouse model of epilepsy (intracortical kainate injections) which reflects many key aspects of human TLE. Changes in interastrocytic coupling were assessed by tracer diffusion studies in acute slices at different time points post *status epilepticus*. These studies revealed a pronounced reduction of coupling before onset of neuronal death and hyperactivity and a complete loss of coupling during the chronic phase, providing strong evidence that this dysfunction is a crucial factor in epileptogenesis. Mechanistically, pro-inflammatory molecules appeared to cause the uncoupling, since no seizure-induced reduction of coupling could be found in toll-like receptor four knockout mice. Moreover, induction of inflammation by LPS injection as well as incubation of acute slices with inflammatory cytokines resulted in a comparable inhibition of astrocytic communication. Fate mapping studies revealed that astrocytes in HS do not transdifferentiate into another cell type but rather acquire another functional phenotype. These data challenge the common view of epileptogenesis according to which changes in neurons are considered the prime cause of this condition.

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## P797

### THE EFFECTS OF ESLICARBAZEPINE ON TRANSIENT Na<sup>+</sup> CURRENTS IN CHRONICALLY EPILEPTIC HUMAN HIPPOCAMPUS

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**Purpose:** Loss of use-dependent block of transient Na<sup>+</sup> channels is a suggested key mechanism underlying pharmacoresistance to carbamazepine (CBZ) at the cellular level, both in human and experimental epilepsy. This study was aimed to determine the activity of eslicarbazepine, the major active metabolite of eslicarbazepine acetate, in modulating transient Na<sup>+</sup> channels in epileptic tissue from patients with therapy refractory seizures.

**Method:** Whole cell patch-clamp recordings were performed on dissociated granule cells from the human hippocampus obtained from therapy refractory epileptic patients (n = 26) under control conditions and after application of CBZ and eslicarbazepine.

**Results:** Consistent with previous published observations, only a slight but significant slowing of fast recovery was observed upon CBZ application (mean ± SEM, in ms):  $\tau = 11.0 \pm 1.1$  and  $11.7 \pm 1.7$  before and during application of 100  $\mu\text{M}$  CBZ, respectively, n = 8, p = 0.05. A subsequent application of eslicarbazepine exerted a pronounced and significant additional slowing of fast recovery rates  $\tau = 21.8 \pm 3.0$  during application of 300  $\mu\text{M}$

eslicarbazepine. The effects of eslicarbazepine were concentration-dependent:  $57.9 \pm 8.6\%$ ,  $120.0 \pm 23.5\%$  and  $121.1 \pm 21.7\%$  increase following application of 30, 100 and 300  $\mu\text{M}$  eslicarbazepine, respectively. Accordingly, eslicarbazepine significantly inhibited neuronal firing in human granule cells.

**Conclusion:** These results indicate that eslicarbazepine exerts use-dependent effects resulting in reduced firing frequencies of excitatory neurons, in pharmacoresistant human epilepsy and potentially overcomes a cellular resistance mechanism to conventional AEDs. This does not preclude additional effects of eslicarbazepine on other properties of sodium channels, i.e. slow inactivation processes.

This study was sponsored by Bial – Portela & C<sup>a</sup>, S.A.

## P798

### EFFECTS OF AGE AND GENDER ON THE PHARMACOKINETICS OF VALPROATE AND PHENOBARBITAL

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**Purpose:** To establish the dosage regimen to maintain sodium valproate (VPA) and phenobarbital (PB) to be at effective steady state plasma concentration in Wistar rats of different ages in different gender.

**Method:** The subjects were postnatal 15 days age (P15) and postage 35 days age (P35) Wistar rats. All rats were divided into many groups with different dosage regimen.

**Results:** (1) The dosage regimen to maintain VPA and PB to be at effective steady state plasma concentration in P15 male rats were 75 mg/kg (12/day), 10 mg/kg (2/day) and the dosage regimen in P35 male rats were 350 mg/kg (6/day) 35 mg/kg (2/day);

(2) With 200 mg/kg (6/day) dosage regimen, the VPA plasma concentration in P15 and P35 male rats were  $150.00 \pm 0.00 \mu\text{g/ml}$ ,  $34.83 \pm 8.47 \mu\text{g/ml}$ , however with 30 mg/kg (2/day) dosage regimen, the PB plasma concentration in P15 and P35 male rats were  $42.15 \pm 6.34 \mu\text{g/ml}$ ,  $13.00 \pm 3.47 \mu\text{g/ml}$ ;

(3) With dosage regimen of 200 mg/kg, 300 mg/kg and 400 mg/kg (6/day), the VPA plasma concentration were higher in male rats than in female rats, but with dosage regimen of 45 mg/kg, 60 mg/kg (2/day) the PB plasma concentration were higher in female rats than in male rats;

(4) The effective dose and lethal dose of VPA were closely 2400 mg/kg/day, 2700 mg/kg/day.

**Conclusion:** (1) The dosage regimen to maintain VPA to be at effective steady state plasma concentration in P15 and P35 male rats were 75 mg/kg (12/day), 350 mg/kg (6/day), and the dosage regimen of PB were 10 mg/kg (2/day), 35 mg/kg (2/day);

(2) The rate of VPA and PB metabolism were age-dependent;

(3) The rate of VPA metabolism were faster in female rats than male rats while the rate of PB metabolism were faster in male rats than female rats.

## P799

### DEXTROMETHORPHAN ATTENUATES SEIZURE SUSCEPTIBILITY IN MICE FOLLOWING SYSTEMIC INFLAMMATION

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**Purpose:** Systemic inflammation leads to a number of the mediated physiological changes in central nervous system. The underlying mecha-

nisms and the signaling pathways involved in these phenomena remain yet well understood. We hypothesized that peripheral inflammation leads to increased neuronal excitability arising from a CNS immune response. The research aim was to investigate the role of activated microglia in seizure susceptibility of the mice following sepsis.

**Method:** We induced inflammation by administration (i.p.) of lipopolysaccharide (LPS) to adult male mice. Seven days later, the LPS-treated mice were randomly assigned to treat daily with vehicle, dextromethorphan 5 and 15 mg/kg. To examine the excitability of the brain in vivo, we administered pentylenetetrazole (i.p.) to evoke clonic seizures. In vitro hippocampal slices from the mice were performed to measure spontaneous interictal burst firing.

**Results:** The LPS-treated mice exhibited a marked, persistent inflammatory response within the hippocampus, characterized by microglial activation. Mice treated with dextromethorphan showed decreased susceptibility to PTZ seizures compared with those with vehicle treatment. In vitro hippocampal slices from LPS-treated mice showed increased spontaneous interictal burst firing, which was attenuated in the dextromethorphan-treated mice.

**Conclusion:** Peripheral inflammation induced persistent neuro-inflammation and, such as microglia activation, and increased seizure susceptibility in mice. By inhibition of microglia activation, dextromethorphan demonstrated to attenuate intrinsic excitability in hippocampus and recovery seizure threshold in LPS-treated mice. Our finding of a microglia-mediated increase in CNS excitability provides insight into potential mechanisms underlying the disparate neurological change following systemic inflammation.

#### P800

##### ATTENTION DEFICIT CAUSED BY EARLY LIFE INTERICTAL SPIKES IS IMPROVED WITH ACTH

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**Purpose:** There is a well-described association between childhood epilepsy and cognitive and behavioral deficits including working memory impairments, ADHD and autism spectrum disorder. However, the precise role of epileptiform discharges in these deficits remains unclear. In order to understand the relationship between epileptic discharges during neurodevelopment and cognition later in life, we developed a model of frequent focal interictal spikes (IIS).

**Method:** Postnatal day (p) 21 rat pups received intracortical injections (0.5 µl) of 200 µM bicuculline methiodine into the prefrontal cortex (PFC) whilst EEG was continuously recorded. Within seconds of injection, focal spikes were recorded at the injection site. Injections were repeated in order to achieve 5 days of IIS. Short-term plasticity (STP) and behavioral outcomes were assessed, and the therapeutic impact of adrenocorticotropic hormone (ACTH) was also studied.

**Results:** IIS resulted in a significant increase in STP bilaterally in the PFC. In a delayed non-match-to-sample task IIS rats showed marked inattentiveness without deficits in working memory. Rats also demonstrated deficits in sociability, an autistic phenotype. The attention deficits were partially ameliorated by ACTH, a drug widely used to treat early-life seizures.

**Conclusion:** Early-life focal IIS in the PFC have long-term consequences for cognition and behavior at a time when IIS are no longer present. Focal IIS during development can disrupt neural networks, lead to long-term cognitive deficits and thus may have important implications in

ADHD and autism. Some of the consequences of IIS may be reduced with pharmacological treatment.

#### P801

##### FIRING PROPERTIES AND REACTIVATION OF HIPPOCAMPAL PLACE CELLS IN RATS WITH EPILEPSY DURING SLEEP

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**Purpose:** Memory consolidation is thought to occur by the reactivation of neural activity during the waking period in the following sleep period. We hypothesize that this process is impaired in the lithium-pilocarpine model of epilepsy in rats.

**Method:** A cohort of rats (four controls and seven epileptics) were tested in the Morris Water Maze task (MWM) and a reaction-to-novelty task (RNT) to study spatial memory. This was also used for Timm staining for mossy fiber sprouting and Cresyl violet staining for the thinning of the cell layers to confirm epileptogenesis. Another cohort (four controls and four epileptics) was trained to run clock-wise in a circular maze for 15 mins (RUN, >20 turns) followed by a rest period for 1 h (POST). We recorded multiunit activity and local EEG in the CA1 layer of the hippocampus, EMG, and the rat's location throughout the experiment.

**Results:** Rats with epilepsy showed impaired performance in both the MWM and the RNT tasks. Cells recorded from epileptic rats showed increased firing rates in all three states during POST. Place cells recorded from epileptic rats showed lower coherence, higher out of field firing rate, and larger place fields than controls. Real-time analysis of reactivation showed no differences between the groups in the strength and number of replay events as well as the maximum correlation coefficients. As sleep was decompressed to look for reactivation at smaller time scales, epileptic rats were found to consistently have an increased number of reactivation events across multiple decompressions.

**Conclusion:** In this study, we present the first evidence of the disruption of the reactivation of neuronal networks during sleep in epilepsy. Rats with epilepsy displayed higher number and strength of reactivation events than controls across multiple time scales, indicating a system-level increase in reactivation.

#### P802

##### DECREASE IN MULTIFOCALITY AND SPATIAL COMPLEXITY CONTRIBUTE TO SEIZURE TERMINATION

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**Rationale:** Traditionally, epileptic seizures are characterized as pathological and extreme forms of synchronization of neural activity. Recent



studies demonstrate that that excessive synchronization may play an important role in seizure termination. In this study we studied the spatio-temporal profile of synchronization during the course of in vitro seizures to examine network mechanisms how seizures terminate.

**Methods:** The experiments were performed in vitro on rat hippocampal slices perfused with artificial CSF containing low calcium (0.2 mM). Field potentials from the hippocampal CA1 region were recorded using multiple extracellular electrodes.

**Results:** Spontaneous seizures were characterized by a complex spatio-temporal evolution which was characterized by progressive slowing of instantaneous frequency of ictal discharges and decrease in complexity. During the initial part of seizures, ictal discharges initiated in multiple areas of CA1. With seizure progression a small localized area of CA1 became the dominant pacemaker of ictal activity and resulted in a uniform propagation pattern of ictal activity. These changes in spatial organization were accompanied by increases in global synchronization index and phase coherence, which reached maxima during the final stage of seizures.

**Conclusion:** This study demonstrates complex evolution of the spatial organization of neuronal networks involved in seizure genesis. Spontaneous termination of seizures is an emergent phenomenon which involves critical slowing of activity combined with high spatial organization of network activity. The stereotypic spatial profile of the late stage ictal activity means that the progressive prolongation of refractory neuronal states can ultimately prevent the re-excitation at the network level and thus act as endogenous large-scale anticonvulsant mechanisms.

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## P803

### FUNCTIONAL IMPAIRMENT OF ADULT HIPPOCAMPAL NEUROGENESIS IN PATIENTS WITH CHRONIC MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Mesial temporal lobe epilepsy (MTLE) is a syndrome characterized by a history of an early initial injury and followed by a latent period of years before chronic epilepsy develops. Semiologic elements in MTLE comprise an aura that typically includes viscerosensory sensations, impaired consciousness, orolimentary automatisms and a prolonged postictal reorientation.

Hippocampal sclerosis (HS) is the most common pathology underlying drug-resistant mesial temporal lobe epilepsy and is characterized by granule cell dispersion in the dentate gyrus where production of newborn neurons from subgranular neural progenitor cells occurs (adult neurogenesis). In experimental settings, generalized seizures robustly increase adult neurogenesis whereas chronic seizures resulted in a lasting decrease in production of new cells. Theoretical models suggest a role for the new neurons in sustaining efficient pattern separation when high loads of information have to be processed by the hippocampus. Animal studies testing mice with reduced levels of adult neurogenesis in the water maze paradigm confirmed that prediction by identifying specific deficits in spatial learning.

**Methods and Results:** Using a version of the water maze task adapted for humans we here show that subjects suffering from HS show specific

learning deficits that correspond to the findings observed in mice with reduced adult neurogenesis.

**Conclusion:** Our findings indicate that cognitive deficits in patients with MTLE comprise adult hippocampal neurogenesis dependant functions.

## P804

### EFFECTS OF A KCC2 BLOCKER ON NETWORK ACTIVITY IN PIRIFORM AND ENTORHINAL CORTICES

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**Purpose:** The efficacy of inhibitory transmission mediated by GABA<sub>A</sub> relies on low levels of [Cl<sup>-</sup>]<sub>i</sub> that is controlled by cation-chloride cotransporters such as KCC2. KCC2 uses the K<sup>+</sup> gradient to maintain a low [Cl<sup>-</sup>]<sub>i</sub>. Here, we tested the effects of the KCC2 blocker, VU0240551, on the epileptiform activity induced by 4-Aminopyridine (4AP).

**Method:** Adult rat horizontal slices were bathed with standard medium. 4AP (50 μM), VU0240551, (10 μM) and ionotropic glutamatergic antagonists were bath applied. Field potentials were recorded from entorhinal cortex (EC), piriform cortex (PC), and CA3.

**Results:** 4AP induced epileptiform ictal discharges that lasted 171 ± 45 s (±SE) in EC and 182 ± 43.5 s in PC (n = 10). It also induced interictal activity in EC, PC and CA3 with the rate of occurrence of 0.3 ± 0.1, 0.1 ± 0.01, and 0.5 ± 0.1 Hz, respectively. VU0240551 abolished ictal discharges and increased the frequency of the interictal activity in EC, PC, and CA3 to 0.6 ± 0.1, 0.3 ± 0.01, and 0.8 ± 0.2 Hz. During application of 4AP+glutamatergic antagonists only "slow" interictal discharges continue to occur. These glutamatergic-independent events decreased in duration and rate of occurrence by 45% and 34%, respectively, during VU0240551 application.

**Conclusions:** Our results suggest that decreasing the Cl<sup>-</sup> drive with a KCC2 blocker (and thus presumably, shifting the reversal potential of GABA<sub>A</sub> receptor-mediated currents to less negative values) reduces epileptiform synchronization.

## P805

### CHARACTERISTICS OF EPILEPTIC SEIZURES IN WAG/RIJ RATS WITH INDUCED CORTICAL DYSPLASIA

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**Purpose:** The effects cortical dysplasia (CD) were investigated in WAG/Rij rats with absence epilepsy by analyzing the spike-wave discharge (SWD) activity in EEG signals and blood-brain barrier (BBB) integrity

**Method:** A CD model was formed using irradiation. After irradiation, rats were taken back to the animal facility and cared for routinely until birth. At the end of 5 month, the EEGs of rats were recorded and BBB integrity was investigated using horseradish peroxidase (HRP).

**Results:** All WAG/Rij rats exhibited spontaneous SWDs on EEG and behavioral symptoms of absence epilepsy. Those with CD were observed to be more agitated behaviorally in comparison to the controls during their development periods. The SWDs of rats with induced CD were

found to have decreased in number and in duration, while displaying an increase in frequency in comparison to the SWDs of the rats in the control group. Macroscopic examination of HRP stained areas in the brain sections from the experimental groups revealed staining in the cerebral cortex and thalamic nucleus. Moreover, macroscopic observation of brain sections revealed a marked increased pattern of HRP extravasation in cortical and subcortical regions of rats with CD.

**Conclusion:** Our study showed that a widespread and intensive HRP extravasation in cortical and subcortical regions was observed in animals with CD. Furthermore, in seizure formation, cortical lamination was found to play an important role both in the formation of SWDs and their duration as well as frequency patterns.

#### P806

##### EFFECT OF LEVETIRACETAM AND TOPIRAMATE ON KYNURENIC ACID SYNTHESIS IN RAT BRAIN

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**Purpose:** Kynurenic acid (KYNA) is an endogenous brain constituent that inhibits the activity of all three ionotropic excitatory amino acid (EAA) receptors. Cerebral synthesis of KYNA from its bioprecursor L-kynurenine is catalyzed by aminotransferases localized preferentially within astrocytes. In the brain, two distinct kynurenine aminotransferases, KAT I and KAT II, are responsible for the formation of KYNA. The possible role of altered KYNA-mediated modulation of EAA receptors in the human neuropathology has been postulated. The disturbances of KYNA production have been linked to the occurrence of epilepsy. The anticonvulsant and neuroprotective role of KYNA in vivo and in vitro is well documented. In the present study, the influence of the antiepileptic drugs levetiracetam and topiramate on KYNA synthesis was investigated.

**Method:** KYNA was subjected to the HPLC and quantified fluorimetrically.

**Results:** KYNA synthesis in cortical slices: levetiracetam at the concentration of 0.5, 1.0 and 3.0 mM diminished KYNA synthesis in the brain cortical slices to 84% (NS), 72% ( $p < 0.05$ ) and 55% ( $p < 0.001$ ) of control, respectively. Topiramate at the concentration of 0.1, 0.5, 1.0 and 3.0 mM enhanced KYNA production to 108% (NS), 146% ( $p < 0.05$ ), 153% ( $p < 0.001$ ) and 186% ( $p < 0.001$ ) of control, respectively. KAT I activity: levetiracetam at the concentration of 0.001–1.0 mM did not alter KYNA synthesis. Topiramate at the concentration of 0.001, 0.01, 0.1 and 1.0 mM increased KYNA synthesis to 126% ( $p < 0.05$ ), 153% ( $p < 0.001$ ), 166% ( $p < 0.001$ ) and 172% ( $p < 0.001$ ), respectively. KAT II activity: Both, levetiracetam and topiramate at the concentration of 0.001–1.0, did not affect KYNA production.

**Conclusion:** Our data suggested, that antiepileptic drugs, levetiracetam and topiramate could modulate KYNA production in the brain by different mechanisms.

#### P807

##### EFFECTS OF NEWBORN TRANSPLANTATION OF NEUROSPHERES DERIVED FROM MEDIAL GANGLIONIC EMINENCE IN ADULT EPILEPTIC RATS

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Dysfunction of GABAergic interneurons plays a direct role in the development of epilepsy. Cells from medial ganglionic eminence (MGE) have the ability to differentiate into inhibitory interneurons when transplanted into the brain. Here we tested the hypothesis that cells from MGE grown as neurospheres, when transplanted prior to pilocarpine-induced epilepsy in rats, differentiate into inhibitory interneurons and may have an anti-convulsive effect. MGE from GFP<sup>+</sup> embryos (E14) were dissected and the cells were grown as neurospheres for 5 days. Neonatal (P2) Sprague Dawley rats were anesthetized and a total of  $5 \times 10^4$  cells were stereotactically injected in the cortex. At P60, the status epilepticus (SE) was induced by pilocarpine administration. After SE, animals were observed for 188 h to assess the spontaneous seizures (SRS) frequency. Animals were perfused and their brains processed for immunofluorescence for GFP and interneuronal markers. We found a large number of GFP<sup>+</sup> cells in the hippocampus of epileptic animals compared to non-SE animals ( $p < 0.05$ ). There was a co-localization of GFP<sup>+</sup> cells with astrocytes and inhibitory interneurons markers in the epileptic hippocampus, indicating that the MGE cells were able to differentiate into astrocytes and interneurons, however we don't find difference in SRS frequency. These results suggest a different strategy to modulate the function of astrocytes, inhibitory interneurons, and other cells present in neurospheres from MGE in order to obtain a protective effect in epilepsy.

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#### P808

##### NMDA AND GABA-ERGIC MECHANISMS IN THE ANTI-EPILEPTIC EFFECT OF TIANEPTINE IN EXPERIMENTAL MODELS OF EPILEPSY

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**Purpose:** Certain antidepressants have been shown to have proconvulsant properties. Conversely, tianeptine, an antidepressant drug, has recently been reported to possess antiseizure effect. The present study evaluates the antiepileptic effect of tianeptine in experimental models of epilepsy. The role of  $\gamma$ -aminobutyric acid (GABA) and N-methyl-D-aspartate (NMDA) in antiepileptic effect of tianeptine was also studied.

**Method:** Male Wistar rats (175–225 g) were used in different experimental models namely pentylenetetrazole (PTZ, 60 mg/kg; i.p.), maximal electroshock (MES; current intensity-70 mA, duration- 0.2 s), bicuculline (7.0 mg/kg; ip) and NMDA (120 mg/kg; i.p)-induced seizures. Tianeptine was administered orally in three doses of 20, 40 and 80 mg/kg, 60 min before seizure induction. Valproate, 300 mg/kg, i.p. was administered as the standard control in all the groups. Behavioural and oxidative stress parameters were assessed using a battery of tests.

**Results:** Tianeptine exhibited dose-dependent protection against PTZ, MES, bicuculline and NMDA induced seizures. Co-administration of tianeptine with MK-801, an NMDA antagonist, potentiated the anti-convulsant effect of tianeptine suggesting involvement of NMDA receptor. Impairment of learning and memory caused by seizures was reversed by tianeptine. Tianeptine *per se* did not cause any significant change in cognitive function of rats. Seizures caused an increase in oxidative stress which was attenuated by tianeptine.

**Conclusion:** Tianeptine produced protection in different experimental models of epilepsy and also protected against the seizure-induced oxidative stress and cognitive impairment. The protective effect of tianeptine against bicuculline and NMDA-induced seizures suggests the involvement of GABA-ergic mechanisms and NMDA receptors, respectively in the antiepileptic effect of tianeptine.

P809

### FEBRILE SEIZURES IN IMMATURE MICE INDUCE A DECREASE IN REELIN-POSITIVE CELLS AND FACILITATE GRANULE CELL DISPERSION INDUCED BY INTRA-HIPPOCAMPAL KAINITE

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**Purpose:** Febrile seizures (FS) are often reported in the history of mesial temporal lobe epilepsy but their role in its physiopathology remains controversial. Neuropathological post-resective studies have described a hypertrophy and dispersion of the granule cell (GCD) of the dentate gyrus in patients reporting a history of FS. A decrease in the expression of the glycoprotein called reelin has also been suggested to be involved in GCD. In this study, we aimed at the determination of the influence of FS on the kainate-induced GCD and epileptogenesis.

**Method:** We induced hyperthermic seizures (HS) by a 30-min rise of body temperature (40–41°C) in P10 mice and examined their consequences on hippocampal sclerosis induced by intra-hippocampal kainate (KA; 1 nmol) once the animals were adults (P60–70).

**Results:** We confirmed that HS alone did not induce GCD or epilepsy in adult mice. Although we observed no changes during the initial KA-induced *status epilepticus*, we found that HS mice had an increased GCD and hippocampal hypertrophy 3 weeks after KA injection, as compared to sham KA-injected animals. In addition, HS mice developed seizures more rapidly than controls. Using immunostaining, ELISA and/or Western blot in HS and sham naive mice (i.e., without KA at P70), we observed a decrease of neurons expressing reelin that we identified as Cajal-Retzius cells.

**Conclusion:** Our data suggest that HS aggravates the consequences of a subsequent epileptogenic insult via a long lasting reduction of the hippocampal Cajal-Retzius expression of reelin.

P810

### ANGIOTENSIN II OVEREXPRESSION IN THE HIPPOCAMPUS MAY BE RESPONSIBLE FOR THE DEATH OCCURRING DURING PILOCARPINE INDUCED STATUS EPILEPTICUS

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**Purpose:** Previous data of our group showed alterations in renin-angiotensin system (RAS) in the hippocampus of rats after pilocarpine-induced epilepsy. Tonin is an enzyme responsible for the cleavage of angiotensinogen releasing angiotensin II (AngII). In addition, the angiotensin converting enzyme (ACE) releases AngII after cleavage of AngI. Thus, we analyzed if transgenic mice, expressing rat tonin and as consequence high amount of AngII in the brain, were more susceptible to *status epilepticus* (SE).

**Method:** Transgenic mice, expressing high activity of the enzyme tonin in the brain (TGM-rTon) and wild type mice (wt-c57black/6) were submitted to pilocarpine-induced SE (320 mg/kg) or saline-treated. Control groups (saline-treated), Acute groups (3 h of SE), tonic-clonic groups (death after a tonic-clonic seizure) of both lineage were employed. ACE was analyzed in the hippocampi of these mice by real time PCR (mRNA) and by enzymatic activity using fluorescent peptides as substrates. Statistical evaluations were performed using Student's t-test and variance analysis was done followed by Student Newman-Keuls as post-hoc test and  $p < 0.05$  was accepted.

**Results:** Death related to tonic-clonic seizure was very increased in TGM-rTon group, when compared to wt-c57black/6 group, after SE induction. Few transgenic mice survived after SE, showing increased vulnerability of this lineage. Comparing mice from both lineages we found increased activity of ACE in saline-treated, acute and tonic-clonic TGM-rTon mice, when compared to wt-c57black/6 groups, suggesting an increased release of AngII in the hippocampus of these animals.

**Conclusion:** Taken together, these data show that the synchronic action of both converting enzymes (tonin and ACE) may release a large amount of AngII in the hippocampus during SE. This fact may modify all synaptic and vascular hippocampal environments in these animals and promoting their death.

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P811

### LONG-TERM EFFECTS OF SINGLE EARLY-LIFE SEIZURES ON CORTICAL EXCITABILITY

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**Purpose:** The aim of our study is to test the long-term effects of single early life seizures (ELs) on mouse cortical function and excitability. In humans ELs can have long lasting detrimental effects on behaviour and cognition, along with a higher propensity for epilepsy. However, clinical studies of ELs are challenged by the many factors that affect their outcome. In this respect, animal models allow the study of these factors in isolation and hence provide an insight to the underlying mechanisms.

**Method:** In vitro electrophysiological studies were combined with behavioural tests to assess the long-term effects of single PTZ-induced ELs on cortical excitability within the context of overall animal behaviour. In order to address the issue of a critical period for the severity of single ELs, seizures were induced at two distinct developmental periods: P10–15 and P20–25 and mice were left to reach adulthood (>3 mo) for behavioural tests and electrophysiology. Cortical excitability was assessed by recording:

- Spontaneous network activity (Up states) in brain slices,
- The effect of blocking GABA-A receptors on Up states, and
- The induction (i.e. delay to appear after transition from normal to 0 Mg<sup>2+</sup> + slice buffer) and expression (i.e. spectral content) of spike and wave discharges (SWDs) in cortical slices in the 0 Mg<sup>2+</sup> model of epilepsy.

**Results:** Our preliminary results show that single ELs have a minimal effect on the behaviour of mice treated at P10–15 but not at P20–25, with no effect however on up states and SWDs. On the contrary, the onset of epileptiform activity tends to occur faster in mice with ELs as opposed to untreated mice.

**Conclusion:** Single ELs affect neither normal nor paroxysmal intrinsic cortical activity, however they cause the cortex to be less resistant to the induction of seizures.

## P812

**CURRENT SOURCE DENSITY ANALYSIS OF SPONTANEOUS INTERICTAL SPIKES IN VIVO**Flynn SP<sup>1</sup>, Lenck-Santini P-PP<sup>1</sup>, Holmes GL<sup>1</sup><sup>1</sup>Department of Neurology, Geisel School of Medicine at Dartmouth College, Lebanon, NH, USA

**Purpose:** Interictal spikes (IIS) are a common observation in both patients and animal models of epilepsy. Although IIS have been well studied in *in vitro* hippocampal slice preparations, few studies have described spontaneously generated IIS *in vivo*. In this study we investigated the propagation of spontaneous IIS within the hippocampus and entorhinal cortex (EC) of rats exposed to pilocarpine-induced status epilepticus (SE).

**Method:** Male Sprague Dawley rats were administered lithium (127 mg/kg, *i.p.*) followed by multiple doses of pilocarpine (12.5 mg/kg, *i.p.*) until the development of SE, defined by continuous stage 4/5 seizure activity. Seizures were stopped 90 min following the initiation of SE, with lorazepam (2.5 mg/kg, *i.p.*). All recordings were completed at least 2 weeks following SE. For *in vivo* recordings animals were anesthetized with urethane (1.5 g/kg, *i.p.*). A laminar 16-channel silicon probe was lowered into the hippocampus to record from a plane including either CA1-CA3 or CA1-dentate gyrus. Additional EEG wires were placed in the medial EC.

**Results:** Spontaneous IIS were observed in both the hippocampus and EC in pilocarpine-treated rats under urethane anesthesia. In preliminary analysis we observe  $3.0 \pm 0.3$  IIS per minute within the hippocampus. Current source density analysis of the EEG traces containing IIS, combined with histological verification of probe placement will allow for a detailed description of how IIS enter the hippocampus and EC.

**Conclusion:** We have demonstrated that spontaneous IIS can be recorded under urethane anesthesia. Detailed analysis of how IIS enter the hippocampus will help illuminate where individual spikes were generated. There is evidence that IIS help establish epileptic foci and negatively affect cognition, thus understanding how IIS are generated *in vivo* may help guide the development of anti-spike therapies.

## P813

**POSTNATAL TRANSPLANTATION OF NEURONAL PRECURSOR CELLS PROTECTS ADULT MICE FROM PTZ-INDUCED SEIZURES**Calcagnotto ME<sup>1</sup>, Valente MF<sup>2</sup>, Romariz S<sup>2</sup>, Paiva DS<sup>2</sup>, Frussa-Filho R<sup>3</sup>, Mello LE<sup>2</sup>, Longo BM<sup>2</sup><sup>1</sup>UFRGS, Biochemistry, Porto Alegre, Brazil, <sup>2</sup>UNIFESP, Physiology, Sao Paulo, Brazil, <sup>3</sup>UNIFESP, Pharmacology, Sao Paulo, Brazil

**Purpose:** Interneuronal precursor cells from the medial ganglionic eminence (MGE) have the ability to differentiate into inhibitory GABAergic neurons after being transplanted into the mouse brain. MGE-derived cells grafted into postnatal brain could increase the GABAergic inhibition in neurological disorders in which inhibitory synaptic function is altered, such as epilepsy. Thus, our aim was to verify the *in vivo* effects on seizure susceptibility of MGE interneuronal precursor cells transplanted into neonatal mice.

**Method:** MGE region from green fluorescent protein (GFP) embryos (E13.5) was dissected, extracted and the cells were cultured in DMEM-F12 medium supplemented. A total of 100,000 cells were injected in the cortex of neonatal (P4) C57 mice. At P60 these animals were injected with pentylenetetrazole (PTZ) (60 mg/kg) to induce acute seizures. Immediately after PTZ injection, animals were observed for 15 min and the seizures were classified by Racine scale. Immunofluorescence was

performed in the transplanted brains for the identification of MGE-derived inhibitory neurons using GFP and interneuronal markers.

**Results:** Our results show that transplanted cells derived from MGE were able to migrate and differentiate into inhibitory GABAergic interneurons and protect from seizures, by reducing the frequency ( $p < 0.01$ ) and mortality ( $p < 0.01$ ) of PTZ-induced acute seizures, when compared to control group.

**Conclusion:** We conclude that transplanted MGE-derived neuronal precursor cells into neonate brain present and the anticonvulsive effects *in vivo* that can be attributed to the migration, integration and differentiation of MGE-derived cells into mature GABAergic interneurons.

## P814

**LACOSAMIDE REDUCES SPONTANEOUS EXCITATORY AND INHIBITORY POSTSYNAPTIC POTENTIALS AND IS ANTICONVULSANT IN AN IN VITRO NEOCORTICAL SEIZURE MODEL**Krawczyk M<sup>1</sup>, Florez CM<sup>2</sup>, Lukankin V<sup>1</sup>, Stern S<sup>2</sup>, Valiante T<sup>1</sup>, Carlen PL<sup>1</sup><sup>1</sup>Toronto Western Research Institute, University Health Network, Toronto, ON, Canada, <sup>2</sup>University of Toronto, Toronto, ON, Canada

**Purpose:** Previous behavioural and electrophysiological studies have indicated that lacosamide (LCM) acts as an anticonvulsant drug *in vivo*. The purpose of the present study was to investigate the effects of lacosamide in an *in vitro* model of epilepsy.

**Method:** Dual extracellular field potential and intracellular whole cell recordings were obtained from 30 to 60 day old mouse cortical slice preparations.

**Results:** Recordings from layer II/III of the frontal cortex during application of 4-aminopyridine (4-AP) (100  $\mu$ M) showed spontaneous and recurrent epileptiform activity. Application of LCM (100  $\mu$ M) strongly inhibited spontaneous epileptiform activity induced by 4-AP. LCM also increased the amplitude of evoked field responses that were reduced by application of 4-AP and ensuing seizure activity. LCM produced a significant reduction in the incidence of spontaneous excitatory postsynaptic currents (EPSC's) and inhibitory postsynaptic currents (IPSC's) in cortical cells exposed to 4-AP.

**Conclusion:** The results indicate the potential for LCM to inhibit epileptiform activity in an *in vitro* animal model of epilepsy, and support its role in seizure reduction observed in clinical trials.

Supported by UCB Pharma

## P815

**CRITICAL SLOWING AND INCREASED SENSITIVITY TO PERTURBATIONS PRECEDE ONSET OF EPILEPTIC SEIZURES IN VITRO**Jefferys JGR<sup>1</sup>, Cmejla R<sup>2</sup>, Paulus M<sup>3</sup>, Jiraska P<sup>1,4,5</sup><sup>1</sup>Clinical and Experimental Medicine, University of Birmingham, Birmingham, UK, <sup>2</sup>Department of Circuit Theory, Faculty of Electrical Engineering, Czech Technical University, Prague, Czech, <sup>3</sup>Department of Nonlinear Modelling, Institute of Computer Science, Academy of Sciences of Czech Republic, Prague, Czech, <sup>4</sup>Department of Developmental Epileptology, Institute of Physiology, Academy of Sciences of Czech Republic, Prague, Czech, <sup>5</sup>Department of Developmental Epileptology, Charles University in Prague, 2nd Faculty of Medicine, Motol University Hospital, Prague, Czech

**Purpose:** How seizures start remains far from clear. Understanding the dynamics of neuronal networks which lead to transition to seizure, and identifying reliable markers for this process would greatly help with the development both of innovative approaches to preventing transition to seizure, and of methods for seizure prediction. In this study we examined the dynamics of transition to seizure in an in vitro model.

**Method:** The experiments were performed in vitro on rat hippocampal slices perfused with artificial CSF containing low calcium (0.2 mM). Field potentials from the hippocampal CA1 region were recorded using extracellular electrodes. To actively test the dynamical state of CA1 network we used two paradigms 1) Electrical stimulation of alveus to evoke antidromic evoked potentials and 2) application of external depolarizing electric fields.

**Results:** Perfusing slices with low-calcium artificial CSF resulted spontaneous and repeated seizure-like events. Spontaneous seizures did not occur abruptly, but were preceded by a progressive buildup in low-amplitude high-frequency activity at ~200 Hz, with superimposed multiunit activity. This phenomenon manifested as gradual increase in signal variance and autocorrelation. Application of antidromic stimuli showed a progressive pre-ictal increase of the length of the evoked responses. The sensitivity of CA1 to the application of uniform depolarizing electric fields also progressively increased in the run-up to each seizure, so that very weak fields could directly evoke seizures just before the next spontaneous seizure is expected.

**Conclusion:** These results demonstrate that seizures are preceded by detectable changes in brain dynamics. This study also shows that the dynamics of transition to seizures in vitro demonstrates features of critical slowing associated with transitions between various dynamical regimes. Demonstrating that dynamics of epileptic neuronal networks is governed by similar principles to other dynamical systems opens new ways to design more efficient therapies to reverse transition to seizure.

#### P816

##### AN OSCILLATION-BASED FEATURE SET FOR SEIZURE-LIKE EVENTS IN HUMAN TEMPORAL NEOCORTICAL SLICE

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**Purpose:** Using human middle temporal neocortical tissue acquired after resective surgery for epilepsy, we investigated the role of phase coherence (PC) and cross-frequency coupling (CFC) during seizure transitions.

**Method:** Middle temporal neocortical tissue was resected from five surgical candidates having mesial temporal lobe epilepsy. 500 µm coronal cortical slices were placed in artificial cerebral spinal fluid and extracellular electrophysiological recordings were obtained from superficial (layers 2/3) and deep (layer 5) neocortical layers. The kainic and cholinergic receptor agonists kainate (50 nM) and carbachol (50 µM) were used to mimic inhibitory and excitatory drives, respectively (Buhl 1998 et al. Journal of Physiology 1998;513:117–126). Of those slices that showed activation under kainate and carbachol, 10% showed spontaneous seizure-like events lasting 35 ± 25 s. Phase coherence (Lachaux JP et al. Human Brain Mapping 1999;8:194–208.) and modulation index (Tort A et al., Journal of Neurophysiology 2010;104:1195–1210) were used in the frequency analysis of the electrophysiological traces.

**Results:** Transition into seizure was characterized by two consistent trends: 1.) A transition of the lower frequencies involved in CFC from delta (0.5–4 Hz) to theta (4–8 Hz), alpha (8–15 Hz) or beta frequencies (15–30). These lower frequencies were coupled with gamma (>30) and high gamma (>150 Hz). 2.) A loss of phase synchrony between cortical layers in the delta range. Transition out of seizure was characterized by a return of the lower rhythm of CFC to the delta frequency.

**Conclusion:** We describe a feature set associated with ictal state transitions in human middle temporal neocortical slices. Trends in the phase synchrony between superficial and deep neocortical layers and the coupling between frequencies within each layer are associated with the transition into and out of the seizure state.

#### P817

##### CALCIUM BINDING PROTEINS IN FOCAL CORTICAL DYSPLASIA TYPE IA

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**Purpose:** Alterations in GABA-ergic cortical neuronal system have been reported in focal cortical dysplasia (FCD) type Ia, a malformation of cortical development associated with of pharmacoresistant epilepsy. We compared calcium binding proteins (parvalbumin, calbindin and calretinin) in lateral temporal lobe surgical specimens of 18 patients with FCD type Ia to 19 patients who underwent the resection of anterior two-third of a temporal lobe due to hippocampal sclerosis (TLE-HS) as well as eight post-mortem controls.

**Method:** Slides and serial sections stained for neuron-specific nuclear protein (NeuN) and calcium binding proteins were analysed. Parvalbumin-, calbindin- and calretinin-immunoreactive neurons were quantitatively investigated by using a two-dimensional cell-counting technique. Cortical layers II, IV and V as well as subcortical white matter (WM) were assessed separately in all groups.

**Results:** Density of parvalbumin-, calbindin- and calretinin-immunoreactive neurons and their ratios to the densities of NeuN positive neurons were significantly higher in patients with FCD type Ia compared to those with TLE-HS and post-mortem controls in all cortical layers and WM, whereas the absolute number of neurons labelled for NeuN was unchanged in all groups. In TLE-HS vs. post-mortem controls, ratios of calcium binding protein-immunoreactive neurons to NeuN were unchanged in the most instances except for calbindin/NeuN ratios in cortical layers II and IV, which were also significantly increased.

**Conclusion:** Increased expression of calcium binding proteins in presumably inhibitory interneurons in FCD type Ia compared to TLE-HS and post-mortem controls may be determined by neurobiology of the cortical malformation.

#### P818

##### QUANTIFICATION OF LEUCINE-RICH GLIOMA-INACTIVATED 1 (LGI-1) PROTEIN IN SURGICAL TISSUE FROM TEMPORAL LOBE EPILEPSY (TLE) PATIENTS

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**Purpose:** LGI-1 participates in the coordination of excitatory synaptic transmission and modulates dendritic pruning. When mutated, it is associated with increased hippocampal excitability and seizures. Possible mechanisms include reduced binding to disintegrins, ADAM-22 and ADAM-23. Despite classically associated with neocortical TLE in the context of familial epilepsy, seizures in limbic encephalitis associated with anti-LGI-1 autoantibodies indicate also a role in acquired seizures. In this study, we aimed to evaluate levels of LGI-1, ADAM-22 and ADAM-23 in hippocampal and temporal neocortex surgical specimens using western blot.

**Method:** This study was approved by our institution Research Ethics Board. Hippocampi (eight patients and six controls from necropsy) and temporal neocortex (eight patients) were flash frozen at  $-40^{\circ}\text{C}$  in isopentane and stored at  $-80^{\circ}\text{C}$ . Samples were homogenized in laemmli buffer and submitted to SDS-PAGE electrophoresis on denaturing Tris-HCL gel. Proteins were transferred onto Hybond-C nitrocellulose membranes. Membranes were incubated with primary antibodies overnight and immunoreactivity was assessed. Levels were normalized by beta-actin and quantification was performed with ImageJ.

**Results:** We found similar levels of LGI-1 ( $p = 0.491$ ), ADAM-22 ( $p = 0.860$ ) and ADAM-23 ( $p = 0.938$ ) between control and TLE hippocampi. In patients, there was a trend ( $p = 0.117$ ) towards increased LGI-1 in the neocortex ( $2.523 \pm 0.668$ ), compared to the hippocampus ( $1.276 \pm 0.334$ ).

**Conclusion:** In this small series of TLE patients, changes in LGI-1 and related proteins were not found in the epileptogenic hippocampi. Higher neocortical levels of LGI-1 are in agreement with previously described distribution of protein isoforms in the temporal regions.

#### P819

### UP-REGULATION OF DOWNSTREAM TARGETS OF METABOTROPIC GLUTAMATE RECEPTOR TYPE 5 (MGLUR5) SIGNALING PATHWAY IN TEMPORAL LOBE EPILEPSY (TLE) HIPPOCAMPAL SURGICAL TISSUE

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**Purpose:** Metabotropic glutamate receptors (mGluRs) are G-protein coupled receptors that modulate neuronal glutamatergic transmission. Postmortem studies describe increased expression levels of the excitatory group I mGluR5 in Temporal Lobe Epilepsy (TLE) surgical tissue. mGluR5 activation leads to unique  $\text{Ca}^{2+}$  signatures which activate the calcium-dependent pathway mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (ERK). In vitro studies show that activation of this pathway leads to increases in p-mTOR and NR2B synthesis. Here, we examined p-ERK, p-mTOR and NR2B protein levels in human hippocampal tissue resected from refractory TLE patients with (HS group) and without (non-HS group) hippocampal sclerosis and compared these levels to that of non-epileptic autopsy controls.

**Method:** This study was approved by our institution Research Ethics Board. Hippocampal surgical specimens were flash frozen at  $-40^{\circ}\text{C}$  in isopentane and stored at  $-80^{\circ}\text{C}$ . Samples were homogenized in laemmli buffer and submitted to SDS-PAGE electrophoresis on denaturing Tris-HCL gel. Proteins were transferred onto Hybond-C nitrocellulose membranes. Membranes were incubated with primary antibodies overnight and immunoreactivity was assessed.

**Results:** In the HS group ( $n = 26$ ), increases in p-ERK (27-fold;  $p < 0.01$ ), p-mTOR (13-fold;  $p < 0.01$ ) and NR2B (3.5-fold;  $p < 0.01$ )

were observed as compared to non-epileptic autopsy controls ( $n = 15$ ). In the NHS group ( $n = 10$ ), increases were seen only in p-ERK (18-fold;  $p < 0.01$ ) and p-mTOR (8.5-fold;  $p < 0.01$ ).

**Conclusion:** Our results indicate altered expression of hippocampal p-ERK, p-mTOR and NR2B in TLE. Therapeutic strategies aimed at down-regulation of these proteins might have a potential role in treating refractory TLE.

### Poster Session: Clinical neurophysiology B Wednesday, 26 June 2013

#### P820

### THE ORIGINS OF MAGNETISM AND ITS EVOLUTION INTO A NON-INVASIVE BRAIN STIMULATION TOOL

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**Purpose:** 1) To trace the origins of magnetism; 2) To follow its evolution into a clinical non-invasive brain stimulation tool.

**Method:** Extensive literature review and consultations with colleagues experienced in the field of TMS.

**Results:** This tool has gone through several decades of refinement both in terms of the relevant technology and the understanding of its use and applications to become a leading non-invasive clinical tool in many areas of medicine. Further development and more trials are needed in order to exploit its full potential.

**Conclusion:** The idea of stimulating the human brain non-invasively is something that has fascinated and motivated scientists for several centuries. The development and refinement of this technique has taken several hundred years, and non invasive transcranial magnetic stimulation as we know it today was first introduced into clinical use 23 years ago by Anthony Barker in Sheffield.

#### P821

### DIAGNOSTIC ACCURACY OF THE COLOR DENSITY SPECTRAL ARRAY (CDSA) AND AMPLITUDE-INTEGRATED ELECTROENCEPHALOGRAPHY (AEEG) FOR SEIZURE IDENTIFICATION IN THE ADULT NEUROLOGY INTENSIVE CARE UNIT

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**Purpose:** The aim of this study was to evaluate the diagnostic accuracy of the color density spectral array (CDSA) and amplitude-integrated electroencephalography (aEEG), which are commonly used in the adult Neurology Intensive Care Unit (NICU) for seizure identification.

**Method:** Thirty-two continuous EEG recordings performed in adult NICU patients were randomly transformed into 6-channel CDSA and aEEG displays. Two specialized neurophysiologists participated in this study and underwent 4 h of training to identify seizures using CDSA and aEEG. They were then individually subjected to a new series of CDSA and aEEG displays and asked to mark any epochs suspected to be seizures without access to raw EEG recordings. The results were compared to seizures identified using conventional EEG recordings.

**Results:** The 32 EEG recordings in this study comprised a total of 450 seizures over 768 h. The median sensitivity for seizure identification was 81.3% using CDSA and 80.4% using aEEG; the median false-positive rate was 3.9 per 24 h using CDSA and 2.1 per 24 h using aEEG; and the

median false-negative rate was 3.9 per 24 h using CDSA and 2.9 per 24 h using aEEG. In general, the false-positive and false-negative rates were very low. Limb movement and electromyography artifacts affected the false-positive rate because they were mistaken for seizures; while the false-negative rate (i.e., missed identification of seizures) was influenced by low-amplitude, short or focal seizures, and abundant discharges in the background.

**Conclusion:** Both CDSA and aEEG showed a high sensitivity but very low false-positive and false-negative rates for seizure identification in the adult NICU, which suggests that these techniques represent useful screening tools for seizures. Whether CDSA and aEEG display tools are suitable for widespread application in the NICU, ICU, or other places outside the ICU requires further study.

### P822 COGNITIVE EFFECTS OF INTERICTAL EPILEPTIFORM DISCHARGES IN ADULT PATIENTS WITH EPILEPSY IN CHINA

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**Purpose:** Educational difficulties or cognitive deterioration has been seen in many epilepsy patients. Neurophysiological and functional neuroimaging evidence suggests that the epileptic seizures and/or epileptiform activity can be the dominant factor, through effects on inhibition of brain areas. However, previous studies focus on the cognitive performance of children, few studies on adult patients. For this reason, we analyzed a new cohort of adult patients with frequent IEDs.

**Method:** A clinical study of 60 adult patients with epilepsy have been performed. Electroencephalography (EEG)-video recordings and cognitive testing were performed respectively. The IED index was estimated, in wakefulness and in sleep, as percentage of time in four categories (<1%, 1–10%, 10–50% and >50%). The IED categories were correlated to cognitive test results and clinical characteristics. The effect of IEDs frequency, duration, location and sleep-wake cycle on cognitive was compared and analyzed.

**Results:** The group of patients with IEDs >10% showed impaired performance on Chinese Wechsler Intelligence Scale (WAIS-RC), Chinese Wechsler Memory Scale (WMS). This effect was seen independently from other IEDs frequency and independently from other IEDs-related variables, such as duration, distribution and location. The impact of the awake or sleep IEDs was of equal importance, contributing to the WAIS and WMS.

**Conclusion:** It found that the frequent IEDs (in more than 10% of the record) in both awake and sleep EEG can impair cognitive performance in adult patients. Whether patients with a high IEDs frequency and low seizure frequency can benefit from antiepileptic treatment should be examined in further study.

### P823 MEG CAN RESOLVE PARADOXICAL EEG LATERALIZATION: A CASE STUDY

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**Purpose:** Interictal or ictal events in partial epilepsies may project on the scalp contralaterally to the side of the epileptogenic lesion. Such paradoxical lateralization can be observed in EEG in the case of para-sagittal generators, and is likely due to the spatial orientation of the generator, presenting an oblique projection towards the midline.

**Method:** We present here a case of occipital epilepsy investigated using EEG, MEG and stereoelectroencephalography (SEEG).

**Results:** MRI demonstrated a para-sagittal focal cortical dysplasia in the superior margin of the right calcarine fissure. Interictal EEG cartography demonstrated a large field, with left paramedian maximal amplitude. Interictal MEG showed that interictal spikes originated in right occipital cortex with spread to contralateral homotopic cortex. SEEG confirmed MEG data. The generator was para-sagittal, localized in the superior margin of the right calcarine fissure, with an oblique projection towards the midline.

**Conclusion:** In conclusion, MEG can resolve ambiguity on source configurations as seen by EEG. MEG revealed, at the sensor level, an initial activity starting on the side of the lesion and a subsequent bilateral implication of medial occipital areas.

### P824 PREDICTION OF POSTOPERATIVE MEMORY DECLINE IN PATIENTS WITH TEMPORAL LOBE EPILEPSY USING PARAHIPPOCAMPAL HIGH GAMMA ACTIVITY

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**Purpose:** Hippocampal resection, an established surgical option for mesial temporal lobe epilepsy, carries a substantial risk of postoperative memory decline. To avoid the disabling complication, we need to know whether the epileptic hippocampus has viable function or not before surgery. We tested the hypothesis that the distribution of parahippocampal high gamma activity agrees with memory outcomes after surgery on mesial temporal lobe structures.

**Method:** We recorded electrocorticograms from parahippocampal gyri of 18 patients while they executed a memory task paradigm. We obtained memory-related high gamma activity by calculating power amplification of electrocorticography signals in high gamma range (60–120 Hz). Distributions of high gamma activity, as well as preoperative language and memory Wada test, were compared with memory outcomes after mesial temporal lobe epilepsy surgery performed on 11 patients.

**Results:** We observed memory-related HGA mainly between 500 and 600 milliseconds poststimulus. HGAs during successful recognition were significantly higher than those related to unrecognized pictures. Memory evaluations using high gamma activity during successful recognition significantly correlated with postoperative memory outcomes with high agreement ( $p = 0.024$ ,  $\kappa = 0.79$ ), whereas both language and memory Wada tests showed poor agreements with memory outcomes.

**Conclusion:** Parahippocampal high gamma activity could provide useful information for preoperative memory evaluation in patients with mesial temporal lobe epilepsy.

### P825 DISCRIMINATING PREICTAL AND INTERICTAL STATES USING TIME IRREVERSIBILITY OF THE INTRACEREBRAL EEG IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Predicting seizures in refractory epilepsy with clinically useful performance opens the door to a new class of treatment approaches. In this study we investigate the discriminability between preictal and interictal states in patients with mesial temporal lobe epilepsy using a measure of multiscale time irreversibility of intracerebral EEG.

**Method:** 1037 h of continuous intracerebral EEG (filtered at 500 Hz, sampled at 2000 Hz) from 12 patients with mesial temporal lobe epilepsy were investigated. 18 channels from deep mesial temporal lobe structures were analyzed, including 104 seizures. Time irreversibility (Costa et al. Phys Rev Lett 2005, 95:198102) was estimated for 10 scales of EEG signals in 1 min sliding window with 20% overlap, using a time irreversibility index. The index was calculated for three periods of preictal data lasting 5, 10 and 15 min and for interictal data separated by at least 2 h from any seizure. The index was investigated for discrimination power between interictal and preictal periods.

**Results:** For all patients, there was at least one channel for which the interictal distribution of the time irreversibility index was significantly different from all three preictal distributions ( $p < 0.01$ , Bonferroni corrected t-test). The channel with most significant separation was ipsilateral to seizure onset zone in eight patients and contralateral in 2 (two patients had unclear or bilateral focus). Longer preictal periods showed slightly larger differences between distributions than shorter periods.

**Conclusion:** Multiscale time irreversibility shows a discriminative power between preictal and interictal EEG data and could potentially be useful in seizure prediction.

#### P826

##### RELATIONSHIP BETWEEN INITIAL EEG AND PROGNOSIS OF ACUTE ENCEPHALITIS

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**Purpose:** This study aimed to identify the usefulness of initial electroencephalograms (EEG) in the prediction of neurological outcomes of acute encephalitis.

**Method:** Thirty-one patients diagnosed with acute encephalitis between January 2007 and March 2010 were included in the study, all of whom were less than 18 years old. Patients were divided into two groups. Those who had recovered completely were designated group A, and those who had neurological sequelae were designated group B. We compared the severity of EEG background abnormalities according to the Synek classification, and the incidence of interictal epileptiform discharges, electrographic seizures, normal sleep features, and EEG reactivity to pain stimuli between the two groups upon initial EEGs.

**Results:** Compared with group A, group B showed a higher grade of EEG background abnormalities ( $p = 0.004$ ). The incidence of interictal epileptiform discharge ( $p = 0.004$ ) and electrographic seizure ( $p = 0.049$ ) were also higher in group B. Further, Group A had more EEG reactivity ( $p = 0.002$ ) and the incidence of normal sleep features tended to be higher in group A ( $p = 0.081$ ).

**Conclusion:** Initial EEG features including the severity of EEG background abnormalities are helpful in predicting the prognosis of acute encephalitis.

#### P827

##### EVALUATION OF THE PATTERNS OF EEG SPIKE AND SLOW WAVE DISCHARGES: SPATIOTEMPORAL ANALYSIS

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**Purpose:** This study was concentrated on the problem of identification of epileptiform patterns in the process of evaluation of EEG records.

**Method:** The analysis was performed during evaluation of selected EEG records in a group of ten patients presenting various degrees of epileptic reorganization of brain electrical activity. The EEG was recorded using ten-twenty system of electrode localization, sampling rate 250 Hz and various locations of reference electrodes. The EEG was evaluated using mapping techniques presenting both: instantaneous distribution of potentials and spatiotemporal evolution of EEG patterns after transformation of EEG records to color maps representing changes of localizations and magnitudes of electric potentials as well as their modifications due to current source density analysis.

**Results:** Described techniques help to determine precisely the character of epileptic decomposition of the basic EEG rhythms: transformation of some components of alpha or theta waves resulting in appearance of the negative-positive sharp waves or spikes with secondary slow waves- elements of discharges within theta- mainly 4–6/s and delta frequency discharges (2–3/s). Frontal or central spikes usually quickly generalize over both hemispheres- in frontal and central derivations. Decomposition of the occipito-parietal or temporal alpha waves transforming to spikes and sharp waves usually does not have tendency to generalize- except in symmetrical derivations over opposite hemisphere. Coupling between frontal and temporal or occipital discharges leads to very rapid generalization of discharges with frontal predominance.

**Conclusion:** The results illustrate advantages associated with application of the method of spatiotemporal mapping of EEG records during differentiation between epileptiform, transitory and nonepileptiform EEG patterns- resembling spike-slow wave discharges.

#### P828

##### SEMI-AUTOMATIC DETECTION OF HIGH FREQUENCY OSCILLATIONS ON SCALP EEG OF EPILEPTIC SUBJECTS

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**Purpose:** This research aims to detect semi-automatically high frequency oscillations (HFOs) on scalp EEG of epileptic patients to determine how they correlate with seizure onset zones. We believe that HFOs provide a more precise localization, and could be used for a better placement of intracranial electrodes.

**Method:** We look for oscillations in the gamma (40–80 Hz) and ripple (over 80 Hz) frequency range, at least four oscillations long with amplitude standing out of the background. To distinguish HFOs from the background, we decompose the signal into narrow frequency bands. To remove false detections, particularly muscle artifacts, we compare the amplitude of each detection in their narrowband to the broadband signal, removing detections with a ratio higher than a threshold. This threshold and other parameters of the detector are set based on prior information from the spectral, temporal and spatial components of samples marked by an expert for each subject to optimize sensitivity and specificity.

**Results:** On patients with frequent epileptic activity, the detector reaches a sensitivity above 90% while minimizing the false positive rate to 3–15 per minute. Detections can then be reviewed by an expert for more specificity.

**Conclusion:** The current level of performance is already acceptable, but methods are currently developed to use the spatial covariance and coherence of each detection with neighboring channels, and a clustering approach that could allow us to determine if more than one class of HFO is detected for a subject; both methods would aim to increase specificity.



P829

### SPATIO-TEMPORAL FEATURES OF RHYTHMIC CORTICAL ACTIVITY IN EPILEPSY DUE TO CHROMOSOME RING 20

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**Purpose:** The ring chromosome 20 [r(20)] syndrome is characterized by refractory epilepsy and mild to severe cognitive impairment. An EEG pattern constituted by trains of theta-delta waves have been reported in [r(20)] patients although its interpretation is discussed. In this work we report the frequency and spatial features of cortical rhythms in a population of [r(20)] patients using advanced EEG methodological approaches.

**Methods:** Twelve patients with [r(20)] syndrome were studied. As controls we enrolled 12 IGE (idiopathic generalized epilepsy) patients and 12 healthy volunteers (HV). For each case a resting 30-min EEG was obtained. Independent Component Analysis (ICA) was applied to EEG data and the components of interests (COIs) carrying theta-delta activity were submitted to FFT (Fast Fourier Transform) and to sLORETA.

**Results:** ICA and FFT analysis showed a reproducible EEG rhythm characterized by runs of theta-delta activity with a spectral peak between 3–7 Hz. FFT revealed in six cases a double peak laying at a frequency about double with respect to the first one. Source reconstruction shown a sensory-motor cortices involvement at single-subject and at group level. Analogue methodological approach in HV and IGE failed to show similar findings.

**Conclusion:** Our results revealed the existence of a pathognomonic EEG pattern in [r(20)] syndrome, whose recognition could help the diagnostic work-up. Both FFT and sLORETA findings supports the existence of a parallelism between this EEG traits and the “mu” rhythm, which is generated by the sensory-motor system. Such link suggests a sensory-motor system dysfunction in patients with [r(20)] syndrome.

P830

### INTERICTAL HIGH FREQUENCY OSCILLATIONS CORRELATING WITH SEIZURE OUTCOME IN PATIENTS WITH WIDE SPREAD EPILEPTIC NETWORKS IN TUBEROUS SCLEROSIS COMPLEX

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**Purpose:** Multiple tubers in tuberous sclerosis (TS) patients cause intractable epilepsy. The epileptic network with multiple tubers complicated to localize the epileptogenic zone for cortical resection. High frequency oscillations (HFOs) on intracranial video EEG (IVEEG) indicated the epileptogenic zone. Our purpose is to clarify that resection of cortex with wide spread HFOs in TS patients achieves good seizure outcome.

**Method:** We analyzed occurrence rate (OR) of interictal HFOs at 80–200 Hz (ripple) and  $\geq 200$  Hz (fast ripple) between groups A (seizure free) and B (residual seizure). We analyzed resection ratio of area including seizure onset zone, electrodes with high OR of ripple, and fast ripple.

**Results:** We collected 10 patients (A: seven patients; B: 3). The distribution of fast ripples was extensive (A: 12–40 electrodes [mean 25]; B:

9–66 [31];  $p = 0.59$ ) and scattered to multiple clusters (A: 1–6 clusters [mean 3.7]; B: 1–4 [2.3];  $p = 0.26$ ). The resection ratio of electrodes with high OR of fast ripples showed significant difference between groups A and B (A: 65–100% [mean 78%]; B: 24–78% [51%];  $p = 0.035$ ; correlation ratio = 0.60). There was no significant difference of resection ratio of both seizure onset zone and electrodes with high OR of ripples between groups A and B.

**Conclusion:** The extensive and multiple areas with fast ripples indicated wide spread epileptic network in TS patients. Resection of cortex with interictal fast ripples on IVEEG correlated with good seizure outcome.

P831

### CARDIAC AUTONOMIC ACTIVITY CHANGES DURING ELECTROCONVULSIVE THERAPY

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**Purpose:** Dynamic heart rate changes have often been described in electroconvulsive therapy (ECT). However, the specific timing of these changes has not been reported. To examine the cardiac autonomic nervous changes during a seizure in refractory epilepsy, we evaluated heart rate and spectral analysis of heart rate variability (HRV) during ECT.

**Method:** Four patients with depression and four patients with schizophrenia who all underwent ECT were included. All ECT sessions were assessed using electrocardiograms (ECG). Heart rate was recorded and analyzed for the HRV indices HF (an index of parasympathetic activity) and LF/HF (an index of sympathetic activity) during 4 min before and after seizure onset. Averaged heart rates over three heart beats pre-seizure and post-seizure onset were compared. Averages of HRV power at 30–100 and 100–170 s following a seizure were assessed.

**Results:** Following seizures, a bradycardia-tachycardia-bradycardia triphasic change was observed. Patients showed a significant prolongation of the average over three heart rates just after a seizure, suggesting parasympathetic dominance at this first phase. The average power of LF/HF significantly increased at 30–100 s after a seizure, while the average power of HF significantly increased at 100–170 s after a seizure, reflecting sympathetic activation in the second phase and parasympathetic activation in the third phase.

**Conclusion:** The evaluation of heart rates and HRV indicated a triphasic change from parasympathetic to sympathetic to parasympathetic cardiac autonomic activity following a seizure.

P832

### LATERALIZATION OF GENERALIZED PAROXYSMAL FAST ACTIVITY IN CHILDREN WITH INTRACTABLE LOCALIZATION-RELATED EPILEPSY

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**Purpose:** Generalized paroxysmal fast activity (GPFA) consists of burst of generalized rhythmic discharges; 100–200 mV; 1–9 s; 8–26 Hz; with

frontal predominance; during NREM sleep. GPFA was originally described as an electrographic feature of Lennox Gastaut Syndrome (LGS). We analyzed GPFA in children with intractable localization-related epilepsies (LRE), who underwent intracranial video EEG (IVEEG) to understand significance of GPFA correlating with the epileptogenic hemisphere.

**Methods:** We collected cases with GPFA among the patients with intractable LRE, who underwent scalp video EEG, and IVEEG. We collected 50 GPFA for each patient. We analyzed three parameters; amplitude, duration and frequency of GPFA over the bilateral frontal region.

**Results:** We found 14 (14%) patients (eight females) with GPFA among 103 patients who underwent IVEEG. IVEEG revealed multilobar epileptic zones in 12 patients and frontal lobe epilepsy in two patients. Seven patients had partial seizures and the other seven patients had generalized seizures and epileptic spasms. The amplitude ranged 48–394 mV (mean 134 mV). The duration ranged 0.5–6.3 s (1.7 s). The frequency ranged 6–20 Hz (11 Hz). There were significant differences between surgical and non-surgical sides of GPFA amplitude in 10 (71%) patients, duration in 2 (14%) and frequency in 5 (36%). In eight patients with good seizure outcomes, the amplitude of the epileptogenic hemisphere showed significantly higher than those in non-surgical side ( $p = 0.012$ ).

**Conclusions:** The lateralization of GPFA amplitude may reflect the excitatory focal cortex in the epileptogenic hemisphere proved by IVEEG. GPFA can exist in LRE with secondary bilateral synchrony and generalized seizures.

### P833

#### POSTSURGICAL QUANTITATIVE ELECTROENCEPHALOGRAMS IN REFRACTORY TEMPORAL LOBE EPILEPSY PATIENTS

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**Purpose:** To assess evolutionary changes in the Quantitative Electroencephalograms (QEEG) in patients with refractory Temporal Lobe Epilepsy who underwent Epilepsy surgery.

**Method:** A prospective and longitudinal study was carried out to assess the QEEG before and after Epilepsy surgery in 13 patients with refractory TLE. Presurgical EEG recording was performed at 6, 12 and 24 months after surgery. QEEG measures evaluated were: Delta/ Alpha Index (DAI), Brain Symmetry Index (BSI), Spectral Powers Index (SPI), total discharges frequency (TDF) and interictal epileptiform activity amplitude (IEA). These findings were correlated with clinical evolution using a seizures severity scale.

**Results:** We found a DAI decrease ( $p = 0.026$ ), and BSI increase ( $p = 0.038$ ). On the other hand a decrease of DTF and IEA ( $p = 0.024$ ,  $p = 0.04$ ) respectively were also found. These changes were gradually established until two years after surgery.

**Conclusions:** Refractory TLE patients undergoing epilepsy surgery, evidenced reorganization and cortical activation of both hemispheres, proven by the increased interhemispheric symmetry in QEEG and decreased IDA. The group of patients also showed a significant decrease in cortical excitability and epileptogenicity level, expressed by the DTF and IEA decreases at two years of evolution.

### P834

#### FOCAL ELECTROENCEPHALOGRAPHIC FEATURES IN PATIENTS WITH IDIOPATHIC GENERALIZED EPILEPSY

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**Purpose:** Focal inter-ictal epileptic discharges are generally considered as diagnostic for focal epilepsies. However, focal EEG abnormalities were reported in patients with generalised idiopathic epilepsies (IGE). We studied the characteristics of focal EEG features in patients with IGE.

**Method:** A retrospective study of patients with IGE (ILAE proposed classification 2001) followed up in Neurological department of Razi Hospital between July 2002 and December 2010. Focal EEG features were defined by the presence of focal or generalised inter-ictal epileptic discharges with a clear predominance on a specified brain region. We precised the frequency of focal abnormalities and the main brain's regions involved.

**Results:** We included 301/326 patients with IGE. Focal EEG features were found in 71 patients (23.6%). They were more frequent in JME (38.5%) than CAE and IGE-GTCS (19.4% and 17.9% respectively). Anterior focal features were more common than posterior ones (76% vs. 18.3%). In 2.8% of cases, there were independent anterior and posterior focal features.

**Conclusion:** Our results support previous studies reporting focal abnormalities in patients with IGE. These focal EEG features may be explained by recent findings in functional imaging studies, revealing an abnormal thalamo-cortical circuitry and the prefrontal cortex as a substrate of seizure generation in IGE. Focal EEG features in patients with IGE are more frequent in anterior brain's regions. They usually lead to misdiagnosis of focal epilepsy with secondary generalisation. Hence, their interpretation must be cautious, and the clinical history of the epilepsy remains the main clue for the diagnosis of the epileptic syndrome.

### P835

#### DUAL ARRAY EEG-FMRI

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**Purpose:** EEG provides high temporal resolution to the superior spatial resolution of fMRI. However, EEG recorded inside an MRI scanner is often contaminated by movement artifact. We hereby present a dual-array MR compatible EEG-a device and method aimed to allow optimal separation between brain signal and movement artifact.

**Method:** The study was approved by Tel-Aviv Sourasky Medical Center ethical committee. We implement two arrays of EEG electrodes organized into two sets of intersecting bundles. The EEG was recorded using referential amplifier. Virtual bipolar measurements were taken both along bundles (minimizing artifact) and across bundles (maximizing artifact). Then independent component analysis (ICA) was applied to the data several times with different initiation point. The ICA components were classified according to degree of two-dimensional correlation between ICA coefficients spatial distribution along bundles vs. across bundles. Components with low correlation were removed from the data.

The rest of components were transformed back to the channel space and then reconstructed denoised EEG traces from different ICA trials were averaged. The application of the dual array EEG inside 3 Tesla MRI scanner was demonstrated in seven epilepsy patients.

**Results:** In all cases the movement artifact (both balistocardiogram and non-balistocardiogram) was sufficiently suppressed, allowing clear visualization of epileptic spikes / sharp waves / rhythmic activity in five cases. In two cases no epileptic waveforms were found.

**Conclusion:** The presented new device and method is potentially useful for brain signal and movement artifact separation in EEG recorded inside MR scanner.

**P836**  
**ARE AFTERDISCHARGES BY CORTICAL STIMULATION AT SEIZURE ONSET ZONES SIMILAR TO CLINICAL SEIZURES? A STUDY BY SUBDURAL ELECTRODES IN PARTIAL EPILEPSY PATIENTS**

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**Purpose:** To assess the similarity and differences between spontaneous clinical seizures and afterdischarges induced by cortical stimulation from the view point of EEG parameters such as high frequency activities (HFAs).

**Method:** Two partial epilepsy patients undergoing subdural electrode implantation were recruited. Both afterdischarges and clinical seizures induced by 50 Hz stimulation for functional mapping were recorded (Low frequency filter 0.016/1.6 Hz for spontaneous seizures/induced clinical seizures and afterdischarges. Sampling rate 2000/1000 Hz, high frequency filter 600/300 Hz in Patient 1/2.). Three conditions, i.e., asymptomatic afterdischarges, induced clinical seizures and spontaneous seizures, were compared for semiology, conventional electrocorticographic change and HFAs. Afterdischarges without symptoms, and longer than 5 s were only adopted. This prospective observational study was approved by the University Ethical Committee (C580).

**Results:** Stimulation of seizure onset zones elicited 3 and 1 clinical seizures, and 7 and 1 asymptomatic afterdischarges in Patient 1 and 2, respectively. Spontaneous seizures were 43 and 5, similarly. Induced seizures had complex partial seizure in semiology similar to spontaneous ones. In Patient 1, induced seizures had paroxysmal fast pattern with limited spreading, and HFAs similar to spontaneous seizures. Asymptomatic afterdischarges had only rhythmic alpha pattern. In Patient 2, the induced seizure had polyspike ictal pattern and HFAs similar to spontaneous seizures. Asymptomatic afterdischarges had similar features, but did not show the evolution and spreading patterns seen in spontaneous seizures. They also lacked HFAs.

**Conclusion:** Asymptomatic afterdischarges are electrophysiologically distinct from clinical seizures by

- (1) conventional electrocorticographic changes,
- (2) HFAs. Afterdischarges induced are at times capable of activating and spreading through epileptic network responsible for habitual seizures.

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**P837**

**THE BEST EVENT-RELATED POTENTIAL PARADIGM TO DETECT PRE-ATTENTIVE ABNORMALITY IN PATIENTS WITH TEMPORAL LOBE EPILEPSY**

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**Rationale:** The Mismatch Negativity (MMN), a component of the event-related potential (ERP), is elicited by a deviant following a series of standard stimuli. MMN is thought to reflect pre-attentive sensory memory. The aim of this study was to compare the MMN in response to duration, frequency, and vowel changes in temporal lobe epilepsy (TLE) patients.

**Method:** We examined 12 TLE patients and 12 age- and gender-matched healthy controls (HC). We adopted three oddball paradigms: duration change, frequency change, and vowel change which are the most common paradigms for MMN study. The electroencephalogram was recorded according to the standard 10–20 International system and bilateral mastoid electrodes. We evaluated the mean MMN amplitude at each electrode.  $2 \times 2 \times 2$  repeated-measures analyses of variance (ANOVAs) were performed on MMN with GROUP (TLE and HC) as the between-subjects factor and STIMULUS (duration, frequency, and vowel) and SITE (Fz and Cz, or the right and left mastoids) as within-subjects factors. An alpha level of 0.05 was used in all analyses.

**Results:** The three-way repeated-measures ANOVA revealed that duration and vowel MMN amplitudes at Fz and Cz were greater than frequency MMN amplitudes. MMN amplitudes at the mastoids were lower in TLE compared to MMN in HC. Additionally, two repeated-measures ANOVA showed that duration MMN at mastoids showed most significant difference between TLE and HC than frequency MMN and vowel MMN.

**Conclusions:** The results suggest that duration MMN may be the best indicator among three MMN paradigms to detect pre-attentive abnormality in TLE.

**P838**

**AUTOMATIC DETECTION REVEALS THAT SLEEP STATE INCREASE OF HFO RATES DEPENDS ON ANATOMIC REGION**

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**Purpose:** The automatic detection of HFOs allows in contrary to visual review the analysis of long term dynamics of HFO rates. Important clinical questions are related to the stability of the HFO ratio between seizure onset channels and other brain regions and its dependence on the sleep-wake cycle.

**Method:** Automatic HFO detection using a radial basis function neural network detection was performed in long term recordings of 12 pre-surgical patients investigated with subdural strip, grid and depth contacts. Periods with visual marked sleep stages based on parallel scalp recordings from two consecutive nights were com-

pared to awake intervals. Seizure epochs were excluded from the comparison. Statistical significance was assessed with one way analysis of variance and post hoc pairwise comparisons using Tukey's HSD ( $p < 0.05$ ).

**Results:** HFO rates in seizure onset contacts differed from other brain regions independent of the sleep-wake cycle. For temporal lobe contacts the HFO rate increased significantly with sleep stage. Contacts covering the parietal lobe, including sensory and motor cortices showed a significant increase of HFO rates for intervals joined from sleep stage III and IV against the awake state. No significant HFO rate changes depending on the sleep-wake cycle were found for frontal lobe contacts.

**Conclusion:** Automatic HFO detection could show, that HFO rates in the seizure onset zone differ from rates in contacts covering other brain regions independent of sleep stage. The assumption that HFO rates increase during slow wave sleep could not be proven for frontal contacts in contrast to temporal, parietal, sensory and motoric regions.

### P839

#### CLINICAL AND VIDEO-EEG STUDY OF A FAMILY WITH INFANTILE CONVULSIONS AND PAROXYSMAL CHOREOATHETOSIS (ICCA): NEUROPHYSIOLOGICAL CONSIDERATIONS

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**Purpose:** Co-morbidity of epilepsy and paroxysmal dystonia (PD) is rare, occasionally aggregated within families under the term of infantile convulsions and paroxysmal choreoathetosis (ICCA). In this syndrome, some patients with benign familial infantile seizures (BFIS) develop PD during adolescence. Recently PRRT2 was identified as causative gene in 40–90% of cases.

We describe the neurophysiologic features of a family with ICCA.

**Method:** Sixteen individuals of a three-generation-family were studied clinically (neurologic examination – onset, semiology, frequency and duration of seizures and/or PD), neurophysiologically (EEG, video-EEG-polygraphy) and neuroradiologically. PRRT2-mutations are under investigation.

**Results:** All patients had normal cognitive and motor milestones, neurological examinations and neuroimaging. Nobody suffered from migraine or gait disturbances. Six patients (37.5%) presented with a clusters of focal seizures in early infancy (BIFS); two patients (12.5%) had also a single tonic-clonic seizure in their twenties. Outside the cluster of seizures, all patients had normal EEGs. At age of 13 years, one patient with BIFS developed PD, triggered by stretching or sudden walking/running. We recorded video-polygraphically six dystonic episodes (10–20 s), homo-lateral to the side of stretching (3left /3right) associated with mild confusion+/-brief loss of consciousness and/or aphasia (anamnestically denied). The EEG showed fronto-temporo-central rhythmic delta activity contra-lateral to PD, lasting for 1–2 min after the end of episodes.

**Conclusion:** The family members have BFIS+/-PD, with age-related expression, fulfilling the diagnostic criteria for ICCA, which is

likely caused by disturbances both in the cerebral cortex and basal ganglia (Guerrini et al, 2001). Although neurophysiological documentations of PD are extremely rare, the current understanding is that this reflects the subcortical dysfunction and is considered distinct from reflex epilepsy (Sadamatsu et al, 1999). Our clinico-neurophysiological documentation of ICCA suggests that the cerebral cortex probably plays a role in PD's manifestations, making the boundaries between epilepsy and PD less well-defined in these patients.

### P840

#### CHANGES OF FRONTAL LOBE FUNCTIONS IN PATIENTS WITH JME

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**Purpose:** To investigate the differences of frontal lobe functions between patients with juvenile myoclonic epilepsy (JME) and healthy controls using magnetoencephalography (MEG), neuropsychological investigations and somatosensory evoked potential (SEP).

**Method:** Eighteen patients with JME and 18 age-matched non-epilepsy volunteers performed motor tasks during MEG. We used BESA software to analyze the task-related oscillatory and spontaneous MEG oscillations, compare the difference between patients and controls. Series of neuropsychological tests and SEP were also performed in these two groups.

**Results:** Patients with JME had significantly reduced pre-movement beta event-related desynchronisation in the motor task compared to controls. The regional power analysis of spontaneous MEG oscillations provided statistically significantly higher values of beta frequency in JME patients than controls in frontal and parietal brain regions. The Wechsler intelligence scale examination showed a slightly worse performance in JME patients, reaching statistical significance for picture arrangement, block design, similarities, comprehension and vocabulary. The time between N20 and P25 was statistically significantly longer in JME patients.

**Conclusion:** Altered beta event-related desynchronisation and spontaneous MEG oscillations may represent network specific dysfunction in JME patients, which may offer the potential to understand the pathophysiological basis of seizures. The poorer performance in the intelligence scale examination could indicate frontal dysfunction of JME patients.

### P841

#### IMPROVED EEG SOURCE LOCALIZATION USING A NOVEL 3D SENSOR

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**Purpose:** The novel sensor technique "Flying Triangulation" (FlyTri) enables rapid and motion-robust optical 3D scanning with a resolution of ~150 µm. Using phantom measurements and simulations, we evaluated the use of FlyTri for EEG electrode localization and coregistration with MRI. We hypothesized that this new technique enables improved source

localization in comparison to the current standard method, employing a digitization pen.

**Method:** An independent high-resolution 3D-scanning technique (FaceSCAN3D, 3D-Shape GmbH, Erlangen, Germany) was used to scan a real subject wearing a 68-channel EEG cap and create a digital 3D model. With this, a true-to-size physical model was then created via 3D printing. “True” locations of electrodes were determined using FaceSCAN3D to compensate inaccuracies of the printing process. Electrodes were then localized using a digitization pen (Fastrak, Polhemus, Colchester, VT, USA) and FlyTri. Results were compared and utilized for simulated source analysis of a low-SNR oscillatory source (source in central area, SNR of 0.05, LCMV Beamformer, Nutmeg Software).

**Results:** The digitization pen coordinates deviated from the true locations by an average of 6.6 mm, while FlyTri coordinates deviated by only 1.5 mm. Simulated source location and time course could be accurately reconstructed using FlyTri. Source analysis using pen coordinates failed and yielded a diffuse activity distribution without clear reconstruction of the oscillatory pattern.

**Conclusion:** Accurate localization of EEG electrodes is important especially for localization of low-SNR oscillations, e.g., epileptic high-frequency localizations. The FlyTri technique provides this accuracy, while the standard method seems problematic.

#### P842 HIPPOCAMPOGRAPHY AND HIPPOCAMPECTOMY IN DOMINANT LESIONAL EXTRAHIPPOCAMPAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Symptomatic lesions account for a large proportion of temporal lobe epilepsy with lesions often located outside the hippocampus in neocortex. When medically refractory, the treatment of choice is surgery. Resection usually includes the hippocampus especially if the hippocampal electrocorticogram demonstrates epileptiform abnormalities. But hippocampectomy in the dominant hemisphere entails potential risk to neuropsychological function. We sought to determine the relation between seizure freedom and findings on electrocorticography and whether hippocampal recording (hippocamptography) is helpful in determining extent of hippocampal resection.

**Method:** We conducted a retrospective chart review of clinical data, neurophysiology, neuroradiology, and pathology. Statistical significance was determined using the Wilcoxon rank sum test.

**Results:** We identified 10 patients with dominant temporal extrahippocampal lesions who underwent lesionectomy and anterior temporal lobectomy. Four patients underwent simultaneous hippocampectomy. All in the hippocampectomy group and four of six patients in the non-hippocampectomy group displayed frequent spiking on hippocamptography. Overall distribution of Engel scores was significantly better for the hippocampectomy group ( $p = 0.0201$ ) with a mean score of 1.44 compared to 2.14.

**Conclusion:** The overall distribution of Engel scores was significantly better for patients with dominant lesional extrahippocampal temporal lobe epilepsy who underwent hippocampectomy. Although our sample size lacks adequate power to assess overall value of hippocamptography, active hippocampal spiking merited resection as “frequent spikers” in the hippocampectomy group still had better clinical outcomes than patients in the non-hippocampectomy group with frequent spiking. Similarly though we lack the power to comment on the absence of spiking, our data suggest here the hippocampus may be preserved.

#### P843 IMPACT OF SLEEP ON LOCALIZING VALUE OF VIDEO EEG IN PATIENTS WITH REFRACTORY FOCAL SEIZURES – A PROSPECTIVE VIDEO-EEG- POLYSOMNOGRAPHY STUDY

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**Purpose:** To examine the role of sleep and its stages on the localizing value of video EEG in the evaluation of refractory focal seizures.

**Method:** Seventy patients with refractory focal epilepsy underwent Video-Electroencephalographic (VEEG) evaluation with additional polygraphic electrodes. Localization of Video EEG for each seizure was made based on clinical, ictal and interictal data. Seizure localization in each patient was assessed for concordance with MRI and other imaging data (SPECT, PET) for both wake and sleep seizures. Interictal discharges in sleep and wake were similarly compared for concordance with imaging data.

**Results:** A total of 608 seizures were recorded, 289 in sleep. Overall, concordance with Imaging data was found in 218 out of 322 wake seizures (67.8%) and in 157 out of 286 sleep seizures (54.8%) ( $p = 0.0314$ ). On analyzing the subset of patients with seizures recorded in both wake and sleep states (total 279 seizures recorded, 113 out of sleep), concordance was observed in 93 out of 166 (56%) wake seizures and in 80 out of 113 (70.7%) sleep seizures (OR 2.03, 95% CI 1.17 to 3.56;  $p 0.007$ ). Interictal discharges were more common and more precisely localizing in sleep, mostly in N2 stage.

**Conclusion:** This prospective VEEG-PSG study demonstrates the role of sleep vs. wake state in the localizing value of different components of long-term VEEG recording for patients with medically refractory epilepsy. Our findings show that while wake state ictal EEG has more localizing value in a mixed group of patients, sleep ictal and interictal EEG is significantly more useful in patients who have seizures recorded both during wake and sleep states. In addition, interictal discharges recorded during NREM sleep have high localizing value.

#### P844 EVALUATION OF AUTOMATIC DETECTION OF HIGH FREQUENCY OSCILLATIONS (80–450 HZ) IN MULTIPLE TYPES OF RECORDINGS

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**Purpose:** High Frequency Oscillations (HFOs) are a biomarker of epileptogenicity. Automatic detection is fundamental for its clinical application. Detection in different type of recordings is challenging. Training for each channel could provide reliable detections.

**Method:** We studied 3 min of intracranial EEG of thirteen patients (three children) from four epilepsy centers. Eight patients had depth electrodes; Five had grids. Three had intraoperative electrocorticography. Sampling rate was 2000 or 1024 Hz (two patients). HFOs and baselines (i.e. non-oscillatory segments) were visually marked. The automatic detector was trained in the first half of each channel and tested in the remaining half. Training optimized overlap between automatic detections and visual markings, while minimizing false detections. Performance, ranking of channels with respect to rate, and duration were evaluated.

**Results:** Mean performance across all 290 channels was: sensitivity =  $0.6 \pm 0.33$ , specificity =  $0.99 \pm 0.04$ , false discovery rate =  $0.4 \pm 0.28$  and kappa =  $0.52 \pm 0.34$ . Sensitivity was statistically higher for depth electrodes ( $0.72 \pm 0.27$ ) than for grids ( $0.44 \pm 0.35$ ;  $p < 0.001$ ), specificity was not statistically different (depth =  $0.99 \pm 0.02$ , grids =  $0.99 \pm 0.06$ ;  $p = 0.28$ ). Performance was not statistically different for acute and chronic recordings (Sensitivity: acute =  $0.46 \pm 0.38$ ; chronic =  $0.61 \pm 0.33$ ;  $p = 0.06$ ; Specificity: acute =  $1 \pm 0$ ; chronic =  $0.99 \pm 0.04$ ;  $p = 0.35$ ). Median ranking of channels across patients was 0.19 (range: 0.04–0.62), indicating good agreement in the channel's relevance for most patients. Duration was  $105 \pm 121$  ms for automatic,  $86 \pm 53$  ms for visual markings.

**Conclusion:** The automatic detector had good performance in all groups. Channels' order was preserved. Sensitivity was better for depth electrodes than for grids. By training each channel for a short period, this detector can be used for analysis of long sections and is useful across various types of recordings.

#### P845

##### WIDE-BAND DETECTION AND LOCALIZATION OF NORMAL HIGH FREQUENCY OSCILLATIONS IN EVOKED RESPONSE MAGNETIC FIELDS

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**Purpose:** As a prelude to understanding pathological high frequency oscillations (pHFOs) in epilepsy, we undertook a magnetoencephalography (MEG) study of normal nHFOs occurring in response to electrical stimulation of the median nerve (MN). Because pHFOs are often associated with simultaneous stronger lower frequency interictal spikes, the detection and localization of nHFOs in the MN MEG data should provide a reasonable testbed for developing a subsequent successful pHFO processing strategy.

**Method:** We devised a novel wide-band spatio-temporal method for simultaneously estimating both the stronger lower frequencies (below 80 Hz) and the weaker higher ripple frequencies, then localizing them to cortex using MEG imaging methods. To test the method, we used MN data from the same subject conducted under the same protocol, but collected from three different institutions, each representing one of the three most-widely used MEG whole-head arrays produced (Weisend et al. International Congress Series 2007:1300,615–618). Data were continuously sampled around 2000 samples per second, with the anti-aliasing filters set to nominally 1/3 the sampling rate. We processed both left and right MN data to create eight test arrays (in one instrument, we separated magnetometers from planar gradiometers).

**Results:** In seven of the eight arrays, we detected and localized the same weak nHFO of about 180 Hz (i.e. ripple frequency band) to the contralateral central sulcus, while simultaneously extracting and localizing the stronger fields generated by post-synaptic potentials, results that are consistent with the prior literature.

**Conclusion:** We demonstrated a successful strategy for extracting a simultaneous weak HFO in the presence of much stronger evoked PSP data, independent of the institution and MEG array vendor.

#### P846

##### ANALYSIS OF ICTAL MAGNETOENCEPHALOGRAPHY USING GRADIENT MAGNETIC-FIELD TOPOGRAPHY (GMFT)

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**Background:** Ictal magnetoencephalography (MEG) is useful to detect the epileptic focus, although analyzing ictal MEG with traditional equivalent current dipole (ECD) is relatively difficult. Gradient magnetic-field topography (GMFT) delineates the spatio-temporal dynamics of epileptic activities without resolution of the inverse problem. GMFT is, therefore, favorable to analyze ictal MEG despite of low signal/noise ratio. Purpose of this study is to validate the usefulness of GMFT for analysis of ictal MEG.

**Method:** We analyzed preoperative ictal MEG data by ECD and GMFT (by free MATLAB-based software, hns\_meg; <http://meg.aalip.jp/index-E.html>) on eight patients with epilepsy.

**Results:** Epileptic focus was localized by chronic intracranial electroencephalography (iEEG) in seven patients. ECD at ictal onset was localized in one, regionally scattered in 5, and failed in the rest of two cases. GMFT could analyze ictal MEGs of all patients and demonstrate the spatio-temporal changes of brain surface activities. Early activated areas above 300 femotesla/cm of gradient magnetic-field were considered as ictal GMFT onsets and the distributions were concordant with the ictal onset zone of iEEG in 7. Postoperative outcomes were Engel class I in 3, class II in 2, and class III in 3. Resection area covered ictal GMFT onset in cases of class I. In contrast, cases with residual seizures failed resection or resulted in multiple subpial transection for the area of ictal GMFT onsets in the eloquent cortex.

**Conclusion:** GMFT is useful to analyze ictal MEG and demonstrates the spatio-temporal changes of epileptic activities.

#### P847

##### DIFFERENT CLINICAL FORMS OF EYELID MYOCLONIA WITH AND WITHOUT ABSENCES: ANALYSIS OF EYELID MOVEMENTS

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**Purpose:** Eyelid myoclonia with and without absences (EMA/EM), EEG paroxysms and photosensitivity (PS) are the main features of Jeavons Syndrome (JS). EMA/EM can occur in different epileptic conditions. In JS, as a rule, is linked to the closing phase during eye closure (EC) in a light environment, suggesting a pivotal role of occipital cortices. This is a video-EEG analysis of eyelid movements in different clinical forms of EMA/EM.

**Method:** Twenty EMA/EM patients and 40 controls (20 JME/20 healthy subjects) had a Neuropsychological Video-EEG Protocol with eyelid piezoelectric sensors and blue Carl Zeiss filter lenses F-452 during photic stimulation. Blinking, eyelid opening/closing and ictal phenomena were analyzed. EMA/EM patients were classified in electroclinical groups within JS spectrum according to Covanis, 2005 and Caraballo et al., 2009. Statistical analysis was performed and p-values <0.05 were considered significant.

**Results:** Blinking rate (BR) during rest (12.8/min in healthy controls, 12.1 in JME, 9.6 in EMA/EM patients) ( $p = 0.382$ ) and closing (96.9 ms; 92.9 ms; 97.7 ms) ( $p = 0.809$ ), opening (146.9 ms; 149.3 ms; 152.0 ms) ( $p = 0.938$ ) and total time (243.8 ms; 242.2 ms; 249.7 ms) ( $p = 0.943$ ) of blinking were similar in the three groups. In EMA/EM, 10 patients had frequent limb myoclonia and 18 were

refractory to treatment (Covanis 1, 4, 5, 6 and Caraballo et al.1b and 2). Nineteen had eyelid jerk after EC with generalized spike-wave discharges (GSWD) in 12, spiky posterior alpha in three, polyspike in one and theta rhythm in one. Flutter with GSWD and jerk and flutter with and without EEG abnormalities were observed in one and three cases, respectively. PS, present in six (30%), disappeared with blue lenses in four (66%).

**Conclusion:** Despite normal physiology of blinking, EM/EMA may occur without EEG abnormalities and independently of PS, suggesting the initial participation of motor cortices in EM/EMA generation.

## P848

### NETWORK CHARACTERISTICS OF SPIKE-AND-WAVE DISCHARGE IN PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY

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**Purpose:** Epilepsy has been considered as a disorder of brain network. To study characteristics of functional network during spike-wave discharge (SWD) of juvenile myoclonic epilepsy (JME), graph theoretical analysis of network connectivity was conducted in present study.

**Method:** Sixty-four-channel EEG data were acquired from seven patients with JME. Representative epochs during spike free baseline period and SWD of 1 s were selected. The numbers of selected baseline and SWD were 140 and 98, respectively. As a measure of functional connectivity, the coherence of every electrode pair was calculated in delta (0–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (13–30 Hz), and gamma (30–55 Hz). Node degree was evaluated for varying threshold of coherence. Clustering coefficient, characteristic path length, and small-worldness were obtained using graphs constructed from coherence matrix with upper 95% threshold. The graph measures were compared between baseline and SWD.

**Results:** During SWD, node degree was increased over all frequency bands except one patient, and increasing in delta, theta and beta band was noticeable, especially. Spatial characteristic of connectivity shows that bilateral frontal region was highly involved. The characteristic path length in delta, alpha, and beta bands was significantly decreased. Clustering coefficient did not show difference between baseline and SWD. Small-worldness was slightly increased in SWD, but did not change significantly.

**Conclusion:** In our results, connectivity was increased and characteristic path length was decreased in SWD. Characteristic path length is highly related to efficiency of network. Thus, SWD may occur with pathologically efficient global circuit of JME.

## P849

### PATTERNS OF BRAIN CONNECTIVITY IN EPILEPTIC PATIENTS

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**Purpose:** To study the changes in the structure of epileptic functional brain networks before and after the seizure onset, by using

graph-theoretic analysis. We take into account the effects of volume conduction.

**Method:** Non-invasive scalp EEG is used to monitor epileptic patients for several days each, using 21 electrodes placed according to the 10/20 international system. Seizures have been identified and marked by specialized neurophysiologists. Using a sliding window, we then apply bivariate and multivariate measures of node connectivity and construct networks from 15 min before the seizure onset upto 15 min after the onset.

**Results:** Thus far five patients have been monitored, three with focal onset and two with generalized epilepsy. For three of these patients the brain network changes as follows: before the seizure onset we observed a clustered network with clusters of size approximately 10 nodes; on the other hand, at seizure onset, as well as for a period of several minutes after the seizure has ended, the network becomes significantly less connected and less clustered, where nodes now connect to only one or two neighbours. In one patient, the opposite change was observed, while for another patient no change was observed before, during, or after the seizure.

**Conclusion:** The epileptic brain network is transformed at seizure onset, not only in the number of connections, but most importantly in its structure, moving from a clustered and efficient network to a less efficient one several minutes after the seizure.

## P850

### STIMULUS AMPLITUDE EFFECT IN TIME AND FREQUENCY ON RESPONSES TO SINGLE PULSE ELECTRICAL STIMULATION IN STEREOELECTROENCEPHALOGRAPHIC STUDIES

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**Purpose:** Intracranial Direct Electrical Stimulation (iDES) is a powerful method for exploring excitability of relevant structures in patients with refractory epilepsy. Stereoelectroencephalography (SEEG), in particular, allows a 3D exploration of the epileptogenic network based on a working hypothesis. We studied responses to single pulse (SPES) to assess excitability of seizure onset zones (SOZ) vs. non-SOZ.

**Method:** We recorded responses to iDES in four subjects undergoing presurgical evaluation for temporal lobe epilepsy using SEEG. We compared the responses not only to different stimulation protocols currently used in clinical practice, but systematically explored the role of various pulse parameters in evoking responses. Effects of monophasic vs. biphasic pulses of 1–3 ms as well as intensity-response curves in the interval 0–5 mA (0.25 mA step) were studied. Trains of pseudo-random amplitude pulses having a 15 s inter-pulse interval were applied by using a programmable stimulator (Guideline LP+, FHC Inc).

**Results:** SPES showed stimulus-response curves having a quasi-linear appearance, but also exhibiting saturation at various thresholds that are correlated with the localization within SOZ or outside SOZ. Post-stimulus oscillations in various frequency bands, including HFO and fast-ripples, were observed and their dependence on the stimulus intensity exhibited both a positive and a negative correlation.

**Conclusion:** Evaluation of thresholds from stimulus-response curves as well as oscillations in various frequency bands triggered by SPES can provide valuable complementary information to recording spontaneous activity and responses to standard stimulation protocols for better defin-

ing the epileptogenic network, reducing the duration of the invasive monitoring phase.

### P851

#### THE UTILITY OF ICTAL MEG AS A COMPLEMENT TO ICTAL EEG IN EPILEPSY PATIENTS

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**Purpose:** To elucidate the additional value of ictal MEG to ictal EEG obtained during long-term inpatient scalp video-EEG (vEEG) monitoring, in epilepsy patients undergoing pre-surgical evaluation.

**Method:** We reviewed the medical records of all epilepsy patients who underwent long-term vEEG and who also had, within six months, a 1-h MEG, between February 2008 and January 2012. Our investigation focused on ictal MEG studies. The detectability, localization and concordance of ictal discharges between vEEG and MEG were analyzed.

**Results:** A total of 309 MEGs in 300 patients were examined. Of the 309 MEGs, 139 (45.0%) were done during inpatient vEEG monitoring, while 170 (55.0%) were in an outpatient setting. A total of 39 patients/studies (12.6%) had ictal MEGs, 26 (66.7%) in inpatients, and 13 (33.3%) in outpatients. Although the proportion of positive interictal MEGs is similar between inpatients and outpatients (106/139, 76.3% vs. 122/170, 71.8%,  $p = ns$ , chi-square test), the proportion of ictal MEGs is significantly higher in inpatients than in outpatients (26/139, 18.7% vs. 13/170, 7.6%,  $p < 0.01$ ), probably because antiepileptic drugs were manipulated to maximize the chance of recording seizures during inpatient vEEG. Of the 39 ictal MEGs, 25 (64.1%) were localizable using the single equivalent current dipole method; approximately half of those (14, 56.0%) could not be localized by vEEG.

**Conclusion:** Compared to vEEG studies, ictal MEGs can provide additional information about the seizure onset zone. MEG studies can therefore be especially valuable when recorded during inpatient vEEG evaluations.

### P852

#### EFFECT OF COGNITIVE STIMULATION ON HIPPOCAMPAL RIPPLES IN EPILEPTIC PATIENTS

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Interictal HFOs (ripples and fast ripples) have been repeatedly identified in recordings from depth macroelectrodes in epileptics. In contrast to fast ripples, which are believed to reflect the neuronal substrates of epileptogenicity, ripples are considered to be a signature of both normal and epileptic brain processes. The differentiation of physiological and epileptic ripples in intracranial recordings remains unavailable. We analyzed SEEG recordings in seven patients with intractable partial seizures in whom hippocampal activity was recorded in resting state and subsequently during simple cognitive task with randomly presented frequent and rare visual stimuli. Using automated detection of ripples based on length of power envelope, we analyzed potential differences in ripple rate (RR) in the cognitive vs. resting period, within epileptic (EH) and non-epileptic hippocampi (NH). Further direct impact of cognitive stimuli on

ripples (immediately after the stimulus) was investigated. Ripples have been detected within hippocampal recordings in all the investigated subjects. Mean RR in resting periods was  $11.36 \pm 8.34/\text{min}$  within EH, and  $10.13 \pm 8.75/\text{min}$  within NH. In the cognitive task periods mean RR within EH and NH decreased to  $7.16 \pm 5.75/\text{min}$ , and  $8.75 \pm 7.69/\text{min}$  respectively. The reduction of RR during cognitive stimulation was significant in EH, but not in NH. Interestingly we observed a transient suppression of ripples in both EH (slight) and NH (significant) in the first second after the stimuli onset, followed by a significant increase in RR for both EH and NH. Our results point to different reactivity of ripples within EH and NH to the cognitive stimulation.

### P853

#### SINGLE UNIT RECORDINGS DURING A VIRTUAL WATER-MAZE NAVIGATION TASK

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**Purpose:** The Morris water maze (MWM) has been used to study spatial learning and memory in rodents. Rodent models of temporal lobe epilepsy have shown that epileptic rats have a severe spatial memory impairment in tasks using the MWM. Here, we present results from a virtual analogue of MWM (vMWM) to assess spatial memory in humans with pharmacologically resistant epilepsy.

**Method:** Single units and local EEG were recorded from depth electrodes implanted in patients with pharmacologically resistant epilepsy while the patient performed in the vMWM. The vMWM was administered on a laptop computer and a gamepad controller was provided. The virtual environment consisted of a rectangular room with a cylindrical arena at the center with opaque water, surrounded by multiple distal visual cues. After habituation, subjects were dropped into arena and instructed to find a hidden platform as quickly as possible. This process was repeated 4 times per session for three sessions with a minute of rest in between followed by a probe trial.

**Results:** Performance was analyzed for six patients with epilepsy and eleven healthy controls, and showed that controls were 3.6 times (95% CI: 1.7–8.3) more likely than patients to find the platform ( $p = 0.001$ ). Single units from five patients with epilepsy were analyzed. Concurrent EEG recordings from depth electrodes have shown an increase in theta (4–7 Hz) and alpha bands (8–12 Hz) but not the delta band (1–4 Hz) during searching behavior. Unit firing was studied in relation to EEG activity and player position in the virtual environment during the task.

**Conclusion:** Following from previous work in the lab on analysis showing that performance in the virtual water maze is severely impaired in patients with epilepsy. This study presents the first examples of single unit activity in humans during vMWM.

### P854

#### SEIZURE SOURCE IMAGING BY MEANS OF DIPOLE LOCALIZATION TO DIFFERENTIATE MESIAL AND NEOCORTICAL TEMPORAL LOBE EPILEPSY

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**Purpose:** To assess the utility of computational dipolar source modelling of ictal scalp EEGs to differentiate between mesial and neocortical tem-



poral lobe epilepsy (TLE). Patients were classified as either mesial or neocortical TLE based on intracranial recording or seizure freedom after resection of hippocampal sclerosis.

**Method:** Twenty-two scalp EEG seizures from 10 patients with pharmacoresistant TLE were reviewed. Six patients with neocortical TLE underwent intracranial recordings; epileptogenic zones localized to anterior temporal pole ( $n = 2$ ) and basal temporal region ( $n = 4$ ). Mesial TLE ( $n = 4$ ) were confirmed by intracranial recordings ( $n = 2$ ) or successful temporal lobectomy. All patients had at least 25 electrodes including inferior temporal coverage. Iterative approach of simple forward low-resolution electromagnetic tomography (CLARA) models was used (BESA Research 5.3). Peaks of earliest discernible rhythmical activity were marked (median  $n = 15$ ; 5-37). The time between EEG onset and initial marked peak was average 6s; and 10s from clinical onset. A standard head model was used and source localization (ESI) was visually interpreted as temporal or extra-temporal.

**Results:** All ictal mesial TLE patterns localized to the inferior or mid-temporal region. Half of the neocortical group localized to temporal and the other half to extra-temporal regions (Fisher's exact  $P = 0.01$ ). Basal neocortical focus localized to extra-temporal region in 57% of the cases, whereas basal foci in the remaining 43%.

**Conclusion:** ESI of mesial TLE is confined to the temporal lobe. Ictal ESI to the basal temporal region may imply mesial temporal or basal neocortical focus. Extra-temporal ESI most likely indicates neocortical temporal focus suggesting rapid propagation.

## P855

### SEEING THE INVISIBLE: A SIMULTANEOUS EEG-SEEG RECORDINGS STUDY OF MEDIAL TEMPORAL LOBE INTERICTAL EPILEPTIC GENERATORS

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**Purpose:** Electrical potentials from deep epileptic generators such as medial temporal lobe structures (MTL) are known to be invisible on sole visual analysis of scalp EEG. Our aim was to assess observability of medial versus neocortical temporal lobe interictal epileptic generators based on simultaneous SEEG-EEG recordings.

**Method:** Seven consecutive patients undergoing pre-surgical evaluation of drug resistant temporal lobe epilepsy were selected from a prospective cohort of 28 patients undergoing simultaneous depth and surface EEG since 2009. Among them three were right temporal and four left temporal. Simultaneous SEEG-EEG signals were recorded on the same acquisition system using 128 channels. Intra-cerebral interictal spikes (IIS) were selected from depth EEG signals by epileptologists blinded to EEG. They were characterized and classified as medial, or lateral irritative networks. They were marked with triggers which then serve to average corresponding surface EEG segments. Averaged EEG events were finally characterized (3D mapping, duration, amplitude and statistics).

**Results:** In average, nine depth electrodes (112 recordings contacts) and 16 scalp electrodes recorded  $684 \pm 186$  IIS per patient. Overall intracerebral IIS analysis identified 21 irritative networks that were classified into three categories: mesial (hippocampal formation and collateral sulcus: M,  $n = 9$ ), mesial and neocortical (M+NC,  $n = 5$ ) and pure neocortical (NC,  $n = 7$ ). 3D scalp amplitude map of IIS showed a negative pole in the basal temporal electrodes for all three intra-cerebral networks and

a positive pole on the vertex electrodes only for M+NC and NC networks.

**Conclusion:** Deep medial temporal epileptic generators of IIS are observable on surface EEG after averaging. MTL structures are not closed electrical fields. MTL and neocortical IIS networks have a distinct scalp amplitude map.

## P856

### USEFULNESS OF VIDEO-EEG MONITORING IN CHILDREN

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**Purpose:** To analyze the sensitivity of the v-EEG for detecting clinical events and analyze therapeutic changes after the reading.

**Method:** A retrospective, descriptive study of 178 pediatric v-EEGs recordings at the Hospital Italiano de Buenos Aires from January 2011 to February 2012. The V-EEG were divided in: With epileptic clinical events, with nonepileptic clinical events and Uneventful. We analyzed the therapeutic changes. The data were analyzed using univariate statistics.

**Results:** Age was: 1 month to 17 years (median 9.1). Clinical events were recorded in 120/178 (67.4%), 81/178 (45.5%), were Epileptic and 39/178 (21.4%) non-epileptic. The sensitivity of the v-EEG divided by duration was: 6 h 71.2%, 24 h 68.9% and 48 h or more 78%. According to the age distribution the sensitivity was: 69.8% in preschoolers school, 58.97% in children and 82.14% in adolescents. The sensitivity for detection of clinical events was better in 6 hs. v-EEG in preschoolers ( $p < 0.05$ ) and in 48 hs. v-EEG in all ages ( $p < 0.05$ ). The therapeutic approach was changed in 72/178 (40.4%). AEDs were indicated in 9.75%, AEDs were modified in 63.9%, AEDs were suspended in 2.75%, epilepsy surgery was indicated in 9.75%, 9.75% were referred to mental service health and ketogenic diet was indicated or suspended in 4.1%.

**Conclusion:** The v-EEG was useful for the detection of clinical events in two thirds of the patients and the sensitivity was higher in those that lasted two days or more. The modification of AEDs was the most frequent therapeutic change.

## P857

### LATERALISING VALUE OF BARBITURATE SUPPRESSION TESTS IN CHILDHOOD EPILEPSIES

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**Purpose:** Barbiturate suppression tests have been used to determine autonomous epileptic foci. Morrell and colleagues employed methohexital suppression test (MHXT) in patients with Landau-Kleffner syndrome (LKS) to assess suitability for multiple subpial transections (MST). We report our experience with these investigations.

**Method:** Information on all patients who had intravenous barbiturate suppression tests was obtained retrospectively. Reports of the tests were categorised as clear lateralisation, weak lateralisation, no lateralisation. Other investigations including magnetoencephalography (MEG) were included.

**Results:** Thirty eight patients were included with 40 MHXTs and one amobarbital test performed at a median (range) age of 8.2 (4–17.8) years: 27 with LKS, seven with unclassified epileptic encephalopathy, three with probable Lennox-Gastaut syndrome, and one with autistic regression preceding seizures. MHXT showed clear lateralisation in 17 (44.7%) patients, weak lateralisation in three (7.9%), and no lateralisation in 18 (47.4%). Of 17 patients with clearly lateralised MHXT, eight had MST (three patients corroborated by MEG), and nine did not receive MST (three patients without lateralisation by MEG, one without spike activity during intraoperative EEG). Of three patients with weak lateralisation, one had MST (MEG showing lateralisation). Of 14 patients whose tests did not lateralise, two had MST (one showing lateralisation by MEG). Surgical decisions were influenced by the language level. One patient had electrical status epilepticus during MHXT. No other complications were seen.

**Conclusion:** Barbiturate suppression tests provided evidence of a surgical target in around half of patients and was used in surgical decision-making. MEG has been increasingly used in epilepsy surgery evaluation.

#### P858

##### UTILITY OF THE PHOTO-PAROXYSMAL RESPONSE IN CLINICAL PRACTICE AND PROOF OF CONCEPT RESEARCH; STABILITY OF THE PHOTOPAROXYSMAL RESPONSE OVER THE DAY

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**Purpose:** Photo-paroxysmal response (PPR) evaluation is important in epilepsy and EEG investigations. Change in PPR has been proposed and used in clinical practice and proof of concept trials evaluating efficacy of AEDs. The utility of the PPR as a valid test depends on the assumption of PPR stability throughout the day. However, data exist suggesting that PPR has a diurnal variability (Labate et al., 2007). Demonstration of PPR stability across the day would validate use of change in PPR as an efficacy marker.

**Method:** Adult epilepsy patients taking stable doses of up to 2 other AED's with generalized PPR's were evaluated via a standardised PPR protocol (Kasteleijn-Nolst Trenite et al., 2012) seven times during each test day; (7–9am, 9–10 am, 10–11am, 11am-12md, 1–2 pm, 3–4 pm, and 5–7 pm). All gave informed consent. Ethics approval was obtained prospectively. They were dosed with placebo plus their normal therapy or only their normal therapy on each test day. At each time point the PPR test included IPS on-eye closure, with eyes closed and with eyes open. EEG's were read blind and the resulting PPR data were standardised and recorded as "standardised photoparoxysmal responses" (SPR's). SPSSv19 and NONMEM statistical methods were utilised in data analysis.

**Results:** Ninety-eight patients with data at every time point and in all three eye conditions participated, yielding 2058 evaluable EEG PPR tests. The SPR's were plotted for each eye condition at each time point with 95% C.I.'s.

The results demonstrated that the PPR is stable across the waking day and that the on eye closure condition had the greatest repeatability.

#### Conclusion:

1: EEG PPR and SPR are not dependent on time of day; this has implications: reliably assessing epilepsy patients and for the clinical utility in the PoC Photosensitivity model.

2: Eye closure is the most reproducible PPR-test.

#### P859

##### SIMULTANEOUS RECORDING OF INTRA-CRANIAL EEG, SCALP EEG AND MEG: INITIAL CASE STUDY

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**Purpose:** Magnetoencephalography (MEG), scalp electroencephalography (EEG) and intra cranial EEG (iEEG) are measures often used for pre-surgical evaluation of intractable epilepsy. While the signal recorded in the three modalities captures the same type of neural activity, the relationship between surface and depth recordings is largely unresolved. An ideal approach to address this issue is to perform simultaneous recordings of MEG, EEG and iEEG. Here we present a case study of simultaneous recordings in these three modalities.

**Method:** The patient is a 19 year-old female patient with intractable epilepsy who underwent an iEEG implantation for pre-surgical evaluation. At the end of the evaluation, EEG electrodes were placed on the patient's scalp. Data were then acquired on a 4D BTi MEG system. The patient had both spontaneous activity and visual stimulation recorded (checkerboard). Signals were preprocessed and averaged independently for each modality. Minimum Norm (Hämäläinen et al. Med Biol Eng Comput 1994; 32:35–42) source reconstructions of MEG and EEG were compared with iEEG signal mapped on a 3D reconstruction of the SEEG electrodes.

**Results:** The averaged signals of the three modalities have similar morphology both for evoked response and epileptiform discharges. At the source level, the localizations (MEG and EEG) show patterns that are compatible with the spatiotemporal patterns recorded on iEEG.

**Conclusion:** We show that there is good concordance between scalp and depth signals. This establishes the validity of the MEG and EEG data recorded simultaneously with intra-cranial EEG, and opens a number of perspectives for exploring the origin of these signals.

#### P860

##### INFRAFLOW ACTIVITY AND ICTAL ONSET BASELINE SHIFTS: REPORT OF FIVE PAEDIATRIC CASES

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**Purpose:** Infraslow activity (ISA) has been found to be helpful to localize ictal onset region in adult epileptic patients. There are no reports

of infraslow activity in children with epilepsy undergoing pre-surgical scalp and intracranial monitoring. The purpose of the study was completed to assess the ictal baseline shifts and infraslow activity in five consecutive children who underwent epilepsy surgery.

**Method:** A retrospective EEG analysis was completed of five children who underwent conventional prolonged video LTM-EEG and subsequently underwent successful resective epilepsy surgery. ISA and ictal shifts were identified using previously recommended settings with 0.016 Hz, 0.1 Hz, 0.2 and open pass filters respectively. A total of twenty six seizures were analyzed.

**Results:** The recorded analyzed seizures had over 90% correlate demonstrated by a clear ictal baseline shift and clear identifiable localized infraslow activity that was demonstrated with the recommended filters settings, and not identifiable with conventional frequency band (CFB) analysis.

**Conclusion:** Identification of infraslow activity and ictal onset baseline shifts can be easily achieved in children undergoing evaluations for Epilepsy surgery. Current modern amplifiers allow accurate analysis during scalp and intracranial EEG recordings, specifically applying using protocols that use infraslow activity.

#### P861 COMPARISON OF PHOTOPAROXYSMAL RESPONSES DURING INTERMITTENT PHOTIC STIMULATION WITH INCREASING AND DECREASING FREQUENCIES

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**Purpose:** Intermittent photic stimulation (IPS) is one of the provocation techniques in electroencephalography (EEG). IPS is often used to diagnose especially the photosensitive epilepsies. Recently, a critical review has been published about standardization of IPS since it is known there is great diversity in methodology between centers. One of the recommendations is to go up in frequencies from 1 to 60 Hz and then go down. In this study, we want to investigate the photoparoxysmal responses in terms of density and duration during increasing and then decreasing frequencies.

**Method:** Photosensitive patients with idiopathic generalized epilepsy (IGE) were included. We used the 1-2-8-10-15-18-20-25-40-50-60 flash frequencies in every patient followed by the same frequencies in reverse order. All photoparoxysmal responses were calculated during the go up and go down parts and then compared.

**Results:** Twenty patients fulfilled the criteria for IGE with photoparoxysmal responses. Number of the responses was significantly lower during increasing frequencies than the decreasing part ( $1.62 \pm 0.53$  vs.  $3.12 \pm 0.63$ ,  $p < 0.001$ ). Similarly, the duration of the responses was significantly higher when to use IPS as a second time ( $2.62 \pm 0.70$  vs.  $7.37 \pm 2.08$ ,  $p < 0.001$ ).

**Conclusion:** The data provides evidence that longer photic stimulation reduced the threshold of photoparoxysmal responses. On the other hand, down going frequencies might have a superior effect on generating the discharges but this hypothesis needs further investigation.

#### P862 PHOTOSENSITIVITY AND CARDIOVASCULAR ABNORMALITIES

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**Purpose:** To explore potential cardiac interactions in photosensitive patients.

**Method:** Preliminarily, 18 patients with photosensitive epilepsy were identified on retrospective chart review. Reports of EKG rhythm were noted; available EEGs and charts were reviewed for any evidence of cardiac arrhythmias or other abnormalities.

**Results:** Of 10 males, eight females ranging from 13 months to 79 years (median age 24.4 years), at least nine had either EKG abnormalities or clinical changes reported. These ranged from sinus bradycardia/tachycardia or PVCs or skipped beats to heart rate variability, orthostatic hypotension and one patient who came in with asystole and ventricular fibrillation. Confounding factors included histories of cardiac disease and medications. AEDs included topiramate, levetiracetam, carbamazepine, trileptal, depakote, lamotrigine. Detection of an association with photoparoxysmal response was not possible in this sample. With our large existing sample from previous studies we are further exploring relations between our photosensitive patients and EKG/cardiovascular abnormalities.

**Conclusion:** Previous studies demonstrated that arrhythmias/repolarization abnormalities occur frequently in refractory epilepsy. Others noted that right vs. left temporal lobe seizures can lead to tachycardia vs. bradycardia, and that both epilepsy and AEDs can alter autonomic function in epileptic patients. Carbamazepine has been associated with decreased heart rate responses to deep breathing; phenytoin and valproic acid have not. Investigation into cardiac rhythms in epileptic patients is necessary, and may inform about SUDEP. Photoparoxysmal discharges frequently involve the temporal lobes; programmed heart rate/rhythm monitoring in patients may be helpful. Caution is recommended in history of cardiac disease or temporal lobe seizures.

### Poster Session: Epidemiology Wednesday, 26 June 2013

#### P863 IS PARENTAL CONSANGUINITY A RISK FACTOR FOR EPILEPSY? A CASE CONTROL STUDY ASSESSING EPILEPSY RISKS IN SOUTHERN SAUDI ARABIA

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**Purpose:** To evaluate the role of parental consanguinity (PC) as a risk to develop epilepsy.

**Method:** This is a case-control study, matched for age and sex, conducted among Saudi population in the city of Abha, between January and December of 2012. Data of the epilepsy group was obtained from the epilepsy registry, which was compared to none epileptic control seen for reasons other than epilepsy. Enquiries about the presence or absence of PC (a union between a couple related as second cousin or closer) and family history of epilepsy (FHE) were obtained for both groups.

**Results:** 1086 cases were studied, 543 in each group. Mean age was 27 years (range; 13–85, SD = 13.2 years). There were 536 men (49%). 1st degree PC was significantly seen less in epileptic patients (13 vs. 18%,  $p < 0.05$ , OR = 0.7, 95% CI: 0.5–0.9), while 2nd degree PC increased the risk of epilepsy more than 2 times ( $p < 0.05$ , OR = 2.01, 95% CI: 1.3–3.0). Yet, PC (both degrees) was seen equally in both groups (27 vs. 26%). FHE was significantly seen in epileptic patients (26 vs. 20%,  $p < 0.5$ , OR = 1.4, 95% CI: 1.1–1.9). Multivariate regression anal-

ysis showed that men with 2nd degree PC are three times more likely to have epilepsy ( $p < 0.05$ , OR = 3.0, 95% CI; 1.5–5.8), followed by patients with FHE ( $p < 0.05$ , OR = 1.5, 95%CI; 1.2–2.0).

**Conclusion:** Only the 2nd degree PC increased the risk of developing epilepsy in our population, and when observed in men, has high probability of predicting epilepsy. The heterogeneous etiologies and genetic basis of epilepsy may explain the identified association with PC, but the apparent protective effect of 1st degree PC may be related to avoidance of this type of marriage in families with an epileptic member, probably because of the social stigma of epilepsy.

#### P864

##### EARLY RECURRENT SEIZURES AND DEATH IN HIV+ ZAMBIAN ADULTS WITH NEW ONSET SEIZURE

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**Purpose:** To evaluate the incidence of and risk factors for early seizure recurrence and death in HIV+ adults with new onset seizure.

**Method:** Adults with seizures presenting to Zambia's University Teaching Hospital were screened. Inclusion criteria included being HIV+, having the index seizure in the past 2 weeks, no other seizure history, Karnofsky >50, and consent for lumbar puncture (LP). Risk factors for early mortality and/or recurrent seizures were assessed.

**Results:** In 16 months, 244 patients were screened with 167 being HIV+. Twenty-three died before enrollment. Exclusions included 39 with Karnofsky <50, 38 with prior seizures, and 13 refused LP. Forty-six patients enrolled. Age and gender did not significantly between the enrolled and the eligible. Mean CD4 count was 173 (median 119). Seizures were usually <5 min ( $n = 21$ ; 45%). Focal onset seizures were common ( $n = 17$ ; 37%). Ten participants (22%) had status epilepticus. CSF studies identified JC virus ( $n = 3$ ), CMV ( $n = 2$ ), EBV ( $n = 11$ ), VZV ( $n = 2$ ), and TB ( $n = 2$ ). During follow-up, 8 (17%) died and 7 (15%) had recurrent seizures. No risk factors for recurrent seizure were identified. Female gender was a risk factor for death (30.4 vs. 5.6%;  $p = 0.03$ ), but status epilepticus, CD4 count, and WHO clinical stage were not.

**Conclusions:** HIV+ Zambian adults with new onset seizure have a high risk for recurrent seizure and early mortality. Within the limited power of this study, known risk factors for early HIV mortality and for recurrent seizures in other populations were not found to be risk factors in this population.

#### P865

##### PREHOSPITAL EPILEPSY EMERGENCY SCORE (PEES) FOR DIFFERENTIAL DIAGNOSIS IN EMERGENCY CARE

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**Purpose:** The prehospital emergency management of the clinical phenomenon "convulsive fit" often poses a diagnostic dilemma. It is often not

possible to distinguish between epileptic or psychogenic seizures, syncope or TIA. Structured instruments for the documentation of the incident as reported by witnesses are rarely provided. Therefore, the goal is to develop and evaluate a simple prehospital epilepsy emergency score (PEES). The primary question is whether PEES can be used to differentiate between syncope and seizure.

**Method:** Eight participants are shown four videos, each showing a syncope and three different types of seizure (simple partial seizure (clonic), complex partial seizure, partial seizure evolving to secondary generalized tonic-clonic seizure (ILAE 1981 IA, IB, IC)). The examiner then questions the participants 0, 15 and 60 min after watching the videos, using the PEES. Cut-off:  $\leq 5$ : Syncope.

**Results:** PEES Syncope ( $n = 8$ ) mean: 3.6 (SD 1.7) PEES Seizure IA: mean: 8.6 (SD 0.7); Seizure IB: mean: 8.2 (SD 1.1); Seizure IC: mean: 10.2 (SD 1.1).

PEES after 0 min. 15 min. 60 min.

Syncope ( $n = 8$ ): mean: 3.6 (SD 1.2), 2.6 (SD 1.0), 3.1 (SD 1.3).

Seizure IA ( $n = 8$ ): mean: 8.6 (SD 0.7); 8.2 (SD 0.4); 8.8 (SD 0.8)

Seizure IB ( $n = 8$ ): mean: 8.2 (SD 1.1); 7.8 (SD 1.2); 7.7 (SD 1.8)

Seizure IC ( $n = 8$ ): mean: 10.2 (SD 1.1); 10.5 (SD 1.5), 10.6 (SD 1.7)

**Conclusion:** Pre-evaluation of the PEES has shown that the key clinical characteristics of syncope and epileptic seizures have been registered using the PEES. The  $\geq 5$  cut-off appears suitable for distinguishing between syncope and seizure. Whether the subject is questioned 0, 15 or 60 min after the incident does not seem to have a relevant influence on the result. A continued study has been initiated and further results will be presented soon.

#### P866

##### PREVALENCE AND RISK FACTORS FOR ACTIVE CONVULSIVE EPILEPSY IN SUB-SAHARAN AFRICA: CROSS-SECTIONAL AND CASE CONTROL STUDIES

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**Purpose:** The prevalence of epilepsy in sub-Saharan Africa (SSA) appears to be higher than in other parts of the world, but there is considerable heterogeneity in the estimates. The causes of the higher prevalence and heterogeneity are unknown. We determined the prevalence and risk factors of active convulsive epilepsy (ACE) across five centres, members of the INDEPTH Network in SSA.

**Method:** We surveyed 586 607 people using a three-stage cross-sectional screening process to identify people with ACE. Risk factors for ACE were identified from 1711 cases and 2033 age-matched controls randomly selected using census data from the five centres. Odds ratios (OR) and population attributable fractions were estimated using logistic regression, adjusted for age, sex, education, employment and marital status.

**Results:** There was significant heterogeneity in prevalence between centres and different age groups within centres. Adjusted centre-specific prevalence estimates ranged from 7.0/1000 (95% CI 6.2–7.4) in South Africa to 14.8/1000 (13.8–15.4) in Tanzania. Prevalence varied by age and sex in two centres, but only with age in the other three centres.

In children, ACE is associated with adverse peri-natal events (OR = 10.23, 95% CI 5.85–17.88), ante-natal problems (OR = 2.15, 95% CI 1.53–3.02) and, head injury (OR = 1.97, 95% CI 1.28–3.03), with 33% attributable to ante-natal and peri-natal risk factors. In adults ACE is significantly associated with malaria, toxocarriasis, toxoplasmosis and onchocerciasis, and together these parasites accounted for 35% of adult cases. Hypertension (OR = 2.13; 95% CI: 1.08–4.20) and cysticercosis (OR = 7.03; 95% CI: 2.06–24.00) were risk factors for late onset epilepsy.

**Conclusion:** We found significant heterogeneity in prevalence in SSA, using a standardized methodology. This could be explained by the differences in the prevalence of risk factors between these centres. Programmes to control parasitic diseases and interventions to improve antenatal and peri-natal care may substantially reduce the prevalence of epilepsy in SSA.

#### P867

##### THE EPILEPSY REGISTER IN TIBET, CHINA AND A RELATED EPIDEMIOLOGICAL SURVEY

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**Purpose:** There is a large treatment gap (97%) and patients had very poor quality of life in the Tibet Autonomous Region (TAR) according to our previous survey. In order to provide better medical service for these patients, we tried to establish a hospital-based epilepsy register there. We also performed a further epidemiological survey based on this programme, to evaluate the feasibility of the ongoing register.

**Methods:** We carried the register in the hospitals of Lhasa, Chamdo, Nyngtri and Shigatse. Trained local primary health care physicians carried out screening, treatment, and follow-up. Semi-structured seizure screening questionnaire was used, and those screened positive filled the TAR epilepsy register form. The further epidemiological survey was done in Shigatse as we did in 2006.

**Results:** This Hospital-based registers was conducted from April 15th, 2009 to December 31st, 2012. A total of 234 patients was registered, including 14 in Chamdo, 0 in Nyngtri, 26 in Shigatse, and 194 in Lhasa. From July 1st to July 28th, 2009, a total of 14811 people are screened in Shigatse, and 56 patients were confirmed to have epilepsy. The rough prevalence rate was 3.8‰ (95% CI: 1.1–6.5) and GTCS was the most common form. The most frequent used drugs were phenobarbital and phenytoin.

**Conclusion:** We confirmed the prevalence rate is related lower in TAR (nearly 3‰). However, fewer patients came to see a doctor in the hospital. Because of the relative absence of specialist-trained medical staff in this region, the use of new AEDs is rare in the local hospital. It calls for medical, financial, and social support in this population.

#### P868

##### PREDICTING THE PRESENCE OF FAMILY HISTORY OF EPILEPSY IN PATIENTS WITH EPILEPSY

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**Purpose:** To identify predictors of genetic epilepsy through the presence of family history of epilepsy (FHE) in epileptic patients.

**Method:** This is a one-year retrospective study conducted in Aseer central hospital in Abha, Saudi Arabia from December 2011 to January 2013, where adults with epilepsy registered in our registry were included. Detailed history of epilepsy and epilepsy risk factors were obtained, including the presence of FHE. EEG and high resolution MRI of the brain were performed for most of the patients. Epilepsy classification and etiology were determined. Multivariate regression analysis was performed to predict the presence of FHE.

**Results:** Six hundred and forty patients with epilepsy were included in this study. Mean age of patients was 27 years (SD = 14 years, range: 13–85 years). There were 328 men (51%). Idiopathic was documented in 194 patients (31%), symptomatic in 232 (36%) and cryptogenic in 214 (34%). 165 cases (26%) had FHE. EEG was abnormal in 443 patients (70%) and only 186 patients had an abnormal brain MRI (29%). Regression analysis showed that the presence of temporal atrophy on MRI (with/without mesial temporal sclerosis, MTS) and focal EEG discharges increased the likelihood of having a family member with epilepsy by more than two times (OR = 2.4, and 2.1 respectively,  $p < 0.05$ , 95% CI = 1.4–3.4, and 1.1–5.5), more so than idiopathic epilepsy (OR = 1.7,  $p < 0.01$  95% CI = 1.1–2.7) or young age at the disease onset (OR = 0.97,  $p < 0.01$ , 95% CI = 0.96–0.99).

**Conclusion:** MRI features of temporal lobe epilepsy, along with a focal EEG discharges had a highest prediction of having a family member with epilepsy, which may suggest the presence of familial partial epilepsy, and temporal lobe epilepsy in particular. Idiopathic epilepsy and younger age at presentation were still significant predictors of FHE, which are known to be associated with genetic epilepsy.

#### P869

##### CANADIAN LONGITUDINAL STUDY OF AGING-EPILEPSY ALGORITHM: A PROPOSED TOOL FOR DETECTING EPILEPSY IN POPULATION-BASED STUDIES

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**Purpose:** Estimation of the prevalence and incidence of epilepsy in the absence of physician assessment is challenging. In Canada, the incidence of epilepsy remains unknown while the estimated point prevalence in two reports is based on a single question to screen for epilepsy. The Canadian Longitudinal Study of Aging (CLSA) is a nationwide population study of 50,000 people aged 45–85 years at baseline. We anticipate that the CLSA will include ~1500 subjects with a history of epilepsy, based on available age-specific cumulative incidence estimates. The proposed CLSA-Epilepsy Algorithm (CLSA-EA) aims to serve as an effective tool for the detection of epilepsy in any population-based cohort.

**Method:** The CLSA-EA includes: a self-reported history of epilepsy and antiepileptic medication use; a questionnaire based upon a previously validated nine-item screening tool; and a final component to distinguish lifetime prevalence of epilepsy from that of active epilepsy (defined as any seizure within the last five years and/or continued use of antiepileptic medication). Epilepsy will be defined as probable, suspect or absent. The CLSA-EA, administered by a non-physician, will be validated using a sample of CLSA participants with a blinded epileptologist's clinical assessment as the gold standard.

**Results:** The predictive value of the CLSA-EA as a disease ascertainment algorithm for epilepsy will be the primary outcome of the validation study.

**Conclusion:** It remains important from a clinical, epidemiologic and public policy perspective to accurately ascertain the incidence and prevalence of epilepsy in population-based cohorts. We have proposed an algorithm to detect epilepsy in such populations.

#### P870

##### LONG-TERM MORTALITY IN POOR HEALTH AND LOW INCOME AMERICANS WITH EPILEPSY

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## Abstracts

**Purpose:** To assess long-term mortality and cause of death in poor health and low-income persons with epilepsy (PWE).

**Method:** We performed a retrospective dynamic cohort study using Ohio Medicaid claims data linked with Ohio death certificates. PWE were identified between 1992 and 2008 and followed until the date of death or the end of 2008 ( $n = 68,785$ ). Comorbid conditions were identified at the time of death or the last date of follow-up.

**Results:** There were 12,630 deaths during the median follow-up of 9 years (IQR, 5–15 years). The age-race-sex adjusted mortality rate (MR) was 18.6/1000 person-years with standardized mortality ratio (SMR) of 6.18 (95% CI, 6.05–6.27). The risk of premature death was significantly elevated throughout 16 years of follow-up with the highest mortality during the second year after diagnosis and the lowest mortality during the sixteenth year of follow-up. Among all comorbid conditions, PWE who had metastatic cancer had the highest death rate (MR 141.3/1000 person-years) and PWE who had schizophrenia had the lowest mortality (MR 18.6/1000 person-years). Cardiovascular diseases (proportionate mortality ratio (PMR) 17.6%), cancer (PMR 12.6%), and unintentional injury (PMR 7.4%) were common causes of death in adults Medicaid beneficiaries with epilepsy. Compared to the general population, Medicaid individuals with epilepsy had substantially greater risk of death from pneumonia (SMR 23.1, 95% CI 21.3–24.9), malignant brain tumor (SMR 17.6, 95% CI 15.8–19.5), and drowning (SMR 10.9, 95% CI 8.2–14.2).

**Conclusion:** Poor health and low income PWE carry a substantial risk of premature death. Most deaths are related to comorbid conditions rather than epilepsy-related causes. Funded by the Epilepsy Foundation, the CWRU/CCF CTSA, and the AHRQ.

## P871

## EPILEPSY PREVALENCE IN ADANA CENTRUM

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**Purpose:** Epilepsy is an endemic illness that can be kept under control with a suitable treatment. In this study, we aimed to determine the epilepsy prevalence in Adana centrum.

**Method:** In this study, three districts have been identified in the center of Adana city and the method of random sampling was used in a way so that the sociocultural level of the whole society (upper, middle, and lower) is reflected. Our target population, that needed to be scanned by using the formulas used in epidemiological studies, has been calculated ( $n = 7,052$  people).

**Results:** After the interviews of a total of 7,052 people (aged 0–100), 52 epilepsy patients were identified. Active epilepsy prevalence was found to be 0.7%. Considering the socioeconomic situation, the rate was found to be 1.4% for the lower socioeconomic group, 0.7% for the middle group and 0.3% for the upper group. For the people who were not born in Adana, epilepsy prevalence was 2.29 ( $p = 0.002$ ) times more than those who were born in Adana. (In all of these findings, the OR's have been given being corrected in accordance with the ages and epilepsy prevalence was 95% more).

**Conclusion:** After this study, the results we obtained were similar to the results obtained from other studies done in our country and around the world. As the socioeconomic condition increases, epilepsy prevalence decreases.

## P872

## A SYSTEMATIC REVIEW OF SCREENING TOOLS FOR THE IDENTIFICATION OF SUBJECTS WITH EPILEPSY IN POPULATION-BASED RESEARCH

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**Purpose:** The identification of those with epilepsy within population-based cohorts is a challenge. The primary goal of this systematic review is to identify and evaluate existing questionnaires that may be applied in population-based cohorts to identify participants with epilepsy. This review is pertinent in light of the recently launched Canadian Longitudinal Study of Aging, an ongoing nationwide population study of 50,000 people aged 45–85 years at baseline.

**Methods:** Our search will include studies that detail the development or critical assessment of questionnaires designed to screen adult subjects for epilepsy. We will include questionnaires that may be administered by non-physicians in-person or by telephone. Only published studies, in English or French, will be included. We will search MEDLINE and EMBASE (January 1946 to present; search terms: epilepsy, seizures, questionnaires, mass screening and health surveys) as well as the bibliographies of identified studies. Two reviewers will independently assess all identified studies. The kappa statistic will be reported and disagreements will be settled by consensus.

**Results:** A brief description of each eligible screening questionnaire will be presented. We will describe the questionnaire's components, the population(s) in which it was validated (including number of participants and their mean age as well as the details of any comparator group (including the gold standard) and its reported validity and/or predictive value. The quality of each eligible study will be assessed using the QUADAS-2 quality assessment tool.

**Conclusion:** The proposed systematic review will summarize and evaluate existing screening questionnaires to identify population-based subjects with epilepsy.

## P873

## COMORBIDITIES AND GROUP COMPARISONS OF EPILEPSY-CAUSED MENTAL DISABILITY IN CHINA

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**Purpose:** To estimate the prevalence of comorbidities with epilepsy-caused mental disability (EMD) which is the third leading cause of mental disability in China, and to identify vulnerable Chinese subgroups.

**Method:** The second China National Sample Survey on Disability was used to identify people with EMD based on the WHO International Classification of Functioning, Disability, and Health and the International Statistical Classification of Diseases. Logistic regressions were used to compare comorbidities by sex, age, community, and region.

**Results:** A total of 1,490 respondents were diagnosed with EMD, which was more prevalent in rural communities, in the western region, and among younger people. Brain diseases and organic mental disorders were the most prevalent comorbidities with EMD. Children and people of the eastern region were more likely to have comorbidities with other chronic brain diseases.

**Conclusion:** This understanding of the detailed epidemiology of comorbidities of EMD reveals the vulnerability of children and of people living in rural areas and in the western region of China. The prevalence of comorbidities associated with EMD revealed in this study demonstrates a substantial health burden for individuals with EMD, especially children. And the effect on epileptic and comorbid children demonstrates that extra attention is required for practical and theoretical epilepsy-related services for affected children.

P874

### PREVALENCE AND TREATMENT GAP OF ACTIVE CONVULSIVE EPILEPSY: A LARGE COMMUNITY-BASED SURVEY IN RURAL WEST CHINA

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**Purpose:** Active convulsive epilepsy (ACE) impacts patients greatly, especially in low-income countries where patients do not receive appropriate treatment. In the present study, we measured the prevalence and treatment gap (TG) of epilepsy in rural West China.

**Method:** Six rural areas in West China that have a total population of 3,541,319 were selected to conduct prevalence and TG estimates of ACE via a clue survey. Questionnaire-based interviews were used for the identification of ACE patients, and information was obtained during the survey. TG refers to the ratio of the number of patients with ACE who are not receiving appropriate treatment to the number of all patients with ACE screened in the month prior to identification.

**Results:** A total of 6,547 patients with ACE were identified. The estimated prevalence of ACE was 1.8 per 1,000 in the general population, with the prevalences in males and females determined to be 2.0 and 1.7, respectively ( $p < 0.001$ ). The TG in the general population was 66.3%, and it was 66.6% and 66.0% in males and females, respectively ( $p > 0.05$ ). Prevalence increased as age increased, peaking (2.7 per 1,000) during the period between 30 and 39 years old and then declining gradually to 0.4 per 1,000 in the elderly ( $\geq 80$  years old). The TG figures dropped with advancing age and increased above 30 years of age. Additionally, only 63.9% of the ACE patients included in the study were aware of the disease and had consulted a doctor.

**Conclusion:** We found that numerous patients with ACE failed to see a doctor and even those consulting a doctor did not receive or adhere to an appropriate treatment program, which reflects the need for public education as well as for the training of local physicians.

P875

### PREVALENCE OF DEPRESSION AND ITS IMPACT ON QUALITY OF LIFE IN PATIENTS WITH REFRACTORY FOCAL EPILEPSY (IMDYVA STUDY)

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**Purpose:** Drug-resistant epilepsy (DRE) is usually related to focal epilepsy (FE) and its prevalence is up to 30%. While several studies have found a high rate of depression and poor health related quality of life (HRQL) in DRE patients, there is little information about its rate in the Spanish population. The aim of our study was to identify the prevalence of depression and assess quality of life in patients with DRE compared to controlled epilepsy (non-DRE) in a Spanish cohort.

**Method:** Observational, cross-sectional study in outpatient clinics assessing depression (Montgomery-Asberg Depression Rating Scale, MADRS; Beck Depression Inventory-II, BDI-II) and HRQL (Quality of Life in Epilepsy Inventory, QOLIE-31) in patients with FE with and without DRE.

**Results:** One hundred and thirty investigators included 515 patients (DRE = 248), mean (SD) age 44.3 (15.4) years, 50.5% male. Overall 15.9% had a previous diagnosis of depression (DRE = 22.6%; non-DRE = 9.7%,  $p < 0.001$ ). Prevalence [CI] of depression as per corrected MADRS and BDI-II was 32.6% [27.0–38.2] and 37.2% [31.4–43.0] for non-DRE vs. 62.1% [56.1–68.1] and 64.8% [58.8–70.7] for DRE patients ( $p < 0.001$ ). Depression was associated with poorer mean (SD) QOLIE

31 scores: 46.9 (18.5) vs. 65.4 (18.1) ( $p < 0.001$ ). Mean (SD) QOLIE-31 scores were directly related to the presence or absence of depression.

**Conclusion:** Compared to other studies the rate of depression was high (60% in DRE and 30% in non-DRE patients). MADRS and BDI-II showed a positive correlation. Prior to the study, depression remained underdiagnosed in a large proportion of patients. Clinical diagnosis of depression was associated with poorer mean QOLIE-31 scores.

P876

### EPILEPSY: ANALYSIS OF NUTRITIONAL STATUS AND SERUM VITAMIN D LEVEL (VIT D)

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**Introduction:** In France, the number of people with epilepsy (PWE) is estimated to 500000. Their nutritional status is poorly studied. Impaired nutritional status might play a role in the response to treatment. Vit D might be involved in some forms of epilepsy.

**Purpose:** The main purpose of this study was to describe the nutritional status of patients with epilepsy and analyze their serum vit D level.

**Method:** After consent, 46 PWE with or without drug resistance benefited from a nutritional assessment. Weight, height, body mass index (BMI), waist circumference, triceps skinfold (TS), biceps, supra-iliac, subscapular skinfolds, arm circumference, fat mass (FM) and fat-free mass (FFM) by bioimpedance were measured. The dosage of serum vit D was realized before supplementation (deficiency  $< 30$  ng/ml). Statistical analysis used Student's t test,  $\chi^2$  and ANOVA.

**Results:** The mean age was  $44.5 \pm 14.3$  years, with a sex ratio M/F of 1.3. 60.9% were drug-resistant. BMI was  $28.7 \pm 7.0$  kg/m<sup>2</sup>, with 2.2% of malnourished and 30.4% obese. Vit D concentration was  $15.3 \pm 9.9$  ng/ml with 87% of deficient patients, and 40% with severe deficiency ( $< 10$  ng/ml). The TS was higher in the drug-resistant group ( $p = 0.03$ ). There was no link between drug resistance and nutritional status, other skin fold measures, FM, FFM and vit D level.

**Discussion/Conclusion:** The number of PWE was low, but the study shows that they are rarely malnourished. However, studies focused primarily on clinical cases or African populations. Obesity is common in PWE, possibly iatrogenic and should be deeply studied. Vit D deficiency is very common, often severe, but as nutritional status, seems not playing on the drug-sensitivity of patients studied.

P877

### SOMATIC CO-MORBIDITIES OF EPILEPSY: WHAT ARE THE RISK FACTORS?

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**Purpose:** People with epilepsy seem to have more concomitant medical conditions when compared to the general population. The burden of somatic co-morbidities probably plays an important role in premature mortality remote from epilepsy onset. The relation between somatic co-morbidities and epilepsy remains unclear; several biases exist (causes and treatment of epilepsy).

**Methods:** We collected clinical, demographic and somatic co-morbidity data in over 2016 consecutive people with epilepsy assessed at a referral

centre and in 1297 patients with epilepsy in the community. Underlying causes of epilepsy were not taken as co-morbidities, neither were symptoms of the cause (e.g. hemiparesis in a person with stroke as the cause of epilepsy).

**Results:** Somatic co-morbidities were found in 49% of people at the referral centre and in 35% in the community. Consistent risk factors were found in both cohorts. In a multivariate ordinal regression, older age, shorter epilepsy duration, and absence of underlying brain lesion were independently associated with an increased burden of somatic conditions. Shorter epilepsy duration was a predictor for metabolic, digestive, and musculo-skeletal conditions at the referral centre and for neoplastic, circulatory, and nervous conditions in the community.

**Conclusion:** There are predictors of the burden of somatic conditions in epilepsy. Independently from age, the early period after epilepsy onset appears to be at particular risk, possibly improving subsequently or alternatively leading to a premature mortality. The increased burden of somatic co-morbidities in people without a clear underlying brain lesion could suggest a less favourable genetic background in those people. Further studies are needed.

#### P878

##### EPIDEMIOLOGIC PROFILE OF ACUTE SYMPTOMATIC SEIZURES IN THE MEDICAL WARDS OF A TERTIARY HEALTH FACILITY IN SOUTHEAST NIGERIA

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Acute symptomatic seizures are seizures occurring in close temporal relationship with an acute central nervous system (CNS) insult. Data on the epidemiology of acute symptomatic seizures are sparse in Africa. We aimed at determining the frequency and the causes of acute symptomatic seizures among medical admissions in a tertiary health institution in Southeast Nigeria. It was a two year retrospective study of medical files of patients admitted into the medical wards of the Nnamdi Azikiwe University Teaching Hospital Nnewi between January 2005 and December 2006. During the period under review, there were 94 patients with acute symptomatic seizures (males: 49 (52.1%), females: 45 (47.9%)) accounting for 5.2% (94/1802) of medical admissions. The patients' age range was 18–84 years with a mean age of  $51 \pm 16$  years (males:  $49.8 \pm 16$ ; females:  $53.7 \pm 15.7$ ). The causes of acute symptomatic seizures were CNS infections accounting for 36.2% (n = 34), acute stroke 29.8% (n = 28), metabolic abnormalities 12.8% (n = 12), encephalopathy 10.6% (n = 10) and others 10.6% (n = 10). Those aged below 49 years accounted for 70.6% of CNS infections while those aged 50 years and above accounted for 82.1% of acute stroke. CNS infection and acute stroke were the prominent causes of acute symptomatic seizures. This is an evidence of the double tragedy facing developing countries, the unresolved threat of infectious diseases on one hand and the increasing impact of non-communicable diseases on the other.

#### P879

##### TEMPORAL TRENDS OF PEDIATRIC EPILEPSY SURGERY IN THE USA: 1997–2009

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**Purpose:** Despite clear guidelines for referral of patients to epilepsy surgery, no changes in epilepsy surgery have been detected in the adults with epilepsy. Our study aims to study the rate of epilepsy surgery in children age 0–17 years.

**Method:** Data from the Kids Inpatient Database was used to identify the number of epilepsy surgeries from 1997 until 2009. Data analyzed included number of surgeries per age group, gender, race and primary payer. Rate of epilepsy surgery was calculated based on published prevalence estimates of pediatric epilepsy.

**Results:** Number and rate of epilepsy surgery increased from 1997 to 2009. Number (rate/1000/year) of pediatric epilepsy surgeries were 375 (0.83/1000/year) in 1997, 410 (0.87/1000/year) in 2000, 589 (1.24/1000/year) in 2003, 683 (1.43/1000/year) in 2006 and 706 (1.48/1000/year) in 2009. Rate changes from 1997 to 2009 were consistent across all age group (age 0–4: 1.17/1000/year in 1997 to 1.85/1000/year in 2009; age 5–9: 0.86/1000/year to 1.89/1000/year; age 10–14: 0.51/1000/year to 1.15/1000/year; age 15–17: 1.07/1000/year to 1.37/1000/year), gender (male: 0.72/1000/year to 1.26/1000/year; female: 1.02/1000/year to 1.81/1000/year), race (white: 0.64/1000/year to 1.20/1000/year; black: 0.33/1000/year to 0.62/1000/year; Hispanic: 0.43/1000/year to 1.67/1000/year) and primary payer (Medicaid: 0.40/1000/year to 0.71/1000/year; private insurance: 1.05/1000/year to 2.03/1000/year).

**Conclusion:** Rate of change in pediatric epilepsy surgery in USA increased from 1997 to 2009 across all pediatric demographic and payer categories, indicating increased awareness among health professionals of the benefits of early epilepsy surgery. Rates of epilepsy surgery remained significantly lower for black children and those on Medicaid indicating persisting disparity.

#### P880

##### OBESITY AND EPILEPSY: POSSIBLE FACTORS AFFECTING CO-MORBIDITY

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**Purpose:** Obesity is a serious and growing health risk. Brain regions involved in eating behavior are among the more epileptogenic sites, raising a question of whether people with epilepsy (PWE) might be at increased risk of obesity. The possibility that epilepsy might be associated with a sedentary lifestyle suggests a second risk factor.

**Method:** We administered questionnaires about eating habits and exercise frequency to a sample of epilepsy patients recruited primarily from epilepsy clinics, and to healthy control subjects. Weight and height were recorded to obtain the body mass index (BMI), and waist circumference (WC) was measured. We also administered a simple olfactory test.

**Results:** According to published BMI standards, 42% of our sample of PWE were obese and 71% were overweight; 50% are at risk for cardiovascular problems according to waist circumference. These measures were significantly higher in our patients than in our healthy control subjects. No significant group differences were found on the self-report questionnaires, but there was evidence of olfactory impairment in the epilepsy group.

**Conclusion:** Obesity and epilepsy are highly co-morbid in our sample. We could not control for antiepileptic drugs (AEDs) in this exploratory study. However, it is unlikely that AEDs can account for the entire finding. Indeed, one study that examined obesity in newly diagnosed young patients prior to initiation of AEDs



reported a significantly greater incidence of obesity in the patients than in the general population. The relationship of exercise habits and olfactory acuity to weight in the two groups will be explored.

#### P881

##### THE HEALTH STATUS OF ADULTS WITH EPILEPSY AND INTELLECTUAL DISABILITY IN QUEBEC

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**Purpose:** To identify the health status of adults with an intellectual disability (ID) and epilepsy in a community derived sample of the population of Quebec and compare with their peers without epilepsy.

**Method:** The health of 791 individuals with ID in Quebec was assessed with the Short Form 36 Health Survey (SF-36v2; Ware et al. 1994) and a more detailed health status questionnaire (Morin et al. 2012). The questionnaires were sent by post to the family and answered by the person with an ID and/or a family member or paid caregiver.

**Results:** 19.8% (n = 157) of the sample were identified as having epilepsy. The level of intellectual disability was: mild in 22.3%, moderate in 43.3%, severe in 19.1% and profound in 10.8%. People lived with: their natural family 42%, in an apartment 7.6% or in government-funded residential settings 48.4%. As compared to their peers with no epilepsy the following were significantly more frequent: Constipation (14% vs. 6.7%, p = 0.003), respiratory problems (8.9% vs. 4.6%, p = 0.033), back problems (15.9% vs. 9.8%, 0.029), and accident (6.4% vs. 2.9%, p = 0.033). Results on the Short Form 36 showed a significant correlation between the presence of epilepsy and SF36 physical score (r = -0.161, p = 0.001).

**Conclusion:** Individuals with epilepsy and intellectual disabilities experience poorer health compared to their peers without epilepsy. The management of epilepsy in this group needs to consider the influence of comorbid conditions.

#### P882

##### EPILEPSY AND CO-MORBID DISORDERS IN CANADIAN CHILDREN: DATA FROM THE NATIONAL LONGITUDINAL STUDY OF CHILDREN AND YOUTH

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**Purpose:** National data on the prevalence of various developmental disabilities and comorbid conditions associated with childhood epilepsy in Canada are not presently available. Co morbid conditions likely impact health care utilization, school performance and long term outcomes.

**Method:** We analyzed data from four cycles of Canada's National Longitudinal Survey of Children and Youth. The NLSCY captured, socio-demographic information, as well as age, sex, education, ethnicity, household income, health related conditions from birth to 15 years of age. The presence of epilepsy and other neurological comorbid

conditions was self-reported by the 'person most knowledgeable' (PMK) about the child. The list of responses included co-morbid conditions (cerebral palsy, intellectual disability, learning disability, emotional and nervous difficulties). Prevalence was based on the national cross-sectional sample and used 1000 bootstrap weights to account for survey design factors.

**Results:** In Cycle 1(1994/95, 0–11 years.), Cycle 2(1996/97, 0–13 years) Cycle 3(1998/99, 0–15 years), Cycle 4 (2000/01, 0–15 years) the prevalence rates for epilepsy (n/1000, 95% CI) were estimated to be: 2.3, (95% CI:1.5–3.2), 4(95% CI:2.2–5.8), 5.3 (95% CI:3.0–7.5), 3.75(95% CI:2.1–5.3) respectively. Similarly estimates of the prevalence (n/1000) of co-morbid disorders associated with epilepsy across the four cycles included; cerebral palsy (0.19), (0.84), (1.1), (0.57), learning disability (0.51), (1.2), (1.15), (1.24), intellectual disability (0.46), (0.87), (1.17), (0.67), and emotional/nervous difficulties (0.32), (1.05), (0.82) (Data suppressed for cycle 4 by Statistics Canada).

**Conclusion:** These results provide an initial prevalence estimate of comorbid conditions with epilepsy in Canadian children. Individuals with epilepsy and co-morbid conditions are expected to experience more difficulty in day to day activities and lower success in social outcomes while requiring greater supports and resources. We discuss methodological aspects related to the ascertainment of epilepsy in both surveys, and to the validity and implications of our findings.

#### P883

##### PREVALENCE OF NOCTURNAL FRONTAL LOBE EPILEPSY IN ADULTS IN TWO PROVINCES OF NORTHERN ITALY

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**Purpose:** We aimed to estimate the four-year prevalence (2007–2010) of NFLE in two close areas of Northern Italy, the province of Modena (434.020 inhabitants in 2010) and the city of Bologna (338.268 inhabitants).

**Method:** Sources of data were the databases of the Epilepsy Centers of NOCSAE Hospital, hub of the Modena area, and of IRCCS Istituto delle Scienze Neurologiche, hub of Bologna, in addition to local territorial neurological sources of data. We included all the resident patients who fulfilled each of the following criteria: >14 years; history of sleep-related bizarre motor attacks; attacks mainly during sleep; videopolysomnographic recording of at least one major attack (asymmetric tonic or hyperkinetic seizure) or two stereotyped paroxysmal arousals.

**Results:** Ten subjects (six women, four men) from Modena and 10 (four women, six men) from Bologna met the inclusion criteria. Prevalence was 2.4 per 100,000 inhabitants (95% CI 1.1–4.2) in Modena and 3.0 (95% CI 1.4–5.4) in Bologna. There were three symptomatic cases in Modena and 2 in Bologna. All cases were sporadic.

**Conclusion:** To our knowledge, our study provides the first epidemiological data for NFLE. Due to methodological limits in case ascertainment, our estimate of 2.4–3 per 100,000 adults must be considered as a minimum prevalence. However, the similarity of outcomes from these two areas, collected with different ascertainment settings, reinforces their reliability. We failed to find any ADNFLE case, thus reflecting its lower prevalence compared to the sporadic form.

## P884

**THE SPONTANEOUS REMISSION OF UNTREATED EPILEPSY IN RURAL AREAS IN TIBETAN AREAS**

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**Purpose:** To evaluate the spontaneous remission of people with untreated and under-treated prevalent epilepsy in a rural area of Tibetan areas.

**Method:** During 2006 to 2011, we carried out an door to door epidemiologic community survey in a sample of 60,466 subjects in five rural counties in both Tibetan areas. All the inhabitant were investigated, people with the suspicious symptoms are investigated retrospectively, but only the patients with "active epilepsy" will be registered to our epileptic project. The treatment methods are suggested by local doctors but the willing of treatment is decided by themselves. And all of them are followed up regularly and prospectively.

**Results:** At the survey, we identified 473 (60.7% male) people with convulsive epilepsy, of whom 367 (61.9% male) were active and followed up for mean 41 ± 8.6 months. In the retrospective survey, 22.4% patients with untreated become spontaneous remission for more than 5 years, 31.7% for more than 3 years, 48.8% reach seizure free for only 1 year. During the follow up, 79 (21.5%) patients treat by antiepileptic drug (AED), but only 34 continued the treatment for more than 3 year, 45 (12.3%) patients used traditional Tibetan medicine, and another 243 (66.2%) patients believe that God will cure their illness, so they don't trust AED. 12 (3.3%) subjects died during the follow-up period. About 174 patients are followed up more than 5 years, 48(27.6%) have spontaneous remission. For the 308 who untreated or under treated followed up more than 3 years, 96(31.2%) of them have spontaneous remission. Besides, 19 (55.9%) of 34 who take AED regularly have seizure free after 3 years treatment.

**Conclusion:** Our data suggest that spontaneous remission of epilepsy occurs in a portion of untreated patients. Besides, the AED treatment do have effect to elevate the rate of the spontaneous remission rate.

## P885

**VISITS FOR SEIZURES TO AN EMERGENCY ROOM IN A LARGE COMMUNITY HOSPITAL: DEMOGRAPHIC AND CLINICAL CHARACTERISTICS**

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**Purpose:** Current literature provides evidence that poor seizure control is associated with regular use of the emergency room (ER) and inconsistent follow up with outpatient neurologists. The aim of this study was to describe patients visiting the ER for seizures so that targeted education can be recommended.

**Method:** This retrospective cohort study collected data on 155 adult patients presenting at the ER of Winthrop University Hospital between June 1, 2011 and December 31, 2011 with a first unprovoked, recurrent unprovoked, or provoked seizure.

**Results:** Seizures included recurrent unprovoked (epileptic) seizures (71.0%); first unprovoked seizures (16.8%); and, provoked seizures (12.3%). Subjects with epileptic seizures were 44.9 ± 21.8 years of age on average (range: 18–96) and 58.2% were male. Almost 60% of subjects were Caucasian and 31.8% were African-American. Differences in demographic characteristics were not present when comparing patients presenting multiple times (n = 22, 20%) vs. once. Acute seizure related injuries occurred among 31.6% of patients (n = 49). Though definitive causes for most seizures (59.1%) could not be determined based on evaluation in the ER, others were secondary to medication noncompliance (18.4%), toxic intake (8.7%), and metabolic abnormalities (6.2%).

**Conclusion:** Most acute care evaluations for seizures in the ER were for epileptic seizures. Unlike prior studies, our initial analyses revealed no differences in characteristics between patients with single vs. multiple ER visits. Acute seizure related injuries were common. Further study identifying potential factors associated with ER care for seizures in our patient population could lead to ways to possible minimize ER visits, and shift most care to the outpatient setting, if appropriate.

## P886

**EPILEPSY IN THE ERA OF HIV/AIDS**

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**Purpose:** Epilepsy is a condition in which someone has unprovoked seizures at two or more separate times in their life. A seizure is an abnormal electrical discharge within the brain resulting in involuntary change in movement, sensation, perception, behavior, and/or level of consciousness.

**Method:** This is a descriptive cross-sectional hospital based study. A total of 700 AIDS patients were included in the study. The diagnosis of epilepsy and its subtypes was made by a neurologist based on the clinical signs and symptoms. A full detailed history was taken from each patient and a proper systemic and neurological examination was performed by the authors. The presenting symptoms include history of convulsions, headache, loss of consciousness, mental symptoms, such as confusion and forgetfulness and family history of epilepsy. The history also included symptoms in favour of HIV infection like fever, weight loss and extreme fatigue, chronic diarrhea and difficult or painful swallowing due to Candida infection. The physical signs were grouped into general, systemic/neurological. The following investigations were done/ indicated: TWBC and differential, urine analysis, blood urea and electrolyte, ESR, HB% and blood picture, CSF analysis, ELISA was done for each patient and the diagnosis was confirmed by Weston blot. CPK, NC study, EMG, EEG, Brain MRI and serology for toxoplasmosis and syphilis were done if needed.

**Results:** Up to 70% of HIV patients develop neurological complications. Neurological complications, including seizures, from the human immunodeficiency virus (HIV) may arise from HIV itself, opportunistic infections, tumors, or drug related complications. Seizures can occur at any disease stage

**Conclusion:** AIDS is a great mimicker. It can be present in almost any neurological manifestation. Epilepsy is not an uncommon neurological manifestation associated with AIDS.

P887

### PREVALENCE OF EPILEPSY IN A COHORT OF PATIENTS WITH MULTIPLE SCLEROSIS

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**Introduction:** The prevalence of epilepsy in the general population is between 0.27–1.7%. However, in patients with Multiple Sclerosis (MS), a bigger percent of affected patients has been reported, suggesting this association is not a coincidence.

**Methods:** We retrospectively reviewed 309 patients with diagnostic criteria for MS or Isolated Clinical Syndrome (CIS), who were receiving clinical care since 2009 in our Multiple Sclerosis Center in Pontificia Universidad Católica de Chile.

**Results:** We found nine patients with epilepsy diagnosis (prevalence 2.9%). These patients had an earlier onset of symptoms of MS compared with the MS without epilepsy group (25 vs. 32 years,  $p = 0.04$ ). We didn't find differences among other variables as gender, duration of disease, clinical course or disability scales. The most frequent seizure type was partial with secondary generalization (five patients). Interestingly, two patients presented with convulsive status epilepticus during their disease, and in three patients, seizures were the debut symptom of their MS. The interictal EEG was abnormal in four patients, and the MRI showed cortical lesions in all nine patients. All the patients were in treatment with antiepileptic drugs, as well as immunomodulators.

**Conclusions:** Patients with epilepsy and MS have an earlier onset of symptoms, without developing a different clinical course or poor outcomes on disability scales. Considering that the most frequent type of seizure were the ones with partial onset, the presence of cortical lesions could probably be the pathophysiologic mechanism underlying this association.

P888

### SEROLOGICAL ANALYSIS OF TOXOCARA CANIS ANTIBODIES IN CHILDREN WITH EPILEPSY

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**Introduction:** In Mexico there are about 18 per 1,000 people with epilepsy and toxocarasis is a frequently reported zoonosis in the world. In order to find etiologies for symptomatic epilepsies, infectious agents are a possibility, such as *Toxocara canis*, which in its juvenile phase can reach the human brain and cause damage.

**Purpose:** The aim of the study was to determine anti-T. canis in children with epilepsy attending in the area of neurology at the Hospital Infantil de México Federico Gomez.

**Method:** Serological analysis was used in 57 patients with epilepsy, aged 6–12 years old. The presence of antibodies of *Toxocara canis* was determined by ELISA.

**Results:** We found that 26.3% of the patients with epilepsy had antibodies against antigens of T. canis without significant differences between focal or generalized epilepsies.

**Conclusion:** There is a high frequency of this parasite in children with epilepsy in our hospital, but we will need more patients and consider

other variables in order to pretend establishing a relationship between epilepsy and toxocarasis.

## Poster Session: Epilepsy Surgery C Wednesday, 26 June 2013

P889

### LOCALIZATION VALUE OF PERIICTAL VEGETATIVE SIGNS IN FOCAL EPILEPSIES: A NONINVASIVE VIDEO-EEG STUDY

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**Purpose:** To analyze localization value of periictal vegetative signs (PIVS) for the epileptogenic zone in patients with focal pharmacoresistant epilepsies who were undergone presurgical evaluation.

**Method:** We analyzed video-EEG recordings of 170 patients (82 men and 88 women), age ranged 13–66 years (mean  $34.67 \pm 11.10$ ; Med = 35.00) with medically intractable focal epilepsy. All of the patients underwent a complete presurgical evaluation in the Belgrade Epilepsy Center, comprising long-term noninvasive video-EEG telemetry, magnetic resonance imaging, interictal fluorodeoxyglucose positron emission tomography and interictal and/or ictal HMPAO single-photon emission computed tomography. The diagnosis of lobar epilepsy was established according to the correlation of clinical seizure semiology, ictal EEG findings and neuroradiology findings. In all patients we analyzed video recordings of clinical seizure semiology in order to determine the frequency and types of PIVS in focal epilepsies and their localizing value for temporal lobe epilepsies (TLE) vs. extratemporal lobe epilepsies (ETLE).

**Results:** Ten different types of PIVS occurred in 69 of the 170 patients (40%). The most frequent PIVS were postictal nose rubbing (28.8%) and periictal cough (12.9%). We found PIVS were reliable localizing signs for TLE vs. ETLE (50.0% vs. 23.2%;  $p = 0.001$ ). The most valuable localizing signs were postictal nose rubbing ( $p = 0.008$ ), periictal water drinking ( $p = 0.035$ ) and hypersalivation ( $p = 0.048$ ).

**Conclusion:** We found that PIVS are reliable semiological signs in focal epilepsies for the localization of the epileptogenic zone in temporal lobe.

P890

### DIRECT CORTICAL STIMULATION: A TOOL FOR RESECTION OF BRAIN LESIONS IN ELOQUENT CORTEX

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**Purpose:** To assess the neurological deficit associated with the surgical resection of brain lesions that involve the eloquent cortex using brain stimulation in order to achieve wider resections with safer margins.

**Method:** Follow-up to patients with brain injury related to the premotor eloquent area was made; twelve patients who underwent resection of the lesion with standard anesthetic technique, intra operative cortical stimulation with Ossiris stimulator and neuropsychological protocol; the

resected volume assessment was performed with a day postoperative CT and follow-up at 3 months with MRI, standardized neuropsychological tests were performed to assess neurological deficit.

**Results:** Complete resection of the lesion was achieved in 64% of patients. In the follow-up visit three months after surgery, 73% of patients had no neurological deficit associated with the procedure, only three patients (27%) had mild deficit.

**Conclusion:** Although advances made in anatomic location of brain lesions related to eloquent areas with improving MRI and neuronavigation technology, surgical resection of these lesions poses a high risk of postoperative neurological deficit. Cortical stimulation has been developed as an increasingly useful tool for this type of injury as it opens up the possibility of using it not only to establish a real-time functional map of the cerebral cortex that allows the surgeon to define a safe edge for resection of the lesion but also stimulation of intracranial or intralesional electrodes can be carried out in epilepsy surgery to determine whether a specific injury is the initial foci for specific seizures. Cortical stimulation for resection of brain lesions in eloquent areas is a good tool to preserve neurological function. Moreover, the preoperative cortical stimulation of intralesional and intracranial electrodes in epilepsy surgery is highly useful to verify location of epileptogenic focus.

#### P891

##### STEREOTACTIC MRI-GUIDED LASER ABLATION OF EPILEPTOGENIC FOCI IN CHILDREN

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**Purpose:** A minimally invasive stereotactic procedure may allow for precise thermal ablation of seizure foci. We present our first 18 patients with intractable epilepsy that underwent MRI-guided stereotactic laser ablation (SLA) of their seizure foci.

**Method:** This is a retrospective review of 18 patients (14 male) who underwent SLA between August 2010 and January 2013. Patients had medically intractable epilepsy and were aged 21 months to 18 years. Etiologies included hypothalamic hamartoma (11), focal cortical dysplasia (3), mesial temporal sclerosis (3), and cortical tuber (1). The FDA-cleared Visualase thermal ablation system using a 15 W 980 nm diode laser was employed. Under general anesthesia, an MR-compatible laser catheter (1.6 mm) was placed stereotactically into MRI visible target lesions using a 3.2 mm twist drill skull opening. Patients were then placed into a 1.5T MRI for real-time magnetic resonance thermal imaging (MRTI) during the ablation process. An initial laser test dose confirms proper applicator position prior to thermal ablation doses (10–12 W for 45–120 s).

**Results:** SLA was successful in all cases without significant complications. Post-contrast MRI exhibited a central coagulated region surrounded by a rim of enhancement typical of acute thermal injury that encompassed the targeted foci. The majority of patients were discharged from hospital within 1–2 days. Follow-up ranged from 1 to 29 months (x = 11) with 12 patients seizure-free (67%).

**Conclusion:** Minimally invasive SLA may offer advantages over conventional craniotomy. Use of real-time MRTI feedback control allows excellent visualization of target and protection of critical structures. Short term follow-up outcomes are encouraging.

#### P892

##### CALCIFIED NEUROCYSTICERCUS LESIONS (CNL) AND DRUG RESISTANT EPILEPSY: SURGICALLY REMEDIABLE SYNDROME?

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**Purpose:** Calcified neurocysticercus lesions (CNL) are not known to cause drug resistant epilepsy (DRE). We studied the association between DRE and CNL including the feasibility and outcome of resective surgery.

**Methods:** All patients with DRE who underwent presurgical evaluation and had CNL on imaging from January 2001–2010 were studied. Diagnosis of CNL was based upon the standard diagnostic criteria. Clinical data, interictal and ictal EEG, neuroimaging, and intracranial EEG in selected patients were used to determine the association between CNL and DRE. Suitable candidates underwent resective surgery.

**Results:** Forty-five patients fulfilled inclusion criteria: In 17 patients, CNL was proven to be causative lesion for DRE; In 18 patients, CNL was associated with unilateral MTS; In 10 patients, CNL was proven as incidental lesion. Causative CNL were more common in frontal lobes (12/17) while CNL with MTS were more common in temporal lobes (11/18;  $p = 0.002$ ). Patients with associated MTS had younger age at epilepsy onset than those with causative CNL ( $8.9 \pm 7.3$  vs.  $12.6 \pm 6.8$  years,  $p = 0.003$ ). Perilesional gliosis was more common in causative than incidental group (12/17 vs. 1/10;  $p = 0.006$ ). Four out of five patients became seizure-free following lesionectomy alone in causative group. In CNL with MTS group, four patients underwent ATL alone (one seizure-free) and five underwent ATL combined with removal of CNL (two after intracranial EEG) and all became seizure free.

**Conclusions:** CNL are potential cause for drug resistant and surgically remediable epilepsy as well as dual pathology. Perilesional gliosis contributes to epileptogenicity of these lesions.

#### P893

##### EFFICACY OF MRI-GUIDED STEREOTACTIC RADIOFREQUENCY THERMOCOAGULATION FOR 82 INTRACTABLE EPILEPSY PATIENTS WITH HYPOTHALAMIC HAMARTOMA

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**Purpose:** To evaluate the efficacy of stereotactic radiofrequency thermocoagulation (SRT) for intractable epileptic hypothalamic hamartoma (HH), which is characterized by gelastic seizures (GS) and epileptic encephalopathy.

**Method:** Eighty-two consecutive patients with HH underwent SRT between 1997 and 2012. All but one patient presented with GS, with other types of seizures in 76 patients (93%), precocious puberty in 29 (35%), behavioral disorder in 39 (48%), and mental retardation in 41 (50%). Mean maximum diameter of the HH was 14 mm (range, 5–80 mm). SRT creates multiple 5-mm-spherical lesions within the HH through multiple tracks via the unilateral frontal route. Fifty-three patients were observed for at least 2 years and seizure outcomes were reviewed.

**Results:** Total 104 surgeries of SRT were performed, using 1–9 tracks (mean, 4) and creating 1–36 lesions (mean, 8) without adaptive limitations regardless of size or subtype. No permanent complications persisted after SRT. GS disappeared in 49 patients (92%). Complete freedom from seizures was achieved in 40 patients (75%). Six patients became free from antiepileptic drugs. The overall seizure-free rate was 69% for intrahypothalamic type, 75% for para-hypothalamic type, 86% for mixed-hypothalamic type with unilateral attachment and 60% for mixed-hypothalamic type with bilateral attachment, respectively. Thirty-eight of 40 patients achieved improvement of intelligence or developmental quotient significantly (mean, 9 points).

**Conclusion:** Our SRT reduces all types of seizures caused by HH, and achieves minimal invasiveness and mental or developmental improve-

ment of epileptic children. SRT successfully remedies intractable epilepsy syndrome and epileptic encephalopathy in patients with HH.

**P894**  
**LONG-TERM PROGNOSIS AFTER RESECTIVE EPILEPSY SURGERY FAILURE**

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**Purpose:** We performed a retrospective study to evaluate the long term outcome of patients who were classified Engel IV one year after epilepsy surgery.

**Methods:** We analyzed 30 patients (19 males and 11 females) who had been classified as Engel IV one year after resective epilepsy surgery. The age of patients varied from 8 to 51 (mean 31,3 ± 12,0) years and the duration of epilepsy ranged from 2 to 40 (mean 17,5 ± 10,7) years at the time of epilepsy surgery. The outcome after epilepsy surgery was assessed from 2 to 16.3 (mean 7.7 ± 4.2) years.

**Results:** At the last follow-up, seven out of 30 patients (23.3%) were classified as Engel I, three out of 30 patients (10%) as Engel, II, eight out of 30 patients (26.7%) as Engel III and other 12 patients (40%) as Engel IV. The resective reoperation was performed in five of 30 patients (16.7%). Out of 25 patients who did not undergo resective reoperation, the following reasons were identified: "satisfactory" effect of AEDs adjustment, or change in 6 (24%) cases, absence of plausible hypothesis for re-evaluation in 5 (20%), risk for postoperative deficit in 6 (24%), multifocal epilepsy (bitemporal) in 3 (12%) and neurosurgical contraindication in three patients (12%). One patient refused the surgery (4%).

**Conclusions:** Although the reoperation rate was relatively low in our series, we can achieve the better or even excellent seizure outcome by other procedures in patients in whom the resective surgery initially failed.

**P895**  
**THE ROLE OF INTRAOPERATIVE ELECTROCORTICOGRAPHY IN DETECTION OF FOCAL CORTICAL DYSPLASIA ASSOCIATED WITH HIPPOCAMPAL SCLEROSIS**

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**Purpose:** Patients with hippocampal sclerosis associated with focal cortical dysplasia (FCD IIIa) can have a higher risk of seizure recurrence if both of these pathologies are not removed. The aim of our study was to

determine the role of intraoperative electrocorticography in detection of this dual pathology.

**Method:** Intraoperative electrocorticography recordings were obtained in patients who underwent anteromedial temporal lobe resection. Patients with histopathologically proven hippocampal sclerosis and temporal pole available for analysis were included. Cortical activity was measured prior to the resection using two six-contact strips (sampling from latero-basal and temporo-polar regions respectively) and one four contact strip sampling from mesio-basal temporal cortex. Occurrence of isolated mesial and independent neocortical (basal or lateral) spike activity was evaluated. Patients were divided into two groups according to histopathology: isolated hippocampal sclerosis (n = 23) and hippocampal sclerosis associated with focal cortical dysplasia (n = 23). Data analysis was performed by raters blinded to histopathology.

**Results:** Independent neocortical spikes were identified more frequently in patients with dual pathology (sixteen patients with FCD IIIa vs. four patients with isolated hippocampal sclerosis; p = 0.01). On the contrary, isolated mesial spikes occurred more often in patients with isolated hippocampal sclerosis (19 patients vs. 6 patients with FCD IIIa). In one patient with FCD IIIa no spikes were recorded.

**Conclusion:** Independent latero-basal temporal spikes recorded during intraoperative electrocorticography in patients with hippocampal sclerosis suggest associated dysplastic tissue in neocortex.

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**P896**  
**EPILEPSY SURGERY IN PEDIATRIC INTRACTABLE EPILEPSY WITH DESTRUCTIVE ENCEPHALOPATHY**

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**Purpose:** The aim of this study is to review the clinical characteristics, surgery outcome and parental satisfaction of children with destructive encephalopathy who underwent epilepsy surgery due to medically intractable seizures.

**Method:** We have reviewed 48 patients with destructive encephalopathy who underwent epilepsy surgery at Severance Children's Hospital. Functional outcome and parental satisfaction collected via telephone survey done at 1 year follow up period from the final surgery were assessed.

**Results:** Epileptic encephalopathy, which includes Lennox-gastaut syndrome (33/48, 68.7%), and infantile spasms (2/48, 4.2%), was more prevalent among the patients than LRE (localization related epilepsy) (13/48, 27.1%). The underlying etiology of the encephalopathic conditions of the patients were mostly hypoxic ischemic injury (32/48, 66.7%), and the rest were mainly CNS infection (12/48, 25.0%) and head trauma (4/48, 8.3%). As for the types of epilepsy surgery done for seizure control, 56.3% of the patients underwent resective surgery (27/48) and palliative surgeries done for the rest of the patients were corpus callosotomy (21/48, 43.7%). At last follow-up at the median of 2.7 years, 33.3% (16/48) of the patients were in Engel Class I. Seizure freedom was achieved in 37.0% (10/27) of the resective surgery cases compared to 28.6% (6/21) in corpus callosotomy (p-value = 0.397). According to our telephone interviews, all parents of the Engel Class I patients have reported satisfaction, and among the parents of the rest of the patients (Engel class II-IV), 77.8% of them (14/18) have reported satisfaction for improvement in alertness, hyperactivity, concentration, facial expression, responsiveness and reduction in traumatic fallings.

**Conclusion:** Epilepsy surgery in destructive encephalopathy is effective for controlling seizures. We found that parents reported satisfaction, not only with the outcome of their children's epilepsy surgery, but also with improvement in aspects of cognition and behavioral issues.

#### P897

### DIAGNOSTIC BENEFIT OF INVASIVE EEG RECORDINGS TO CLARIFY MESIOTEMPORAL EPILEPTOGENESIS

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**Purpose:** With improving imaging quality and changes in prevailing pathologies underlying drug-resistant epilepsy, indications and yield of invasive EEG recordings have to be re-evaluated. We report the information gained by intracranial recordings targeting the hippocampal formation at the Epilepsy center Freiburg.

**Method:** One-hundred consecutive patients (47 male, age 10–55 years) undergoing intracranial EEG recordings between 1999 and 2008 including hippocampal tissue were retrospectively reviewed based on electronic charts regarding their diagnostic yield.

**Results:** All patients were implanted with hippocampal depth electrodes (inclusion criterion), 32 bilaterally, 72 in addition with subdural grids or strips. 28 patients had a hippocampal lesion of unknown epileptogenicity, 25 were cryptogenic, 18 had MR evidence of dual pathology (FCD and hippocampal sclerosis), 15 had hippocampal sclerosis but discordant presurgical findings, and five had bilateral hippocampal sclerosis. In 71%, mesiotemporal seizure onset was shown, in 26% hippocampal seizure onset was excluded. In patients with mesiotemporal seizure onset, 52% had additional neocortical seizure generation. In 50% of patients invasive monitoring gave additional information beyond surface EEG and imaging, 25% had hippocampal sclerosis and extrahippocampal seizure onset, 25% had seizure onset from a normal appearing hippocampus. In 81% of implanted patients surgery was recommended (21 selective amygdalohippocampectomy, 27 extrahippocampal resections, 33 combined resections).

**Conclusion:** Invasive recordings did confirm suspected seizure origin from a lesion in half of the patients, but yielded relevant information beyond imaging and non-invasive video-EEG monitoring in another 50% of patients. These results support the continuing relevance of invasive recordings from mesiotemporal structures in properly selected patients. Intracranial EEG allows to identify hippocampal seizure generation also in patients with structurally normal hippocampus and to identify extra-hippocampal seizure onset in patients with hippocampal sclerosis, either of which is relevant for the decision process on surgery and for tailoring resections.

#### P898

### SURGICAL OUTCOME IN PATIENTS WITH MRI-NEGATIVE, PET-POSITIVE TEMPORAL LOBE EPILEPSY

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**Purpose:** The purpose of this study was to determine the long-term surgical outcomes of MRI-negative, Florodeoxyglucose positron emission tomography (FDG)-PET-positive temporal lobe epilepsy (TLE) patients and compare them with those of patients with mesial temporal lobe sclerosis (MTS).

**Method:** One hundred forty-one patients with TLE who underwent anterior temporal lobectomy (ATL) were included in the study. Twenty-four patients who had unilateral temporal FDG-PET hypometabolism without an epileptogenic lesion on MRI were compared with the patients who had unilateral temporal FDG-PET hypometabolism with MTS on MRI (n = 117). Surgical outcomes were compared using Engel's classification at 2 years after surgery. Clinical characteristics, unilateral interictal epileptiform discharges (IED), histopathological data and operation side were considered as probable prognostic factors.

**Results:** Class I surgical outcomes did not differ significantly between the MRI-negative patients and the MTS on MRI group (2 year outcomes were 79.1% for the MRI-negative group and 82% for the MTS group). By univariate analysis, febrile convulsion history, unilateral IED and left temporal localization significantly associated with seizure free outcome. Multivariate analysis revealed that febrile convulsion history, unilateral IED were independent predictors of a good outcome.

**Conclusion:** Our results suggest that epilepsy surgery outcomes in the MRI-negative, PET positive patients are similar to those in patients with MTS. This finding may aid in the selection of best candidates for epilepsy surgery.

#### P899

### LATERALIZING VALUE OF TEMPORAL NEOCORTICAL APPARENT DIFFUSION CO-EFFICIENT (ADC) AND T2 RELAXOMETRY VALUES IN MESIAL TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS

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**Purpose:** To study the utility of apparent diffusion co-efficient (ADC) and T2 relaxometry (T2R) values over the anterior temporal neocortex for lateralization in mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS).

**Methods:** Forty-five consecutive patients who underwent anterior temporal lobectomy (ATL) for drug resistant MTLE-HS and had minimum of two years of postoperative follow-up formed the study group. The 1.5T MRIs were visually evaluated by two radiologists blinded to clinical details for presence of temporal neocortical grey-white matter abnormalities (GWA). We also calculated the ADC and T2R values over the temporal neocortex at 2 cm from the temporal pole bilaterally. We compared the preoperative characteristics and postoperative outcome in patients with and without GWA.

**Results:** Mean age of the group was 27.2 ± 10.1 years at the time of surgery and 25 were males. Eighteen (40%) patients had GWA ipsilateral to HS on visual analysis. Patients with GWA had early

age of epilepsy onset ( $6.7 \pm 5.7$  vs.  $12.1 \pm 7.4$ ;  $p < 0.001$ ), more chances of atypical initial precipitating injury in the form of febrile status epilepticus or perinatal injury and more tendency for seizure clustering. Preoperative seizure frequency, frequency of secondarily generalized seizures, interictal and ictal EEG characteristics and postoperative seizure outcome were similar in both the groups. At mean follow-up of  $4.1 \pm 1.8$  years, 35 (77.7%) patients were seizure free. Mean neocortical ADC ( $925.9 \pm 91$  vs.  $824.9 \pm 50.8$ ;  $p = 0.02$ ) and T2R ( $97.6 \pm 16.6$  vs.  $92.2 \pm 8.4$ ;  $p = 0.03$ ) values were significantly higher on the side of HS. There was positive correlation between severity of visually detected GWA, early age of seizure onset and increasing ADC values ( $p = 0.02$ ).

**Conclusions:** Patients with temporal neocortical GWA have distinct clinical profile than those without GWA. Neocortical ADC and T2R values can help in lateralization of temporal lobe epilepsy.

## P900

### SAFETY AND EFFICACY OF INTRACRANIAL EEG MONITORING: THE QUEEN SQUARE EXPERIENCE FROM 2008 TO 2012

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**Purpose:** To assess diagnostic yield, clinical outcomes and complications related to intracranial EEG evaluations using subdural grid, strip and intracerebral depth electrodes at a single institution

**Method:** Retrospective review of 94 consecutive intracranial EEG investigations performed at the National Hospital for Neurology and Neurosurgery/Queen Square, London, UK from Jan 2008-Dec 2012. Complications were graded according to a six-point scale (Wellmer J et al. *Epilepsia* 2012; 53(8):1322–1332). Surgical outcomes in patients with postoperative follow-up of at least 12 months were determined based on Engel's classification.

**Results:** The median age of patients was 32 (range 17–59) years. Depth electrodes only (avoiding craniotomy) were used in 22%. Intracranial EEG monitoring identified discrete ictal onset zone(s) in 94% of patients. Resections were offered to 76%. Reasons for not offering resection were multifocal onset (11%), ictal onset from eloquent cortex (9%), and ictal onset not identified (6%). Three patients (3%) declined resections. Acute clinically evident complications without long term sequelae, mostly infection related occurred in 5%, none requiring surgical intervention. Procedure related complications evident on imaging without clinical correlate were seen in 40%. Electrodes were revised to increase the diagnostic yield in 2%. Three patients (3%) had permanent neurological deficits related to implantation-associated hemorrhage. There were no deaths. Fifty patients (62%) with at least 12 months (mean 34 months) post-resective follow up had Engel class IA outcome.

**Conclusion:** In appropriately selected patients, intracranial EEG has a high diagnostic yield, with a <5% risk of permanent neurologic complications.

## P901

### PREOPERATIVE ESTIMATION OF SEIZURE CONTROL AFTER RESECTIVE SURGERY FOR THE TREATMENT OF EPILEPSY

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**Purpose:** Predicting seizure control after epilepsy surgery is difficult. The objectives of this work are: a) To estimate the value of surgical procedure, presence of neuroimaging abnormalities, need for intracranial recordings, resection lobe and pathology to predict postsurgical seizure control after epilepsy surgery; b) To provide empirical estimates of successful outcome after different combinations of the above factors in order to aid clinicians in advising patients presurgically about the likelihood of success under their patients' individual circumstances.

**Method:** We report postsurgical seizure control from all 243 patients who underwent resective surgery for epilepsy at King's College Hospital between 1999 and 2011. Among the 243 patients, 233 had lobar or sublobar resections, eight had multilobar resections and two had excision of a hypothalamic hamartoma. We examined the relation between postsurgical seizure control and type of surgical procedure, presence of neuroimaging abnormalities, pathology, resection lobe and the need of intracranial electrodes to identify seizure onset.

**Results:** Among the 243 patients, 126 (52%) enjoyed outcome grade I, 40 (16%) had grade II, 51 (21%) had grade III and 26 (11%) had grade IV. Normal neuroimaging or need for intracranial recordings was not associated with poorer outcome. Patients undergoing temporal resections showed better outcome than those with frontal resections, due to the poor outcome seen in frontal patients with normal neuroimaging. Among temporal resections, there was no difference in outcome between patients with and without neuroimaging abnormalities. Among patients with lesions on imaging, temporal and frontal resections showed similar outcomes.

**Conclusion:** Overall, nearly 70% of patients undergoing resective surgery enjoy favourable post-surgical seizure control. Normal neuroimaging should not discourage surgery in temporal patients but is a negative prognostic sign in normal MRI frontal patients. There were no statistical differences in outcome between patients with neuroimaging lesions in frontal or temporal lobes.

## P902

### VALUE OF MAGNETOENCEPHALOGRAPHY TO GUIDE ELECTRODE IMPLANTATION IN EPILEPSY

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**Purpose:** To investigate if magnetoencephalography (MEG) can identify implantation sites for intracranial recordings (IR).

**Method:** Two groups of 12 patients assessed for surgery with IR with and without MEG were compared (MEG and control groups). In the control group, non-invasive pre-surgical assessment without MEG suggested clear hypotheses for implantation. In the MEG group, non-invasive assessment was inconclusive, and MEG was used to identify implantation sites. Both groups were matched for implantation type. The success

## Abstracts

of implantation was defined by findings in IR: a) Focal seizure onset; b) Unilateral focal abnormal responses to single pulse electrical stimulation (SPES); and c) Concordance between a) and b).

**Results:** In all MEG patients, at least one virtual MEG electrode generated suitable hypotheses for the location of implantations. The proportion of patients showing focal seizure onset restricted to one hemisphere was similar in control and MEG groups (6/12 vs. 11/12, Fisher's exact test,  $p = 0.0686$ ). The proportion of patients showing unilateral responses to SPES was lower in the control than in the MEG group (7/12 vs. 12/12,  $p = 0.0373$ ).

**Conclusion:** The MEG group showed similar or higher incidence of successful implantations than controls.

## P903

### IMMEDIATE IMPROVEMENT OF MOTOR FUNCTION AFTER EPILEPSY SURGERY FOR CONGENITAL HEMIPARESIS: PLASTICITY VS. RELEASE OF FUNCTION

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**Purpose:** Improvement in hemiparesis in a few patients following hemispherectomy was already reported and is generally attributed to plasticity or seizure control, avoiding postictal paralysis. When improvement occurs immediately after surgery, however, the mechanism may be distinct. We report four patients whose motor function improved immediately after resection and raise the issue of release of function as the mechanism behind the improvement.

**Method:** Four patients with congenital hemiparesis and therapy-refractory seizures due to a large pre- or perinatally acquired cortico-subcortical infarct in the territory of the middle cerebral artery underwent epilepsy surgery. Intra-operatively, electrical cortical stimulation of the affected hemisphere demonstrated preserved motor projections from the sensorimotor cortex to the (contralateral) paretic hand in two. A fronto-parietal resection was performed in 2, which included a complete disconnection of all motor projections originating in the sensorimotor cortex of the affected hemisphere. The other two had a temporal lobectomy. Pre- and post-operative fMRI were performed in all.

**Results:** Neurologic examination in all showed a significant functional improvement in the paretic hand immediately after the operation. There was no evidence for a seizure around the preoperative and postoperative examinations. Two are completely seizure free and the other two had a major reduction in seizure frequency.

**Conclusion:** Assessing pre-, intra- and post-operative data allow us to suggest a mechanism of release of function as the basis for immediate improvement. We suggest that in congenital hemiparesis, crossed motor projections from the affected hemisphere are not always beneficial, but can interfere with or inhibit the control of the unaffected hemisphere over the paretic hand. Ipsilateral corticospinal projections, thus, play a major role in recovery.

## P904

### INTERICTAL ESTIMATION OF INTRACRANIAL SEIZURE ONSET IN TEMPORAL LOBE EPILEPSY

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**Purpose:** To evaluate the lateralizing and localizing values of interictal focal slow activity (IFSA), single pulse electrical stimulation (SPES) and <sup>18</sup>F-DG PET, in order to estimate their potential to complement ictal recordings and reduce prolonged monitoring in patients with temporal lobe epilepsy.

**Method:** The study includes 30 consecutive patients with bilateral temporal subdural electrodes and focal seizure onset. IFSA, SPES, and <sup>18</sup>F-DG PET when available, were visually assessed, and their combined lateralization was based on the majority of the individual lateralizing tests.

**Results:** In the 18 patients who had all three tests, lateralization was congruent with seizure onset areas in 15 (83%). In all 12 patients without <sup>18</sup>F-DG PET, lateralization combining IFSA and SPES was congruent with seizure onset, including two with bilateral independent seizure onset on subdural monitoring. Twenty two out of the 23 patients who had surgery enjoyed favorable outcome (Engel I or II).

**Conclusion:** Intracranial IFSA and SPES can reliably predict the side and site (mesial vs. lateral temporal) of seizure onset when they lateralize to the same side. These techniques are simple, fast and cheap, with the potential to reduce telemetry time, and its risks and costs if performed early in the telemetry period.

## P905

### LATE ONSET AMNESIA AFTER TEMPORAL LOBECTOMY

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**Purpose:** To describe a late severe complication of temporal lobectomy for intractable epilepsy

**Method:** A case of amnesia occurring 24 years after surgery is described and five similar cases from the literature reviewed.

**Results:** Mean age at surgery (five right) was 40 years (19–62 years), three female. Four of five tested had impaired visual and verbal memory preoperatively but not sufficient to contraindicate surgery. Pathology was mesial temporal sclerosis in 3, 1 cavernoma, 1 DNET and 1 normal. Postoperatively, four were seizure free 3–12 years off medication and two continued with seizures. There was no unexpected postoperative memory change until incapacitating anterograde amnesia developed 1–24 years after surgery. In five patients, this followed definite or possible status epilepticus resulting in new mesial temporal sclerosis on the opposite side in the 4 that were investigated by MRI. One patient developed a glioblastoma in the opposite temporal lobe.

**Conclusion:** Late recurrence of or continuing seizures after temporal lobectomy can result in global amnesia if status epilepticus occurs. Other new lesions on the opposite side to surgery can also have the same effect.

## P906

### CORTICAL DYSPLASIA ALONG WITH ANOTHER PATHOLOGY: SURGICAL TEMPORAL LOBE EPILEPSY SERIES

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**Purpose:** To describe our surgical series of patients presenting cortical dysplasia (CD) along with another pathology and intractable temporal lobe epilepsy.

**Method:** We retrospectively reviewed 99 patients who underwent complete Electrocorticography (ECoG) guided lesional/epileptogenic zone (s) resection at the National Institute of Neurology and Neurosurgery and ABC Medical Center in Mexico City from January 2005 to December 2011, with histopathological diagnosis of CD along with another pathology. Presurgical evaluation comprised a modified international protocol including integral review of past medical/ seizure history, MRI, surface EEG, Video-EEG, neuropsychological and neuropsychiatric evaluation and, in selected cases, fMRI, PET and SPECT.

**Results:** Mean age at seizure onset was 15 ( $\pm 12.5$  SD) years, 48% were men, presurgical mean seizure frequency/month was 16.5 ( $\pm 28.1$  SD). *MRI findings:* 35% clear evidence of CD, 27.3% with tumor, 6.1% with Cavernous Malformation (CM) and 58.6% with Mesial Temporal Lobe Sclerosis (MTLS). *Etiology:* 27.3% CD and low-grade tumor (ganglioma-DNET), 66.6% CD and MTLS and 6.1% CD and CM. *Histopathology of CD:* 10.1% Ia, 2% Ib, 39.4% IIa and 48.5% IIb. *Surgical outcome:* Engel I 80%, Engel II 13%. Engel III 3% and Engel IV 4% at last follow up, mean follow-up 5.2 years. Morbidity included 32.3% visual field deficit, 2.2% surgical site infection, 1.1% cerebrospinal fluid leak, mortality 0%.

**Conclusion:** Given the unexpected high association of CD and its still to be clarified meaning in terms of epileptogenicity, we suggest that tailored corticectomy plus lesionectomy by ECoG provides the better long term outcome in these cases.

#### P907 SURGICAL TREATMENT OF INTRACTABLE PEDIATRIC EPILEPSY USING THERMAL LASER ABLATION

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**Purpose:** We describe the first nine patients with intractable epilepsy at our institution who have been treated with laser thermal ablation. This novel treatment approach allows the minimally invasive removal of a seizure focus when the extent of the focus can be determined preoperatively.

**Method:** Since May 2011, Miami Children's Hospital has treated nine patients (in 10 procedures) using laser thermal ablation. We report all such subjects, including follow-up time, anatomical result, seizure outcome, and complications.

**Results:** Nine children were treated with laser thermal ablation. The mean age at surgery was 14.92 (range 11.5–20.6). Average time of follow-up was 10 months (range 4–21). Five of the nine patients had undergone prior conventional resection (56%), and had failed. The anatomical goal was achieved with the thermal probe in 7 (78% of patients, and 80% of treatments). The epilepsy has been completely controlled for five of the nine subjects (56%), although one required a second laser treatment,

and one required conversion to conventional surgery. Complications included post-op surgical site pain in all patients (less than conventional surgery, easily controlled), and clinically relevant edema in one. All children went home within 48 h of the treatment, and none had an infection or unintended neurological injury.

**Conclusion:** Laser thermal ablation is a well-tolerated treatment for children with intractable epilepsy. Identification of the epileptogenic zone is critical, but early results suggest that its effectiveness compares favorably to conventional resection.

#### P908 DEPTH ELECTRODE INVESTIGATION AND FOCUSED LASER THERMAL THERAPY FOR PRIMARY INSULAR SEIZURES

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**Purpose:** Refractory insular onset seizures represent an important subset of intractable complex partial epilepsy. However, diagnostic and surgical treatment of insular seizures remains difficult. We utilized intraoperative MRI-guided stereotactic depth electrode recording and laser interstitial thermal therapy (LITT) for treatment of a patient with insular epileptic seizures.

**Method:** A 54 year old man with a history of refractory complex partial seizures for 17 years underwent video-EEG, which showed seven complex partial seizures with left hemispheric diffuse EEG onset and evolution. A brain MRI revealed encephalomalacia in the left insula. A PET scan revealed hypometabolism in the left insula. An ictal SPECT injection during a typical complex partial seizure revealed hyperperfusion in the left insula in the region of MRI-defined encephalomalacia. He underwent stereotactic placement of left insular depth electrodes and left frontotemporal strip electrodes with intraoperative stereotactic MRI navigation. The intracranial video-EEG showed five complex partial seizures with left insular onset followed by left frontal and temporal propagation. Ablation of the insular lesion using laser ablation interstitial thermal therapy (LITT) was performed to target the seizure-onset zone, and surrounding encephalomalacia, including both the anterior, and posterior insula.

**Results:** Postoperatively, the patient reported symptoms of anxiety, with associated mild dysarthria, which improved over the first six months of follow-up. He remained seizure free at his last follow-up, six months after surgery.

**Conclusion:** This case shows multimodality localization of left insular seizures, followed by LITT for surgical treatment of the epileptogenic focus, demonstrating usefulness of these diagnostic and treatment approaches for insular seizures.

#### P909 SEIZURE AND DEVELOPMENTAL OUTCOMES AFTER HEMISPHEROTOMY FOR REFRACTORY EPILEPSY IN CHILDHOOD AND ADOLESCENCE

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We aimed to evaluate the seizure and developmental outcomes after hemispherotomy for refractory epilepsy in childhood and adolescence and to identify their predictive factors. We retrospectively studied the clinical courses and outcomes of 52 children with refractory epilepsy who underwent hemispherotomy in the Epilepsy Center Freiburg between 2002 and 2011. Age at epilepsy onset ranged from birth to 8 years (mean 1.8 years) and age at surgery was 6 months to 18 years (mean 6.7 years). The underlying etiology was congenital in 22 (42%) children, acquired in 24 (46%) and progressive in 6 (12%). At final follow-up of 1–9.8 years (mean 3.3), 43 (83%) children were seizure free. Seizure outcome was not related to etiology, with the exception of hemimegalencephaly that was linked to poor seizure control. Presurgical development was impaired in all but one child and markedly determined postsurgical development. Patients with acquired or progressive etiology, later epilepsy onset and subsequent later surgery presented higher presurgical developmental status that substantially determined postoperative developmental outcome. Improved postsurgical development was determined by acquired etiology and seizure freedom off antiepileptic drugs. In our study, the vast majority of selected children and adolescents achieved seizure freedom, including those with congenital etiology. Developmental outcomes, however, were superior in patients with acquired etiology and older age at surgery, underlining that it is never too late to reap the benefits of this procedure in terms of both epilepsy and development.

#### P910 EPILEPSY SURGERY IN THE HOSPITAL SAN JUAN DE DIOS IN GUATEMALA

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**Purpose:** Identifying patients with epilepsy surgery criteria. Determine the types of surgical procedures.

**Method:** Prospective – descriptive.

**Results:** A three patients underwent epilepsy surgery, representing 2.7%, procedures performed on patients who underwent surgery was performed a callosotomy in a patient of 12 years who was diagnosed with Lennox Gastaut Syndrome, existing as a complication of the procedure intraparenchymal hematoma surgery because there was a condition of the superior sagittal sinus, having need of treatment in the intensive care unit in immediate postoperative period, moving towards improvement and with a residual hemiparesis. In their post surgical evaluations as ranked by Modified Engel, Engel was an IV A and be given up to one year after surgery. In the second case we made a lesionectomy a patient of 37 years of the display a cystic lesion highly suggestive of NCC in the right parietal area, persitiendo one body hemihypoesthesia left as a complication of it, as Engel clasificándose IA, after a year postoperatively be evaluated, and the result sent to histopathological material was reported Neurocysticercosis pathology. In the third case was resected left temporal cortex, a male patient of 21 years who presented an image suggestive of malignancy in the lateral region of the left temporal lobe, which was reported only in pathological inflammatory tissue sample, no having regard to surgical complications, and is not classified according to Engel as only attended twice for postoperative evaluation.

**Conclusion:** - The surgical procedures performed were a callosotomy, a lesionectomy and extratemporal resection.

- According to the epidemiological characteristics in our study it was determined that the most affected sex was female and the age range was the predominant from 21 to 30 years and the majority of patients treated with a primary school were enrolled.

#### P911 EFFECT OF DEEP BRAIN STIMULATION IN EPILEPSY (DBS-E) ON SLEEP QUALITY AND SLEEP STRUCTURE; STIMULATION OF THE ANTERIOR NUCLEUS THALAMICUS, ANT, USING THE STIMULATORSYSTEM “ACTIVA” BY MEDTRONIC, USA

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**Purpose:** To evaluate the effect of DBS in Epilepsy (with stimulation of the Anterior Nucleus Thalamicus, ANT;) on sleep quality and sleep structure.

**Method:** We investigated 4 Patients with refractory focal epilepsy and Deep Brain Stimulation of the ANT (all patients were repetitively stimulated with 5 V, ON Time 1 min, OFF Time 5 min) with polysomnographic recordings. Their medical histories will be briefly discussed, also their outcome on DBS therapy; MRI Data will be shown, visualizing the exact position of the electrode in the Tractus mamillothalamicus. Exemplaric PSG data of all patients will be discussed, in order to show the time locked effect of the single DBS activation on Arousel, Sleep Stage and Sleep Discontinuation. Thereafter hypnograms of all patients are presented in order to show the effect of the continued DBS activity on sleep quality and structure over the whole night.

IN 1 Patient we switched off the DBS in a second PSG night in order to obtain a clearer comparison in one other patient we reduced the DBS power on 2.5 V in a second PSG night. Also these data will be discussed.

**Results:** In all four patients we saw a strong effect of DBS on sleep with Induced Arousel, Awakenings and Sleep Discontinuation in 80, 72, 54 and 30% of DBS Activations, together with a high sleep fragmentation in all patients and a decline of deep sleep N3 in two patients. Reducing the DBS power on 2.5 V let to a clear reduction of these effects, switching off DBS stopped them.

**Conclusion:** DBS of the ANT leads to sleep fragmentation. This might be the reason for DBS – side effects as mood disorder, memory problems or even seizure continuation. Reducing DBS power at nighttime could be helpful.

#### P912 INTRACRANIAL ELECTROGRAPHIC PATTERNS AT SEIZURE ONSET AS PROGNOSTIC FACTORS FOR EPILEPSY SURGERY

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**Purpose:** Predicting the outcome of epilepsy surgery is difficult. The objective of this work is to investigate if the intracranial EEG patterns at seizure onset can be used to predict surgical outcome.

**Method:** Ictal onset patterns were analysed retrospectively in 305 seizures from 53 patients who underwent intracranial EEG recording (iEEG) prior to surgery. The seizure onset pattern was classified by visual analysis into diffuse electrodecrement (DED) and localised fast activity, spikes, spike-wave, sharp waves or theta activity. Presence of these seizure onset patterns was correlated with the surgical outcome. Engel surgical outcome scale was used. Grades I and II were considered favourable outcome, while grades III and IV were considered as poor outcome. One tailed Fisher's exact test was used to establish associations between surgical outcome and the different seizure onset patterns.

**Results:** The mean surgical follow up was 82 months. Diffuse electrodecremental event was the most common onset pattern seen (34%), followed by localised fast activity (30%), spike-wave (11%), sharp waves (9%), spikes (7%), theta activity (5%) and polyspike (4%). Among the 18 patients with DED at onset, nine had favourable outcome whereas among the 35 patients without DED, 23 showed favourable outcome ( $p = 0.2$ ). Among the 16 patients with fast activity at onset, 13 had favourable outcome whereas among the 37 patients without fast activity, 19 showed favourable outcome ( $p = 0.038$ ).

**Conclusion:** DED at onset should not discourage surgery despite being a diffuse change because it is not associated with poor surgical outcome. Presence of localised fast activity is associated with favourable outcome.

### P913

#### THE EFFECTS OF VAGAL NERVE STIMULATION ON GENERALIZED-PARTIAL SEIZURE COUNT AND MEDICAL TREATMENT IN ADULT DRUG RESISTANT EPILEPSY PATIENTS

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The aim of this study is to find out if VNS affects to the generalized-partial seizure count and medical treatment on adult drug resistant epilepsy patients. This study included 20 patients (>18 years of age), who were diagnosed with drug-resistant epilepsy between 2001 and 2010 at Neurosurgery Departments of Ufuk University Faculty of Medicine and Gulhane Military Medical Academy, and underwent Vagus Nerve Stimulator (VNS) implantation operation according to the decision of Epilepsy Surgery Council. Retrospective data gathered from the hospital databases of Ufuk University Faculty of Medicine and Gulhane Military Medical Academy. If a significant difference is found, a comparison is made by *Wilcoxon Signed Ranks test* and *Pairwise*. Differences are shown with *box-plot graphics*. For the differences between the scores that measured at different time periods, percentages are calculated. For all the group analyses, the statistical significant rank is accepted as the value of  $p < 0.05$ . Bonferroni correction is made when it is needed at pairwise comparisons. Changes in frequencies of generalized seizures after VNS implantation revealed a 60.4% reduction in 2nd month, 70.6% reduction in 6th month, and 84.9% reduction in 12th month. Partial seizures were decreased after VNS implantation 57.8% at 2nd month, 59.2% at 6th month, 54.9% at 12th month. Analyses of medical treatment between preoperative and postoperative period revealed that there were no changes in medications. Patients neither changed nor decreased their antiepileptic drug doses. Finally, we found that VNS decreases the scores of generalized-partial seizures with a statistically significant value. The doses of anti-epileptic drugs could not be decreased and medical treatment resume as before VNS is implanted. When we

compare our results with the literature, they are found to support each other.

### P914

#### IMPACT OF SEIZURE FREQUENCY ON IMPROVEMENT IN QUALITY OF LIFE IN MEDICALLY AND SURGICALLY TREATED PATIENTS WITH EPILEPSY: RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

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**Purpose:** To assess the impact of baseline seizure frequency on the proportion of patients treated medically and surgically who achieve minimal clinically important differences (MCID) in quality of life (QOL) at 6- and 12-months.

**Method:** We analysed QOL in a randomized controlled trial (RCT) of temporal lobe epilepsy (Wiebe et al, NEJM 2001). QOL was assessed with QOLIE-89 and QOLIE-31, self-administered at baseline, 6 months and 12 months. MCID for QOLIE-89 and QOLIE-31 was defined as 10.1 and 11.8 points in total score, respectively. We categorized average monthly seizure frequency as low (1-4 per month) or high (>4 per month).

**Results:** 40 patients were randomized to medical and 40 to surgical therapy. In analyses including both patient groups and both measurement periods (6 and 12 months), the largest proportion of MCIDs occurred among surgical and medical patients with high baseline frequency of dyscognitive (65% 95CI 49-78%) and all seizures (72% 95CI 54-85%). Among surgical patients, the proportion achieving MCID tended to be higher among those with more seizures (high = 62%, low = 37%;  $p = 0.25$ ), but not in medical patients (24% each).

**Conclusion:** In this RCT, higher baseline seizure frequency correlated with larger improvements in QOL in surgical patients. QOLIE-31 was more sensitive to detect these changes. Other explanatory variables are explored.

### P915

#### A SURGICAL METHOD FOR SAFELY IMPLANTING LARGE SUBDURAL ELECTRODE ARRAYS IN CHILDREN

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**Purpose:** Patients with non-lateralized or atypical epilepsy usually do not undergo phase 2 surgical evaluation. We sought to develop a surgical technique which allows a meaningful evaluation of these challenging patients. Our purpose is to develop a method which allows large subdural electrode arrays to be safely implanted in children.

**Method:** A surgical approach, which includes placing water-tight dural expansion grafts at the time of electrode implantation, will be described. Sixteen consecutive patients treated at our hospital, using this approach will be presented.

**Results:** From November 2011 to November 2012, sixteen children underwent placement of large bilateral subdural electrode arrays, using our surgical method. The number of electrodes implanted ranged from 102 to 226, with a mean number of electrodes implanted of 167. Our patients tolerated the electrode implantation well. Monitoring with the intracranial electrode arrays lasted from 3 days to 30 days, with an average duration of 9.5 days. There were no infections, hemorrhages or CSF leaks in our series. The expanded electrode recordings led to resective surgery in all patients. Five patients achieved ILAE class 1 outcome, four ILAE class 3 outcome and seven ILAE class 4 outcome.

**Conclusion:** Large subdural electrode arrays can be safely implanted in children. With increased cortical coverage, a more complete understanding of seizure onset and propagation can be achieved. Using this approach, successful resective surgery can be performed, resulting in satisfactory seizure control.

#### P916

##### VERTICAL PERITHALAMIC HEMISPHEROTOMY IN PEDIATRIC CATASTROPHIC EPILEPSY: A SINGLE CENTER EXPERIENCE OF 38 CHILDREN

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**Purpose:** In hemispheric epilepsy there are two concepts to perform a complete disconnection of the affected hemisphere. A lateral perinsular hemispherotomy with various modifications that have consistently been reported to be safe and effective and the vertical parasagittal hemispherotomy introduced by O Delalande. However, apart from Delalande's report published in 2007, there are no large series from other centers reporting on the long-term experience with this special technique. We evaluated long-term safety and seizure outcome of this technique.

**Methods:** Between 1998 and 2012 38 patients underwent a vertical perithalamic hemispherotomy. We retrospectively analyzed our prospectively collected data of these patients.

**Results:** There were 21 male and 17 female patients (median age 5.5 years; range from 4.4 mo – 20.1 years). The affected hemisphere was left in 25 and right in 13 patients. The patient median age at seizure onset was 1.3 years (range from 1 day – 11.6 years). The median duration of epilepsy before surgery was 3.8 years (range from 4.4 mo – 15.8 years). The underlying hemispheric pathology was ischemic vascular in 19, malformation of cortical development in 11, Sturge Weber Syndrome in 2, gliosis after tumor resection in 2, and Rasmussen encephalitis, posthemorrhagic, postencephalitic and cavernoma pathology in 1 each. We encountered no serious intraoperative complications. One 4 year-old patient died on the 4th postoperative day due to intractable hyponatremic brain edema. Three patients developed CSF disturbances, but only one needed a permanent VP-shunt (2.6%). 35/38 children (92.1%) were seizure free (class 1a) after a median follow-up time of 3.5 years (range from 6 mo – 14.4 years). Only three patients were classified as class 5.

**Conclusion:** According to our results, we confirm Delalande's concept to be an effective and safe method in terms of seizure outcome and safety.

#### P917

##### SURGERY FOR EXTRATEMPORAL FOCAL CORTICAL DYSPLASIA FOLLOWING A NON-INVASIVE PRESURGICAL PROTOCOL: THE PORTO ALEGRE SERIES

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**Purpose:** Focal cortical dysplasia (FCD) is the most frequent cause of medically refractory neocortical epilepsies. MRI has improved detection of FCD lesions, but most Centers only consider epilepsy surgery after chronic intracranial EEG studies. We present the approach to evaluation and surgical results in the long-term for 40 patients with MRI-positive neocortical FCD who did not undergo chronic intracranial EEG studies.

**Method:** All patients underwent routine presurgical evaluation and had surgical resection guided by acute ECoG and cortical stimulation. 28 had lesions over or adjacent to eloquent cortex, and only 12 away from eloquent regions. Mean age of seizure onset and at operation were, respectively, 6.4 and 14.6 years. Fifteen patients were re-operated. Mean follow-up at final visit, after single or second operation, was 6.3 years (2–18). Outcome was assessed yearly. Engel's classification was used.

**Results:** Continuous or bursting ECoG discharge patterns were found at operation in 34 patients (85%). One year after operation, 23 patients (58%) were seizure free, but in 9 of these seizures recurred between 1 and 6 years after surgery. At last visit, 17 (43%) were seizure free: 8/12 (66%) with lesions away from eloquent cortex and 9/28 (32%) with lesions adjacent or over eloquent regions. Complete resection of the lesion and of the regions displaying continuous ECoG spikes correlated with surgical results at year 1 and last outcome. No patient had unexpected worsening of neurologic function.

**Conclusion:** Surgery for neocortical FCD can be effectively and safely performed following non-invasive evaluation and guided by acute ECoG and cortical stimulation. Delayed seizure recurrence is frequent. Results have a tendency to correlate with lesion proximity to eloquent cortex and should be compared with series including a majority of patients with lesions surrounding eloquent regions. Anticipation of deficits may allow seizure freedom even in these latter patients.

#### P918

##### “FROM THE BACK”: POSTERIOR CALLOSOTOMY FOR THE TREATMENT OF DROP ATTACKS – THE FIRST 30 PATIENTS UNDERGOING A NOVEL SURGICAL APPROACH

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**Purpose:** The impact of callosotomy to prevent sudden epileptic falls is still unclear. One- or two-stage total callosotomy consistently leads to better results than incomplete, anterior-based sections. We hypothesized that the better outcome with total callosotomy is specifically related to

the section of the fibers crossing through the posterior half of the CC, most of which are left intact in the anterior-based approaches. Thus, we present a unique series of 30 patients who underwent selective posterior callosotomy to control drop attacks.

**Method:** All 30 patients had refractory, frequent epileptic drop attacks and underwent inpatient presurgical evaluation to rule out focal epilepsy. 28 had variable degrees of mental retardation. All had a selective posterior callosotomy to the level immediately anterior to the isthmus. Comparisons between a number of practical variables were performed before and after surgery. A neurological examination to test for disconnection syndromes and a post-op MRI were also performed. Mean post-op follow-up was 7 years.

**Results:** At the last visit, 50% of the patients were free from drop attacks and an additional 20% had a dramatic reduction in the frequency of these disabling seizures; only nine patients failed to improve significantly. This was paralleled by a similar marked reduction in the percentage of patients needing constant supervision. Marked improvement in behavior was observed in two-thirds of patients. None had significant motor or cognitive worsening in the long-term. No clear correlations were found with a number of epilepsy variables.

**Conclusion:** Selective posterior callosotomy is a safe and effective novel surgical approach for refractory epileptic drop attacks. Results are comparatively better than those reported with any subtotal, anterior-based section and complications are much less significant than those reported with total callosotomy. Recent tractography findings lend anatomical support to the excellent results found with selective posterior sections.

## P919

### TEMPORAL LOBE TUMORS WITH REFRACTORY EPILEPSY: SEIZURE AND NEUROPSYCHOLOGICAL SURGICAL OUTCOME

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**Purpose:** Low grade glial tumors (LGT) can be seen in temporal lobe epilepsy (TLE – Van Breemer et al., 2007). The extent of surgical resection predicts seizure freedom in Low-Grade Temporal Lobe Brain Tumors (LGT – Englot et al., 2012), however limited data exist comparing surgical approach with neuropsychological outcomes. The aim of this work was to discuss the surgical and memory outcomes in patients with LGT with refractory TLE.

**Method:** Retrospective review of 29 operated patients with LGT and refractory TLE at Federal University of Sao Paulo, between 2003 and 2011. We assessed histopathology, gross of resection, surgical and neuropsychological outcome features. Verbal and no verbal delayed recall memory and verbal learning test were performed pre and post operative. Hippocampal functions were considered: impaired; partially impaired or normal. We evaluated seizure outcomes according to the Engel classification.

**Results:** Twenty-five (86.20%) patients were Engel 1 and twenty-one (72.41%) were completely seizure free. Ninety-six percent (23/24) of patients with gross total tumor resection evolved to Engel 1, while 40% (2/5) from the group of residual tumor were Engel 1 (p = 0.012). Eighteen patients had pre and post surgical neuropsychological evaluation, 13 of them had the hippocampus involved by tumor (seven with contralateral functional deficits preoperatively). In five the memory function improved after surgery.

**Conclusion:** LGTT with refractory epilepsy have excellent surgical outcome when a gross total tumor resection is possible. The presence of functional deficits contralateral to the hippocampus encroached by tumor was not related to a worse prognosis of seizure control or of functional deficits after surgery.

## P920

### EPILEPSY SURGERY IN GUATEMALA: OUR EXPERIENCE IN 6 YEARS

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**Purpose:** Describe the evolution of the patients were under surgery for drug resistant epilepsy from 2006 to 2012.

**Method: Patients and method:** From a universe of 3,648 patients, we chose 239 with truly diagnosis of drug resistant epilepsy. All the patients underwent a study protocol for drug resistant epilepsy, we made 73 video-EEG with medical suppression (AD), subtemporal electrodes were implanted in two patients, 31 intraoperative electrocorticografías, 2 72-h chronic electrocorticography, 41 patients were operated. We exclude in this report, seven patients because the postoperative time.

**Results:** Thirty-four patients were operated as follows addressing them, right temporal lobectomies 15, left temporal lobectomies 7, callosotomy 1, hemispherostomy 1, lesionectomy more corticectomy left parietal (with surgery in two times)1, frontal corticotomy 3 and lesionectomy, temporal lesionectomy 2, and 3 cases were treated with vagus nerve stimulation (VNS). Follow-up, from the Patients with TLE Engel I 13 patients Engel II 9 (n = 22), the other patients Engel I 3 patients Engel II 9 patients One patient post callosotomy was in Engel II until his death 12 months after surgery, from complications of virus A-H1N1, we observe significantly improved in comparison tests of working memory and long term in TLE.

#### Conclusion:

- Epilepsy surgery is possible to do in Guatemala with current resources, maintaining international quality controls.
- The best results as in the World Series have been obtained with temporal lobectomy patients the effect of crisis management has maintained long-term, however, it has been possible to make virtually all types of epilepsy surgery, keeping furthermore, without the morbidity and mortality associated standard.

## P921

### A RANDOMIZED CONTROLLED TRIAL OF CATHODAL TRANSCRANIAL DIRECT CURRENT STIMULATION IN PATIENTS WITH MULTIFOCAL EPILEPSY REFRACTORY TO PHARMACOLOGICAL TREATMENT

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**Introduction:** Transcranial direct current stimulation (tDCS) is a safe, non-invasive method that modulates cortical excitability and has emerged in recent years. tDCS has been used in different neurological and psychiatric conditions, including epilepsy. Many of these studies have been merely exploratory and the positive results have yet to be reproduced. In the case of epilepsy, it has been attempted to reduce the number of seizures and epileptiform patterns by cathodal stimulation and its apparent hyperpolarization effect.

**Purpose:** Evaluate the efficacy (reduction of seizure frequency  $\geq 50\%$  and decrease of epileptiform activity [amplitude and frequency]) and safety of tDCS in patients with multifocal pharmaco-resistant epilepsy.

**Methods:** Clinical trial randomized, prospective, patient-blinded of 5 arms (4 active [tDCS 2 mA; 3 Hz], 1 placebo) with patients diagnosed with multifocal pharmaco-resistant epilepsy, from our Epilepsy Clinic (February–December 2012). We described the clinical and socio-demographic variables, monthly frequency of seizures and epileptiform activity on EEGs before and after, at 1 month, 2 months of the intervention were recorded. Adverse effects were reported. Descriptive statistic and 4-way ANOVA were used.

**Results:** Thirty-five patients were included 7 (placebo; tDCS) 7 [1 session/30 min], 9 [1 session/60 min], 5 [3 sessions/30 min] and 7 [5 sessions/30 min]. The 45.7% (16/35) of the patients reported an itching sensation on the site of stimulation. The therapies of 60 min, 3 sessions/30 min and 5 sessions/30 min showed a significant reduction ( $\alpha = 0.05$ ), up to  $-26\%$  on the second month.

**Conclusion:** The tDCS therapy of 60 min, 3sessions/30 min and 5sessions/30 min showed a significant reduction in the number seizures of  $-26\%$  without achieving  $\geq 50\%$ . The tDCS showed to be safe and well tolerated.

## P922

### PROGNOSIS AND MORBIMORTALITY IN EPILEPSY SURGERY USING GRID (ECOG) OR DEPTH (SEEG) ELECTRODES OR BOTH (ECOG +SEEG)

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**Purpose:** Analyze the prognosis and complications of patients requiring NFI with different implantation strategies.

**Method:** Retrospective observational study of 52 consecutive patients between 2005 and 2011 that were evaluated by NFI focal epilepsies. We analyzed demographics, prognosis, morbidity and mortality.

**Results:** Of the 52 patients there were 27 females and 24 males with a mean age of 21.1 (1–45). All were chronically implanted in 15 (28.8%) with depth electrodes (SEEG), 16 (30.7%) with subdural grids (ECOG) and 20 (38.4%) with both methods (SEEG + ECOG). Four (7.7%) did not undergo resection. The last Engel I + II obtained at follow-up of all the population was: 82.8% (40/48 patients). No significant differences in prognosis between the three groups of strategies implants. Transient complications were 28.8% (15/52) and 19.2% permanent (10/52). Patients implanted with grids had just highest number of permanent complications 43% ( $p < 0.05$ ). The only recorded death was in a patient with combined implantation.

**Conclusion:** In our study we found no significant differences in the prognosis of seizures NFI using different strategies. Complications were more frequent in the implanted only with grids and mortality was observed only when using combined implementation. The lowest number of permanent complications were observed using SEEG.

## P923

### MULTICENTER EXPERIENCE WITH MINIMALLY INVASIVE STEREOTACTIC LASER THERMAL AMYGDALOHIPPOCAMPOTOMY FOR MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Stereotactic laser thermal ablation of the amygdala and hippocampus (SLTAH) is a minimally-invasive alternative to open amygdalo-hippocampectomy or temporal lobectomy for mesial temporal lobe epilepsy (MTLE). The purpose of this study is to examine the effectiveness and safety of this procedure in a prospective, non-controlled, multi-center cohort of patients with MTLE.

**Method:** MRI-guided SLTAH was performed via optical fiber using a computer-controlled, saline-cooled system with real-time MR thermal imaging in 40 patients (repeat procedure in 2) with MTLE at 9 epilepsy centers. Thirty-six patients had mesial temporal sclerosis (MTS) and 4 had normal MRIs.

**Results:** At six months follow-up thus far, 8 of 12 patients (67%) with mesial temporal sclerosis (MTS) are seizure-free. While 0 of 4 MTS-patients are seizure-free, two of these have only contralateral onsets post-operatively. Complications included two visual field deficits (one superior quadrantanopsia; one homonymous hemianopsias due to deviated cannula), and three hematomas (one acute subdural hematoma evacuated and two intracerebral hematomas, all without sequelae).

**Conclusion:** SLTAH may offer a minimally invasive alternative to open resection in patients with MTLE. Longer-term outcomes (6 month follow-up will be available on 38 patients by time of presentation) and more patients will be necessary to determine comparative effectiveness and safety vs. open resection.

## P924

### CLINICAL RESULTS IN SURGICAL TREATMENT OF REFRACTORY EPILEPSY IN SAN IGNACIO HOSPITAL: 3 YEAR RETROSPECTIVE STUDY

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**Purpose:** Evaluate the clinical results and complications in the surgical management of epilepsy at the San Ignacio Hospital.

**Method:** We searched the database and statistical and we found 57 patients who were taken to surgery for treatment of intractable epilepsy between November of 2009 to December of 2012 (3 years). Medical records were analyzed to study the clinical course of epilepsy and its complications.

**Results:** We treated 57 patients with epilepsy, aged 4–53 years. Of these, 35 patients had focal pathologies, and 18 multifocal. We performed the following surgical procedures: temporal lobectomy, frontal lobectomy, Hemispherectomy, Lesionectomy, Vagus nerve stimulator, Callosotomy. No patients were lost to follow up. According to Engel's classification, 77% of patients are in grade 1, 17% in grade 2, and 6% in grade 3. In postoperative complications one (1) patient had of cerebrospinal fluid fistula that resolved with medical management, one (1) patient had nominal aphasia that resolved with time, and one (1) patient had cerebrospinal fluid fistula associated with hydrocephalus that required to be derived. 90% are free of complications.

**Conclusion:** Epilepsy surgery is an option to consider in patients with intractable epilepsy, there was better response in focal epilepsy than in the multifocal. Most patients have no major complications related to the procedure, so it is a relatively safe option.

## P925

**CLINICAL OUTCOME DURING SEQUENTIAL CHRONIC STIMULATION OF THE NUCLEUS ACCUMBENS AND THE ANTERIOR THALAMUS FOR PHARMACORESISTANT EPILEPSY – 1ST PART: 6 MONTH STIMULATION OF THE NUCLEUS ACCUMBENS**

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**Purpose:** Only for the anterior thalamus (ANT) a controlled study of deep brain stimulation (DBS) showed reduction of seizure frequency and severity. However, depression was reported as one adverse event. The nucleus accumbens (NAC) has an important relais function for frontal and temporal lobe circuitry; DBS of the NAC has successfully been applied for major depression. The following uncontrolled, observational, open study summarizes the clinical outcome of 6 months of DBS in the NAC.

**Method:** Sequential NAC and ANT stimulation for pharmacoresistant patients with focal epilepsy was approved by the Ethics Committee of the University Magdeburg. The first period included 6 months of NAC stimulation, the second period ANT stimulation, respectively. Already 6 months before surgery, the antiepileptic drug regimen remained unchanged. All patients underwent video-eeg-monitoring before surgery and after the 6 month stimulation period. Changes of Beck-test-score, Liverpool-Seizure-Severity-Scale (LSSS) and seizure frequency were prospectively assessed. Due to pronounced interindividual heterogeneity in the baseline period, all variables were related to the individual baseline values and expressed as fraction of 1. The results of four patients, who have completed the first NAC stimulation period, are reported.

**Results:** After NAC stimulation the relative LSSS reduced to  $0.81 \pm 0.11$  ( $p = 0.014$ ). The sum of disabling seizures (defined as generalized tonic-clonic seizures plus complex partial seizures) showed a tendency toward reduction ( $0.66 \pm 0.34$ ;  $p = 0.091$ ). The number of non-disabling seizures and the Beck-test did not change after the NAC stimulation period. From the four subjects, in two patients frequency of disabling seizures reduced to <59% and only the responder (reduction to 22%) had a diffuse electroencephalographic seizure onset pattern.

**Conclusion:** NAC stimulation proved to be efficacious concerning seizure severity. A larger cohort is necessary to show a potential reduction of seizure frequency or the electrophysiological characteristics of responders.

*FC Schmitt and J Voges were equally contributing to this study.*

## P926

**REPORT OF 9 CLINICAL CASES: FUNCTIONAL HEMISPHERECTOMY FOR EPILEPSY REFRACTORY TO MEDICAL MANAGEMENT**

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**Purpose:** To report the clinical results and complications of nine cases of hemispherectomy for treatment of intractable epilepsy at the Hospital Universitario San Ignacio.

**Method:** We reviewed the database of the Hospital Universitario San Ignacio and found nine cases of patients who underwent functional hemispherectomy for intractable epilepsy from November 2009 to November 2012. We observed clinical outcomes and complications of the procedure.

**Results:** There were nine patients with an age range from 6 to 44 years, predominantly male, which had intractable epilepsy criteria. 100% of the patients underwent follow-up. Seven patients who underwent functional hemispherectomy are in engel 1, 2 are in engel 2. Procedure-related complications were 1 cerebrospinal fluid fistula resolved with medical management and 1 CSF fistula that required treatment with DVP.

**Conclusion:** The functional hemispherectomy is an effective method for reducing the frequency in patients with ictal refractoriness criteria to medical management in specific syndromes.

## P927

**EPILEPSY SURGERY IN THE DOMINICAN REPUBLIC**

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**Purpose:** Identify lesional epilepsy and Histological type.

**Method:** The methods used were Stereotaxy surgical site and neuronavigation.

**Results:** There have been 15 patients with lesions whose clinical presentation were crises seizures which were most focal (13) and only two all with characteristic generalized refractoriness, ages ranged from 9–61 years, with male gender predominance in eight and seven female. The locations were divided in temporal lobe 8 and 7 in the frontal lobe, the right hemisphere being dominant with nine cases.

**Conclusion:** The pathology results were six cases with grade II astrocytoma, five with oligodendroglioma and four with cavernomas.

## P928

**PROVOCATIVE TEST BY ELECTRICAL STIMULATION OF THE ENTORHINAL AREA PREDICTS MEMORY IMPAIRMENT FOLLOWING AMYGDALOHIPPOCAMPECTOMY**

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**Purpose:** Amygdalohippocampectomy (AHP) has been widely applied for medically refractory temporal lobe epilepsy (TLE). However, its indication for the verbal dominant hemisphere is limited due to the possibility of postoperative memory impairment. To prevent this disabling complication, methods with strong predictive power are required. Here, we describe the efficacy of provocative test by electrical stimulation of the entorhinal area in predicting postoperative memory impairment.

**Method:** We performed the abovementioned provocative test on 10 consecutive patients with refractory TLE involving the dominant hemisphere. Prior to AHP, depth electrodes were implanted to the entorhinal area with stereotaxic technique. Using electrical stimulation through the depth electrodes, provocative tests for memory functions were performed. Following electrical stimulation during memory encoding, delayed recall and/or recognition were evaluated with verbal and/or

visual memory tasks. The pre and postoperative memory function were compared in six patients who underwent AHP, using Mini-Mental State Examination (MMSE) and Wechsler Memory Scale-Revised (WMS-R).

**Results:** A positive test was found in 6 out of 8 for delayed recall and in 6 out of 10 for recognition for verbal memory. Among the 6 who underwent AHP, postoperative memory impairment developed in two patients with positive tests in both delayed recall and recognition for verbal memory. In contrast, memory function was intact in three with negative tests and in one with positive test in only delayed recall for verbal memory. None demonstrated provoked visual memory disturbance. AHP was considered not applicable to the remaining four patients based on the result of the provocative test.

**Conclusion:** Our results suggest that recognition tasks following electrical stimulation during memorization is the most predictive for the possibility of postoperative memory impairment. Provocative test using depth electrodes implanted in the entorhinal area is a promising predictive tool for possible memory impairment following AHP of dominant hemisphere.

## P929

### EXPERIENCE IN EPILEPSY SURGERY IN PEDIATRIC PATIENTS WITH REFRACTORY EPILEPSY IN MEXICO

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**Introduction:** The epilepsies are a disease with chronic seizures and recurrences of diverse etiology. The frequency in the pediatric neurology service are 40% of the medical attention and the control it is 70% of the cases; included new and old antiepileptic drugs. But in 20% it is necessary additionally treatment included epilepsy surgery.

**Objective:** Present information about experience of epilepsy surgery in pediatric population in Medical Center La Raza México.

**Material and methods:** Included pediatric patients in the program of epilepsy surgery with refractory epilepsy between January 2008 to June 2012 and with attention in Pediatric neurology and neurosurgery of Medical Center La Raza. The previous evaluation consisted in: confirmation of refractory epilepsy, number of antiepileptic drugs, videoEEG, Magnetic resonance, SPECT and neuropsychological exam, included in graphs and tables.

**Results:** Included 15 patients, with predominant female 9, infants 70% and the type of surgery was: frontal lobectomy, functional hemispherectomy and callosotomy. In 6–12 months the efficacy was 75%, and number of antiepileptic drugs for control of seizures with classification of Engels obtained in III phase. The resolution of surgery obtained 3–4 years of arrived to attention in the hospital.

**Conclusion:** This preliminary information concluded it is very necessary it is more brief the surgery procedures for best quality of life.

**Key Words:** Refractory epilepsy, surgery in epilepsy, antiepileptic drugs.

## P930

### SURGICAL RESECTION OF HIGH-FREQUENCY OSCILLATION REGIONS PREDICTS FAVORABLE OUTCOME IN NEOCORTICAL EPILEPSY

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**Purpose:** High-frequency oscillations (HFO) are utilized as new electrophysiological marker to delineate the resection margin before epilepsy surgery. Wider clinical application of HFO is limited by high inter-patient variability in spatiotemporal distributions of HFO and by lack of exact quantitative measures to reliably determine the brain area necessary to remove. Here we adopted a new approach to identify HFO and examined novel parameters to predict surgical outcome in cases of neocortical epilepsy.

**Method:** Fifteen patients with neocortical seizure onsets who underwent intracranial EEG monitoring were included. A fully automated algorithm was used to detect HFO. The spatial association of HFO distribution and the seizure onset zone (SOZ) was evaluated. To address the issue of high inter-subject variability in HFO properties, we evaluated a statistical parameter, which identifies regions of high-rate HFO in each patient. The relationship between surgical resection of HFO-generating region and post-operative outcome was examined.

**Results:** Grouped analysis revealed that fast ripple (FR) and ripple (R) rates were significantly increased in the SOZ. In within-patient comparison, either FR or R rate localized the neocortical SOZ in eleven patients. High-rate HFO regions were defined by individually adjusted thresholds, and they partially overlapped with the SOZ. Favorable outcome was observed in patients in whom high-rate HFO regions were removed in addition to SOZ. In contrast, leaving even a small area of high-rate HFO unresected predicted poor outcome. The extent/ratio of SOZ or irritative zone resection, however, did not differ between seizure-free and seizure-persistent groups.

**Conclusion:** This study demonstrates that high-rate HFO can mark the areas of high epileptogenicity and the crucial component of neocortical epileptic network which should be completely removed to achieve good surgical outcome. The ability to define a quantitative parameter identifying high-rate HFO regions facilitates prospective application of HFO in presurgical evaluation.

## Poster session: Genetics B Wednesday, 26 June 2013

### P931

#### PITFALLS IN DIAGNOSTIC SEQUENCING: THE STORY OF SCN1A MUTATIONS BEING MISSED IN DRAVET SYNDROME

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**Purpose:** The most important gene implicated in the development of Dravet syndrome (DS) is *SCN1A*, which encodes for the alpha-1 subunit of the neuronal voltage-gated sodium channel Na<sub>v</sub>1.1. Mutations in *SCN1A* explain ~75% of DS patients, of which 90% arise *de novo*. To identify the missing heritability in the remaining DS patients we performed whole exome sequencing (WES) in patient-parent trios.

**Method:** DS patients were selected based on the proposed core DS phenotype (Dravet C., 2011). Prior to inclusion, *SCN1A* mutations and deletions/duplications were excluded by Sanger sequencing and MLPA or MAQ analysis. WES was performed on 28 DS patients who fulfilled all inclusion criteria and their parents if available (n = 25/28).

**Results:** Unexpectedly, WES showed that eight out of 27 patients carried a *de novo* *SCN1A* mutation, previously missed by Sanger sequencing. All mutations and their *de novo* occurrence were confirmed by repeat Sanger sequencing. After re-evaluation of four of the original Sanger sequencing trace files, we identified several reasons for missing these variants: one patient was thought to be sequenced but actually never was; one mutation was overlooked in the trace files; one mutation was lying 7 base pairs into the intron and was therefore dismissed as not significant and one mutation could not be observed in the original trace files. The latter mutation was re-sequenced with the same primer pair by the referring laboratory and the mutation could be visualized using a lower annealing temperature.

**Conclusion:** Hereby, we show that direct Sanger sequencing, which is considered to be the gold standard in sequencing, can have numerous pitfalls leading to misinterpretation of the genetic diagnosis of patients. This valuable lesson emphasizes that patients with DS must be carefully investigated for a pathogenic *SCN1A* mutation and increases the overall rate of *SCN1A* mutations in DS to +80%.

### P932

#### AUTOSOMAL DOMINANT NOCTURNAL FRONTAL LOBE EPILEPSY CONFIRMED GENETICALLY IN TEN PATIENTS

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**Purpose:** The aim was to evaluate patients who have fulfilled criteria of Autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE).

**Method:** We have analyzed ten patients (two men and eight women) from two unrelated families aged from 6 to 70 years with an aver-

age of 7.8 ± 2 years at Department of Neurology in Brno. All patients have fulfilled criteria of ADNFLE, which is an epileptic syndrome mostly manifested in the first two decades of life. The accurate prevalence is not known, more than one hundred families are identified worldwide. The mutations of genes encoding various nicotinic acetylcholine receptor alpha- and beta-subunits, and corticotropin-releasing hormone are associated with this syndrome. Available molecular genetic testing confirms the diagnosis in less than twenty percent of patients with positive family history. Nocturnal partial seizures occur typically in clusters, they are brief, stereotypical and hypermotoric. It is important to differentiate epilepsy from other conditions, particularly non-rapid eye movement sleep disorders. The resistance to antiepileptic drugs is about thirty percent. All of our ten patients were genetically examined in Center of Molecular Biology and Gene Therapy.

**Results:** Amplification and sequence analysis allowed us to confirm the mutation (p.S280F, heterozygote) in the *CHRNA4* gene (neuronal nicotinic acetylcholine receptor alpha-subunits) in all ten patients. This influences a function of channel and causes the ADNFLE phenotype. Only one patient had daytime seizures and none of them had interictal EEG epileptiform abnormalities. All patients had normal magnetic resonance imaging. They were taking from one to five antiepileptic drugs.

**Conclusion:** ADNFLE is a lifelong disease with periods of remissions and relapses. Routine electroencephalography is not beneficial enough in some cases and the syndrome is misdiagnosed with parasomnia. This is one of the reasons why the exact prevalence is not known. It is assumed that the prevalence is underestimated.

### P933

#### EVIDENCE POINTING TO FAILURE IN NEUROGLIAL DIFFERENTIATION IN FOCAL CORTICAL DYSPLASIA (FCD) TYPE II

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**Purpose:** FCD is characterized by a spectrum of abnormalities in the development of the laminar structure of the human cerebral cortex. Microscopically, FCD is usually associated with cell abnormalities, giant/dysmorphic neurons and balloon cells. Since dysplastic tissue is highly epileptogenic, patients with FCD frequently need surgery to control their seizures. To date, the mechanism underlying the development of FCDs is poorly understood. Our main objective was to determine whether abnormal microRNA regulation could be present in FCD. More specifically, we wanted to evaluate microRNA expression pattern in FCD and to identify potential microRNA target genes whose expression would be deregulated in FCD.

**Method:** We used total RNA isolated from brain tissue obtained after epilepsy surgery performed in 17 patients with type II FCD and 20 controls from autopsy. MiRNA expression profile was assessed by Affymetrix GeneChip platform miRNA array. Quantitative PCR (qPCR) was used to validate results miRNAs experiments and to access expression of target genes.

**Results:** MicroRNA expression studies using microarray revealed 39 microRNAs which were downregulated and only one microRNA overexpressed. Decreased expression of three miRNAs was confirmed by qPCR: **hsa-miR-31**, **hsa-miR34a** and **hsa-let-7f**. In addition, we found that *NEUROG2*, a possible target gene regulated by hsa-miR-31 is over expressed in FCD.

**Conclusion:** The three microRNAs confirmed to be downregulated act as tumor suppressors and may lead to the abnormal histopathological features seen in FCD type II. Furthermore, overexpression of *NEUROG2*, would lead to failure in the transition between neurogenesis and gliogenesis and could explain the existence of immature or poorly differentiated cell types, such as balloon cells, which are typical of FCD type II.

#### P934

##### EPILEPSY-APHASIA SPECTRUM DISORDERS ARE CAUSED BY MUTATIONS IN *GRIN2A*

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**Purpose:** The epilepsy-aphasia syndromes (EAS) are a group of rare, severe epileptic encephalopathies (EE) of unknown etiology with a characteristic EEG pattern and developmental regression, particularly affecting language. Rare pathogenic deletions that include *GRIN2A* have been implicated in neurodevelopmental disorders. We sought to delineate the pathogenic role of *GRIN2A* in the etiology of diverse epilepsy syndromes.

**Method:** We conducted targeted massively parallel resequencing of *GRIN2A* in a cohort of 519 probands with a spectrum of EE to identify novel pathogenic variants in the gene.

**Results:** We identified four probands with *GRIN2A* variants that segregated with the disorder in their families. Strikingly, all four families presented with EAS, accounting for 9% of epilepsy-aphasia cases. We did not detect pathogenic variants in other EE (n = 475), nor in 81 probands with benign childhood epilepsy with centro-temporal spikes.

**Conclusion:** We report the first monogenic cause for EAS. *GRIN2A* mutations are restricted to this group of patients, with important ramifications for diagnostic testing and treatment, as well as novel insights into the pathogenesis of this debilitating group of conditions.

#### P935

##### TREATMENT OUTCOME OF GENETIC 7P21.3 DELETION WITH EEG ABNORMALITIES AND AUTISM PHENOTYPE IN A 5-YEAR OLD MALE

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**Purpose:** This single-case reviews treatment outcome of Lennox-Gastaut EEG pattern and epilepsy with autism phenotype in a 5-year old male with 7p21.3 deletion. This genetic variant has been associated with temporal lobe epilepsy, language delay, autism phenotype, as well as possible Dandy Walker. This presentation is potentially responsive to anticonvulsant combination therapy, reducing manifestation of a debilitating disorder.

**Method:** Medical and developmental testing included serial EEG and video EEG monitoring, brain 3T MRI (normal) ADI-R (autism pheno-

type, initially) language (PPVT and EVT) as well as social (ADOS). Genetic testing through Athena laboratory.

**Results:** This five-year old male initially met criteria for autism. Patient was noted to have atypical absence seizures and subsequently developed atonic head drops. Initial EEG showed 2–3 Hz generalized polyspike and slow wave discharges, semicontinuous right temporal slowing appearing like Lennox-Gastaut variant. Genetic microarray found 7p21.3 (190 kb) deletion while ruling out sodium channelopathy, Fragile X, and Angelmanns and Phelan-McDermott syndromes. Valproic acid had minimal clinical or affect on EEG change. Clinical and EEG normalization occurred after adding felbamate and clobazam, then tapering valproic acid. Brain 3T MRI was also negative. Treatment response involved EEG normalization and reduction of autistic-like features over a 3-month course of felbamate and clobazam. After EEG improvement, resolution of autism phenotype was documented via ADOS and ADI-R within 3-months.

**Conclusion:** Clinical treatment with known 7p21.3 chromosomal deletion showed resolution of atypical absence and head drop seizures and normalization of EEG in a 5-year old with Dooose or a Lennox-Gastaut variant. This outcome documents that some genetic variants linked to autism phenotype and epilepsy co-morbid conditions may respond well to treatment of EEG, and in such cases may even resolve autism phenotype. Comparable outcome has been documented in rare familial cases of 7q36 deletion in Amish families using valproic acid. This child required modified combination treatment. Data sharing of such cases is critical to improve our understanding of environmental and genetic factors in autism and epilepsy.

#### P936

##### WHOLE EXOME SEQUENCING IDENTIFIES THE NOVEL GENE (MYOCLONIN 4) IN CHILDHOOD ABSENCE EPILEPSY WITH EYELID MYOCLONIA EVOLVING TO JUVENILE MYOCLONIC EPILEPSY

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**Purpose:** Identification of the causal gene of childhood absence epilepsy with eyelid myoclonia (CAE/EM) evolving to juvenile myoclonic epilepsy (JME).

**Method:** We analyzed one large family by linkage mapping and Genome scan with 440 microsatellites, and then applied whole exome sequencing. The family of four generations, with 51 members of which 8 were clinically and 2 were EEG affected, was ascertained through a proband affected with CAE/EM evolving to JME. MLINK was used 2 diagnostic models assuming 70% penetrance, disease allele frequency of 0.001 and phenocopy and gene mutation rates of 1%.

**Results:** LOD score (2.41 for D12S1042, q = 0, m = f) identified 8 more microsatellites on chr 12p11.23 to form a haplotype that segregated with 8 CAE/EM- and 2 EEG-affected members across four generation. Whole exome sequencing isolated R638W missense mutation of Myoclonin 4 on chr 12p11.23. The same mutation is absent in 342 controls matched for ethnicity and ancestral origin. Three other mutations (Q332K, I640V, G1016V) of Myoclonin 4 were observed in four families and two singletons with CAE/EM, CAE evolving to JME or JME.

**Conclusion:** This result strongly suggests that Myoclonin 4 is a causal gene of childhood absence epilepsy with eyelid myoclonia evolving to

juvenile myoclonic epilepsy. Knockout of Myoclonin4 in mice to prove causality is in progress.

**P937**  
**IDENTIFICATION OF *ATPIA3* MUTATIONS BY EXOME SEQUENCING AS THE CAUSE OF ALTERNATING HEMIPLEGIA OF CHILDHOOD IN JAPAN**

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**Purpose:** Alternating hemiplegia of childhood (AHC) is a rare disorder characterized by transient repeated attacks of paresis and epilepsy. AHC was thought to be caused by genetic abnormalities, although the responsible gene has not been determined. Using exome analysis, this study aims to identify the genetic abnormality behind.

**Method:** A total of 24 sporadic AHC patients were recruited. Exome sequencing was performed for the 8 patients with typical AHC. Verification of candidate genes was done by Sanger sequencing.

**Results:** In the eight sporadic AHC patients, 712,558 single nucleotide variations were found. After a series of exclusions, mutations in *ATPIA3* became candidate causes for AHC. Each patient harbored a de novo heterozygous missense *ATPIA3* mutation; these included G755C, E815K, C927Y and D801N. *ATPIA3* mutations were identified in 22 patients (91.7%). E815K was identified at a frequency of 46.8%.

**Conclusion:** *ATPIA3* heterozygous missense mutations are a cause of AHC. E815K mutations are frequent occurrences in AHC patients.

**P938**  
**THE CLINICAL AND GENETIC FEATURES OF AUTOSOMAL DOMINANT LATERAL TEMPORAL LOBE EPILEPSY IN ITALY**

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**Purpose:** To report the overall clinical and genetic spectrum of autosomal dominant lateral temporal lobe epilepsy (ADLTE) in Italy.

**Method:** In a collaborative study of the Commission for Genetics of the Italian League against Epilepsy encompassing a 12-year period (2000–2012), we collected 37 ADLTE families. The probands' DNAs were tested for LGI1 mutations by direct sequencing and, if negative, were genotyped with SNP array to search for disease-linked CNV. The disease penetrance in mutated and non-mutated families was assessed as a proportion of obligate carriers who were affected.

**Results:** The 37 families included a total of 137 affected individuals, whose age at onset ranged between 2 and 60 years (mean 18.7 years). Focal seizures were present in 97 patients (70%) and were characterized by auditory auras and aphasic seizures in 68% and 20% of the cases, respectively. Other symptoms included complex visual hallucinations, vertigo, and déjà vu. Tonic-clonic seizures occurred in 86% of the overall series. LGI1 mutations (missense in 10 and a microdeletion in 2) were found in 12 families (32%). The patients belonging to the mutated and not mutated groups did not differ except for penetrance estimate, which was 62.5% and 35% in the two groups, respectively (chi-square,  $p = 0.011$ ).

**Conclusion:** In this large Italian ADLTE series LGI1 mutations have been found only in one-third of families. There was a significantly lower penetrance rate in non-LGI1-mutated families compared with LGI1-mutated pedigrees, suggesting that a complex inheritance pattern may underlie a proportion of these families.

**P939**  
**SINGLE NUCLEOTIDE POLYMORPHISMS IN GENES RELATED TO INFLAMMATION MOLECULES IN MEXICAN PATIENTS WITH DRUG-RESISTANT EPILEPSY**

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**Purpose:** More than 30% of patients develop a drug-resistance epilepsy (DRE). The Temporal Lobe Epilepsy (TLE), Mesial Temporal Sclerosis (MTS) tend to be refractory. It has been documented that some inflammatory molecules enhances neuronal excitability<sup>1</sup>, like Tumor Necrosis Factor- $\alpha$  (TNF- $\alpha$ )<sup>2</sup>. Also, the Cyclooxygenase-2 (COX-2) is related with antiepileptic drug transport<sup>3</sup>. Due to the impact of inflammation in seizures and because DRE could be a polygenic disorder, we analyzed the risk effect of five single nucleotide polymorphisms (SNPs) in TNF- $\alpha$ , COX-2 and complement receptor 1 (CR1) genes.

**Method:** Genotyping was performed by qPCR, in 35 clinically diagnosed patients with DRE (12 TLE and 23 MTS cases) and 47 controls of Mexican population. Allelic frequencies were analyzed with a Chi-square test.

**Results:** The SNP located in CR1 gene could be linked with a risk increased of DRE ( $p = 0.03$ ). When we analyzed allele frequencies separating TLE and MTS patients, we realized that the effect of this allele would be exclusive for the MTS patients ( $p = 0.007$ ).

**Conclusion:** The preliminary results suggest a possible association of the SNP analyzed in CR1 gene with the development of MTS in Mexican population.

**References**<sup>1</sup>Vezzani A, et al. *Epilepsia*. 2005; 46(11):1724–43. <sup>2</sup>Stellwagen D, et al. *J Neuroscience*. 2005; 25:3219–28. <sup>3</sup>Holtman L, et al. *Epilepsy Research*. 2010; 91:49–56. **Acknowledgments** This work was conducted in accordance with current ethical standards in biomedical research of the Instituto Nacional de Neurología y Neurocirugía. Authors acknowledge the financial support of FONSEC SSA/IMSS/ISSSTE-CO-NACYT(No. 069899).

#### P940

### INVESTIGATING THE ROLE OF MICROGLIAL ACTIVATION MEDIATED BY MICRORNA-124 IN THE PILOCARPINE EPILEPSY MODEL

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**Purpose:** MicroRNAs regulate gene expression and are important in many key biological functions such as development, oncogenesis and inflammation. One microRNA, miR-124, is known to be expressed exclusively in the central nervous system and has been implicated in the maintenance of microglial cells in a non-activated, or quiescent, state. It is well known that activation of microglia must be properly and tightly regulated to maintain normal tissue homeostasis, avoiding tissue damage. The aim of the present study was to analyze expression of miR-124 in the acute phase of the pilocarpine epilepsy model. Thus, investigating whether abnormalities of microglial activation, usually observed in this model, could be mediated by microRNA deregulation.

**Method:** We obtained total RNA from hippocampus of animals at 1, 3, 6, and 24 h, as well as 5 days after induction of status epilepticus (SE) by pilocarpine, and from control animals. We quantified expression of miR-124 by quantitative real-time PCR. Only tissue obtained from rats which presented SE were used in our experiments. In addition, we used TargetScan 6.2 in order to identify target genes related to epilepsy that could be regulated by miR-124.

**Results:** We found that expression of miR-124 was significantly decreased after SE, about 60%, in comparison with control samples. MiR-124 expression was decreased already at 1 h after SE and remained low until 5 days after SE. Using TargetScan 6.2 we identify many candidate genes, including glutamate receptors, potassium channel sub-units and genes involved in neurogenic differentiation.

**Conclusion:** Our results indicate that regulation by microRNA, especially by miR-124, can play a role in microglia activation after SE induced by pilocarpine. Thus, opening the possibility of using microRNA-based therapies in epilepsy.

#### P941

### DEEP BRAIN STIMULATION FOR THE MANAGEMENT OF SEIZURES IN MECP2 DUPLICATION SYNDROME

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**Purpose:** MECP2 duplication (MECP2-dup) leads to cognitive delay, minimal or absent speech and dysmorphic features. Here we describe clinical features of an adult with severe seizures of multiple types, and their management challenges, including response to deep brain stimulation (DBS).

**Method:** Developmental delay was recognized at 9 months. At 14 years of age he began experiencing complex partial, atonic, tonic, secondarily generalized tonic-clonic, and eating reflex seizures. Several antiepileptic drugs failed to control his seizures. At the age of 23 years his monthly seizure frequency was of 125. The patient then received DBS to the anterior thalamic nuclei.

At 35 years of age microarray analysis showed a clinically significant 0.641 Mb duplication in chromosome region Xq28 which involves 25 RefSeq genes including eight genes ABCD1, L1CAM, AVPR2, NAA10, MECP2, OPN1LW, OPN1 MW, and FLNA.

**Results:** Treatment with DBS caused 65% decrease in seizure frequency. Despite a significant seizure improvement, his cognitive and motor skills continue to deteriorate. Frequent respiratory infections are the most severe and life-threatening events.

**Conclusion:** MECP2-dup is a condition rarely seen/diagnosed in adults. Almost 40% of all boys with MECP2-dup that were reported until 2009 died before completing 25 years of age. This case shows that cognitive and motor dysfunction continue to deteriorate as patients age. It also shows that seizures may be extremely difficult to treat and DBS may improve seizure control. As opposed to some other genetically determined severe epilepsies such as Dravet syndrome, seizure frequency and severity do not improve in adulthood.

#### P942

### CLN6 MUTATIONS CAUSE TEENAGE-ONSET PROGRESSIVE MYOCLONUS EPILEPSY

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**Purpose:** Progressive myoclonus epilepsy (PME) afflicts mainly teenagers. PME in young children and adults is mostly caused by neuronal ceroid lipofuscinosis (NCL). Using a whole-exome sequencing (WES) approach, we find that NCL is also a cause of teenage-onset PME.

**Methods:** A 24 year-old Pashtun Afghani man presented with myoclonus at age 15 years. Seizures and cognitive decline appeared later. Two cousins had the same disease and age of onset. Both died around age 30 with severe dementia. Investigations showed cortical myoclonus, multifocal epileptiform discharges, and generalized brain atrophy. Testing for known causes of teenage-onset PMEs were negative. Homozygosity mapping and WES, were performed to identify the disease gene.

**Results:** 600,000 SNPs were genotyped in the proband and one affected cousin. Homozygosity mapping revealed two shared regions of homozygosity. WES yielded 41,597 genetic variants of which only two were exonic, novel, nonsynonymous, and located within one of the shared homozygous regions. One variant was expressed in testis. The other variant was a homozygous sequence change in the CLN6 gene. This variant segregates with the disease in the pedigree. Sequencing for it in 268 con-

trol individuals, including 176 Pashtun, revealed it in one Pashtun, in heterozygote state.

**Conclusion:** The patients in our study closely resemble Kufs disease generally<sup>5,7</sup> and the teenage-onset cases of Arsov et al. in particular<sup>7</sup>. Combining this with our findings that the CLN6 sequence change we identified affects a highly conserved amino acid, is the only homozygous exomic alteration in a brain-expressed gene in a shared region of homozygosity, and is not present in homozygous state in vast control sequence datasets and 176 ethnic matches, confirms that CLN6 c.768C>G (D256E) is the mutation in our family. Combined WES and homozygosity mapping in two patients from one family without a priori hypothesis led directly to the causative defect.

#### P943

##### DRAVET SYNDROME: SEIZURE CONTROL AND GAIT IN ADULTS WITH DIFFERENT SCN1A MUTATIONS

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**Purpose:** Most cases of Dravet syndrome (DS) are caused by SCN1A gene mutations. This study aimed to correlate different types of SCN1A mutations and seizure control, frequency of convulsive status epilepticus (cSE), and the presence of crouch gait in adult patients.

**Methods:** Chart review and physical examination were completed in 10 adults with DS caused by SCN1A. Mutations were divided in four different groups based on location or effect on the gene product. Four SCN1A mutations have not been previously described. Greater than 90% seizure reduction was observed in 6/7 patients with missense mutations in the pore forming region (PFR) of the Na<sub>v</sub>1.1 protein (group A) and nonsense mutations (group B). One patient with a splice-site mutation (group C) and another with a mutation outside the PFR (group D) stopped having seizures. cSE after the age of 19 years was observed in only one patient. Crouch gait was observed in 5/7 patients from groups A and B.

**Results:** This study shows that seizure control improves and cSE become less frequent in adult DS, independently of their SCN1A mutation type. Complete seizure freedom was seen in two patients (groups C and D). Finally, crouch gait was observed in 50% of adults.

**Conclusion:** Although no definite statistical correlations could be drawn due to the small number of patients, it is interesting to note that crouch gait was only observed in those patients with SCN1A non-sense mutations or mutations in the PRF. Future studies with larger cohorts will be required to confirm this later finding.

#### P944

##### MESIAL TEMPORAL LOBE EPILEPSY AND SEROTONIN: THE ROLE OF HTR2A RECEPTOR

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**Purpose:** Evidences from animal models have demonstrated that depletion of brain serotonin (5-HT), a neurotransmitter with a pivotal role in neurodevelopment and brain plasticity, lowers the threshold to induced

seizures. It was also demonstrated that anti-epileptic drugs increase endogenous 5-HT concentrations. Studies in brain tissue from Mesial Temporal lobe Epilepsy (MTLE) patients have showed that serotonin type 2a receptor (HTR2A) is downregulated in these patients. HTR2A expression levels may be modulated by a 102 T>C polymorphism. The aim of this study was to analyse the association between 102T>C polymorphism and the development and clinical features of MTLE-HS in a Portuguese population.

**Methods:** A cohort of 112 MTLE-HS patients (62F, 50M, mean age = 44 ± 11 years, age of onset = 13 ± 9 years, 97 patients with drug refractory epilepsy) was compared with a cohort of 183 healthy individuals (HI). Genotyping was performed by Real Time PCR using High Melting Resolution methodology.

**Results:** HTR2A 102 T>C genotype frequencies were similar between patients and controls (TT: 24.1% vs. 25.1% in HI; TC: 45.5% vs. 43.2% in HI; CC: 31.3% vs. 31.7% in HI). No association was found between this polymorphism and MTLE-HS clinical features (age of onset, FS antecedents and anti-epileptic drug response).

**Conclusion:** The present results do not provide evidence that HTR2A polymorphism 102T>C may confer susceptibility to MTLE-HS. Nevertheless a possible role for the serotonergic system in epileptogenesis cannot be excluded. The study of other 5-HT receptors and transporters is underway.

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#### P945

##### HEMIMEGALENCEPHALY: ADULT EVOLUTION

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**Purpose:** Provide improved characterization of the evolution of Hemimegalencephaly (HME) in adult patients. HME is a rare neurological migration disorder resulting in the enlargement of one hemisphere. Depending on the severity of the enlargement, clinical manifestations may include macrocephaly, colpocephaly, epilepsy, and impaired psychomotor development. HME may also be associated with various neurocutaneous syndromes. One neurocutaneous syndrome is Hypomelanosis of Ito (HI). The main characteristics of HI are hypopigmented skin areas along the lines of Blaschko, which appear as streaks and patches.

**Methods:** Retrospective chart review on patients diagnosed with HME examining seizure frequency, family history, treatment, associated conditions, cognitive evolution, neuroimages, and EEG findings. Out of 1600 patients seen in our Epilepsy Clinic, four were diagnosed with HME.

**Results:** Diagnosis of HME was determined after the onset of early childhood or infantile epilepsy. Neuroimaging involving CT, MRI, and angiogram confirmed an enlarged hemisphere with dilated ventricles. Imaging findings revealed: loss of grey-white matter differentiation, heterotopias, and ventricular enlargement. Treatment with anti-epileptic medications did not provide complete seizure control. Two of the patients with seizure frequencies exceeding 15 seizures/day underwent hemispherectomy at ages 2 and 9 years. While these patients continue to experience daily seizures, seizure control significantly improved. Of the four patients, three presented hypomelanotic patches on their neck, trunk, arms, and legs. All patients exhibit some form of psychomotor developmental delay and varying degrees of mental retardation or learning disabilities.

**Conclusion:** We present four adult patients previously diagnosed with HME; three showing signs of HI in association with HME. While there have been numerous case studies and literature reviews on HI and HME, in association with each other or not, all current studies involve children or infants with few detailing adult cases. We reviewed the literature to discuss the adult evolution of HME.

## P946

## AICARDI SYNDROME: LONG-TERM EVOLUTION

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**Purpose:** Aicardi syndrome (AS) is a disorder characterized by the triad: corpus callosum agenesis, infantile spasms and chorioretinal lacunae. The long-term evolution of AS is severe due to high early mortality, considerable morbidity and poor developmental outcome. Few adult cases have been reported. Here we review two adult cases of AS, aged 24 and 27, their varying clinical spectrums and long-term evolution.

**Methods:** We conducted a retrospective chart review on patients diagnosed with AS examining their psychomotor development, family history, seizure frequency, seizure classification, current antiepileptic drug (AED) use, MRI findings, continuous video-EEG recordings containing seizures, systemic problems and overall treatment. Out of 1600 patients seen in our Epilepsy Clinic, we identified two patients with confirmed clinical diagnosis of AS.

**Results:** Both patients diagnoses at a few months of age were based upon the classic triad of infantile spasms, corpus callosum agenesis and chorioretinal lacunae. Infantile spasms began six weeks after delivery. Neither patient has any family history of similar illness. Both patients experience multiple seizure types daily and take more than three AEDs. Seizure control has moderately improved with medication. Each patient exhibits some form of psychomotor impairment and varying degrees of mental retardation. Medical problems these patients face are bladder/bowel retention and severe hypoxemia during tonic-clonic seizures.

**Conclusion:** We present two adult Aicardi cases, the clinical spectrum and long-term evolution. Although there have been numerous case studies and literature reviews on infant and child Aicardi cases, few adult cases have been reported as not many patients live to adulthood. The long-term evolution of Aicardi syndrome is severe. Seizure frequency and severity do not improve as the patients age. However other signs of neurodegeneration (such as those seen in Rett syndrome, or Dravet syndrome) were not observed in our adult cases.

## P947

## EXTENDING THE SPECTRUM OF KCNQ2 ENCEPHALOPATHY: DESCRIPTION OF 11 ADDITIONAL PATIENTS

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**Purpose:** Recently we reported *de novo* KCNQ2 mutations in eight patients with severe neonatal epileptic encephalopathy (EE). In this follow up study, we aimed to determine the frequency of KCNQ2 mutations in a cohort of patients with neonatal EE, and to provide a detailed description of clinical features of mutation carriers.

**Method:** Eighty-four patients with an unexplained EE with onset on the first month of life were screened for KCNQ2 mutations using classical Sanger sequencing.

**Results:** We identified nine different heterozygous *de novo* KCNQ2 missense mutations in 11 of 84 (13%) patients. Seizures at onset were mostly tonic and often accompanied by apnea and desaturation. We delineated three clinical subgroups: Six patients had frequent seizures at onset that sometimes remitted after several months to several years, and they had profound intellectual disability (ID). Three patients presented in a similar way, generally had earlier seizure remission (2–11 months) and had mild to moderate ID. In the third group of two patients seizure frequency at onset was less dramatic and although their EEGs showed epileptic activity, there was no typical burst-suppression pattern or frequent multifocal activity. Outcome ranged from moderate to profound ID. Patients with a recurrent mutation had a similar phenotype. In four patients seizures with ictal bradycardia were registered. One patient died of probable SUDEP shortly after diagnosis.

**Conclusion:** KCNQ2 mutations are a frequent cause of neonatal EE with a wide spectrum of severity. The co-occurrence of desaturation and bradycardia during seizures may lead to an increased risk for SUDEP.

## P948

## NOCTURNAL FRONTAL LOBE EPILEPSY (NFLE): CLINICAL AND GENETIC CHARACTERIZATION OF A LARGE COHORT

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**Purpose:** To describe the clinical and genetic features of a large cohort of Italian NFLE patients, both sporadic and familial.

**Method:** From a pool of patients referred to our Department for sleep-related motor events suggestive of seizures, we selected a final population diagnosed with NFLE, according to the clinical and video-polysomnographic criteria. All patients underwent a full clinical, neurophysiological and neuroradiological examination. The genetic study comprises molecular analysis of known genes for NFLE, subunits of nAChRs: CHRNA4, CHRN2 and CHRNA2 and a preliminary screening for mutations in a recently identified gene, KCNT1.

**Results:** The sample includes 192 NFLE patients, 164 sporadic and 28 familial cases. Among the latter, 10 patients belong to four definite NFLE pedigrees. 18 NFLE cases reported a positive family history for focal epilepsy, NFLE and/or extra-frontal, to the 4th degree of kinship. 31% of patients were drug resistant. Neuroradiological abnormalities were detected in 12 cases. Eight cases underwent surgery with seizure control in 2 (Engel class IA). Mutational analysis did not identify mutations in the 18 familial nor in the 75 sporadic cases screened for mutations in *CHRNA4*, *CHRN2* and *CHRNA2*. Two sporadic cases had a heterozygous polymorphism in *CHRN2*. Screening of *KCNT1* was conducted in 43 cases (18 familial). A missense mutation c.2386T>C (p.Tyr796His) was identified in the four affected members of a three generation-ADNFLE pedigree showing an early age at epilepsy onset, refractory seizures and intellectual disability with psychiatric disorders in two individuals.

**Conclusion:** Mutations in nAChRs and *KCNT1* account for a low rate of our large cohort, confirming the etiologically heterogeneity of the syndrome and suggesting the contribution of other genes in our cases.

#### P949

##### APOE ISOFORMS IN FOCAL EPILEPSIES: AN ASSOCIATION STUDY IN A PORTUGUESE POPULATION

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**Purpose:** Apolipoprotein E (ApoE) is the main lipoprotein secreted in brain. It has a critical immuno-modulatory function, influences neurotransmission and is involved in repairing damaged neurons. ApoE ε4 allele is an isoform of ApoE with altered protein function previously associated with refractoriness and early onset epilepsy. Our purpose was to investigate if apoE isoforms are risk factors for partial epilepsy and to correlate genotypes with anti-epileptic drug response.

**Methods:** A cohort of 230 epileptic patients with partial epilepsies from the outpatient clinic at HSA-CHP [109F, 121M; mean age = 44 ± 13 years, age of onset = 15 ± 13 years; 168 patients with Drug Refractory Epilepsy (DRE)] was compared with a cohort of 301 healthy individuals (HI) in a case control study. ApoE isoforms were genotype by RFLP-PCR methodology.

**Results:** ApoE ε4 allele frequency was higher in epileptic group when compared with HI (10.6% vs. 7.6%, p = n.s., OR = 1.44, 95% CI: 0.945–2.20). Anti-epileptic Drug response was not influenced by apoE isoforms.

**Conclusion:** Our results suggest that ApoE ε4 may be a risk factor for partial epilepsy development. ApoE ε4 is associated with CNS network instability, with lower protection against oxidative and inflammatory cascade. These could influence neuronal growth and recovery leading to a chronic vicious cycle of damage and neuronal loss contributing to seizures development. These observations should be confirmed in a larger cohort.

#### P950

##### THE ROLE OF *SCL2A1* IN MYOCLONIC ASTATIC EPILEPSY AND SEVERE ABSENCE EPILEPSY WITH VARIABLE ONSET

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**Purpose:** Mutations in *SLC2A1*, encoding the glucose transporter of the blood-brain barrier (GLUT-1), was first associated with an encephalopathy and more recently found in rare dominant families with various forms of epilepsy e.g. early onset absence epilepsy (EOAE), myoclonic astatic epilepsy (MAE) and idiopathic generalised epilepsy (IGE). The study aimed to investigate the role of *SCL2A1* in MAE and severe absence epilepsy with variable onset.

**Method:** Fifty-nine probands with MAE and 28 cases with severe absence epilepsy with variable onset were screened for *SCL2A1* mutations by sequence analysis. Extensive phenotyping was performed in patients and family members.

**Results:** Mutations in *SLC2A1* were detected in 2/28 patients with severe absence epilepsy and in 0/59 patients with MAE. A maternally inherited mutation was found in a 9 year old girl with medical resistant absence epilepsy since the age of 5 years. In addition, array CGH revealed a 15q13.3 microdeletion in the patient, which further increases risk of absence epilepsy. Inheritance of the microdeletion is yet to be determined. In relation to diagnosing the daughter, the presumably unaffected mother reported that she had always experienced episodes with lack of awareness, clumsiness and syncope. The mother had an EEG, showing multifocal epileptiform discharges with secondary bilateral synchrony. The other mutation occurred *de novo* and was found in a 7 year old boy with onset of medical resistant epilepsy with myoclonic absences at 1.5 years of age.

**Conclusion:** Our study confirmed a role of *SLC2A1* mutations in severe absence epilepsy and demonstrated that *SLC2A1* do not seem to play a major role in MAE. Ketogenic diet is a well known treatment option in GLUT-1-deficiency and this study confirms that *SLC2A1* mutations should be strongly considered in patients with medical resistant absence epilepsy.

#### P951

##### EXTENDING THE PHENOTYPIC SPECTRUM ASSOCIATED WITH *PCDH19* MUTATIONS: DESCRIPTION OF SIX AFFECTED FEMALES

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**Purpose:** Mutations in the gene encoding protocadherin 19, *PCDH19*, cause Epilepsy and Mental Retardation limited to Females (EFMR). EFMR has marked phenotypic heterogeneity with additional patients further informing the phenotypic spectrum. This study aimed to identify and phenotype patients with *PCDH19* mutations.

**Method:** Ten unrelated females with a wide spectrum of epilepsies with onset before the age of 36 months, were screened for mutations in *PCDH19*. Detailed phenotyping was performed in the patients and their affected relatives.

**Results:** Three (15%) novel *PCDH19* missense mutations were identified in three probands. Two of the mutations are located in the

extracellular portion of the protein and one is located in the cytoplasmic domain. All three mutations were inherited and family studies revealed mutations in six affected females, three unaffected females, and two unaffected males. One unaffected male was shown to be mosaic for the mutation. The predominant clinical features in the females were clusters of seizures and aggressive behaviour, with marked variability between the females. Seizure onset ranged from 8 months to 11 years of age. Affected females had normal development prior to seizure onset but 4/6 had neurocognitive and/or psychiatric problems at 2–3 years of age. Psychiatric problems including OCB, psychosis, (suspicion of) schizophrenia, depression and ADHD were observed in one family with four affected females. Furthermore, migraine was also diagnosed.

**Conclusion:** *PCDH19* mutations are a relative frequent cause of idiopathic early onset epilepsy in Danish females. Here we present an unaffected mosaic male carrier. Importantly we extend the onset age of EFMR to late childhood (11 years) and expand the psychiatric comorbidities to include OCB, psychosis, (suspicion of) schizophrenia, depression and ADHD.

#### P952

##### EPILEPSY ASSOCIATED WITH RARE CHROMOSOMAL ABNORMALITIES

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**Purpose:** Many chromosomal abnormalities are associated with different neurological conditions, including epilepsy. There were about 400 different chromosomal imbalances described with seizures or EEG abnormalities. In this paper we present some rare chromosomal rearrangements associating epileptic seizures.

**Method:** Hundred children with epilepsy, other neurological features, and/or dysmorphic features were evaluated by clinical, dysmorphological, neurological and psychological examinations, EEG, imaging studies (CT, MRI), biological studies, genetic investigations (karyotype, FISH, array CGH).

**Results:** Twenty-five cases with epilepsy and a chromosomal abnormality were identified, including three children with Down syndrome, 12 children with Angelman syndrome, two children with Miller-Dieker syndrome, one child with trisomy 18, one child with Williams syndrome, translocation (4p16;8p23) in a girl with severe global development delay, epilepsy, dysmorphic features. Six cases presented some very rare chromosomal rearrangements: 3p26 duplication in a girl with global development delay, epilepsy, congenital cerebral malformation, microcephaly; translocation (4p16; 10q26) in two sibling with severe mental retardation, epilepsy, dysmorphic features; proximal deletion of 8p in a girl with severe mental retardation, autistic features, epilepsy, dysmorphic features; translocation 3qter;20qter in a boy with severe mental retardation, epilepsy, dysmorphic features, behavior problems.

**Conclusion:** If in some cases, like translocation (4p16; 10q26), translocation (4p16.; 8p23), 8p deletion, we identified some genes which are known to be involved in epilepsy, in other cases (3p26 duplication, trisomy 3qter) no specific genes for epilepsy are known to be located in these regions. Further studies are needed to understand the mechanism of epilepsy associated with chromosomal abnormalities.

#### P953

##### CLINICAL AND GENETIC ASPECTS IN CHILDREN WITH DRAVET SYNDROME: ROMANIAN EXPERIENCE OF 3 YEARS OF RESEARCH

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**Purpose:** Clinical and genetic spectrum of Dravet Syndrome are currently intensively studied. We present the Romanian experience concerning clinical, therapeutic and genetic aspects in Dravet Syndrome.

**Method:** From 34 Dravet phenotype patients selected from Romanian databases in the project 6EUROC, partner of RES EuroEpinomics Consortium, 19 were tested for SCN1A gene mutations (16 in, 3 in other labs). We identified clinical data including age and type of onset, seizure types, EEG aspect, response to medication, genetic aspects. Data were collected in both Romanian and Bench databases. Phenotype/genotype correlations were analysed in tested patients.

**Results:** Sixteen tested patients were SCN1A positive (7 unpublished mutations) and three negative; seven patients had classical and 12 – borderline phenotype. Patients with new mutations did not associate a particular phenotype. Clinical, EEG and genetic correlations were analyzed. Polytherapy was given to all patients; ketogenic diet was associated in some.

**Conclusion:** Particularly – our group included mostly borderline SMEI. Key for clinical diagnosis was: prolonged febrile seizures, association with vaccination, development disturbance. No clear correlation between clinical, EEG, treatment aspects and genetic mutation could be done. There is hope for treatment using pathophysiological philosophies, thus new research of molecular mechanisms of these syndromes is necessary.

#### P954

##### POLYMORPHISMS IN GENES OF TAU PROTEIN, GSK3β AND HSP70, AS POTENTIAL MARKERS OF RISK IN THE DEVELOPMENT OF TEMPORAL LOBE EPILEPSY AND MESIAL SCLEROSIS

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**Purpose:** To determine the presence of single nucleotide polymorphisms (SNP's) in genes encoding the protein TAU, GSK3β and HSPs in Mexican patients with Temporal Lobe Epilepsy (TLE) and establish whether there is any association between these polymorphisms and the presence or absence of Hippocampal Sclerosis (HS).

**Method:** Nine SNPs were genotyped by PCR-Real Time, in DNA of 35 patients with TLE (23 with and 12 without HS) and 50 controls. Allele frequencies were obtained and X<sup>2</sup> test was performed. Subsequently haplotypes in each group were analyzed and compared with controls.



**Results:** When we compared polymorphism of all patients with TLE vs. control subjects, we do not found significant differences. However when compared those with HS, with the control group, differences were found in the polymorphism rs2227956 ( $p = 0.03$ ), whereas comparison between group without HS and control, differences were observed in the polymorphisms rs2471738 ( $p = 0.04$ ) and rs334558 ( $p = 0.04$ ). Analyzing haplotypes statistical significance was found in seven of them for TLE and after separating the groups; we obtained four haplotypes statistically significant for the HS group and 5 to the group without HS. Our results were consistent with recent studies that suggest that the TAU protein is involved in the pathogenesis of drug resistant epilepsy (DRE) [Xi ZQ, et al. Synapse. 2009; 63:1017–1028] [Xi ZQ, et al. Medical Hypotheses. 2011; 76:897–900].

**Conclusion:** The presence of polymorphisms in the Tau protein gene may be associated as differential markers between patients with HS and without HS.

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## P955

### CLINICAL PHENOTYPES, EPILEPSY AND GENETICS IN A COHORT OF 52 PATIENTS WITH NON SYNDROMIC AND SYNDROMIC POLYMICROGYRIA

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**Purpose:** To study the phenotypes, epilepsy, radiological and genetic data in a cohort of 52 patients with nonsyndromic and syndromic polymicrogyria (PMG).

**Methods:** Inclusion of any type of PMG, excluding confirmed congenital CMV/toxoplasmosis. We performed detailed review of medical records; karyotype and/or CGH and/or genomic SNP microarray; and specific gene analysis when indicated.

**Results:** We studied 48 sporadic patients and two families with two siblings each. 25/52 (48%) had associated brain malformation(s), including 6/25 nodular heterotopia, 4/25 microcephaly, 2/25 corpus callosum dysgenesis, 2/25 brainstem hypoplasia, 2/25 hemimegalencephaly, 1/25 focal cortical dysplasia, 1/25 optic chiasm hypoplasia. 10/50 (20%) had PMG as part of a syndrome. Epileptogenicity was heterogenous, from no seizures to various epileptic phenotypes of variable severity. One karyotype showed a reciprocal translocation 46, XY t(8;22)(p23.1;p11.2). Of 28 CGH microarray results, 24 (85%) were normal. The detected CGH

anomalies included a 22q11del, a 1p36del, a 2p21del of unknown significance, and a 2p13.3-p16.3duplication. We fine mapped a subgroup of bilateral perisylvian polymicrogyria (BPP) patients to 2p16.1-p16.3. We identified a novel and de novo TUBB2B mutation in exon 4 in a sporadic patient with polymicrogyria and associated anomalies of the corpus callosum, basal ganglia and brainstem.

**Conclusions:** Polymicrogyria is markedly heterogeneous, clinically, radiologically and genetically. Our results support previous suggestions of PMG loci on chromosomes 22q11 and 1p36. We have narrowed a novel locus for BPP to 2p13.1-p16.3. These data can help to identify the causative genes located in these regions. We found a novel and de novo TUBB2B mutation in a patient with complex PMG. Identification of associated brain malformations and phenotypic anomalies, as well as recognition of specific syndromes, can help to orient the genetic testing and diagnosis.

## P956

### SOME CASES OF JUVENILE MYOCLONIC EPILEPSY ARE GENETICALLY RELATED TO PROGRESSIVE MYOCLONIC EPILEPSY

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**Purpose:** To investigate which mutated gene products might be shared between a relatively mild clinical phenotype, Juvenile Myoclonic Epilepsy (JME) and a severe clinical phenotype, Progressive Myoclonic Epilepsy (PME). Both conditions are considered to be genetically heterogeneous.

**Method:** Review of protein mutations reported in each disorder in OMIM, in the literature, and predicted by exome sequencing in Heinzen et al (2012).

**Results:** *KCTD7* (OMIM 611725), encoding a potassium channel tetramerization protein seven has two different mutations in JME, one predicting a substitution pThr64Arg in 2/279 JME patients, and pMet80Thr in another JME patient (1/280 tested); all three were heterozygotes, and these mutations were not found in over 2000 controls. Mutations in *KCTD7*, at other sites in the protein, have been reported in a number of patients with infantile- and childhood-onset myoclonic epilepsy, PME (OMIM#611726, EPM3). Most of the mutations (including the heterozygous JME mutations reported in Heinzen et al) fall in the highly conserved tetramerization domain.

A deleterious heterozygous mutation in *CLN6* (OMIM 606725), encoding the ceroid lipofuscinosis neural protein 6, predicts the substitution Thr93Met in the second transmembrane domain of a multipass membrane protein in another JME patient (1/280 tested). Homozygous mutations at other locations in *CLN6* have been reported in autosomal recessive adult-onset Kufs disease (OMIM #204300). Subtype A of the recessive form of Kufs disease is characterized by severe PME.

The autosomal dominant form of Kufs disease (OMIM #162350), also characterized by PME, is linked in some families to *DNAJC5*, encoding cysteine string protein, which is part of the presynaptic proteome, but which has not thus far been found to be mutated in JME.

**Conclusion:** There is gene sharing amongst the myoclonic epilepsies (ranging in severity from the progressive and devastating to the relatively mild), which were not previously known to be genetically related.

## P957

### QARS: A CANDIDATE GENE IN FAMILIAL MALIGNANT MIGRATING PARTIAL SEIZURES OF INFANCY

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**Purpose:** Migrating partial seizures of infancy (MPSI) constitute a severe epileptic encephalopathy first reported in 1995. It is characterized by (i) seizure onset within the first six months of life, (ii) seizures “migrating” randomly between cortical regions and hemispheres, (iii) pharmacoresistant epilepsy and (iv) a poor cognitive and motor outcome with microcephaly. Recently KCNT1 has been identified as a major MPSI gene linked to 50% of sporadic cases. Here we report the results of exome sequencing in two sibs from non-consanguineous parents with MPSI.

**Method:** Whole exome sequencing was performed in unaffected parents and the 2 sibs with MPSI.

**Results:** Compound heterozygous missense mutations (c.1543C>T/p.Arg515Trp and c.169T>C/p.Tyr57Hys) were identified and confirmed by Sanger sequencing in the QARS gene in both children. Both mutations affected evolutionary conserved amino acid residues. The analysis of QARS sequence in 10 additional sporadic patients with MPSI and negative for KCNT1 did not disclose any pathogenic variant.

**Conclusion:** Our results further demonstrate the genetic heterogeneity of MPSI and suggest QARS, encoding the human glutamyl-tRNA transferase, as a candidate gene for familial MPSI. Aminoacyl-tRNA transferases are involved in translation and mutations in several members of this large protein family have been linked to human neurological diseases. We propose that defective protein synthesis might be a possible pathophysiological mechanism underlying MPSI.

## P958

### A NOVEL HETEROZYGOUS MUTATION IN SODIUM CHANNEL SUBUNIT BETA-1 (SCN1B) INVOLVED IN GENERALIZED EPILEPSY WITH FEBRILE SEIZURES PLUS (GEFS+) PATIENT

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**Purpose:** This study was conducted to roll out the genetic basis of GEFS+ patients in the indigenous population of Pakistan.

**Method:** The patients having GEFS+ were selected on medical data and family history basis. DNA of the affecteds was isolated and screened for SCN1B mutations. Primers for the amplification of exons 1, 3, 4 & 5 were designed by using the Primer3 program and PCR amplification was performed to amplify the 300–650 bp DNA segments. Sequence analysis was performed with the ABI PRISM Big Dye Terminator Cycle Sequencing. Homology and blast search was performed using individual and wild sequence at the national centre for biotechnology information and data was analyzed.

**Results:** We report here a novel heterozygous IVS2-1G>T transversion mutation in splice acceptor site of exon 3 of SCN1B gene with autosomal dominant inheritance pattern.

**Conclusion:** This study will be helpful to add genetic information for global data bank for this disorder which will ultimately lead to development of tools for molecular diagnosis, prenatal testing and further research establishment.

## Poster session: Neuroimaging B Wednesday, 26 June 2013

### P959

#### IN VIVO AND EX VIVO MR RELAXOMETRY CHANGES IN TLE ARE ASSOCIATED WITH TISSUE ASTROGLIOSIS

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**Purpose:** Increased T2 relaxation time (RT) is a common finding in the hippocampus of patients with drug-resistant temporal lobe epilepsy (TLE). Histopathological examination of the hippocampus often reveals astrogliosis, which is commonly associated with the increased T2 signal. Magnetic resonance imaging (MRI) studies have shown that signal alterations observed in vivo (IV) can be seen in ex vivo (EV) MRI of fixed brains. Our aim was to evaluate if the association between astrogliosis and RT can be observed in EV MRI.

**Method:** Patients with TLE (n = 26) and age-matched voluntaries (VC, n = 12) were scanned (IVRT, TE = 20/40/60/80/100 ms; TR = 3 s) in a 3T MR scanner. After surgery, a coronal section from hippocampus of TLE patients was fixed for 8 days, and a similar relaxometry was performed (EVRT). Age-matched autopsy tissues (AC, n = 6) went through the same EV MRI protocol. Astrogliosis was evaluated as GFAP immunopositive area in paraffin embedded sections.

**Results:** TLE patients presented increased relaxation time when compared to controls (p = 0.005 for IVRT and p = 0.006 for EVRT). No correlation was observed between IVRT and EVRT in TLE. Increased immunopositive GFAP area was observed in the hippocampus of TLE patients, when compared to AC, in granule cell layer, hilus, CA4, CA3, CA2, CA1 prosubiculum and subiculum (p ≤ 0.009). The IVRT correlated with GFAP area in the subiculum (r = 0.541; p = 0.0296) and the EVRT correlated with the GFAP area in the hilus (r = 0.422; p = 0.0445) in TLE patients.

**Conclusion:** IVRT and EVRT can detect astrogliosis in the hippocampus of TLE patients. Since the IVRT is affected by functional and structural characteristics of the tissue and the EVRT is influenced only by structural factors, this may account for the lack of correlation between both. Taken together, our data suggest that structural and functional changes affect MR signal, and EV MRI can identify structural alterations.

### P960

#### A RESTING STATE FMRI STUDY IN NON-LESIONAL EPILEPSY PATIENTS

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**Purpose:** The resting state fMRI study in Non lesional epilepsy patients, using the algorithm of low-frequency fluctuation observed amplitude increased and decreased in the circumstances, in order to understand the patients resting state brain activity and abnormal brain regions in non-focal seizures in the role.

**Method:** The low frequency fMRI were performed in non-lesional epilepsy group and normal controls group in non-attention state, 16 cases with a history of more than 2 years, aged 10–38 years, frequent grand mal epilepsy patients. After pre-processing of resting-state fMRI data, with which a whole-brain in low frequency fMRI fluctuations was calculated to investigate the changes of the Low-frequency amplitude changes.

**Results:** Compared with normal subjects, the regions showing increased ALFF in NLE patients were distributed in right temporal lobe (15,-90,21), medial frontal lobe (0,24,-24), ventral anterior cingulate (-12,30,27) and the right cerebellar hemisphere (51,-57,-4); (2) while the regions showing decreased ALFF covered the areas of the left cerebellar hemisphere (-48,-15,39), posterior cingulum gyrus (60,-21,33) and precuneus (-6,-54,66).

**Conclusion:** (1) NLE patients shows abnormal brain functional organization in resting state.

(2) The increased ALFF is considered the facilitation such as the epileptic activity generation and propagation; while the ALFF decreased is able to considered the function inhibition in these regions.

## P961

### HIPPOCAMPAL SUBFIELD SEGMENTATION ON SUB-MILLIMETRIC MRI AT 3 TESLA

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**Purpose:** Due to limited grey-white contrast and partial-volume, crucial anatomical boundaries may not be visible on 1 mm T1-weighted images, diminishing sensitivity to detect subtle pathology. We developed a standardized protocol for hippocampal subfields volumetry on multispectral sub-millimetric MRI.

**Method:** We obtained T1-weighted ( $0.6 \times 0.6 \times 0.6 \text{ mm}^3$ ) and T2-weighted ( $0.4 \times 0.4 \times 2 \text{ mm}^3$ ) images in 24 consecutive patients with drug-resistant temporal lobe epilepsy (TLE) and 20 controls on a 3T-scanner with 32-channel head-coil. Images were registered into stereotaxic space to adjust for differences in brain volume and orientation. T1- and T2-weighted images were then co-registered and resampled into 0.4 mm isotropic voxels. The hippocampus was partitioned into subiculum, CA1-3, and CA4-dentate.

**Results:** Compared to controls (2SD cut-off), in 11/24 TLE patients we found ipsilateral atrophy across all regions, although more marked in CA1-3. Volumes were normal in 4/24. Conversely, 9/24 had hypertrophy in at least one sub-region, bilateral in 7. Isolated CA1-3 hypertrophy or combined with CA4-dentate lead to increased total hippocampal volume in 5/9. Conversely, hypertrophy confined to CA4-dentate (4/9) was associated with normal total hippocampal volume. Available surgical specimen in patients with hypertrophy showed isolated gliosis, while all patients with atrophy had neuronal loss and gliosis.

**Conclusion:** In about half of our TLE patients, subicular and hippocampal subfield atrophy co-occurred and were associated with hippocampal sclerosis. Conversely, about 40% had subfield hypertrophy. In these patients, timing and interplay between structural pathology and remodeling of neuronal circuitry may favour astroglial response and neurogen-

esis, masking neuronal loss, thus resulting in MRI-apparent tissue hypertrophy.

## P962

### INTERMITTENT LIGHT STIMULATION-DEPENDENT CBF CHANGES IN PHOTOSENSITIVE AND CONTROL BABOON

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**Purpose:** Photoparoxysmal responses are best triggered by intermittent light stimulation (ILS) at 20–25 Hz in photosensitive (PS) baboons. We compared ILS rate-dependent CBF changes between PS and healthy (CTL) baboons.

**Method:** Thirteen adult baboons (8PS/5CTL) underwent H<sub>2</sub><sup>15</sup>O-PET (ILS at 5, 10, 15, 25 Hz, and two resting) scans. The baboons were sedated using intravenous ketamine and paralyzed with vecuronium. Regional CBF changes (averaged across all frequencies) differed significantly from resting CBF in 26 cortical/subcortical regions. Group z-score images were obtained by comparing group-averaged resting scans and at each ILS frequency in these regions.

**Results:** In CTL baboons, occipital CBF increases were maximal at 10–15 Hz. Significant CBF regional changes were noted in 65 (63%) trials (5 Hz in 11, 10 Hz in 19, 15 Hz in 19, 25 Hz in 16 regions). Significant activations across all ILS frequencies were noted in five regions, deactivations in 2. Occipital CBF increases in the PS baboons were maximal at 25 Hz. Significant CBF changes were noted in 89 (86%) trials (5 Hz in 24, 10 Hz in 19, 15 Hz in 22, 25 Hz in 24 regions). At 25 Hz, significant activations were noted in eight regions (visual cortices, lateral geniculate nucleus, bilateral orbitofrontal cortices, right subthalamic nucleus and mid-brain), deactivations in 16 regions. CBF responses were significant across all ILS frequencies in 19 (activations in 6 and deactivations in 11) regions.

**Conclusion:** This study confirms that regional CBF responses are greatest at 25 Hz in PS baboons, the frequency of maximal photosensitivity. However, PS baboons respond differently to ILS across a range of frequencies, reflecting both frequency-specific activation of cortical-subcortical networks and disruption of physiological networks.

## P963

### VOXEL-BASED MORPHOMETRY ANALYSIS IN PARTIAL EPILEPSY: SIGNIFICANCE OF THALAMIC INVOLVEMENT IN MEDIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Previous studies have demonstrated that epilepsy is a progressive disease. The neural circuits undergo progressive structural and functional alterations in response to seizures, inducing brain damage. We investigated whether the progressive structural changes in the brain were different between medial temporal lobe epilepsy (MTLE) and extra-temporal lobe epilepsy (ETLE). We also evaluated whether seizure induced brain damage in intractable partial epilepsy.

**Methods:** A total 34 patients with chronic partial epilepsy were divided into the group of drug-controlled epilepsy (DCE, n = 13) and the group of drug-resistant epilepsy (DRE, n = 21). Of the patients with DRE, the patients with MTLE were 12, and nine patients had ETLE. We also recruited the patients with newly diagnosed partial epilepsy (NDE, n = 26). We analyzed the volume of gray matter in the brain by using MRI voxel-based morphometry (VBM).

**Results:** As compared to the patients with NDE, the thalamic involvement was very strong in the patients with MTLE than ETLE. As compared to the patients with DCE, more widespread involvement of gray matter was evident in the patients with MTLE than ETLE. In addition, reduction of the thalamic volume was significant in the patients with DCE compared with NDE.

**Conclusion:** MTLE seems to be a progressive disease than ETLE, especially involvement of thalamus in MTLE. Seizure induced brain damage looks like to occur in MTLE but not in ETLE. Even though seizures are well controlled, thalamic involvement may be possible in chronic epilepsy.

#### P964

##### TO WHAT EXTENT IS INCOMPLETE HIPPOCAMPAL INVERSION RELATED TO EPILEPSY?

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**Purpose:** To establish the prevalence of the incomplete hippocampal inversion (IHI) in a epileptic populaion of our catchment area and to investigate possible correlations between clinical/neurophysiological results and IHI in epileptic patients.

**Method:** Epileptic outpatients performing 3T-MRI from 20.04.09 till 31.12.12 were included in the survey. IHI prevalence has been therefore calculated. Clinical and neurophysiological data have been collected and statistically analyzed.

**Results:** Forty out of 277 (14.4%) epileptic patients performing 3T-MRI according to Epilepsy Protocol satisfied criteria for left-sided IHI, as isolated abnormality. Of these (M = 20; F = 20) median age was 57 years, ranging from 19 to 71 years, with median epilepsy onset of 33.5 years (range 2–65 years). Thirty-one patients (77.5%) presented with focal seizures; eight patients (20%) presented with GTCS and only one with multiple types of seizures. Paroxysms at EEG were founded in 28 (70%) whose 20 (71%) with temporal lobe involvement and 2 (7%) as extra-temporal; three out of 28 (11%) presented generalized abnormalities whereas other 3 (11%) showed multiple EEG abnormal patterns. 28/40 (70%) patients underwent at assessment time a single AED whereas 8/40 (28.5%) underwent polipharmacy and 4/40 (10%) were drug-free at time.

**Conclusion:** IHI, as defected fetal development, has been often described in epileptic subjects. Although in previous studies prevalence data are discordant probably due to different methodological approaches, our results effort the hypothesis of a reliable correlation between IHI and epilepsy. In our study left-sided IHI has been exclusively founded and EEG/IHI coherence has been impressively higher than in previous series. Prospective studies are mandatory in order to measure epileptogenic risk of IHI.

#### P965

##### RELIABILITY OF FMRI TEST-RETEST FINDINGS DURING VERBAL AND NONVERBAL LEARNING IN HEALTHY SUBJECTS

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**Purpose:** Repeating fMRI studies of patients with temporal lobe epilepsy (TLE) after surgical intervention may identify changes in brain activity related to resection of the dysfunctional region. To interpret meaningfully any differences found during performance of memory tasks, however, it is critical to know the test-retest reliability of the measures used in healthy subjects. Here, we sought to examine whether two forms of our clinically-based learning test results in differences in cortical activation in healthy individuals.

**Method:** Fourteen healthy subjects were scanned twice over a 12 month period. During each session, they were administered one of two equivalent forms of a learning and recognition task similar to that used for neuropsychological evaluation of TLE patients in our clinic. Scans for each subject were analyzed using the software package Statistical Parametric Mapping 8 (SPM8). For all analyses, we used a small volume correction applying an image of the hippocampi and parahippocampal gyri. The Monte Carlo simulation was used to establish, at the cluster level, the number of voxels required for significance within the masked area of interest. Two-sample t-tests were performed to compare behavioural responses between scans during recognition trials.

**Results:** Comparisons between Scans 1 and 2 revealed no significantly active clusters on any behavioural condition of our task. Further, there was no significant difference in the number of correct responses for any trial of the two test forms.

**Conclusion:** The results suggest that different but equivalent forms of our test will yield similar activation reliably in healthy subjects tested at two different times, and, importantly, that fMRI retesting of subjects with a same measure should activate the same brain regions if nothing has intervened to change that subject. Such findings have important implications about the validity of observed changes in cerebral functioning in TLE patients before and after surgery.

#### P966

##### FUNCTIONAL NEAR INFRARED SPECTROSCOPY-EEG STUDY OF INTERICTAL SPIKES

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**Purpose:** Functional Near-Infrared Spectroscopy (fNIRS) acquired simultaneously with electro-encephalography (EEG) is one of the promising non-invasive neuroimaging approaches for localization of the epileptic focus. We have previously shown that it allows monitoring and localizing concentration changes in oxy-hemoglobin (HbO), deoxy-hemoglobin (HbR), and total hemoglobin (HbT) during focal epileptic seizures. In this research, we looked at hemodynamic changes associated with interictal spikes.

**Method:** Forty patients with refractory focal epilepsy underwent continuous fNIRS-EEG recording. The EEG were reviewed by trained epileptologists and all interictal spikes were marked. Recorded fNIRS data (60–90 min long) was processed using a General Linear Model (GLM) using a toolbox based on SPM8 and NIRS-SPM. Euler Corrected (EC) and uncorrected contrast topographic maps were generated, reflecting concentration change responses due to epileptic spikes. The epileptic foci locations, determined by multimodal analysis of structural (MRI), electrophysiological (MEG, scalp or intracranial EEG) and functional (PET, ictal SPECT), were compared with the contrast maps. Sensitivity was defined as whether activation was found in the contrast images as expected. Specificity was defined as whether the activation found at

expected place was the most significant. A division of each hemisphere into four major regions (temporal, parietal, occipital and frontal) was assumed for the comparison.

**Results:** Four patients were excluded from further analysis because too few spikes were identified or no optodes covered the focus region. We reported good sensitivity on 28/36 and good specificity on 9/36 patients, based on HbR maps. fNIRS results improved for cortical epilepsies (28/30 and 9/30 respectively) and decreased for mesial temporal epilepsies (no sensitivity or specificity in all six cases).

**Conclusion:** The sensitivity (78%) of this fNIRS-EEG approach is encouraging, while methods to improve specificity (25%) remain to be investigated.

### P967

#### OCURRENCE OF EPILEPTIC SEIZURES AFTER THE ADMINISTRATION OF IV CONTRAST MEDIA IN NEUROIMAGING

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**Purpose:** To examine the potential role of iv contrast media administration during neuroimaging in inducing epileptic seizures.

**Method and Results:** A 42 year old male presented in the A and E department with two episodes of grand mal seizures within 15 min. The patient did not have any previous seizure history. A previous history of Left MCA stroke 6 months before, with LICA occlusion due to dissection was reported. According to the referring doctor, the patient had performed an MRI with iv contrast (Contrast agent: Gadopentetate Dimeglumine) 3 h before the initiation of the seizures. A resting state EEG was performed that revealed low amplitude slow wave activity, in particular delta rhythm in the left hemisphere. The seizures were adequately controlled with valproic acid.

**Conclusion:** This is a rare case of grand mal seizures that occurred in a patient without any previous seizure history and not immediately after the injection of the contrast media, as it was till now reported in the literature.

### P968

#### DEVELOPMENT OF TOOLS FOR BRAIN MAPPING OF ELOQUENT CORTEX: DATA FROM HEALTHY SUBJECTS AND PATIENTS WITH EPILEPSY

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**Purpose:** In patients with seizures who experience no relief when taking certain anti-epileptic drugs, brain surgery is an increasingly common and effective treatment. In such cases, advance knowledge of eloquent zones can facilitate surgical planning and reduce morbidity associated with resection of critical sensory, motor or language zones.

**Method:** We report data from a multidisciplinary research effort at the Montreal Neurological Institute directed at enhancing the surgical treatment of patients with Epilepsy. We have developed a systematic protocol for the preoperative identification of eloquent areas for surgical planning using a 3T Siemens scanner and functional magnetic resonance imaging (fMRI) and diffusion tensor tractography (DTT). Using BOLD fMRI, 14 healthy right-handed subjects were scanned while performing sensory, motor and lan-

guage tasks. We also initiated deterministic tractography (FACT algorithm) on identified regions-of-interest of white matter subjacent to the maximal activity identified in the fMRI condition-of-interest. We then applied this method to patients undergoing neurosurgical interventions and integrated these techniques with the results obtained from depth electrode implantations (via post-operative imaging).

**Results:** We have developed a protocol for obtaining BOLD-fMRI and DTT for integration in image-guided neurosurgery (IGNS) for the surgical treatment of patients with seizure disorders. Our method has use for epilepsy patients, permitting the effective planning and execution of minimally invasive neurosurgical procedures.

**Conclusion:** Presurgical brain mapping can provide the surgeon with a margin of safety to make larger removals of pathological tissue, improving patient outcome, and hence quality of life.

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### P969

#### ASYMMETRY OF PLANUM TEMPORALE PREDICTS LANGUAGE LATERALIZATION IN CHILDREN WITH LEFT-SIDED SYMPTOMATIC FOCAL EPILEPSY

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**Purpose:** Atypical language dominance is common in individuals with early onset left focal epilepsy. Surprisingly, many patients fail to show interhemispheric shifts of language despite having epileptogenic lesions in proximity to eloquent language cortex. It has remained unexplored if neuroanatomical asymmetries linked to human language modify the likelihood of atypical lateralization in this population.

**Method:** Fifty-one children (mean age 13.3 years) with lesional focal epilepsy and 36 controls underwent fMRI-scanning using a verb-generation task. The fMRI-laterality index within Broca's region was correlated with clinical predictors and neuroanatomical measures including the length of the planum temporale (PT).

**Results:** Atypical language lateralization was observed in 19 patients (38%) and in four controls (11%). Language laterality was increasingly right-sided in patients who showed atypical handedness, a left perisylvian ictal EEG focus, and a lesion in left superior temporal or inferior frontal regions. Most striking was the relationship between rightward PT asymmetry and atypical language ( $R = 0.70$ ,  $p < 0.0001$ ); patients with a longer PT in the right hemisphere were more likely to have atypical language dominance. The length of the right PT was the main predictor of language lateralization in the epilepsy group, accounting for 48% of variance, with handedness accounting for only a further 5%.

**Conclusion:** We conclude that although asymmetry of the PT may be unrelated to language lateralization in healthy individuals, the size of the right, contra-lesional PT region may reflect a "reserve capacity" for interhemispheric language reorganization in the presence of a seizure focus and lesions within left perisylvian regions.

### P970

#### RETROSPECTIVE QUANTITATIVE ANALYSIS OF MRI FROM NONLESIONAL EPILEPSY SURGERY CANDIDATES

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**Purpose:** To assess if quantitative MRI analysis can identify subtle structural changes in patients with refractory nonlesional focal epilepsy candidate for surgery.

**Method:** Epilepsy surgery candidates evaluated between 2006 and 2012 with a normal MRI based on qualitative analysis were identified. Presurgical MRIs were reviewed to retain only those of adequate quality. The quantitative analysis comprised two types of measure: cortical thickness (Freesurfer) and volumetric analysis of the hippocampus and amygdala (Freesurfer and FSL). The control group was composed of 39 subjects between the ages of 18 and 35. We created a z-score map for each patient and compared those two measures using a standard deviation of 2 and a minimum of 10 nodes/voxels. Results were compared to the epileptic focus determined by a comprehensive presurgical evaluation (video-EEG, ictal SPECT, MEG, and intracranial EEG).

**Results:** We identified 54 epileptic patients with reportedly nonlesional refractory focal epilepsy. After excluding MRIs with too much noise/artefacts, 35 MRIs from 21 subjects were deemed adequate for further quantitative analysis (mean age 26; range 18–35; 9 mesiotemporal, 7 lateral-temporal, 10 extratemporal). Increases and/or decreases in cortical thickness were noted in all subjects. Increases and/or decreases in hippocampal volume were noted in 4 (19%) subjects. These structural changes were identified within the epileptic focus in 56%. However, other intralobar (78%), extralobar (94%) and contralateral (89%) changes were also noted. Guided review of areas of increased thickness by a neuroradiologist could not confidently identify any underlying cortical dysplasia.

**Conclusion:** Retrospective structural image analysis of a series of nonlesional refractory epileptic patients evaluated for epilepsy surgery disclosed complex changes within and outside the focus. Prospective data acquisition is ongoing to determine what extent structural image analysis can contribute to the management of epilepsy surgery candidates.

#### P971

##### COMPARISON OF TWO NORMALIZATION METHODS OF EPILEPSY PATIENTS MRI AFTER SURGERY

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**Purpose:** Several neuroimaging studies of epilepsy require the normalization procedure (warping of individual brain images to a common template space) in order to perform a group study. Satisfactory normalization algorithms are available for anatomically normal brains; however, this is not a solved problem for brains with lesions or undergone surgery. Some previous works have shown that MRI normalization of these atypical brains, using different methods can dramatically affect partially or the whole final normalized brains (Ripollés et al., *NeuroImage* 60, 2002, 1296–1306; Brett et al., *NeuroImage* 14, 2001, 486–500; Crinion et al., *NeuroImage* 37, 2007, 866–875).

**Method:** In this work, we sought to compare two popular methods of MRI T1 image normalization, FSL and SPM8/Dartel, for our particular group of patients:

- A 8 epilepsy patients that had undergone surgery;
- B 9 epilepsy patients' candidates for surgery; and
- C 9 healthy patients. Performance evaluation was quantified through variance per voxel and ANOVA test.

**Results:** We have observed visually that SPM8/Dartel perform better than FSL the registration/normalization process, that is, the first present less deformation comparing the images of the three groups. Statistical analysis of intra- and inter-groups and different registration methods, also, shown that SPM8/Dartel presented the smaller variance in all cases of comparison between methods. Variance of group A, B, and C using FSL: 4149.8, 4166.5, and 3659.4, respectively; using SPM8/Dartel: 1995.0, 1881.1, and 1746.2.

**Conclusion:** In this work, we observed superior and robust performance of DARTEL algorithm in our MRI data. However, a larger number of patients would be desirable for more statistically significant results.

#### P972

##### SURFACE-BASED MAPPING OF LOCAL STRUCTURE-FUNCTION RELATIONSHIPS IN TEMPORAL LOBE EPILEPSY

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**Purpose:** In temporal lobe epilepsy (TLE), imaging research has shown structural and functional compromise of multiple cortical regions. As most studies separately analysed structural and functional data, the exact inter-relation of these changes remains unclear. Task-free functional MRI (fMRI) allows studying spontaneous functional activity. The majority of previous work in TLE focused on assessing inter-regional functional connectivity. Conversely, the amplitude of low-frequency fluctuations (ALFF) is a local marker of functional integrity. To assess local structure-function relationship in TLE, we jointly analyzed ALFF and cortical thickness.

**Method:** We acquired task-free fMRI and structural MRI in 45 drug-resistant TLE patients and 23 controls. Functional time-series were pre-processed using standard tools and mapped onto co-registered cortical surface models. In all subjects, we measured ALFF and cortical thickness. To control for global changes, both measures were z-scored in each participant prior to the analysis.

**Results:** Relative to controls, patients showed decreased ALFF in insulo-opercular, temporo-parietal, and posterior midline regions, together with orbitofrontal and occipito-temporal increases. Cortical thinning displayed a different spatial distribution, occurring mainly in fronto-central, opercular, and marginally in lateral temporal regions.

**Conclusion:** Point-wise surface mapping of ALFF derived from task-free fMRI revealed alterations in local functional integrity of limbic and default-mode networks, whereas cortical thinning predominated in fronto-central regions. These findings indicate a divergent distribution of structural and functional alterations in TLE. While cortical thinning likely represents cumulative effects of seizures, limbic and default-mode functional alterations may be secondary to hippocampal disconnection.

#### P973

##### BRAIN FUNCTIONAL MODULARITY IN TEMPORAL LOBE EPILEPSY

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**Purpose:** Focal epilepsy syndromes, in particular temporal lobe epilepsy (TLE), can be much improved by the surgical removal of a localized structural pathology. Nevertheless, these syndromes need to be conceptualized as network diseases in which the interplay is disturbed between brain regions immediately affected by the structural pathology and those remote to them. We hypothesized that the network architecture in patients with temporal lobe epilepsy is significantly different to that of healthy volunteers reflecting semiological features of the epilepsy syndrome.

**Method:** We used graph theoretical methods based on fMRI functional connectivity to study in detail the modular network structure in patients with TLE in comparison to healthy controls with special reference to the vigilance state.

**Results:** Compared to healthy controls, link density was reduced in TLE (=higher modularity in TLE). Node degree (=number of ties, a node has) in the amygdala was reduced in TLE compared to controls while in the posterior cingulate, it was higher in TLE than in controls.

**Conclusion:** Network modularity which quantifies the strength of interaction between functional modules, was decreased in TLE compared to controls paralleling our findings with deepening sleep, which is a physiological condition of reduced consciousness and limited cognitive functioning. The decreased node degree in the amygdala reflects its reduced connectivity to other network nodes, possibly linked to memory dysfunction often observed in TLE. The higher node degree in the posterior cingulate, an integral part of the “default mode” network, indicates an “over connection”, which might explain an increased susceptibility of the DMN in TLE for its suspension associated with impaired consciousness.

#### P974

### METHODOLOGICAL PROCEDURE TO IDENTIFY ANATOMICAL LOCATION OF DEPTH ELECTRODES IN THE CLINICAL EVALUATION OF EPILEPSY SURGERY CANDIDATES BASED ON OPEN SOURCE SOFTWARE

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**Purpose:** Rapid and precise localization of depth intracranial electrodes (IE) during invasive explorations of epilepsy surgery candidates, are a critical issue for surgical planning and in the interpretation of neurophysiologic results that has great potential to affect outcome.

To readily resolve this critical aspect related to the confident anatomical localization of IE, during the first instances of invasive explorations we describes a very reliable and easy to implement workflow for the precise localization of IE and its relation with automatic labeled surrounding cortex.

**Method:** Post-implant CT and high resolution T1 MRI, are first rigidly and then affinely aligned together using a Mutual Information metric to measure similarity across modalities. We performed this using the BRAINSFit module of the 3DSlicer package (<http://www.slicer.org>). Using this transforms, we then fit an automated parcellation of the brain

generated with Freesurfer image analysis suit (<http://surfer.nmr.mgh.harvard.edu/>). It is obtained subdividing the T1 MRI of the patient to a gyral based region that represents individual, valid and reliable anatomical context labels.

We performed all steps using open source licensed software requiring minimal user intervention, without the need of time consuming computational processing or specialized human resource.

**Results:** The method presented here was a useful and effective approach to easily identify the precise anatomical localization of IE, as recognized in four patients that underwent epilepsy surgery with successful outcomes.

**Conclusion:** This methodological procedure may assist epileptologist and neuroscience scientist in the identification of IE and the precise relation of the intracranial EEG signal to anatomical structures. It can be applied on individual patients and also for reporting in standardized large scale for group analysis, using open source licensed software with minimal human resource preparation.

#### P975

### THE DORSAL HIPPOCAMPAL COMMISSURE IN TEMPORAL LOBE EPILEPSY

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**Purpose:** Although Temporal lobe epilepsy (TLE) is often unilateral, spread to the contralateral temporal lobe is not uncommon. One of the possible pathways of spreading of the temporal lobe seizures is the dorsal hippocampal commissure. Our purpose was describe the characteristics of the dorsal hippocampal commissure in patients with temporal lobe epilepsy (TLE) using diffusion tensor tractography and compare them against healthy controls.

**Method:** Fifteen patients with TLE were scanned in a 3 T MRI, as well as 30 healthy controls. Tractography of the hippocampal commissure was performed using hippocampal seed regions and variables were recognized: number of tracts, Fractional anisotropy (FA) and mean diffusivity (MD), these averaged along the tract and at the mid-sagittal plane, and dominance of tracts at one side in respect to the contralateral homologous region.

**Results:** The mean age for patients with TLE was 34 and for controls was 30 years. The patients had a mean epilepsy duration of 14.4 years. Significant differences were found in the mean FA, reduced both along the tracts ( $p = 0.018$ ) and at the mid-sagittal plane ( $p = 0.011$ ). The length of the tracts was significantly decreased in patients than in controls ( $p = 0.02$ ). There was also a significant difference in the proportion of tracts on left to right, with more tracts in the left hemisphere in the epilepsy patients ( $p = 0.024$ ).

**Conclusion:** This is the first study comparing the tractography of the dorsal hippocampal commissural tract in patients with TLE. Significant differences between patients with TLE and healthy controls were found that might be due to their longstanding epilepsy and the characteristics of their seizures.

#### P976

### REORGANIZATION OF MEMORY CIRCUITS IN TEMPORAL LOBE EPILEPSY (TLE) DEMONSTRATED ON PRE-AND POSTOPERATIVE FUNCTIONAL MRI STUDY: RIGHT TLE DOES BETTER

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**Purpose:** A longitudinal study in potential memory circuits' reorganization over time across pre- and post-ATL has rarely been performed.

**Method:** Nineteen adult patients with medically intractable TLE and 15 healthy controls were enrolled. Ten patients underwent left ATL and 9 underwent right ATL. Group analyses of a novelty scene-encoding paradigm comparing areas of BOLD signal activation pre- and post-ATL were performed and separately analysed between left (LTLE) and right TLE (RTLE) patients. Further analysis comparing post-operative activations at <1 year and ≥1 year after the surgery was also performed in each group. SPM2 was used to process the data and to perform statistical analyses. Whole brain group analysis was performed by using a mixed-design analysis of variance model with  $p \leq 0.001$  (uncorrected) and cluster size ≥10 voxels.

**Results:** *fMRI activations:* Pre-op: Whole brain analysis: extratemporal activations were seen in both LTLE and RTLE, demonstrated by comparing with controls and also within groups comparison between pre- and post-op activations. ROI analysis: greater activations on contralateral hippocampus and parahippocampus. Post-op: increased ipsilateral neocortical temporal activations (left fusiform gyrus in LTLE and right superior temporal gyrus in RTLE). Better ipsilateral temporal lobe recruitment was demonstrated at 1 year or more in LTLE. Earlier recruitment at <1 year and more widespread activations at 1 year or more were seen in RTLE patients.

**Conclusion:** Increased extratemporal and increased asymmetries with predominant contralateral HC/PHC recruitments were observed during pre-operative period in both LTLE and RTLE patients. After the surgery, ipsilateral neocortical temporal recruitments were seen in both groups, more robust in RTLE. This post-operative dynamic change in recruitment pattern was earlier seen in RTLE, at less than 1 year. Even more widespread recruitment including extratemporal areas was also observed in RTLE at more than 1 year after the surgery.

## P977

### GRAPH ANALYSIS OF RESTING STATE FMRI DATA REVEALS REDUCED CONNECTIVITY FROM BILATERAL PHONOLOGICAL ANALYSIS REGIONS AND RIGHT INFERIOR FRONTAL GYRUS IN FOCAL EPILEPSY PATIENTS WITH READING DIFFICULTIES

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**Purpose:** We have recently observed that reading difficulties are present in ~10% of patients with focal epilepsy. Here we investigate whether whole brain patterns of fMRI based resting state functional connectivity in this group differ from that in focal epilepsy patients without reading difficulties and controls.

**Method:** We obtained resting state fMRI data in focal epilepsy patients with (n = 9) and without (n = 37) reading difficulties (+RD and -RD, respectively) and in healthy controls (n = 47). We measured functional connectivity between every pair of voxels and generated images of "whole-brain" functional connectivity by counting the number of functional connections of each voxel.

**Results:** When contrasted with the -RD and control groups, the +RD group had decreased connectivity ( $ui < 0.01$ ,  $FDRc < 0.05$ ) from bilateral posterior superior temporal regions and right inferior frontal gyrus.

**Conclusion:** These results indicate that the +RD group shows reduced connectivity arising from bilateral posterior regions involved in phonological analysis, and from the right hemisphere homologue of Broca's area. Studies of reading difficulties consistently implicate a failure of phonological awareness as the fundamental underlying deficit. The reduced functional connectivity observed in the +RD group could impli-

cate disrupted integration across the language network as a basis of reading difficulty.

## P978

### REGIONAL DIFFERENCES IN THALAMIC INVOLVEMENT IN LENNOX GASTAUT SYNDROME

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**Purpose:** To explore cortical and thalamic involvement during (a) slow spike-and wave (SSW), (b) generalised paroxysmal fast activity (GPFA); characteristic discharges of Lennox-Gastaut syndrome.

**Method:** Fifteen subjects (11–56 years), with Lennox-Gastaut Syndrome. Inclusion criteria were (1) interictal EEG with SSW and GPFA; (2) recurrent tonic seizures on video-EEG monitoring or history.

Up to 60 min of fMRI (3T GE Signa-LX; EPI, TR 3.0 sec.) were acquired during continuous EEG (in-house hardware/software), analysed using SPM8 and the iBrain Analysis Toolbox. Timings of EEG discharges were used in an event-related fMRI analysis for each subject, combined in a second-level group analysis.

Spherical regions of interest (ROIs) were placed in: (a) "Attentional" and "REST" areas; (b) primary cortical structures, and (c) four thalamic subregions.

**Results:** GPFA – Simultaneous fMRI activity increases in "attentional" and "REST" areas of association cortex, plus caudate and pons, leaving primary cortical areas relatively spared. Anterior and medial thalamic regions involved, but lateral and posterior thalamic regions uninvolved.

SSW – Reduced activity in posterior cingulate, precuneus and primary cortical areas, but pre-SSW rises in fMRI activity. Anterior, medial and lateral thalamic regions show fMRI changes of similar timecourse, with the posterior thalamus uninvolved.

**Conclusion:** There is diffuse association network activation during GPFA. fMRI activity in association cortex rises pre-SSW, then falls when SSW appears on the scalp.

Anterior and dorso-medial thalamic regions are involved during GPFA and SSW. The posterior region (pulvinar) appears uninvolved. Lateral thalamic regions (connecting to primary sensory cortex) are relatively uninvolved in GPFA.

## P979

### AUTOMATIC DISSECTION AND STRUCTURAL CONNECTIVITY OF THE LIMBIC SYSTEM

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**Purpose:** Current techniques such as diffusion tensor imaging (DTI) are extremely useful in clinical practice allowing in-vivo and non-invasive reconstruction of white matter (WM) tracts [Honey PNAS;2009;106:2035–2040]. Despite enabling the study of brain connectivity and detection of patients' brain networks abnormalities, these analyses are time consuming and require technical expertise [Lacerda et al;2012;29th ESMRMB]. In this work, a new automatic tool for the analysis of structural connectivity (SC) was developed and applied to the study of the limbic system (LS) of a post-traumatic epilepsy (PTE) patient.



**Method:** This study enrolled 16 (8 males) healthy volunteers (controls) and 1 PTE male patient. Data was acquired in a 1.5T MRI scanner. Volumetric T1-weighted data was acquired for anatomy visualization. DTI data was acquired using a spin echo-based diffusion sequence with 20 non-collinear gradient diffusion directions and  $b = 0.1000\text{s/mm}^2$ . Data was resampled into 2 mm isotropic voxels, prior to tensor estimation and tractography. The developed tool was used to automatically dissect the LS according to 14 predefined regions (both hemispheres): Amygdala, Caudate, Cingulate Gyrus (anterior and posterior division), Corpus Callosum, Hippocampus, Nucleus Accumbens, Putamen, Paracingulate Gyrus, Parahippocampal Gyrus (anterior and posterior division), Putamen, Subcallosal Cortex and Thalamus. SC matrixes for each subject were calculated from the number of tracts connecting each pair of LS regions, and were compared between controls and patient.

**Results:** It was observed that the PTE patient yielded an overall loss of SC (reduced number of tracts) in the LS. However, an increase in number of connections between the Right Paracingulate Gyrus and Right Cingulate Gyrus (anterior division) was also observed, suggesting reorganization of brain-networks in the area of trauma.

**Conclusion:** An automatic tool was developed for the study of the LS. SC analysis of LS may provide complementary information in the study of PTE patients and other neurological disorders alike.

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#### P980

##### MAGNETIZATION TRANSFER RATIO CAN LATERALIZE HIPPOCAMPAL SCLEROSIS

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**Purpose:** To test the hypothesis the Magnetization transfer ratio (MTR) can identify hippocampal sclerosis (HS).

**Method:** We studied 32 patients with epilepsy for unilateral mesial temporal lobe sclerosis, eighteen on the right, with a 3T MRI equipment. All patient had hippocampal sclerosis histopathologically proved after temporal lobectomy. The images were automatically segmented with FreeSurfer software. The MTR maps were calculated as well as quantitative T2 for comparison. The segmentation labels were used to extracted values for MTR, volume and T2-relaxometry. The data was analyzed using a Discriminant Analysis with cross-validation and the normalized difference between hippocampus was also calculated.

**Results:** MTR lateralized 29 cases of 32 (91%), T2-relaxometry time lateralized 28 (87.5%), and volumetry 30 cases (94%). The highest lateralization ratio was achieved combining the three metrics (97%).

**Conclusion:** MTR can detect HS and may be used to provide complementary information of hippocampal pathology. For lateralization of epileptogenic focus and preoperative examination, the combination of techniques represents better accuracy.

#### P981

##### COMPARATIVE STUDY OF 4-EXSO-MUSIC, S(W) LORETA, AND MUSIC PERFORMANCES FOR DISTRIBUTED EEG SOURCE LOCALIZATION (ESL)

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**Purpose:** ESL has been used for more than twenty years to estimate the origin of pathological signals such as interictal/ictal spikes in focal epilepsy. In this context we have recently proposed a new method, called 4-ExSo-MUSIC, designed to account for sources that are spatially distributed over a focal or multi-focal area ("extended sources"). This method exploits the high degree of synchronization within the source - a necessary condition to detect epileptic signals on surface recordings - and is particularly insensitive to perturbations due to the background activity and or to errors in the forward model. Although 4-ExSoMUSIC has shown promising results on simulated interictal-like activity compared to other MUSIC-like methods, this algorithm has not yet been compared to other distributed inverse solutions and has not been evaluated on real data. The purpose of our study is to compare 4-ExSo-MUSIC with methods commonly used for distributed EEG source localization (sLORETA, swLORETA) as well as with a distributed implementation of MUSIC.

**Method:** The performance of each method is quantified using realistic simulations of epileptic spikes in various scenarios (source location, source synchronization, number of EEG electrodes and number of spikes). The different methods are also evaluated on real epileptic data.

**Results:** In the context of simulated spikes we show that 4-ExSoMUSIC outperforms the three other methods in most of the source configurations considered. In particular, our method is robust with respect to desynchronization within the source. The limits of the method are also pointed out in situations where sources are closely located and emit synchronous activity. In patients, in whom a strong hypothesis on the origin of epileptic spikes exists, the accuracy of 4-ExSoMUSIC is clearly established.

**Conclusion:** This comparative study demonstrates the gain on performance achieved by 4-ExSoMUSIC and argues for its use in the work-up of patients with focal epilepsy.

#### P982

##### FOCAL CORTICAL DYSPLASIA: MRI AND HISTOPATHOLOGY OF 83 CASES

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**Purpose:** To review the spectrum of MRI appearance of the different types of Focal Cortical Dysplasia (FCD) based in the 2011 ILAE consensus.

**Method:** Data review of 83 patients with histopathological diagnosis of FCD after epilepsy surgery from 2001 to 2011. All "dual pathology" and not complete documented cases were excluded. The same imaging protocol was used, but with both 1.5 and 3 Tesla MRI equipment. Two radiologists reported the lesions and all the patients were submitted to the same presurgical protocol including structural and functional neuroimaging, neuropsychological examination, video-EEG and eventual invasive monitoring. The histopathology was reviewed by two expert pathologists.

**Results:** From the cohort of 83 patients, 17 were diagnosed histologically as type I (including types a, b and c), 39 as type 2 (including types a and b), and 26 patients as type III (a = 7, b = 11, d = 9 and no type c). Forty-one percent of the MRI were reported as normal. Atrophy and abnormal signal intensity of the white matter (WM) were the findings more frequent in Type I. Gray matter (GM)/WM boundary blurring, abnormal WM intensity, and cortical thickening were more frequent in type II. Tumor and gliosis were the misdiagnosis reported.

**Conclusion:** The MRI data of this series was similar to the literature. The normal MRI was reported more frequently in FCD type I. The type II was the most detected based on increased cortical thickness, abnormal gyral patterns, increased T2 WM signal and transmantle sign.

**P983**  
**MOTOR SYSTEM HYPER-EXCITABILITY IN SIBLINGS OF PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY**

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**Purpose:** To establish whether motor system hyper-excitability during a working memory task in a functional magnetic resonance imaging study (fMRI) is an endophenotype of juvenile myoclonic epilepsy (JME).

**Method:** We investigated seven unaffected siblings of JME patients and seven healthy controls with an fMRI visual-spatial working memory (n-back) task. The same task was previously employed in a cohort of JME patients (Vollmar et al. Brain 2011;134:1710–1719). The fMRI analysis was performed using SPM-8. A group comparison between JME siblings and healthy controls was carried out to investigate differences in activation patterns with a moderate and high working memory load. The level of significance was set at  $p < 0.001$  uncorrected.

**Results:** JME siblings and healthy controls were comparable for age, gender and verbal IQ. Both groups performed equally well on the n-back task. Siblings showed higher motor cortex activation during moderate working memory load. In addition to the motor cortex, increased prefrontal activation was observed in unaffected JME siblings which was more prominent during high working memory load.

**Conclusion:** This pilot study identified abnormal motor cortex co-activation with increasing memory load in unaffected siblings, similar to the changes seen previously in JME patients. In the context of the high heritability of this syndrome, our findings support the hypothesis that motor system hyper-excitability is an endophenotype in JME.

**P984**  
**MAPPING AND VOLUMETRY OF HESCHL'S GYRUS BY VOXEL BASED MORPHOMETRY AIDS IN PLANNING TEMPORAL LOBE RESECTION IN PATIENTS WITH "TLE WITH AUDITORY AURA"**

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**Purpose:** TLE with auditory aura (TLE-AA) form a specific subgroup of patients where the ictal onset zone extends to Heschl's gyrus (HG). After anterior temporal lobectomy (ATL), TLE-AA patients seldom become seizure-free. Through VBM of HG, we analyzed the reasons for surgical failure in them.

**Methods:** Of 456 consecutive patients operated for TLE from 2000–2010, we identified TLE-AA patients. Their HG was mapped by VBM pre-and post-surgically. Automated anatomical labeling using T1 image "normalized" to customized template was then "segmented" into GM, WM and CSF using probability maps. "Modulation" and "smoothing" with a 12-mm isotropic Gaussian Kernel was done. The volume of the HG (cm<sup>3</sup>) was computed by multiplying and summing voxel-by-voxel volume. Bivariate followed by multivariate logistic regression model analysis was performed comparing TLE-AA from patients with other auras. Pre-and-post-surgical VBM of HG was compared by ANOVA.

**Results:** Of 456 patients who underwent ATL, 344 (75.4%) had aura; 19 (5.5%) were TLE-AA. 11/19 (57.8%) with TLE-AA had prior encephalitis ( $p = 0.006$ ), 10/19 (52.6%) had normal MRI and 8/19 (42.1%) had normal histopathology ( $p = 0.000$ ). 10/19 had persistent seizures after surgery vs. 86/325 with other auras ( $p = 0.01$ ). 7/10 (70%) patients underwent left ATL ( $p = 0.01$ ). HG was intact in 9/10 patients (90%) who had seizures postoperatively. In 9 patients without seizures, the HG was disrupted completely by more than two-third its volume (mean pre- vs. post-surgery volume, 3.02 cm<sup>3</sup> vs. 0.41 cm<sup>3</sup>,  $p = 0.001$ ).

**Conclusions:** Volumetric mapping of HG pre and post-surgically in patients with TLE-AA confirmed that major disruption or removal of HG will only make the patient seizure-free. A presurgical VBM-HG mapping to incorporate it in resection should be attempted by anatomic landmarks or by neuronavigation.

**P985**  
**TRACTOGRAPHY-BASED CORTICAL CLUSTERING**

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**Purpose:** Tractography-based parcellation of the cortex aims at delineating distinct cortical regions presenting specific connectivity pattern. Recent works demonstrated a close agreement between tractography-based and cytoarchitectonic atlases. In this preliminary work, we present a method for investigating the cortical connectivity pattern in a group of healthy controls.

**Method:** All subjects underwent T1 and 32 directions DTI acquisitions on a 3T Philips MRI scanner. T1 images were processed using the FreeSurfer suite and cortical surfaces were parcellated into 5995 ROIs. DTI were corrected for Eddy currents, head motion and distortions using dedicated methods. For all subjects, 1,000,000 fibers were traced by seeding all brain voxels using the probabilistic tractography software MRtrix. Connectivity matrices were obtained for each subject by counting the number of fibers across all pairs of ROIs and a first-level clustering identified 20 distinct clusters using the spectral clustering Ncut algorithm. In addition, a second-level clustering identified the cluster correspondence across individuals and allowed us to compute cluster stability and reproducibility.

**Results:** We were able to map and identify reproducible clusters across the subjects.

**Conclusion:** We introduced an innovative method for clustering cortical regions in healthy subjects which, in future works, may be used to highlight structural connectivity disorganization in epileptic patients.

**P986**  
**MAPPING FIBER DENSITY ON SUBCORTICAL STRUCTURE SURFACE MODELS**

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**Purpose:** Subcortical structures play pivotal role in the study of epilepsy and surface models were developed to investigate abnormal shape and

positioning variations in epileptic patients. In this work, we propose a new way of constructing surface models, based on local surface curvature, to define surface templates and match individuals' anatomy. In addition, local fiber density was mapped on subcortical surfaces and registered to a common template.

**Method:** T1 and DTI images were acquired from a healthy controls and temporal lobe epilepsy patients using a 3T Philips MRI scanner. Surface models were obtained using the automated segmentations of the subcortical structures of interest (with Freesurfer, namely hippocampus, thalamus, putamen, caudate and accumbens). A template was computed for each structure using an iterative non-linear registration procedure based on surface curvature. Therefore, a non-linear transformation was found between each subject's subcortical surface model and corresponding template, ensuring anatomical correspondence across subjects. Fiber density was mapped on each surface by counting the number of fibers locally intersecting the surface model and was registered to the surface template using the predetermined transformation.

**Results:** For each structure, we obtained a non-linear surface model and mapped the local fiber density in patients and in healthy subjects.

**Conclusion:** Our proposed method may be a valuable tool for localizing connectivity differences in the subcortical structures involved in epilepsy.

#### P987

### CONTRIBUTION OF MAGNETIC RESONANCE IMAGING IN RESEARCH OF ETIOLOGY OF EPILEPSY

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**Purpose:** Epilepsy is a chronic disabling disease and a major health problem worldwide. The magnetic resonance imaging (MRI) is currently the best imaging choice for the exploration of epilepsy in the etiologic assessment and pre surgery. Our study aims to evaluate the contribution of this technique in the epileptic pathology.

**Method:** This is a retrospective descriptive study covering a period of one year (from 1 August 2011 to 31 July 2012) in which 135 patients have been referred to our service for the exploration of epilepsy. Epidemiological, clinical, EEG and MRI results were analyzed.

**Results:** The average age of our patients was 25.7 years, ranging from 1 month to 80 years. Adults accounted for 67.4% (n = 91) of the population. The series consisted of 79 men and 56 women is a sex ratio of 1.4. Partial seizures were present in 35.6% of patients, generalized seizures in 12.6%. EEG-MRI concordance was present in 21 patients. MRI was normal in 40% of cases. The lesions most frequently found were: atrophic lesions in 21%, vascular lesions in 15.9%, tumors in 14.8%, hippocampal sclerosis in 9.7%, cerebral malformations in 4.9% and phacomatoses in 2.5%.

**Conclusion:** MRI because of its high diagnostic performance remains the examination of choice in exploring the etiology of epilepsy, although it should always be guided by clinic and EEG. The emergence of new modalities of advanced MRI help to highlight lesions not detected by conventional MRI.

#### P988

### DIFFUSE GRAY MATTER ATROPHY DIFFERS IN RIGHT AND LEFT MESIAL TEMPORAL LOBE EPILEPSY

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**Rationale:** MRI studies show that patients with mesial temporal lobe epilepsy associated with hippocampal sclerosis (MTLE-HS) have structural brain abnormalities beyond the hippocampus. However, there is no consensus about the differences of the atrophy pattern of right and left MTLE-HS.

**Objectives:** To compare the pattern of gray matter (GM) atrophy in patients with right and left MTLE-HS.

**Method:** We evaluated 118 patients with diagnosis of MTLE-HS (65 with left and 53 with right MTLE). For detection of GM atrophy, voxel-based morphometry (VBM) was performed with VBM8/SPM8 (two-sample T-Test, FDR = 0.05) in T1-weighted images acquired in 3T scanner. A control group of 82 healthy subjects was used for comparison.

**Results:** The two groups did not differ in sex, age, duration of epilepsy, age of epilepsy onset, seizures frequency, response to anti-epileptic drugs, history of status epilepticus, seizures remission and family history of epilepsy. Patients with left MTLE-HS had a higher frequency of initial precipitating insult than patients with right MTLE-HS (p = 0.01). Both groups showed GM atrophy in the ipsilateral mesial temporal structures, bilateral pre-central gyrus and bilateral thalami. GM atrophy was observed in contralateral anterior temporal lobe, ipsilateral caudate, and medial frontal areas only in left MTLE-HS. GM atrophy was observed in occipital regions and ipsilateral insula only in right MTLE.

**Conclusion:** Patients with right and left MTLE-HS have distinct networks of GM atrophy. The knowledge of the different structures involved in these networks may help the discovery of target areas for specific treatment for different groups of MTLE-HS.

#### P989

### IN VIVO METABOTROPIC GLUTAMATE RECEPTOR TYPE 5 (MGLUR5) ABNORMALITIES IN PATIENTS WITH PERIVENTRICULAR HETEROTOPIA

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**Purpose:** Metabotropic glutamate receptor type 5 (mGluR5) modulates neuronal plasticity and excitability. Analysis of surgical specimens from patients with epilepsy have shown strong mGluR5 immunoreactivity in heterotopic neurons. However, pathological studies are limited by the scope of the surgical resection. Therefore, we utilized positron emission tomography using the radioligand [<sup>11</sup>C] ABP688, which binds specifically to the transmembrane allosteric site of mGluR5 to examine vivo whole brain mGluR5 availability. The study assessed [<sup>11</sup>C] ABP688 binding potentials (BP) in patients with nodular periventricular heterotopia (PVH) and PVH extending toward the cortex.

**Method:** Four patients with radiologically confirmed PVH and epilepsy (3 female, mean age of 23), and 29 healthy controls (6 female, mean age of 41) were included in the study. [<sup>11</sup>C]ABP688 PET scans consisted of a dynamic acquisition following [<sup>11</sup>C]ABP688 injection, in the ECAT High Resolution Research Tomograph (HRRT) PET scanner. PET volumes were coregistered to each subjects' s T1-weighted MRI and resampled to standard space. [<sup>11</sup>C]ABP688-BP maps were generated using a simplified reference tissue method. We compared average [<sup>11</sup>C] ABP688-BP from select regions of interest (ROI) and performed a voxel-wise whole brain z-test of [<sup>11</sup>C]ABP688-BP between each PVH patient and the control group.

**Results:** Patients with PVH showed no voxel-wise z-score differences in the cortex. As expected, positive z-score were found within the PVH relative to controls. Patients with nodular PVH showed reduced average [<sup>11</sup>C]ABP688-BP in the PVH ROI relative to the cortex, whereas patients

with PVH extending towards the cortex had equal [ $^{11}\text{C}$ ]ABP688-BP in the PVH ROI and the cortex.

**Conclusion:** Our findings in this small group of patients confirm abnormalities of [ $^{11}\text{C}$ ]ABP688-BP in PVH. The results highlight differences between patients with nodular PVH and PVH extending toward the cortex.

#### P990

### T2 HYPERSIGNAL IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY WITH AND WITHOUT HIPPOCAMPAL SCLEROSIS

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**Purpose:** T2 relaxometry is sensitive for detecting tissue abnormalities in patients with temporal lobe epilepsy (TLE). Our objective was to evaluate hyperintense T2 signal in temporal lobe structures and its correlations with clinical features in TLE patients with (TLE-HS) and without (TLE-NL) MRI evidence of hippocampal sclerosis (HS).

**Method:** We selected 180 consecutive patients with TLE: 110 with TLE-HS and 70 with TLE-NL. Healthy controls (N = 76) were used as comparison. T2 multi-echo images obtained with a 3T MRI were evaluated with in-house software. T2 signals decays were computed from six original echoes in ROIs in the hippocampus, amygdala and white matter of anterior temporal lobe (TLWM). Values higher than 2SD from the mean of controls were considered abnormal.

**Results:** T2 signal increase was observed in the hippocampus in 84% of TLE-HS and in 34% of TLE-NL; in amygdala in 17% of TLE-HS and in 21% of TLE-NL; and in TLWM in 22% of TLE-HS and in 23% of TLE-NL. Patients with drug refractory seizures had higher frequency of hippocampus hyperintense signal (72%) than patients with good seizure control (50%) ( $X^2$ :  $p = 0.004$ ), however, this difference was not observed for amygdala and TLWM. Patients without family history of epilepsy had higher frequency of hyperintense signal in hippocampus (71%) than those with positive family history (57%) ( $X^2$ :  $p = 0.049$ ).

**Conclusion:** Hyperintense T2 signal occurs in mesial and neocortical structures in both TLE-HS and TLE-NL. Hippocampal hyperintense signal is more frequent in patients with refractory TLE and in those without family history of epilepsy.

#### P991

### FINDING THE OCCULT: SURFACE-BASED MORPHOMETRY AND MACHINE LEARNING AIDS IN THE DETECTION OF "MRI-NEGATIVE" FOCAL CORTICAL DYSPLASIA

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**Purpose:** Focal cortical dysplasia (FCD) is the most common etiology in pediatric epilepsy and the second most common etiology in adults with treatment resistant epilepsy. Seizure freedom after surgery is reported at

66% with a detected lesion, but only 29% in MRI-negative patients. Yet, 70–80% of histologically-confirmed FCD cases go undetected by visual inspection of the MRI. Here, we test surface-based quantitative MRI processing methods and machine learning algorithms to determine their utility in the pre-surgical detection of MRI-negative FCD lesions.

**Method:** Twenty-three MRI-negative patients in whom no focal lesion was detected during routine visual radiological analysis and 7 MRI-positive patients were re-scanned before surgery at 3T using a T1-weighted MRI sequence. All patients subsequently underwent intracranial EEG monitoring and resection of the epileptic focus. In all patients, pathology showed the presence of focal cortical dysplasia. Sixty-one controls were scanned using the same imaging parameters. Morphometric routines with surface-based spherical averaging techniques were used to align anatomical structures between individual brains and to calculate six features at each vertex, including cortical thickness, gray-white contrast, local gyri-fication, sulcal depth, jacobian distance and curvature. A logistic regression classifier was trained on normal control data and the data from the FCD region of MRI-positive patients to classify, in MRI-negative patients, vertices into lesional and non-lesional.

**Results:** The logistic regression approach correctly classified lesions within the resection zone in 14 out of the 24 (58%) MRI-negative patients. The overall false positive rate (by vertex) was never greater than 1.05%.

**Conclusions:** Quantitative MRI can aid in the pre-surgical detection of FCD lesions, even in patients whose clinical MRI was read as normal. An automated, quantitative approach has the potential to increase the number of patients suitable for surgery and improve electrode placement and surgical outcome in patients with invisible lesions on routine clinical MRI.

#### P992

### WHITE MATTER INTEGRITY IN TLE PATIENTS WITH AND WITHOUT FAMILY HISTORY OF EPILEPSY

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**Purpose:** White matter abnormalities in patients with temporal lobe epilepsy have been described in both temporal and extratemporal regions. However, few studies have aimed to evaluate the influence of family history (FH) of epilepsy in the pattern of brain structural abnormalities. In this study, we used diffusion tensor imaging (DTI) to investigate the influence of family history of epilepsy on white matter (WM) integrity.

**Method:** We scanned 173 patients (105 females, mean age  $46.9 \pm 10.4$  years SD) with temporal lobe epilepsy and unilateral hippocampal sclerosis and 129 healthy volunteers (82 females, mean age  $41.4 \pm 14.6$  years SD) at 3.0T using DTI with 2 mm isotropic resolution and 32 directions. Patients were classified in four groups according to family history (FH) of epilepsy and side of hippocampal sclerosis, therefore we had: left-FHpos(36patients), left-FHneg(56patients), right-FHpos(36patients), right-FHneg(45patients). Four white matter tracts including, corticospinal tracts, uncinate fasciculus as well as both anterior and inferior portions of cingulum were identified using a deterministic streamline tractography method based on a priori knowledge of anatomy. Diffusion parameters (mean Fractional anisotropy -FA and Mean Diffusivity -MD) were compared between groups for each tract. For statistical analyses we used ANOVA with post-hoc Tukey HSD.

**Results:** DTI demonstrated reduced FA in all four tracts for the four groups compared to the control group: (anterior cingulum  $p = 0.001$ , inferior cingulum  $p = 0.003$ , corticospinal tract  $p < 0.0001$  and uncinate fasciculus  $p < 0.0001$ ). However we only observed an elevated MD in anterior cingulum in left-FHneg group (post-hoc Tukey HSD,  $p = 0.011$ ),

as well as a trend for elevated MD in uncinate fasciculus in the same group (Tukey HSD,  $p = 0.059$ ).

**Conclusion:** DTI tractography demonstrates widespread white matter abnormalities in all patients including extratemporal regions. Our preliminary analyses suggest that patients without family history and left side hippocampal sclerosis present more severe damage to WM integrity.

### P993

#### EVALUATION OF EFFECTIVE CONNECTIVITY OF LANGUAGE NETWORK IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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**Purpose:** To investigate the effective connectivity networks among overlapped core regions associated with semantic aspects of language function in patients with temporal lobe epilepsy (TLE) by means of conditional Granger causality and graph-theoretic method.

**Method:** Thirty-two TLE patients and 32 age- and sex matched healthy controls were recruited. All subjects performed the classic verb generation fMRI task. The acquired images were processed using statistical parametric mapping (SPM) software. Nine ROIs were selected according to the both group activation patterns and previous reports. The conditional granger causality (CGC) method for effective connectivity analysis was performed among the selected ROIs during verb generation using an in-house program coded in MATLAB.

**Results:** The comparison of activation in functional magnetic resonance imaging during covert word generation task between two groups showed that epilepsy patients had significant increased activity in left fusiform gyrus, right precuneus and left PCC. Compared with healthy controls, TLE patients revealed more effective connections and relatively higher In-Out degrees in bilateral insula, right Supplementary motor area, left frontal middle lobe and left PCC during verb generation task, while relatively lower In-Out degrees were found between right insula and left precentral gyrus.

**Conclusion:** The present study confirms the previous studies associated with brain plasticity in patients with temporal lobe epilepsy and extends previous results by a data-driven Granger causality approach in identifying condition-dependent effective connectivity, suggesting that insula and PCC may be the core structure responsible for the impaired language network in TLE patients.

### P994

#### REGIONAL AND FUNCTIONAL CONNECTIVITY ALTERATIONS IN TEMPORAL LOBE EPILEPSY AFTER SURGERY: A LONGITUDINAL RESTING-STATE FMRI STUDY

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**Purpose:** To characterize the alterations of network function in refractory TLE patients before and after surgery.

**Method:** Seventeen (10 right TLE and 7 left TLE) refractory TLE were recruited. ALL patients went through the baseline MRI scans before surgery and were rescanned 4.5 months after surgery. The amplitude of low-frequency fluctuations (ALFF) of blood oxygen level-dependent signals was used to characterize regional cerebral function. Twenty-seven regions of interest were selected as seed areas and followed by ROI wise functional connectivity analysis. Changes in these measures after surgery were examined to characterize effects of focal surgical excision on regional function and functional integration.

**Results:** After surgery, decreased functional connectivity were found in right TLE patients in a relative large scale network between right inferior orbital frontal lobe and right caudate, right inferior frontal lobe and right superior parietal lobe, right thalamus and right superior orbital frontal lobe, right thalamus and right caudate, left thalamus and left superior frontal lobe. Meanwhile, in left TLE patients, decreased functional connectivity was demonstrated between left putamen and right putamen. However, the functional connectivity of left medium orbital frontal lobe and right middle frontal lobe was increased. These alterations were associated with clinical measurements.

**Conclusion:** Our study demonstrated alterations of regional synchronous neural activity occurs and decreased functional integration across widely distributed neural networks after focal surgical excision. This finding contributes to the understanding of the pathological mechanism in TLE.

### P995

#### VALUE OF AUTOMATED CORTICAL THICKNESS ANALYSIS IN DETECTION OF OCCULT EPILEPTOGENIC LESIONS IN MRI OF PATIENTS WITH NONLESIONAL REFRACTORY INSULAR CORTEX EPILEPSY (NLRICE)

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**Purpose:** To explore the utility of automated cortical thickness analysis to detect subtle epileptogenic lesions in patients with NLRICE candidate for surgery.

**Method:** Nine consecutive patients with NLRICE (confirmed by MEG, intracerebral EEG and/or post-insulectomy seizure freedom) were identified. Their presurgical 3T MRI T1-weighted images were processed with Freesurfer to obtain a 3D segmentation of the cortical surface, a cortical thickness map and an individual vs. control-group node-to-node correspondence to assess regions with increased cortical thickness. The control group was composed of 40 right-handed subjects between the ages of 18 and 35. The same analysis was applied to six patients with nonlesional extrainsular epilepsy.

**Results:** In two subjects, an increase in cortical thickness was noted in the location of the insular epileptic focus. For one of them, guided review of the MRI allowed identification of a subtle cortical dysplasia

previously missed. For all nine subjects, other areas of increased thickness were however noted within the epileptic insular lobe (but not in the vicinity of the focus) (33%), in extrainsular lobes (100%) and contralaterally (89%). Furthermore, in six subjects with nonlesional extrainsular epilepsies (3 frontal, 3 temporal), an increase in cortical thickness was observed in the ipsilateral and contralateral insula in 17% and 67% respectively.

**Conclusion:** Automated cortical thickness analysis reveals insular areas of increased thickness both in patients with NLRICE and extrainsular epilepsy. It did allow however identification of one subtle cortical dysplasia previously missed (out of 9 patients). Further combined analyses are required to increase specificity.

### P996

#### PROGRESSING THE WHITE MATTER CHANGES ASSOCIATED WITH SURGERY ON TEMPORAL LOBE EPILEPSY

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**Purpose:** To evaluate the white matter changes during 4.5 months after surgery on patients with temporal lobe epilepsy (TLE).

**Method:** Ten right TLE patients who underwent right anterior temporal lobectomy or selective amygdalo-hippocampectomy were recruited. DTI was performed before surgery, and 4.5 months follow-up using a gradient-echo echo-planar imaging (EPI) sequence on a 3T MR imaging system (EXCITE, General Electric, Milwaukee, USA). The fractional anisotropy (FA) was calculated using DtiStudio software. Voxel based analysis of the FA maps between baseline and 4.5 months after surgery was performed with paired t test by using the SPM8. Pearson correlation coefficients were calculated to evaluate the relationship between some clinical variables (duration, frequency and interval days of scanning) and the mean values of FA within the VOIs. The significance levels were set at  $p < 0.05$  (two-tailed).

**Results:** The FA values significantly reduce diffused in the left inferior temporal gyrus, bilateral middle frontal gyrus and left putamen. The increased FA areas include the left parahippocampal gyrus, left temporal lobe, right inferior frontal gyrus. There is a correlation between the changes of FA values of right frontal gyrus and ages, and the left inferior temporal gyrus correlated with the postoperative follow-up interval.

**Conclusion:** Our study provides the neuroimaging evidence of white matter alteration pattern in TLE patients after surgery. The potential mechanism of TLE still needs further study.

### P997

#### RESTING STATE FUNCTIONAL CONNECTIVITY PREDICTS POST-SURGICAL COGNITIVE OUTCOME IN ANTERIOR TEMPORAL LOBECTOMY PATIENTS

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**Purpose:** The aim of this study is to determine if pre-operative resting state functional connectivity can predict postoperative cognitive morbidity in ATL patients.

We hypothesize that the more connections observed in the ipsilateral, to be resected temporal lobe, the more at risk the patient will be for cognitive decline postoperatively.

**Method:** We recruited 25 TLE patients (14 left; 11 right) who performed both resting state fMRI and neuropsychological tests as part of presurgical evaluations, and underwent standard temporal lobectomy with at least one year of postoperative follow-up. A gradient-echo fMRI sequence was obtained from each patient, and connectivity was measured by a voxel based calculation of the degree of correlation coefficient for each voxel within the brain hemisphere and within medial or medial/lateral temporal lobes to ipsilateral and contralateral to the seizure focus. Analysis of rs-fMRI connectivity was correlated with preoperative and postoperative change scores obtained on a battery of neuropsychological tests.

**Results:** Verbal memory scores on the Selective Reminding Test (SRT) were positively correlated with the left hippocampus and performance on the Boston Naming Test (BNT) showed similar positive correlations with left hippocampus, left superior/middle temporal and parahippocampal gyri, using whole brain mask. Rs-fMRI connectivity also correlated with pre-post change scores on verbal memory tests as well on the BNT.

**Conclusion:** These findings suggest that impairments in cognitive function in TLE patients are reflected in the intrinsic functional connectivity of the brain. Impairments of verbal learning and naming in TLE patients showed alterations in dominant temporal lobe structures in good agreement with the previous knowledge of memory and language networks. This study also demonstrated a relationship between pre and postoperative test scores and rs-fMRI connectivity, indicating rs-fMRI may be a useful predictor of cognitive outcome in patients undergoing ATL.

## Poster session: Neuropathology Wednesday, 26 June 2013

### P998

#### ASTROCYTIC P2Y RECEPTORS: CONTRIBUTION TO EPILEPTOGENESIS

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**Purpose:** G-protein coupled purinergic P2 receptors, P2Y1 (P2Y1) and 2 (P2Y2) are astrocyte-dominant ATP receptors. P2Y1 is known to act as direct inhibition of excitatory neurons and P2Y2 is involved in astrocytic migration and proliferation. We investigated expression of P2Y1 and P2Y2 in epileptic human brain with cortical malformations, and discussed the role of these receptors in epilepsy.

**Method:** Surgically resected specimens from patients with intractable epilepsy with 23 focal cortical dysplasia (FCD) and four tuberous sclerosis complex (TSC) were examined. We prepared 24 controls of non-epileptic autopsied brains. We performed immunohistochemistry (IHC) of either P2Y1 or P2Y2 receptors, which was double-labeled with glial fibrillary acidic protein (GFAP). Furthermore, we counted the number stained cells, and calculated the rate of the number of double-marked cells over that of GFAP+ cells in each observation area.

**Results:** P2Y1 and P2Y2 were expressed only in astrocytes. The P2Y1 rates of FCD and TSC were  $56.9 \pm 23.3$  (mean  $\pm$  SD)% and  $66.2 \pm 21.2\%$ , respectively. Those were significantly higher than controls ( $0.9 \pm 2.8\%$ ). The P2Y2 rates of FCD ( $86.6 \pm 19.5\%$ ) and TSC ( $99.3 \pm 1.6\%$ ) were also significantly higher than controls ( $4.8 \pm 14.1\%$ ).

**Conclusion:** The results indicated that P2Y1 and P2Y2 expressed in astrocytes of epileptic foci. It is suggested that astrocytes fall into dysfunctions of P2Y1 and P2Y2. Diminished rate of P2Y1+ astrocytes may lead to accelerate neuronal excitation. Moreover, increase of P2Y2+ astrocytes rate is thought to reflect the secondary change of regional astrogliosis.

#### P999

##### EXPRESSION OF HMGB1 AND TOLL-LIKE RECEPTORS IN THE HIPPOCAMPUS OF HUMAN INTRACTABLE TEMPORAL LOBE EPILEPSY

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**Purpose:** Inflammation of the brain has received widespread attention as an important factor in acquired epileptogenicity. Recently, Maroso et al. reported that the epileptogenic pathway is activated when high-mobility group box-1 (HMGB1) released from neurons and glia bind to toll-like receptor 4 (TLR4), a receptor that plays an important role in natural immunity. Therefore, to clarify inflammation mediator expression in intractable temporal lobe epilepsy patients, we used the hippocampus of epilepsy patients to perform immunostaining for HMGB1, receptors TLR4, and the receptor for advanced glycation end products (RAGE) and investigated the expression for each of them.

**Method:** This study targeted 20 patients, HS (+) n = 10, mean age 34.5yo; HS (-) n = 10, 38.2yo, who underwent extirpative surgery of the hippocampus or lateral temporal lobe as treatment for intractable epilepsy at the Juntendo School of Medicine. Immunostaining was performed for KB, GFAP, TLR4, HMGB1, and RAGE receptors, and results were comparatively investigated.

**Results:** Strong immune reactions for HMGB1, TLR4, and RAGE were observed in the pyramidal neurons, astrocytes of HS (+) specimens. Meanwhile, in HS (-) cortexes, HMGB1 was detected in ubiquitous glia and neuronal nuclei, but we did not observe TLR4 or RAGE expression. These include perinuclear stain for HMGB1 in neurons, astrocytes and expression of TLR4 in astrocytes and neurons, both stains are showing low expression in HS (-). HMGB1 interacts with TLR4, which can normally be found on the surface of but also abnormally on other astrocytes and neurons in sclerotic hippocampal tissue.

**Conclusion:** This study suggested that expression of HMGB1 and TLR4 increases in hippocampus with HS. HMGB1-TLR4 pathway also plays an important part in human epileptogenesis. It was discovered that in

human hippocampal epilepsy, HMGB1 acts chronically in localized areas and TLR4 becomes involved. This may then enhance hippocampal sclerosis and atrophy.

#### P1000

##### FIRST AUTOPSY REPORT OF A PATIENT WITH ACUTE ENCEPHALITIS WITH REFRACTORY, REPETITIVE PARTIAL SEIZURES

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**Purpose:** Acute encephalitis with refractory, repetitive partial seizures (AERRPS) or febrile infection-related epilepsy syndrome (FIRES) is a devastating disease with refractory status epilepticus and subsequent intractable epilepsy. Neuroimaging studies do not show specific findings and the underlying pathogenesis is poorly understood. We report a first autopsy case to reveal the pathophysiology of AERRPS or FIRES.

**Patient:** A 11-year-old previously healthy boy was admitted with sudden onset of clustering partial seizures preceded by febrile illness. He was given multiple anticonvulsants and steroid. All of diazepam, midazolam, phenytoin, and phenobarbital failed to control seizures. Seizures ceased by continuous intravenous thiamylal with induction of burst-suppression EEG pattern. However seizures recurred when thiamylal was decreased. Diffusion weighted images at 7th day showed high intensity in bilateral hippocampi, amygdala and pulvinar of thalami. After 2 weeks of continuous thiamylal infusion, we started phenobarbital to replace thiamylal. Then he developed systemic skin eruption and multiple organ failure, which were supposed to be a drug-induced reaction. He died two months later in spite of repeated plasmapheresis and dialysis.

**Autopsy findings:** The CA1 and CA4 areas of hippocampus showed severe neuronal loss and astrocytosis. Although neuronal loss and astrocytosis were also seen in amygdala, thalamus and cerebellum, they were milder. There were multiple focal lesions of neuronal loss and astrocytosis in the frontal, parietal, temporal and occipital neocortex.

**Conclusion:** The extensive neuronal loss and astrocytosis may be caused by long-lasting seizure activities. The multifocal hippocampal and neocortical lesions may induce subsequent epileptogenesis of AERRPS.

#### P1001

##### MALDISTRIBUTION OF INTERNEURON BETWEEN CORTEX AND BASAL GANGLIA IN FOCAL CORTICAL DYSPLASIA: CONSIDERATION OF EPILEPTOGENESIS

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**Purpose:** The balance of excitation and inhibition of neurons and neuronal network is very important to perform complete neuronal function. Damage or loss of inhibitory  $\gamma$ -aminobutyric acid (GABA)-ergic interneuron is associated with impaired inhibitory control of cortical pyramidal neurons, leading to hyperexcitability and epileptogenesis. In the present study, we investigated distribution of interneuron subtypes between cortex and caudate nucleus in focal cortical dysplasia cases.

**Method:** We performed immunohistochemistry of GABA, glutamic acid decarboxylase (GAD), calretinin (CR), calbindin (CB), parvalbumin (PV) and neuropeptide. We used surgical materials of four focal cortical dysplasia (FCD) cases, having lesions of cortex and caudate nucleus, and eight age-matched autopsy controls. Student-t test was used for comparison between two parts at a significance level of  $p < 0.05$ . All cerebral tissues used in the present study were approved for research usage by the parents and ethical committees of the hospital and institute.

**Results:** The pathology showed three FCD IIa, containing dysmorphic neurons, and one FCD IIb, balloon cells. In the cortex, the concentrations (each positive cell number/all cell numbers in the evaluated field) of GAD+ ( $p = 0.0194$ ), CR+ ( $p = 0.0472$ ) and CB+ ( $p = 0.035$ ) cells were significantly lower in FCD than in controls. On the contrary, in the caudate nucleus those of CR+ ( $p = 0.0475$ ) and CB+ ( $p = 0.0017$ ) cells were significantly more in FCD than in controls.

**Conclusion:** The interneuron imbalance between the cortex and basal ganglia may affect the epileptogenesis of FCD.

#### P1002 PRECOCIOUS AND DELAYED NEOCORTICAL SYNAPTOGENESIS IN FETAL HOLOPROSENCEPHALY

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**Background:** Predictable temporal and spatial patterns of synaptophysin expression previously were demonstrated in the normally developing foetal cerebral cortex, reflecting synaptogenesis without regard to neurotransmitter type.

**Methods:** We studied six human fetal brains with holoprosencephaly in the mid-2nd and 3rd trimesters with immunocytochemical antibodies against synaptophysin and other markers of neuronal maturation.

**Results:** All brains were micrencephalic for gestational age. We found not only abnormal patchy patterns of synaptic vesicle reactivity within the disorganized cortical plate, but also loss of precise timing of genetically programmed synaptogenesis. Precociousness in synaptophysin reactivity relative to age-matched controls was demonstrated in five cases, and delayed reactivity in one. Abnormalities were more severe in paramedian than in more lateral regions of the cerebral cortex, following a mediolateral gradient in the horizontal axis. Extrajugal heterotopia exhibited early synaptogenesis. The nodular histological architecture of paramedian zones of cortex contains randomly oriented branching microcolumns of neurones, a unique feature. The hippocampus and subcortical structures did not show precocious synapses, except for delay in our single case of cortical delay.

**Conclusions:** Synaptic precociousness occurs often in holoprosencephaly but is limited to the cerebral cortex; synaptic delay occurs in other

cases and is more global. Precociousness may limit synaptic plasticity and contribute to earlier epileptogenic circuitry with a poorer prognosis for infantile epileptic syndromes. Faulty genetic programming alters not only cortical histological architecture but also the timing of onset of synapse formation.

#### P1003 LOW HIPPOCAMPAL GABA CONCENTRATION IN THE EPILEPTIC RAT BRAIN PRECEDES THE ONSET OF SPONTANEOUS SEIZURES IN THE PILOCARPINE MODEL OF TLE

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**Purpose:** Repetitive activation of the GABAergic system leads to GABA-A receptor desensitization in refractory human temporal lobe epilepsy (TLE) and in the rat pilocarpine model. These findings suggest an impairment of GABA signaling in the epileptic brain. In this work we analyzed GABA release and loss of two major GABA interneuron populations (parvalbumin and somatostatin) in the ventral hippocampus at different time-points after pilocarpine-induced status epilepticus (SE) in the rat, i.e. during development and progression of the disease.

**Method:** GABA release was measured using in vivo microdialysis under basal and K<sup>+</sup> evoked conditions, 24 h after SE (acute phase), during latency (7–9 days after SE), at the time of the first spontaneous seizure, in the early (1 month) and late chronic period (2 months after SE). The survival of parvalbumin and somatostatin positive interneurons was analyzed.

**Result:** (i) During latency there is a loss of GABA cells and the basal GABA release is reduced, but the system contrasts seizures, because an increased GABA release takes place in response to stimulation; (ii) at the time of the first spontaneous seizure the increased responsiveness to stimulation of the GABA release system disappears and no compensation for GABA cell loss is available. The dysfunction remains the constant until the late phase of the disease.

**Conclusion:** Our data suggest that a GABAergic hyper-responsiveness protects from the occurrence of seizures during latency, while impaired GABA release in the hippocampus favors the occurrence of spontaneous recurrent seizures and the maintenance of an epileptic state.

#### P1004 HUMAN HERPESVIRUS-7 (HHV-7) IN BRAIN TISSUES FROM ADULTS WITH INTRACTABLE EPILEPSY: A PATHOLOGICAL ROLE IN SOME CASES OF HIPPOCAMPAL SCLEROSIS?

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**Purpose:** Human herpesvirus-7 (HHV-7) is a  $\beta$ -herpesvirus which has been associated with febrile seizures in children. An association between HHV-7 and intractable epilepsy has not, however, been confirmed. Thus, the purpose of this study is to investigate the presence of HHV-7 protein (KR4) in brain tissue from 305 people with intractable epilepsy and to determine whether inflammatory molecules are activated and inflammatory responses are associated with the presence of HHV-7 infection.



**Method:** We used immunocytochemistry to detect HHV-7 protein KR4 in 305 patients with intractable epilepsy. Nested PCR was used to detect HHV-7 DNA in 63 liquid nitrogen-preserved hippocampal samples from the same people. [11] Inflammatory molecules including Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), Transforming growth factor- $\beta$  (TGF- $\beta$ ), Interleukin-1 (IL-1) and Interleukin-6 (IL-6) were identified by rt-PCR and immunohistochemistry. [11] Are they from the same 305 people? Yes, they come from the same people.

**Results:** There were 201 males. Mean age of individuals was 23.9, SD 6.2 years (range 15 to 45 years). The commonest pathological finding was hippocampal sclerosis (69 cases, 22.6%). HHV-7 protein was detected in 27 (8.9%) of the 305 samples and in none from the 30 controls. Factors associated with HHV-7 infection were hippocampal sclerosis (11/69), glial scar (8 of 58 cases) and vascular malformation (4 of 52 cases). Significant staining for HHV-7 antigen was distributed mainly in or around the nucleus of astrocytes in deep white matter. HHV-7 DNA was detected in 20 of 63 HS hippocampal sclerosis samples. The expression of inflammatory factor TGF- $\beta$  was up-regulated in samples positive for HHV-7 protein.

**Conclusion:** These findings suggest a possible association between HHV-7 positivity and intractable epilepsy especially hippocampal sclerosis, and activation of TGF- $\beta$ . Further studies are needed to confirm this result.

#### P1005 INCREASED OLIGODENDROGLIAL LIKE CELLS CORRELATING WITH INTRACTABLE FOCAL EPILEPSY IN CHILDREN

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**Purpose:** Recent studies suggest that glia influence epileptogenesis. Studies of specimens from epilepsy surgery reported increased oligodendroglial-like cells (OLC) in the white matter. Oligodendrogliosis is defined as clusters or linear arrays of OLC (Olig2-reactive). We examined the OLC population in the resected specimens from children with intractable focal epilepsy.

**Method:** We retrospectively collected 17 cases (9 female) who underwent intracranial EEG. The neuropathological findings were correlated with the clinical data. The neuropathology examination utilized H&E/LFB and immunohistochemical staining for NeuN, GFAP and Olig2. OLC were counted in three sites: (a) gray matter, (b) junction of gray/white matter, and (c) white matter. We also examined the correlation between the density of OLC among the three sites and the clinical features (seizure type, diagnosis).

**Results:** Seizure types consisted of partial seizures in 12 patients, epileptic spasms (ES) in 4, and partial seizures with secondarily generalization in 1. We found focal cortical dysplasia in 10/17 (59%) cases and oligodendrogliosis in 7/17 (41%) cases. OLC were observed in all 17 cases. The density of OLC at (b) and (c) significantly increased than (a) ( $p < 0.01$ ). The density of OLC at (b) and (c) significantly increased in seven oligodendrogliosis than others ( $p < 0.05$ ). Four patients with ES showed significantly increased the density of OLC at (b) than 13 patients without ES ( $p < 0.05$ ).

**Conclusion:** Increased OLC in white matter may correlate with intractability of epilepsy in children. The increased OLC at the junction of gray/white matter in patients with ES may indicate the wide spread epileptic network to provoke spasms.

#### P1006

#### ROLE OF INFLAMMATION ON GENE EXPRESSION IN A MURINE MOUSE MODEL OF TEMPORAL LOBE EPILEPSY

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**Purpose:** Temporal Lobe Epilepsy (TLE) is one of the most represented form of epilepsy in human. Recently, immune system activation and inflammatory mediators have been found having a role in epileptogenesis and seizure occurrence in TLEs. In order to study hippocampal gene expression changes during chronic seizures in conjunction with systemic inflammation, we set up a murine experimental model of kainic acid (KA)-injected mice treated with Lipopolysaccharide (LPS).

**Method:** Two groups of mice had been unilaterally injected with an intrahippocampal dose of kainic acid (KA). After three weeks mice were injected or not with an intraperitoneal dose of LPS to mimic peripheral infection. A set of animals had been recorded by EEG to assess the frequency and the strength of epileptic seizures after LPS administration. On the other hand, hippocampi had been explanted 4 and 24 h later the LPS injection, and used for subsequent gene expression analysis by microarray and RT-qPCR.

**Results:** First, EEG recordings showed an increased seizure number in LPS-treated mice with chronic seizures in comparison to controls. Microarray analysis showed that KA+LPS treatment exacerbated the expression of many inflammatory genes already observed in KA- or LPS-treated hippocampi, encompassing chemokines, interleukines, CD receptors, and vascular adhesion genes. Subsequent RT-qPCR analysis largely confirmed microarray data about differential gene expression observed among the experimental groups.

**Conclusion:** These data suggest that LPS-mediated inflammatory insult may strengthen inflammatory gene expression changes that occur during chronic epilepsy, and that these molecular changes are associated with an enhanced propensity to spontaneous seizures.

#### P1007

#### CELL INJURY AND PREMATURE NEURODEGENERATION IN FOCAL MALFORMATIONS OF CORTICAL DEVELOPMENT

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**Purpose:** Several lines of evidence suggest that cell injury may occur in malformations of cortical development associated with epilepsy. Moreover, recent studies support the link between neurodevelopmental and neurodegenerative mechanisms.

**Method:** We evaluated a series of focal cortical dysplasia (FCD, n = 21; type I and II) and tuberous sclerosis complex (TSC, n = 6) cases. Sections were processed for TUNEL labeling and immunohistochemistry using markers for the evaluation of apoptosis signalling pathways and neurogeneration-related proteins/pathways.

**Results:** In both FCD II and TSC specimens, we observed significant increases in both TUNEL-positive and caspase-3-positive cells compared to controls and FCD I. Expression of  $\beta$  amyloid precursor protein was observed in neuronal soma and processes in FCD II and TSC. In these specimens, we also observed an abnormal expression of death receptor-6. Immunoreactivity for phosphorylated tau was only found in older patients with FCD II and TSC. In these cases, prominent nuclear/cytoplasmic p62 immunoreactivity was detected in both dysmorphic neurons and balloon/giant cells.

**Conclusions:** Our data provide evidence of complex, but similar mechanisms of cell injury in focal malformations of cortical development associated with mammalian target of rapamycin (mTOR) pathway hyperactivation, with prominent induction of apoptosis signalling pathways and premature activation of mechanisms of neurodegeneration.

#### P1008

##### PROLIFERATIVE OLIGODENDROGLIAL HYPERPLASIA IN EPILEPSY (POGHE): A NOVEL DIAGNOSTIC ENTITY

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**Purpose:** The histopathological diagnosis of human focal epilepsies is challenging comprising a broad spectrum of entities. Here, we describe a novel diagnostic entity which involves the white matter of the frontal lobe and shares features of both, malformations and tumors.

**Method:** We identified eleven patients with increased cellularity within the white matter of the frontal lobe reviewing the clinico-pathological data base of the European Epilepsy Brain Bank. All patients suffered from drug-resistant focal epilepsy and were submitted to epilepsy surgery. Particular emphasis was put on the quantitative evaluation of Olig-2 immunoreactive oligodendroglial cell densities. Cellular proliferation was quantified using Ki67-labeling. Double immunofluorescence experiments were applied to further characterize the proliferating cells. The results were compared to other epilepsy-associated lesions and autopsy controls.

**Results:** Presurgical evaluation suggested focal cortical dysplasia in all patients. Histopathological examinations did not reveal any gross architectural abnormalities of the cortical ribbon. We found increased oligodendroglial cell numbers in the white matter, extending into adjacent subgranular cortical layers. Glial cell numbers and proliferation was increased compared to controls. There was no evidence for tumor infiltration nor inflammation as reassessed by immunohistochemistry (p53, IDH1, CD68, CD45). In five patients, double-immunofluorescence stainings confirmed an oligodendroglial lineage of 53–100% of proliferating cells. In four cases, Olig-2 positive cells were proliferative in 20–46%. We were not yet able to identify the lineage of Olig2-negative prolifera-

tive cells in these patients (yet non-neuronal, non-astroglial, non-inflammatory).

**Conclusion:** Here, we describe a novel diagnostic entity and propose the term “Proliferative Oligodendroglial Hyperplasia in Epilepsy (POGHE)”. Histopathological analyses and available long-term follow-up in our patient cohort virtually exclude a neoplastic nature. We suggest to classify this intriguing lesion into the spectrum of Malformations of Cortical Development. The epileptogenic potential is difficult to clarify, but may be related to the involvement of subgranular cortical areas.

#### P1009

##### ASSOCIATION BETWEEN HUMAN HERPES VIRUS 6B AND APOLIPOPROTEIN E4 IN PATIENTS WITH REFRACTORY MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** To investigate the relationship of apolipoprotein E4 (ApoE4) and human herpes virus 6B (HHV-6B) in hippocampal tissue of refractory mesial temporal lobe epilepsy with hippocampal sclerosis (rMTLE-HS).

**Method:** We used nested PCR and immunohistochemistry to detect and quantify viral DNA of HHV-6B in resected brain tissues. ApoE gene polymorphism was also analyzed by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP).

**Results:** A total of 65 participants were recruited into this study, including 46 rMTLE-HS cases and 19 controls. Higher positive rates of ApoE4 and HHV-6B (30.4% and 39.1%) was observed in rMTLE-HS patients' hippocampus compared to controls (p = 0.049 and p = 0.037 respectively). Eight out of 14 (57.1%) ApoE4 positive cases with rTLE were HHV-6B carriers; however 10 out of 32 (21.4%) ApoE4 negative cases were demonstrated to have HHV-6B (p = 0.115 > 0.05). Among HHV-6B positive cases with rMTLE-HS, virus DNA mean expression was 25.44 (E + 07 copies/10<sup>6</sup>cell) for those with ApoE4 and 96.53 (E + 07 copies/10<sup>6</sup>cell) for those without ApoE4 (p = 0.213 > 0.05). Additionally for those with both ApoE4 and HHV-6B in rMTLE-HS group, average onset age was 8.87 ± 3.79 years, lower than that of those with either ApoE4 (17.50 ± 7.14 years) or HHV-6B (15.30 ± 9.13 years), with p = 0.013 and p > 0.05 respectively.

**Conclusion:** We have observed an elevated expression of ApoE4 and HHV-6B in hippocampal tissue of patients with rMTLE-HS. Those with positive ApoE4 expression might gain a higher chance to carry HHV-6B. Further researches were needed to investigate the relation and potential mechanism.

#### P1010

##### HIPPOCAMPAL HISTOPATHOLOGY IN A KINDLING REFRACTORY EPILEPSY SPRAGUE-DAWLEY RAT MODEL INDUCED BY CORIARIA LACTONE

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**Purpose:** Temporal lobe epilepsy (TLE) is the most common form of refractory epilepsy. Meanwhile, hippocampus sclerosis is an usual pathogenesis for TLE. Nowadays the clinico-pathological classification of hippocampus sclerosis has become a research focus. Accordingly, we intend to identify the hippocampus histopathological category of a kindling refractory epilepsy Sprague-Dawley (SD) rat model induced by Coriaria Lactone (CL), which has been demonstrated to be a mesial temporal lobe

epilepsy (MTLE) model in our previous work (Wang Y et al. *Epilepsia* 2003;44:475–488).

**Method:** We established the epilepsy model in SD rats by repeated intramuscular injection of subthreshold dosages of Coriaria Lactone, while the control group by equal Normal Saline. The brain specimens were specifically stained by immunohistochemistry (IHC) with the neuronal nuclear antigen NeuN. Neuronal cell numbers were semi-quantitative measured under microscopy, three randomly visual fields at 200 fold magnification, in hippocampal subfields CA1-CA4 respectively.

**Results:** In hippocampal subfields CA1-CA4, the neuronal cell numbers were significantly different between kindled group and control group in CA4 ( $p < 0.05$ ), while in the other subfields the differences were non-significant.

**Conclusion:** According to the clinico-pathological classification system proposed by Blümcke et al., postsurgical outcome was worse in the atypical MTS, especially MTS type 3 (severe neuronal loss restricted to the hilar region). Our findings indicated that the CL kindling MTLE rat model was in accordance with the MTS type 3. Therefore, this special epilepsy model may be a better choice for future researches of refractory MTLE, especially for the multiple pharmacoresistant mechanism and post-surgery anti-epilepsy therapy.

#### P1011

##### LAFORA BODIES TYPE II: ORIGIN AND POTENTIAL FUNCTIONAL SIGNIFICANCE: OBSERVATIONS MADE IN A K-O LAFORIN-DEFICIENT MICE MODEL

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**Purpose:** Laforin-deficient mice show neuronal death occurring at early age in the absence of Lafora bodies (LFBs). They also show neurodegenerative changes contradicting current views establishing a causality relation between Lafora bodies and neural derangement. Formation of LFBs (types I and II) remains obscure. We describe the morphological sequence that leads to the formation of the LFBs Type II, and discuss a potential dynamic and functional role for this kind of LFBs.

**Method:** Laforin-deficient K-O and wild mice were sacrificed and samples of the nervous system, liver and muscle were taken for microscopical studies.

##### Results:

- (1) Type I LFBs are abundant dust-like structures and ubiquitously present in neuronal cytoplasm and neurites. Type II, are elegant and large structures, always located in the cytoplasm of large neurons and their number is limited.
- (2) Type II LFBs are seldom seen outside the nervous system.
- (3) We have already described that the Type II LFBs display a strong immunoreaction to Neurofilament L, revealed as a circular array of globules in their outer ring, and potentially linking Type II LFBs with the neurocytoskeleton.
- (4) For the first time, our light- and electron-microscopy studies show a sequence of morphological steps that clearly demonstrate the complex way in which the type II Lafora bodies are formed.

**Conclusion:** Our findings demonstrate the presence of neurodegenerative changes as well as neuronal death (non-apoptotic) long before the LFBs reach a large size and/or a large number. The special sequence of formation of LFBs type II and their morphological features, allows us to say that they do not represent a simple cul-de-sac accumulation of badly formed molecules. We postulate that Type II inclusions are elaborated structures produced by a genetic response (adaptive ???) that just a few neurons are capable to present.

#### P1012

##### CHRONIC LOW-LEVEL VIRAL REPLICATION IN REFRACTORY EPILEPSY FOLLOWING HERPES SIMPLEX VIRUS ENCEPHALITIS

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**Purpose:** Neurologic deficits frequently follow Herpes simplex virus (HSV) encephalitis (HSVE). Chronic inflammation is reported in animal, post mortem and epilepsy surgery brain specimens following HSVE. While HSV DNA has been isolated from these specimens, it is unclear whether this represents latent or replicating virus. As such, it is unclear whether the inflammation identified is a viral- or immune-driven process.

**Method:** Four patients aged 6–25 years underwent surgery for refractory epilepsy following HSVE. Histopathology, and immunohistochemistry (IHC) to detect T and B cells and HSV protein, was performed on brain tissue. HSV DNA PCR was performed on brain tissue and cerebrospinal fluid. IHC for HSV protein was performed on control brain tissue from three children with Rasmussen encephalitis and three with non-lesional epilepsy.

**Results:** Histopathology revealed chronic encephalitis with a T-cell predominance. No viral inclusions were seen. HSV DNA was detected by PCR in brain tissue in all patients; HSV PCR was negative in the cerebrospinal fluid. IHC was positive for HSV proteins in all patients, each specimen showing occasional cells with granular cytoplasmic staining. HSV IHC was negative in control specimens.

**Conclusion:** The presence of HSV proteins indicates active viral replication and suggests low-level persistent or reactivating HSV infection is the cause of the chronic encephalitis and possibly seizures following HSVE. Consideration should be given to long-term antiviral therapy following HSVE.

#### P1013

##### ANGIOCENTRIC GLIOMAS ARE CHARACTERIZED BY UNMETHYLATED MGMT-PROMOTER AND DO NOT HARBOR BRAF OR IDH1/2 MUTATIONS

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**Purpose:** Angiocentric glioma is a rare epilepsy-associated cerebrocortical tumor of uncertain relationship to other neuroepithelial tumors. Recently IDH1/2 mutations have emerged as a hallmark of diffuse astrocytomas and oligodendrogliomas and BRAF V600E point mutations are common in gangliogliomas and pleomorphic xanthoastrocytomas. The presence and putative role of these mutations in angiocentric glioma is still unclear.

**Method:** We here analyzed a series of 12 resected angiocentric gliomas from 11 patients for mutations of IDH1/2 and BRAF by immunohistochemistry (H09 and VE1) and direct sequencing. Additionally MGMT

promoter methylation was assessed by methylation specific PCR and pyrosequencing.

**Results:** All cases were negative for H09 (IDH1 R132H) and VE1 (BRAF V600E) immunohistochemistry. Consistent with this, sequencing of IDH1, IDH2 and BRAF revealed wild type status in all investigated cases. None of the investigated cases demonstrated a methylated MGMT promoter.

**Conclusion:** We conclude that IDH1/2 and BRAF mutations are not a common feature of angiocentric glioma. These genetic alterations may be useful for the differentiation of this rare epilepsy-associated tumor type from IDH1 mutated diffuse gliomas as well as from BRAF mutated gangliogliomas and pleomorphic xanthoastrocytomas. Furthermore, lack of MGMT promoter methylation might predict temozolomide as unpromising in cases not treatable by surgery or radiotherapy.

#### P1014 THE NEUROPATHOLOGICAL BASIS OF POLYMICROGYRIA

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**Purpose:** Polymicrogyria (PMG) is known to be a common endpoint of various insults (genetic and environmental) occurring at different time-points in the developing brain, resulting in a highly heterogeneous clinical, imaging and histological phenotype. PMG can result in early-onset intractable seizures including infantile spasms, as well as in ESES or localization-related epilepsy with relatively favorable prognosis.

**Method:** Medical records, EEG, imaging and complete autopsy data of 70 patients were reviewed. The cortex was defined as PMG when the normal cortical architecture was replaced by one or more festooning bands.

**Results:** We examined 22 fetuses  $\leq 28$  weeks gestation, 21 between 29 weeks gestation and term, 11 infants, seven children and seven adults. The number of cortical layers did not correlate with (presumed) etiology and both 2- and 4-layered cortex could occur in the same patient. Fusion of the molecular layers was present in 73% and different patterns were observed. PMG was frequently associated with periventricular (23%), subcortical (38%) or white matter (24%) heterotopia. Leptomeninges were normal in 18% and thickened with neuroglial invasion in 77%. Pyramidal tracts were hypoplastic or absent in 41/60 patients. Two patients had a confirmed genetic diagnosis, 25 had a possible genetic cause (multiple congenital anomalies or a positive family history), 15 had evidence of hypoxic ischemic injury with middle cerebral artery infarct in 5, 6 had congenital infections (CMV 5, toxoplasma 1). There was no clue to etiology in 23. Deaths were seizure-related in two adults and six infants.

**Conclusion:** This is most extensive series of brain autopsy findings in PMG patients. Our study illustrates that PMG is often associated with diffuse microscopic migration disorders that may contribute to the epileptogenesis in patients with PMG. Future studies including advanced staining techniques, genetic and imaging studies are necessary to further address the anatomic-clinical correlation in PMG.

## Poster session: Neuropsychology B Wednesday, 26 June 2013

### P1015 ADAPTIVE INDEPENDENCE DIFFICULTIES IN CHILDREN WITH INTRACTABLE EPILEPSY ON THE SCALES OF INDEPENDENT BEHAVIOR – REVISED (SIB-R)

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**Purpose:** Children with epilepsy are not achieving the desired levels of life outcomes. According to anecdotal and emerging research evidence, attaining independence presents as a potential challenge. Left unaddressed difficulties may persist into adulthood. This population-based study examined the adaptive functioning of students with intractable epilepsy who struggle academically.

**Method:** Forty-five children (5–13 years; male = 24) attending an “epilepsy-specific” classroom due to academic and/or psychosocial needs participated. Measures of adaptive (SIB-R) and intellectual (IQ) functioning were administered. Results were compared to the normative population and analyzed based on learning profiles, seizure variables, and co-morbidities.

**Results:** Indices from the IQ and SIB-R measures were significantly different than normative data ( $p < 0.001$ ). Other than Community Living, IQ was not significantly correlated with the SIB-R. Students learning profiles were broadly classified as learning disabled (LD,  $n = 15$ ), slow learner (SL,  $n = 16$ ), and intellectual disability (ID,  $n = 14$ ). Motor Skills did not differ among groups. Broad Independence, Social-Communication Skills, Personal Living, and Community Living differed significantly between LD and SL ( $p < 0.05$ ) and between LD and ID ( $p < 0.01$ , except for Personal Living;  $p < 0.05$ ). No differences were evident between SL and ID; Broad, Personal, and Community independence consistently fell  $< 2$ nd percentile, whereas their Social-Communication Skills fell at the 5th and 1st percentiles, respectively, in keeping with IQ. Seizure variables (i.e. type, age of onset, duration, frequency, polytherapy vs. monotherapy) were not related to IQ or SIB-R indices. Having co-morbidities ( $n = 14$ ; ADHD, PDD, Anxiety/mood disorder) was not related to SIB-R indices.

**Conclusion:** The adaptive independence of students with both intractable epilepsy and learning difficulties is significantly lower than age-related peers and, overall, is not related to IQ. Parent ratings of adaptive or functional independence can be informative in understanding children's needs, guiding further evaluation, and planning intervention to facilitate independence.

### P1016 ABSTRACT VERBAL LEARNING USING VISUAL OR AUDITORY ADMINISTRATION: DOES MODALITY MATTER?

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**Purpose:** Verbal memory tests generally use concrete words, which can invoke nonverbal strategies (visualization) to encode the words and recruit nondominant memory structures. Abstract words are difficult to visualize, affording a more accurate measure of verbal

memory and, therefore, the integrity of left medial-temporal structures in temporal lobe epilepsy. In rare instances, learning and retention are better for abstract words, which we present visually, than for concrete words, which we present auditorily. We hypothesized that this observation is dependent upon better visual than auditory processing ability. Using the *Nicole* Abstract Verbal Learning Test (*nAVLT*), we aimed to explore the extent to which learning a list of words is affected by the modality in which the words are presented (i.e. visual or auditory).

**Method:** Forty healthy undergraduate university students, aged 18–23 years, were randomly divided into two groups. In one group, the *nAVLT* words were given and tested visually (shown on a computer screen; written responses), and in the other group, the words were given auditorily (read to the subject; spoken responses).

**Results:** There were no significant differences between the visual and the auditory groups for learning or retention. Similar results were found in groups of francophone subjects.

**Conclusion:** The *nAVLT* can be given to epileptic patients using either a visual or an auditory administration format because both were shown to be equivalent. These results have important implications for testing patients with visual or hearing problems and for overcoming language barriers in the testing situation.

#### P1017 MEMORY AND COGNITION 20-PLUS YEARS AFTER SURGICAL TREATMENT OF TEMPORAL LOBE EPILEPSY

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**Purpose:** Healthy adults experience some cognitive decline as they age. People with temporal-lobe epilepsy (TLE) demonstrate specific deficits, especially for memory, related to their epilepsy, and typically they show further impairment after surgical intervention. We investigated whether temporal-lobe resection exacerbates age-related cognitive decline.

**Method:** We administered tests that sampled general intellectual function, attention, language, executive function and verbal and nonverbal learning and memory. Subjects were patients who had undergone resection from an epileptogenic temporal lobe (8 left-, 9 right-sided) at least 20 years prior to surgery and who were age 55 or older (mean age 63.9, range 56–82). The control group was 16 healthy subjects (HC) with the same mean age and education as the patients. We obtained 3T structural MRIs to assess age-related atrophy in all subjects and extent of removal in the patients.

**Results:** The left TLE patients differed from HC on word finding, the Similarities IQ subtest, and verbal memory. The right TLE patients differed from HC on the Digit Symbol IQ subtest, on a spatial (block-tapping) span test and on a measure of nonverbal memory. Both patient groups differed from HC on speed of reading. No differences were found on the remaining tasks.

**Conclusion:** Compared to aging healthy subjects, specific deficits related to resection from the left or right temporal lobe continue to exist 20 or more years after surgery in people who had been operated as treatment for TLE, while other cognitive functions remain unimpaired. Thus, the pattern of strengths and weaknesses of TLE patients is stable over time, and the rate of age-related memory decline is not greater in people who have undergone surgical treatment of TLE than in the healthy aging population.

#### P1018 IMPROVING THE READINESS OF EPILEPSY SURGERY CANDIDATES DURING ELECTRICAL STIMULATION THROUGH INVASIVE EEG

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**Purpose:** To improve the readiness of patients in cognitive tasks during electrical stimulation through invasive EEG (iEEG) in presurgical evaluation of epilepsy surgery candidates.

**Method:** Two to five training sessions, 30 min each, are performed by a neuropsychologist about one or two weeks before iEEG. These ones consist of an explanation of the positive or negative responses that may occur during electrical stimulation related to planned tasks. It is also given information to patients about the characteristics of the whole procedure to provide more confidence and optimal cooperation.

**Result:** Seven patients were assessed in 2012. Four patients explore the temporal lobe, two in the occipital lobe and one frontal lobe. Were considered: age, education level, baseline cognitive status, psychiatric diagnosis, type of epilepsy, area to explore, implant type and type of cognitive task. We observed that these patients showed commitment, sustained attention and improved quality of response. Changes were considered subjectively in relation to the experience of previous years.

**Conclusion:** Responsiveness and reliability are better when patients know and are engaged in the relevance of responses obtained during electrical stimulation to optimize the surgical treatment.

The neuropsychologist intervention in the patient training has become essential.

#### P1019 CLINICAL UTILITY OF THE LEONARD TAPPING TEST IN EPILEPSY PATIENTS

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**Purpose:** Dis-coordination in humans with frontal-lobe lesions has been reported using the Thurstone Tapping Task. Here, we aim to demonstrate the clinical utility of a new computerized tapping task for a sample of epileptic patients.

**Method:** Included were all patients aged 55 or younger who were administered tapping as part of their clinical seizure workup over the last three years. We excluded all left handers, those with Full Scale IQ ratings less than 75, those with active psychosis, and those for whom no information about seizure focus was available. Blind to tapping scores, patients were assigned to one of four groups (17 diffuse, 20 right temporal, 25 left temporal, and 25 frontal) based on EEG, structural MRI, operation report or neuropsychology conclusion. There were six tapping conditions: right and left sequential (quickly tapping according to a set pattern), balanced (both hands tapping in same spatial pattern), unbalanced (simultaneously tapping in different spatial patterns), and right and left speed tapping. Using age- and sex-appropriate norms, the scores were converted into z scores to determine pass/fail rates for each group for each condition. Chi-square analyses were used to examine whether any of the groups differed from the expected pass rate.

**Results:** Groups were well matched for age, education, IQ and years with seizures. The diffuse group differed on right and left sequential tapping and the frontal group differed on unbalanced tapping.

**Conclusion:** Scores on the Leonard Tapping Test can be used clinically to indicate putative location of epileptic dysfunction.

#### P1020

### FRONTAL LOBE DYSFUNCTION IN CHRONIC MESIAL TEMPORAL LOBE EPILEPSY IN PATIENTS OF TERTIARY CARE CENTRE OF SOUTH INDIAN POPULATION

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Mesial temporal lobe epilepsy (MTLE) patients have problems with memory. It was found that MTLE patients also experience executive deficits that may impair day to day functioning of individuals. Identification of impairment leads to predictions of likely loss or gain of functions after surgical resection. Aim is to evaluate frontal lobe dysfunction in mesial temporal lobe epilepsies and to study the effect of age of onset, duration of illness, number of antiepileptic drugs, side of lesion, seizure burden on the frontal lobe function.

Ninety consecutive patients with unilateral MTLE attending epilepsy clinic in Nizam's Institute of Medical Sciences were studied. They underwent clinical and neurological examination, prolonged video-EEG monitoring, High-resolution MRI brain, neuropsychological assessment for frontal dysfunction by various tests like attention (digit span), fluency (Phonemic and categorical fluency), set shifting, perseveration (WCST), working memory, (N back (verbal & visual), psychomotor speed, cognitive flexibility (TMT A & B), response inhibition (Stroop effect), planning (Tower of London) in addition to IQ (WAIS III), HAM- D to assess comorbidities, QOLIE – 31 for quality of life, verbal (RAVLT) and visual memory (Rey complex figure test).

Statistically significant differences noted in all tests of frontal dysfunction. Age of onset, number of AEDs seem to have an effect on the executive function.

Mesial temporal lobe epilepsy has effects beyond temporal lobe suggesting its effects on networks including function which may have implications for day to day life.

#### P1021

### THE RELATIONSHIP BETWEEN NUCLEAR MEDICINE EXAMINATIONS AND THE RESULTS OF PRE- AND POSTOPERATIVE EVALUATION OF NEUROPSYCHOLOGICAL TESTS IN PATIENTS WITH MESIAL TEMPORAL EPILEPSY ON NON-DOMINANT HEMISPHERE FOR MEMORY

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**Purpose:** We assessed the relationship between nuclear medicine examinations and the results of pre- and postoperative evaluation of neuropsychological tests in patients with mesial temporal epilepsy (MTLE) on non-dominant hemisphere for memory.

**Methods:** We evaluated seven patients with MTLE who had anterior temporal lobectomy. Their Engel's classifications were I for six patients and II for one patient. All patients had nuclear medicine examinations such as ECD- and/or IMP- SPECT, IMZ-SPECT, and FDG-PET. The patients underwent Wechsler Adult Intelligence Scale-Revised (WAIS-R) and Wechsler Memory Scale-Revised (WMS-R) as neuropsychological evaluations. We evaluated pre-to-post operative neuropsychological ratios (PPNR) described at 2 years after operation.

**Results:** The average of PPNR in patients were as follows: WAIS-R; full-scale intelligence quotient (IQ) 1.06, verbal IQ 1.05, performance IQ 1.06, WMS-R; General 0.98, Verbal 1.04, Visual 1.04, Attention 1.07, Delayed 0.99. For six patients bilateral hypoperfusion on ECD- and/or IMP-SPECT was demonstrated. In those patients, neuropsychological scores were strongly improved in two patients with short epilepsy history. On all patients demonstrated ipsilateral hypometabolism on FDG-PET and one of them with bilateral hypometabolism and the worse neuropsychological scores were shown.

**Conclusions:** Epilepsy surgery improved neuropsychological state of the patients with MTLE regardless temporal lobe show bilateral hypoperfusion. On the other hand, bilateral hypometabolism on preoperative FDG-PET would indicate postoperative neuropsychological state was not improved.

#### P1022

### AN EXPLORATORY QUALITATIVE ANALYSIS OF THE PSYCHOLOGICAL PROCESSES UNDERLYING NON-EPILEPTIC SEIZURES

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**Purpose:** Many psychosocial variables have been correlated with Psychogenic Non-epileptic Seizures (PNES), but an understanding of their underlying psychological mechanisms remains elusive. We aimed to explore these mechanisms targeting self-identity development because a well-formed identity is fundamental to normal psychological functioning, and qualitative differences between "healthy" and pathological self-identity have not been examined in PNES patients relative to controls.

**Method:** Twenty PNES patients (13 female; mean age 43.6 ± 15.3 years) recruited through Austin Health were compared to 20 age, education, and sex-matched healthy controls. A 90-min semi-structured interview was administered to both groups covering themes about self-identity development, emotional-control, and relationships. Interpretative Phenomenological Analysis was used to identify and analyze key themes present in >50% of each group.

**Results:** No theme was common to both groups. Thirty-eight themes were identified in the PNES sample and consolidated into four categories; maladaptive childhood experiences, underdeveloped self-identity, and limited understanding of one's own and others thoughts and emotions. Impaired self-identity was described by 95% of PNES patients, with 95% purporting PNES was integral to their identity, yet beyond their control. Typically this accompanied psychosocial difficulties, including childhood abuse during the critical years of self-identity development. In contrast, 14 themes representing a well-developed self-identity were reported by healthy controls, such as performing complex life-roles and experiencing rich relationships.

**Conclusion:** This study proposes a framework of poor self-identity development for understanding the emergence of PNES. Themes representing poor self-identity provide a basis for understanding interactions between psychosocial factors and the emergence of psychogenic seizures, presenting a new treatment focus.

#### P1023

### LACK OF CONCORDANCE BETWEEN DICHOTIC LISTENING AND WADA TEST IN EVALUATION OF LANGUAGE LATERALIZATION

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**Purpose:** Several authors have shown high concordance between ear asymmetry on dichotic listening and speech lateralization on the Wadatest. Dichotic listening has been suggested as part of non-invasive regimes for detecting speech lateralization. This study evaluates concordance between dichotic listening and Wadatest in speech dominance evaluation.

**Method:** Forty-six patients (25 males/21 females, mean age 33.2 years, 39 right-handed/7 left-handed) underwent Wadatest before planned brain surgery. Speech dominance was determined as either left or right-sided. All patients were given a dichotic listening test with CV-syllables. All had epilepsy, i.e. one left frontal, one right frontal and temporal, 21 right and 23 left temporal epilepsy. Etiology was hippocampal sclerosis (n = 23), various medial temporal tumors (n = 13), temporal cavernomas (n = 5), temporal AVM (n = 3), left frontal heterotopia (n = 1) and frontotemporal developmental disorder with hippocampal atrophy (n = 1). All used AED; i.e. 26 (1 AED), 11 (2 AEDs), 8 (3 AEDs) and 1 (4 AEDs).

**Results:** Three patients showed right and 43 left hemisphere speech dominance. In dichotic listening, two right dominant patients had no ear advantage and one left ear advantage. Twenty-four left dominant patients had right ear advantage, 4 no ear advantage and 15 left ear advantage. Mean correct scores in the left dominant group were 13.5 for right ear and 12.3 for left ear.

**Conclusion:** Almost half the patients with left speech dominance did not show the dichotic listening right ear advantage expected, and difference between right and left ear correct answers was smaller than in normals. Thus, dichotic listening do not in itself prove a good indicator of speech laterality in preoperative patients with epilepsy.

#### P1024 CORRELATION BETWEEN COGNITIVE COMPLAINT, QUALITY OF LIFE AND COGNITIVE ASSESSMENT IN PATIENTS WITH EPILEPSY

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**Purpose:** Cognitive changes that may occur during the treatment of epilepsy, and its impact on quality of life (QOLIE), may become more disabling than seizures. Usually these changes are not reported. The aim of this study is to relate the cognitive complaint, subjective measures of QOLIE and objective neuropsychological tests (NPS) in patients with epilepsy.

**Method:** We performed a prospective study in adult patients with epilepsy treated at the Ramos Mejia Hospital. They were asked about complaints in memory, attention and language. Self-administered questionnaire QOLIE-31 and NPS were performed assessing memory, attention and language. We also evaluated the presence / absence of symptoms of depression and anxiety.

**Results:** We evaluated 24 patients with focal epilepsy. The mean age was 28.25 (18–46) years, 13 male and 11 female. Six began monotherapy, and 18 continued in polytherapy.

Eighteen had cognitive complaints (12 memory, 7 attention, 13 language), 18 had symptoms of depression and anxiety associated.

The absence of cognitive complaints related to better cognitive subscale score on QOLIE-31 and memory tests, the presence of cognitive complaints with poor performance in tests of memory and attention. Attention disorders and language did not change QOLIE scores.

Depression increases cognitive complaint and worsens performance in NPS.

**Conclusion:** The complaint of memory disorders is clearly perceived and objectified by NPS. Attention disorders and language seem to be forgone. Therefore it is always necessary to investigate the cognitive complaint during the clinical interview.

#### P1025 JEAVONS SYNDROME: VARIABILITY OF COGNITIVE FUNCTION IN COVANIS GROUP FIVE OF EYELID MYOCLONIA WITH JUVENILE MYOCLONIC EPILEPSY

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**Introduction:** Eyelid myoclonia with absence (EMA) was described in 1977 as a homogeneous condition characterized by EMA, eye closure-induced seizures/EEG paroxysms and photosensitivity; onset 2–14 years; predominance in females and frequent resistance to treatment; normal neurological examination and MRI. EMA have also been reported as a seizure type defining a clinical heterogeneity in patients with eyelid myoclonia (EM). Jeavons Syndrome (JS) has been considered more difficult to treat and high frequency of GTCS may lead to intellectual impairment.

**Purpose:** Analyze cognitive function in a group of patients with EMA classified according to Covanis (Covanis, 2010).

**Methods:** Neuropsychological evaluation was performed in nine patients (7 females) with EMA and Juvenile Myoclonic Epilepsy (JME) and nine (7 females) with JME matched with respect to age, gender and schooling using WAIS-III for intelligence; attention, verbal and visual immediate and delayed memories, executive functions and verbal fluency. Statistical analysis was performed by Mann-Whitney test considering  $p < 0.05$ .

**Results:** Mean IQ of patients with JS were  $102.4 \pm 12.5$  and for those with JME  $100.9 \pm 13.0$ . Patients with JS had a better performance in immediate visual memory ( $p < 0.01$ ). However, both groups had lower average performance with respect to executive function, immediate verbal memory, delayed visual/verbal memories and intellectual level. Patients with JS were more refractory to treatment (3 patients seizure free) than patients with JME (6 patients seizure free).

**Conclusions:** Patients with EMA with JME do not differ from patients with JME since both groups had similar performance in neuropsychological assessment.

**Keywords:** Neuropsychology, Jeavons Syndrome, Cognition.

#### P1026 SHORT TERM MEMORY DEFICITS ARE ACCOUNTABLE FOR MODALITY-SPECIFIC COGNITIVE IMPAIRMENTS FOLLOWING HIPPOCAMPAL SCLEROSIS IN EPILEPTIC PATIENTS

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**Purpose:** To test whether the memory deficits often reported following temporal lobe epilepsy and mesial sclerosis are related to an encoding or a consolidation deficit.

**Methods:** Eight patients, aged between 9 and 19 years, who presented unilateral hippocampal sclerosis (left: 6; right: 2) and seizure onset during childhood or adolescence (age at onset: 2–14) were submitted to a battery of neuropsychological tests. These included IQ (WISC-IV or WAIS-III scales) and memory (CMS or WMS-III, CVLT and Rey complex figure) assessments. The IQ measurements were subdivided into their verbal, non-verbal, auditory and visual attention factors. The memory batteries were also divided in terms of their visual or verbal components.

**Results:** With relationship to their respective IQ, all children who presented a left hippocampal sclerosis showed a significantly lower ( $p < 0.05$ ) working memory factor (assessing auditory attention). This auditory attention deficit was accompanied by lower scores in verbal comprehension ( $n = 3$ ) and verbal memory ( $n = 2$ ) in some patients. By contrast, patients who had a unilateral right hippocampal sclerosis showed deficits in tasks assessing visual processing speed and hence, visual attention. This deficit was accompanied by visual memory impairments in all patients.

**Conclusions:** The verbal or visual memory and cognitive deficits encountered in cases of unilateral sclerosis may be tributary of the corresponding modality-specific attention (verbal or visual) limitations that prevent adequate encoding and processing of information.

#### P1027

### MINDFULNESS-BASED PSYCHOLOGICAL TREATMENT AND SOCIAL SUPPORT INTERVENTION FOR DRUG-RESISTANT EPILEPSY: A RANDOMIZED, ASSESSOR-BLINDED, CONTROLLED TRIAL

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**Purpose:** Purpose of this study was to evaluate mindfulness-based psychological treatment (MBT) and social support (SS) as complementary group treatment for drug-resistant epilepsy.

**Method:** It was a prospective randomized, assessor-blinded, controlled trial ( $n = 60$ ). Participants with drug-resistant epilepsy were randomized into either MBT or SS. Treatment protocols consisted of four 2.5-h-long sessions delivered by registered clinical psychologist bi-weekly for six to eight PWE per group. Both groups included psycho-educational components and lifestyle regulation. MBT aimed to facilitate experiential practices on mindfulness and nonjudgmental awareness whereas SS group provided platform for peer supports among PWE without active psychological intervention. Therapeutic effects were measured using seizure indexes (seizure frequency, Seizure Severity Questionnaire), quality of life (QOL, Patient-Weighted Quality of Life in Epilepsy Inventory), psychological states (Beck Depression Inventory II; Beck Anxiety Inventory) and neurocognitive functions (standardized neurocognitive assessment). Assessments were conducted at six weeks before and six-week after intervention. Seizure frequency was recorded during the two six-week intervals.

**Results:** Paired sample t-tests indicated that both MBT and SS significantly reduced seizure frequency [MBT:  $t(1,29) = 4.69$ ;  $p = 0.000$  and SS:  $t(1,29) = 2.17$ ;  $p = 0.038$ ] and severity ( $t = 3.51$ ;  $p = 0.001$  and  $t = 2.03$ ;  $p = 0.052$ ); improved short-term verbal memory ( $t = -5.66$ ;

$p = 0.000$  and  $t = -3.14$ ;  $p = 0.004$ ) and visual memory ( $t = -3.31$ ;  $p = 0.003$  and  $t = -2.18$ ;  $p = 0.038$ ); reduced depressive symptoms ( $t = 6.13$ ;  $p = 0.000$  and  $t = 3.22$ ;  $p = 0.003$ ) and improved QOL ( $t = -4.70$ ;  $p = 0.000$  and  $t = -2.97$ ;  $p = 0.006$ ). One-way ANOVA revealed significant group differences. MBT was more efficacious than SS on reducing seizure frequency [ $F(1,59) = 4.05$ ;  $p = 0.049$ ] and improving performances on neurocognitive tests included verbal short-term memory ( $F = 14.52$ ;  $p = 0.000$ ), visual short-term memory ( $F = 6.11$ ;  $p = 0.016$ ) and attention ( $F = 6.68$ ;  $p = 0.012$ ).

**Conclusion:** Findings reinforced the role of complementary psycho-behavioural intervention on PWE resistant to pharmacological treatment. Mindfulness-based intervention was more efficacious than social support in terms of improving seizure manifestations, mood, QOL and attention-related performance on neuropsychological tests.

#### P1028

### EFFECT OF EPILEPTIC SEIZURES ON THE FUNCTION OF SPEECH AND WRITING IN CHILDREN AND THEIR MEDICAL TREATMENT

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**Purpose:** Explore dysfunction of speech and writing in children with seizures, the impact of antiepileptic therapy.

**Method:** In accordance with the purpose and objectives of the study we have over 5 years in the dynamics were examined 110 children aged 10 to 15 years with various forms of epilepsy, who were hospitalized in the neurology department, and registered at the clinic. Of these, 43.6% of girls, boys 56.4%. The average age of the boys was 13 years, mean age of the girls 12 years. Later in the survey process, we have formed three groups: those who have epileptic seizures and impaired speech (58 children), with seizures without speech disorders (52 children), the third group of control – were 50 apparently healthy children of the same age without seizures.

**Results:** Among patients with epilepsy speech disorder was diagnosed in 52.7% of children. Violation written speech was the most common speech disorder in children suffering seizures, which were detected in 37.2% of patients. Violation oral speech was found in 15.5%. Children with seizures in combination with speech impairment differ more low-functional maturation of the brain, which is confirmed by the results of the EEG study. The EEG of children with epilepsy in violation of oral and written language found some differences from that of children without speech disorders: lower the maximum representation of the alpha and beta rhythms, higher amplitude delta and theta rhythms than healthy.

**Conclusion:** Epileptic focus is the disorganizers of brain functions, including speech disorders. With the suppression of epileptic activity there is stabilization of of speech functions. In the treatment of children with epilepsy with impaired speech and writing leading role belongs to medicines valproic acid.

#### P1029

### PREDICTING LONG-TERM NEUROPSYCHOLOGICAL OUTCOME OF LATE-ONSET RASMUSSEN ENCEPHALITIS (RE) IN CHILDREN TREATED VIA LEFT HEMISPHERECTOMY: A CASE IN POINT

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**Purpose:** Provision of neuropsychological outcome data on children with late-onset left hemisphere RE to facilitate parent counseling regarding surgical treatment, i.e. left hemispherectomy.

**Method:** Results of multiple, serial pre- and postoperative neuropsychological assessments for a previously right-handed, typically developing girl (Case MF) with left hemisphere language laterality, onset of left hemisphere RE at age 7 years, and left hemispherectomy at age 11 with Engle I outcome are presented and compared to data from 14 similar published cases (Pulsifer et al. 2004; Loddenkemper et al. 2003; Hertz-Pannier, 2002) for intellectual functioning (WISC), receptive vocabulary (PPVT), and behavior/psychosocial functioning (CBCL).

**Results:** Preoperative vs. post-operative per cent change in Full Scale IQ differed between cases reported by Pulsifer et al. (mean = -2.88%) and others (mean = -22.38%), a difference likely attributable to proximity of preoperative assessments to surgery (3 to 29 days vs. 4.13 years). Less difference was evident for receptive vocabulary (-0.15% vs. 10.16%) in Pulsifer and case MF, though expressive language/word reading were severely impaired. Total behavior problems were minimal pre- and post; however, serious social problems and diminished competence emerged.

**Conclusion:** Cognitive outcome for children with RE undergoing left hemispherectomy after 8 years of age is generally poor, most notably for expressive language and intellectual functioning despite evidence from Pulsifer et al. (2004) that there is minimal change in levels of functioning. Until more optimal treatment is available, parents should be counseled that RE may be curable by left hemispherectomy but has devastating long-term consequences on cognition and social functioning.

#### P1030

##### NEUROPSYCHOLOGICAL EVALUATION OF PATIENTS WITH FAMILIAL CORTICAL TREMOR AND EPILEPSY

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**Purpose:** To assess the neuropsychological features of patients with familial cortical tremor and epilepsy.

**Method:** Two families, eight patients and nine normal controls were enrolled. A battery of neuropsychologic tests comprised Auditory Verbal Learning test (AVLT), Logical Memory test (LMT), Digital Symbol test (DST), Stroop Color Word test (SCWT), Trail Making test (TMT), Verbal Fluency test (VFT), WAIS Block design test (WBDT), WAIS Digital span test (WDST) and Boston Naming test (BNT). Both the patient and control groups were balanced in sex, age and educational level.

**Results:** Patients with familial cortical tremor showed a worsening in TMT ( $p < 0.05$ ), SCWT ( $p < 0.05$ ) and WBDT ( $p < 0.01$ ), compared to the normal controls from same family, indicating impairment of attention and psychomotor speed. There was no difference between patient and control group in function of verbal memory, visuospatial memory and language.

**Conclusion:** we reported neuropsychological deficits of attention and psychomotor speed in patients with familial cortical tremor and epilepsy, which may also contribute to pathogenic study of this syndrome.

#### P1031

##### ASSESSMENT OF SYNTACTIC AND SEMANTIC SENTENCES COMPREHENSION IN CHILDREN WITH ROLANDIC EPILEPSY AND INVESTIGATION OF COGNITIVE AND BEHAVIORAL ASPECTS

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**Purpose:** First, our aim was to realize an exhaustive neuropsychological and behavioral investigation of children with Rolandic epilepsy (RE) by focusing on syntactic and semantic sentence comprehension. In this syndrome, we know that abnormal epileptic activity is found in central and temporal regions of the brain, including regions involved in reading and syntactic comprehension (Overvliet, 2011). Consequently, we adapted to French Canadian children a reading task involving syntactic and semantic complexity, earlier developed by Schafer (2011).

**Method:** Nine children with RE (age =  $11.0 \pm 1.3$  year; 6 boys) and 13 healthy children (age =  $12.0 \pm 1.5$  y.; 10 boys) did a task in which they read a pair of syntactically complex sentences and decided whether the target sentence (the second sentence in the pair) is true or false given the meaning of the first one. In addition, a standard neuropsychological assessment was also conducted with each child and their parents completed behavioral and affective questionnaires.

**Results:** In the syntactic and semantic sentences comprehension task, children with RE showed significantly less accuracy compared to controls ( $p = 0.037$ ,  $F = 5.2$ ). Moreover, they showed specific cognitive deficits, although the IQ is within the normal range (Wechsler Intelligence Scale for Children-IV). In verbal tasks, these children have specific difficulties to read words ( $p = 0.009$ ,  $F = 8.4$ ) and pseudo words ( $p = 0.006$ ,  $F = 9.6$ ) (Wechsler Individual Achievement Test-II). In fine motor skills, children with RE had significantly worse performance on complex task ( $p = 0.000$ ,  $F = 17.283$ ) (Purdue Pegboard). Concerning executive functions, parents noticed attention problems ( $p = 0.000$ ,  $F = 21.89$ ) and difficulties in working memory ( $p = 0.002$ ,  $F = 13.40$ ) and initiation ( $p = 0.001$ ,  $F = 14.27$ ) (Child Behavior Checklist; Behavior Rating Inventory of Executive Function).

**Conclusion:** We created a new syntactic comprehension task and revealed behavioral difference between groups. Furthermore, we mentioned various cognitive impairments presented by RE children, which could have implications in everyday life.

#### P1032

##### REY COMPLEX FIGURE TEST: COMPARISON BETWEEN A TRADITIONAL SCORING SYSTEM AND A QUALITATIVE SCORING SYSTEM ON MEMORY ASSESSMENT AFTER TEMPORAL LEFT AND RIGHT LOBECTOMY

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**Purpose:** Rey Complex Figure Test (RCFT) was designed by Rey in 1941 and tests copy and memory of a complex design. Taylor's (Strauss, E. et al, 2006;811-841) (18 items) and Loring's (Loring, D.W. et al, Archives of Clinical Neuropsychology, 1988;3 (3):239-247) (11 items) scoring systems of the RCFT are the most used. The aim of this study is to compare these two scoring systems and identify the sensitivity/specificity of each item to differentiate visual memory deficit on epileptic patients.

**Method:** This prospective study includes 36 left and 30 right patients with unilateral temporal epilepsy confirmed by MRI and VEEG who have undergone Anterior Temporal Lobectomy (ATL). The mean of years after ATL at the time of the assessment was  $7.9 \pm 0.8$  and the

majority (67.20%) of the patients were free of seizures (Engel 1a). Each item of these two scoring systems was analyzed separately in order to detect differences between left and right ATL patients performance.

**Results:** As expected, right ATL patients performed significantly worse than left on delayed memory ( $p = 0.02$ ) on traditional scoring. Items 5 ( $p = 0.01$ ) and 7 ( $p = 0.006$ ) are the most significant to differentiate left and right lesions. Loring's analysis suggested that 80% of the right ATL patients presented two or more errors on qualitative system, whereas only 39% of the left ATL. The qualitative errors 1 ( $p = 0.009$ ), 4 ( $p = 0.003$ ) and 10 ( $p = 0.04$ ) are the most significant.

**Conclusion:** The results suggested that a detailed analysis of specific items, on both scoring systems, might help to differentiate right and left patients. Further studies are needed to determine better clustering of items to increase sensitivity/specificity.

### P1033

#### QUALITY OF LIFE OUTCOME ACROSS YEARS AFTER ANTERIOR TEMPORAL LOBECTOMY FOR DRUG RESISTANT TEMPORAL LOBE EPILEPSY

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**Purpose:** Although over 2/3rds of patients with drug resistant temporal lobe epilepsy (TLE) become seizure-free following anterior temporal lobectomy (ATL), there is scarcity of data on long term quality of life (QOL) outcome following ATL and various factors influencing it. We extensively evaluated the impact of ATL and various clinical, demographic and social factors on QOL of patients who have undergone ATL across years in the long-term.

**Methods:** Between March 1995-March 2007, 436 patients who underwent ATL (192 right, 244 left) with mean follow-up of  $5.29 \pm 3.05$  years (range-1-12 years) were studied. 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 age at onset of epilepsy was  $10.8 \pm 3.5$  years and duration of epilepsy was  $19.02 \pm 9.32$  years. Mean education of the group was  $10.8 \pm 3.5$  years. The mean baseline QOL score pre-ATL was  $50.22 \pm 11.45$ . Overtime following ATL, steady improvement in QOL score documented which peaked at 1 year after which it tended to remain stable ( $p \leq 0.001$ ). QOL was better when patients were seizure-free and medication free and when they remained unemployed ( $p = <0.001$ ). Patients with psychiatric co-morbidity and who never had seizure-freedom for at least 2 years following ATL had poor QOL ( $p = <0.001$ ).

**Conclusions:** In patients with drug resistant TLE, ATL results in steady improvement in QOL over time. Complete seizure-freedom and absence of psychiatric co-morbidity were the most important determinants of QOL outcome following ATL.

### P1034

#### WORKING MEMORY PERFORMANCE IN TEMPORAL LOBE EPILEPSY PATIENTS AFTER CORTICOAMYGDALOHIPPOCAMPECTOMY

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**Purpose:** To investigate performance of patients with mesial temporal lobe epilepsy with mesial temporal sclerosis (MTLE-MTS) after left (L) and right (R) corticoamygdalohippocampectomy (CAH) considering the multiple component model of working memory.

**Methods:** Fourty literate, right-handed patients (aged 18-55 years) with MTLE-MTS (20 L-CAH, 20 R-CAH), were matched by age, gender, hand dominance and schooling to 20 healthy subjects. All subjects were submitted to neuropsychological assessment to investigate working memory: the operation span test (a measure of working memory capacity/the episodic buffer), forward digit span (to assess the phonological loop), the Corsi Blocks task (to assess the visuospatial sketchpad) and the digit span backward, to evaluate executive functioning. Data were submitted to ANOVA followed by Tukey test; significance level set at 5%.

**Results:** L-CAH patients were impaired only in the operation span task compared to controls ( $p < 0.01$ ). R-CAH patients demonstrated no deficits.

**Conclusions:** The multiple component working memory model enables the determination of specific cognitive impairment for L-CAH, who displayed significant deficits in a measure of the episodic buffer or working memory capacity. This is likely to impact patients' lives as this concept is linked to many other cognitive abilities such as intelligence, emotion regulation and long term memory. Working memory is preserved in MTLE-MTS after R-CAH.

### P1035

#### CHILDREN WITH A HISTORY OF ATYPICAL FEBRILE SEIZURES SHOW ABNORMAL STEADY-STATE VISUAL EVOKED POTENTIALS

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**Purpose:** Febrile seizures (FS) represent the most common seizure disorder among children between the ages of 0 and 5 years. Fifteen percent of these seizures are atypical, presenting a risk factor for cognitive sequelae and the onset of epilepsy. Steady-State Visual Evoked Potential (SSVEP) is a method used to test the oscillatory capability of the neuronal networks involved in visual information processing, in which phase alignment values are measured at each frequency. Alpha and theta range SSVEPs are often used to assess cognitive processes. An increase in the SSVEP response with age is observed in healthy children. We therefore hypothesized that children presenting a history of atypical FS would show an altered low-frequency SSVEP response.

**Method:** A retrospective study, approved by the Sainte-Justine Hospital Ethics Committee for Human Experimentation, comparing children with a history of atypical FS ( $n = 10$ ) vs. healthy controls ( $n = 11$ ) was conducted using Intermittent Photic Stimulation (IPS), a widely used routine EEG test that elicits SSVEPs, at 5, 7.5, 10 and 12 Hz.

**Results:** First, a correlation between age and phase alignment was found (5 Hz,  $p = 0.036$ ). Also, an interaction between stimulus type and group was found ( $D = 5.5$ ,  $p = 0.03$ ). Specifically, the atypical FS group showed reduced 5 (F = 5.984,  $p = 0.02$ ) and 7.5 Hz (F = 6.398,  $p = 0.02$ ) phase alignment values.

**Conclusion:** Children presenting a history of atypical FS therefore showed reduced cerebral synchronization as compared to controls. We speculate that these altered responses could cue toward the future cognitive and neurological development of the child.

### P1036

#### AUTOBIOGRAPHICAL MEMORY IN DRUG RESISTANT EPILEPSY PATIENTS

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**Purpose:** To identify the characteristic features of autobiographical memory (AM) in a population of patients with temporal and extratemporal epilepsy in surgical candidates.

**Method:** Twenty patients were evaluated (15 male, age mean 31.50 years, years of education mean 10.9 years, IQ mean 87). Sixteen patients had temporal lobe epilepsy (12 left, 7 right and 1 bilateral) and 4 had extratemporal lobe epilepsy. Epilepsy onset age mean 9 years.

AM was assessed with the Autobiographical Interview (Levine B et al. *Psychol Aging* 2002; 17 (4):677–689) validated to Spanish language. Subjects are asked to recollect memories from five different time periods (early childhood, teenage years, early adulthood, middle adulthood and last year). The information given were segmented and scored to obtain quantitative data. The results were analyzed considering the described variables and compared vs. healthy subjects. All patients were evaluated with our neuropsychological assessment protocol.

**Results:** Patients tend to produce fewer internal details and more external details and referred less emotional change than healthy subjects, although the difference was not significant. Patients with an onset age below 10 years, showed higher scores when asked how clear they visualize the event narrated.

**Conclusion:** Our group of patients does not showed significant abnormalities in AM compared with a control group. It appears to be no significant influence of the onset age, laterality, type of epilepsy and disease duration in their AM. In the future, the results showed will be compared with a postsurgical population.

#### P1037 MEMORY AND LANGUAGE OUTCOME IN PRESERVED PATIENTS SUBMITTED TO SURGICAL TREATMENT

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**Purpose:** To evaluate the change in naming and verbal delayed recall after Corticoamygdalohippocampectomy (CAH) in patients with left mesial temporal sclerosis (LMTS) whose functions were preserved preoperatively.

**Method:** Forty-three right handed patients submitted to CAH underwent neuropsychological assessment pre- and postoperatively with preserved naming and/or delayed verbal memory (words and stories) preoperatively. We compared the raw values obtained (ANOVA  $p \leq 0.05$ ) in both periods. The performance was ranked according to the percentile and considered improvement or worsening when there was change in classification between the periods of each patient.

**Results:** There was impairment in delayed verbal memory in words ( $p < 0.01$ ), stories ( $p < 0.06$ ) and naming ( $p < 0.007$ ) tests. In naming, the low average group (LAG) and the average group (AG) improved in 25% and 26.6% and worsened 50% and 53.3%, respectively, while those in high average group (HAG) worsened 50%. In delayed verbal memory (stories), the LAG and the AG improved 40% and 7.1%, and worsened in 40% and 78.5%, respectively. In verbal memory (words), LAG improved

18.1% and worsened 72.7%, while in AG, improved 6.66% and worsened 46.6% and those patients in HAG, worsened 100%.

**Conclusion:** In our data, 50% of patients of LAG and AG improved or maintain in the same range in naming, while in HAG all patients worsened. In delayed recall stories, the LAG has more chance to improve or maintain while AG are more likely to worsen. On the other hand, in words recall, AG patients seem less likely worsened than LAG or HAG.

#### P1038 DURATION OF EPILEPSY VS. AGE AT SURGERY IN PREDICTING POST-OPERATIVE COGNITIVE OUTCOME

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**Purpose:** Post-operative cognitive outcome is one among several factors in assessing success of resective epilepsy surgery. Younger age at time of surgery is thought to be a predictor of better cognitive outcome, presumably due to the plasticity and resilience of the young brain. The current study examines age at time of surgery, vs. duration of epilepsy at time of surgery, in relation to cognitive outcome.

**Method:** Between 2005 and 2012, 30 children underwent resective epilepsy surgery, including pre- and post-operative neuropsychological evaluations. Mean age at surgery was 11.3 years ( $SD = 4.4$ , 4–19). Mean duration of epilepsy was 6.3 years ( $SD = 4.7$ , 1–18). Thirteen patients underwent surgery in the left hemisphere. Five patients were left-handed. Mean post-operative FSIQ was 82 ( $SD = 16$ , 54–119).

**Results:** Post-operative FSIQ was significantly correlated with duration of epilepsy ( $r = -0.53$ ,  $p < 0.01$ ), but not with age ( $r = -0.29$ ,  $p = 0.19$ ). Among children with epilepsy duration  $\leq 5$  years, FSIQ was significantly higher ( $N = 15$ ,  $M = 96$ ) than among those with duration  $>5$  years ( $N = 15$ ,  $M = 72$ ) ( $t = 3.89$ ,  $p = 0.01$ ).

**Conclusion:** Our data support the increasingly recognized trend toward operating sooner in the disease course, regardless of the age of the child. While younger brains are more resilient in many ways, our results suggest that longer duration of epilepsy, at any age, is associated with more deleterious cognitive outcome, than is the age of the brain alone.

#### P1039 COMPARATIVE STUDY OF QUALITY OF LIFE OF MALE AND FEMALE EPILEPTIC PATIENTS RECEIVING TREATMENT IN THE GENERAL HOSPITAL SAN JUAN DE DIOS, GUATEMALA

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**Purpose:** This is a study about the Quality of Life of male and female epileptic patients. The objective of the study was to identify the existence or not of differences in terms of quality of life

**Methods:** The study group was comprised of 50 patients 25 males and 25 females, patients with epilepsy in an age range between 15 and 60 years.

The instrument utilized was the Quality of Life Scale, Qolife-10, which was created by the World Health Organization; it is composed of 10 questions and evaluates seven essential facets in regards to health. The investigation was designed to be descriptive-comparative. The patients were subject to neuropsychological evaluation

**Key Findings:** It concluded that statistically there is no significant difference in the Quality of Life in epileptic patients between both gender

## Abstracts

with similar conditions; The groups scored averages 29 and 27 which according to the scale is within the expected range.

**Significance:** In the quality of life there were no different, both groups were subject to stigma, social and job discrimination.

It was recommended that similar investigations should be done to promote techniques to enhance quality of life; programs that integrates all the aspects, areas of social education and emotional support; re-educate families and psychological intervention.

**Keywords:** Quality of life, Epilepsy, psychological intervention, Gender.

## P1040

### RESTING STATE FUNCTIONAL CONNECTIVITY AND EXECUTIVE FUNCTIONING IN TEMPORAL LOBE EPILEPSY PATIENTS

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**Purpose:** To explore the relationship between memory and executive functioning in patients with Temporal lobe epilepsy and to examine the underlying functional connectivity networks in these patients.

**Method:** Thirty-seven patients with localized TLE (21 left; 16 right TLE) performed both resting state fMRI and neuropsychological testing including tests of verbal and non-verbal memory and executive functioning. Resting state connectivity was analyzed using degree measures and results correlated with neuropsychological testing.

**Results:** Demonstrable impairment in patients with TLE were observed for both memory and tests of executive functioning. Examination of resting state connectivity patterns showed correlations with neuropsychological memory performance as well as performance on tests of executive functioning.

**Conclusion:** Cognitive dysfunction in TLE patients extend to extra-temporal regions and a number of patients have executive functioning deficits. This corroborates previous studies demonstrating “cognitive phenotypes” in patients with TLE. These results further support the importance of resting state connectivity in understanding the neural underpinnings of cognition in patients with TLE.

## P1041

### SUBJECTIVE PROSPECTIVE AND RETROSPECTIVE MEMORY FAILURES OF EPILEPSY PATIENTS: PRELIMINARY QUESTIONNAIRE STUDY

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**Purpose:** Epilepsy patients ranked cognitive deficit one of the biggest problems with having the disorder. Common cognitive impairments of epilepsy patients include intellectual decline, reduced information processing speed, attention deficit, and memory decline. The present study compared epilepsy patients' subjective PM and RM failures.

**Method:** Forty-three patients who visited or admitted to the neurology department of two university affiliated hospitals in Korea participated.

They were diagnosed as having epilepsy with heterogeneous etiologies. There were 18 male (25 female) patients, and their average age was 49.96. They answered a Korean-translated “Prospective retrospective memory questionnaire (PRMQ)” (Smith et al., 2000), which has 16 items.

**Results:** The effects of memory type (PM vs. RM), duration (short-term vs. long-term), and memory cue (self-initiated vs. environmentally-cued) on subjective memory failures were examined by performing a 3-way within-subject ANOVA. The analysis revealed that type ( $F(1, 42) = 14.46, p < 0.001$ ), duration ( $F(1, 42) = 25.14, p < 0.001$ ), cue ( $F(1, 42) = 12.73, p < 0.001$ ), type \* duration interaction [ $F(1, 42) = 13.39, p = 0.001$ ], type \* cue interaction [ $F(1, 42) = 8.73, p = 0.005$ ], duration \* cue interaction [ $F(1, 42) = 31.74, p < 0.001$ ] were significant. The results shows that the participants complained more memory failures with PM task, short duration, or self-cue than with RM task, long duration, or environmental cue. More interestingly participants complained more PM failures with short duration than with long duration, whereas there was no RM difference. Moreover, the effects of memory type varied when other factor, such as duration or cue, were considered. This applies to duration and cue, too.

**Conclusion:** The patient reported more memory failures with PM task, short duration, or self-cue than with RM failures, long duration, or environmental cue.

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## P1042

### LOW-DOSE VS. HIGH-DOSE ACTH THERAPY IN PATIENTS WITH WEST SYNDROME

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**Purpose:** To summarize available literary data related to comparison of efficacy of “low-dose” and “high-dose” adrenocorticotropin hormone (ACTH) therapy in patients with West syndrome and then present the own experience with that treatment.

**Method:** Research of literary data and basic descriptive statistics. Twelve patients with West syndrome, who underwent ACTH treatment with the average individual dose 0.33 mg/kg (2.66 IU/kg) during 6.1 week in diameter were observed. Changes in interictal EEG pattern and reduction of clinical seizures were the main monitored parameters within the 1-year follow-up.

**Results:** Seventy-five percent of patients we classify as responders – total clinical remission (100% reduction of seizures lasting over one year) in 58.3%, total, but temporary remission in 16.6% of patients. In 83.3% the improvement of EEG pattern was found. No patient had to stop the treatment due to adverse events.

**Conclusion:** Therapeutic scheme of depot form of ACTH with the average individual dose 2.66 IU/kg for the duration of 6.1 week seems to be effective and safe, which is in deuce with literary data.

## P1043

### LONG-TERM VIDEO-EEG MONITORING FOR EVALUATION OF PAROXYSMAL EVENTS IN CHILDREN

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**Purpose:** Long-term video-EEG monitoring (LTM) is used in patients with epilepsy when seizure semiology or syndrome type is unclear and in patients with other paroxysmal events. The purpose of this study was to evaluate the use of LTM in pediatric patients referred in our tertiary unit.

**Method:** Recordings of patients admitted in the years 2011 and 2012 were reviewed. Age, duration of recording, number of ictal episodes, pre-admission and final diagnosis concordance and refinement in diagnosis were analysed. Refinement in diagnosis was made in epilepsy patients on the basis of whether or not it resulted in further ictal classification.

**Results:** Forty-nine patients were included. Mean age was 10 years (range: 2–19 years), mean duration of LTM was 50 h (range: 4–122 h).

Epilepsy was confirmed in 39 of 40 patients, pre-admission and final diagnosis was not concordant in one patient with non-epileptic psychogenic events; The final diagnosis was epilepsy in 2 of 4 with suspected epilepsy and non-epileptic (anoxic and cardiogenic) event in another two patients. The diagnosis was concordant in both two patients with the movement disorder and in both two patients with non-epileptic psychogenic events. LTM enabled differentiation in one patient having both epileptic and non-epileptic psychogenic events.

Habitual seizures were recorded in 75% (30/40) of epilepsy patients. Refinement of the diagnosis was possible in 29 patients.

**Conclusion:** This study disclosed high concordance of pre-admission and final diagnosis as only 3 of 49 (6%) mismatched. High yield of LTM in refinement in diagnosis of epilepsy patients reflects selected population of drug resistant epilepsy patients entering presurgical evaluation in our center. In our experience LTM is safe and provides extremely relevant clinical information for the further management of patients.

#### P1044

##### SEIZURES AND MENTAL DISORDERS IN PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX

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**Purpose:** Psychiatric disorders in patients with tuberous sclerosis complex (TSC) include: autism spectrum disorder, mental retardation, attention deficit hyperactivity disorder and mood disorders. The influence of epilepsy to psychiatric profile of these patients is challenge.

**Method:** The study included 33 patients (16 males, 17 females, average age 18.31 ± 9.89) diagnosed as TSC, and treated at the Clinic of Neurology and Psychiatry for Children and Youth in Belgrade, Serbia. Data relating the psychiatric diagnoses and clinical response to therapy at follow-up were assessed.

**Results:** Epilepsy was diagnosed in all but 3 (90.91%) patients. Group of 30.0% had a history of infantile spasms. Focal epilepsies were diagnosed in 93.34% of patients. In 13 (46.29%) secondary generalized seizures occurred. In 10 out of 27 (37.04%) patients complete, long-term seizure control was achieved. Antiepileptic monotherapy was used in five patients only. Most frequently used actual therapy included valproate (20), carbamazepine (13) and lamotrigine (12). Infantile spasms were mainly treated by vigabatrin. Mental deficiency was noted in 16 patients (57.14%). Frequency of mental retardation was significantly higher in patients with infantile spasms than in patients without such history ( $p < 0.05$ ). Five (19.23%) out of 26 patients developed psychosis. None of patients with psychosis was seizure free. Autism or autistic traits were recognised in four (14.28%) out of 28 patients. Three of them were seizure-free, while remaining patient had near complete seizure control. Favorable seizure control was associated with both behavior or

mood disorder only in one third of cases. Better seizure control and suppression of paroxysmal EEG abnormalities showed indirect benefits on behavioral problems associated with TSC.

**Conclusion:** There are no uniform relations between seizure control and psychiatric disorder in TSC patients. Differently from psychotic TSC patients and those with behavior/mood disorder, subgroup with autistic spectrum disorder achieved long-term favorable seizure control.

#### P1045

##### SLEEP DISORDERS AND MELATONIN SYSTEM IN CHILDREN WITH EPILEPSY

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Sleep disorders are a frequent comorbidity of childhood epilepsy and may have in common an altered function of melatonin system.

**Purpose:** To examine the profile of sleep disorders and characterize the melatonin system in children with epilepsy.

**Method and Subjects:** We investigated 246 children, 5–18 years of age (152 children with epilepsy, 67 males, 85 females and 94 control children, 38 males, 56 females) using Sleep Disturbance Scale for Children (SDSC) filled in by parents. Out of these children, we enrolled 80 children (29 control group, 12 males, 17 females and 51 child with epilepsy, 26 males, 25 females) to study melatonin secretion and excretion patterns.

**Results:** In the epilepsy group, 48% children had sleep-wake transition disorders (SWDT), 28% excessive somnolence (DOES), 14% sleep breathing disorders (SBD). In the control group, 21% had SWDT, 14% DOES, 5% SBD (group comparisons, chi-square,  $p < 0.005$  for SWDT, DOES and total SDSC). Children with epilepsy had significantly higher scores on all subscales of SDSC ( $p < 0.05$ ). DA, SHY and total SDSC scores were significantly higher among children having night seizures.

The diurnal profiles of melatonin secretion and excretion showed high inter-subject variability, but circadian rhythm was preserved in both study groups. A subgroup of children with epilepsy had very high peak nocturnal salivary melatonin concentrations (9/50; 18%).

**Conclusion:** Sleep disorders were more frequent in the group of children with epilepsy. Further studies of melatonin in children with epilepsy and sleep disorders are warranted.

#### P1046

##### METHYLPREDNISOLONE FOR THE TREATMENT OF CHILDREN WITH REFRACTORY EPILEPSY

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**Purpose:** To evaluate the use of methylprednisolone in the treatment of children with refractory epilepsy.

**Method:** Observational, retrospective case series. The study included 14 patients with refractory epilepsy (M:F = 11:3; age 9.8 ± 7.3 years). For three- five consecutively days, each patient received methylprednisolone by intravenous administration at a dosage of 20 mg/kg/day, once a month for 3 months. The frequency of epileptic seizures and possible related side effects were evaluated every month during the three months before, during, and after administration of methylprednisolone.

**Results:** The frequency of epileptic seizures was reduced by more than 50% in 12/14 patients during methylprednisolone treatment. The median number of seizures before treatment with methylprednisolone was 10.1; during the treatment: 2.1; and after treatment: 3.1.

**Conclusion:** Methylprednisolone reduces the frequency of epileptic seizures in children with refractory epilepsy.

#### P1047

### SENSORY MODULATION DYSFUNCTION IN CHILDHOOD-ONSET GENERALIZED EPILEPSY

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**Background:** Sensory modulation is the ability to regulate and organize reactions to sensations in a graded and adaptive manner and the term may refer to either physiological or behavioral adjustments in response to sensory stimulation. Sensory modulation dysfunction is defined as inability to process sensory stimuli in a graded manner and to execute behaviors that are suitable to the degree, nature or intensity of the sensory stimuli and as such may affect function, behavior and quality of life in a negative manner. The sensory profile of children with generalized epilepsy has not been fully clarified.

**Purpose:** Assess possible sensory modulation dysfunction within all sensory modalities in children with generalized epilepsy.

Patients: 48 children at the age of 6–10.9 years participated including 22 patients with generalized epilepsy compared with 26 age and gender matched controls.

**Methods:** A standardized Short Sensory Profile (SSP) questionnaire including 38 items was filled out by caregivers reporting on measured tactile and taste/smell sensitivities, movement sensitivity; underresponsive/seeks sensation, auditory filtering, low energy/weak sensation and visual/auditory sensitivity.

**Results:** Children with generalized epilepsy had significantly higher sensory modulation dysfunction in all sensory modalities compared with controls and particularly demonstrated extreme patterns of underresponsive / sensation seeking.

**Conclusions:** The present study further delineates the growing bulk of data recognizing that generalized epilepsy among children is a multi-faceted neurological disorder with diverse functional disabilities also including sensory modulation dysfunction.

#### P1048

### ABSENCE SEIZURES FROM THE PERSPECTIVE OF CHILDREN AND ADOLESCENTS WITH THIS CONDITION

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**Purpose:** In this work the results of a local research are presented, in which children and adolescents with absence seizures were invited to par-

ticipate with the objective to know from their perspective how they live their illness in their everyday.

**Method:** The model in which it is to rely on is the experience of illness; this approach integrates the mind-body dichotomy within the social context, acknowledging that individuals are more than physiological entities; overcomes the limitations inherent in the medical model and ensures that patients are treated as persons and not as objects. We utilized for this work a methodology based in humanities and narrative (novel, in which we are starting to research in our country). It employs in this case drawing and narrative of children and adolescent (about their seizures and their context), in neurology pediatric area, to explore one of more frequency in this subspecialty.

**Results:** The fundamental of present work is that provided the opportunity to participants to express free and creatively about their emotions, difficulties, points of view, etc, which very seldom are taken in consideration. This is due to the fact that children are considered passive recipients of adults' protection and care. They have been considered invisible objects and voiceless of concern, and not understood as competent autonomous persons who have a point of view.

**Conclusion:** We conclude that like child health professionals interested to promote the children development and well-being as well as to achieve an eager patient compliance is essential that the practitioners in their clinical practice to get more involved to obtain knowledge not only of the disease also of the illness experience. It will extend their knowledge and it will improve the attention process too, creating better conditions of childhood in the future.

#### P1049

### EFFICACY AND SAFETY OF INTRAVENOUS LACOSAMIDE IN CHILDREN: A PILOT EVALUATION IN EIGHT CHILDREN WITH REFRACTORY NON-CONVULSIVE STATUS EPILEPTICUS/SEIZURE CLUSTERS

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**Purpose:** To evaluate the efficacy and safety of intravenous (IV) Lacosamide (LCM) in epileptic children suffering from non-convulsive refractory status epilepticus (SE) or seizure clusters (SC)

**Method:** Eight children with epilepsy (4 girls and 4 boys) aged 2–13 years old (mean: 8 years old) treated with IV LCM were retrospectively evaluated. Efficacy was measured as a persistent disappearance of SE/SC after 48 h of first IV LCM administration. Safety was evaluated by the appearance of any adverse event during infusion. All patients fulfilled refractory epilepsy criteria (ILAE 2010) and were treated at least with two oral antiepileptic drugs. Three patients were taking oral LCM. All patients except one were previously treated with other IV antiepileptic drug before use of IV LCM (valproate, midazolam, phenitoin, levetiracetam). Etiology was symptomatic in six patients (2 mitochondrial encephalopathies, 1 tuberous sclerosis, 1 remote due to neonatal hypoglycemia, 1 cerebral palsy, and 1 polymalformative syndrome with polymicrogyria). The other two patients suffered from focal cryptogenic epilepsy. The mean LCM dose was 5 mg/Kg/day, using a loading dose of 2–3 mg/Kg. A parental Informed Consent and hospital manager approval was obtained for every patient, for the compassionate use of IV LCM.

**Results:** Six patients (87.5%) reached 100% control of SE/SC state between 1 and 24 h after first administration of IV LCM. Only one patient with myoclonic status experienced a 25–50% seizure reduction. No severe adverse events were registered during or after infusion. One patient experienced dose-related insomnia

**Conclusion:** Intravenous lacosamide could be an effective and safe anti-epileptic drug to be used in non-convulsive status epilepticus and seizure clusters in refractory epileptic children

#### P1050

##### THE COMORBIDITY OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN WITH EPILEPSY

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**Purpose:** Attention Deficit Hyperactivity Disorder (ADHD) is known to be more common in children with epilepsy than in the general population. Thirty one to forty percent of ADHD is accompanied with epilepsy. Few studies regarding this matter have been reported in Korea. This study was aimed to evaluate the comorbidity of ADHD in children with epilepsy.

**Method:** This is a two center based, retrospective and controlled study. Thirty four ADHD children with epilepsy from Chungbuk National University hospital and 38 ADHD children without epilepsy from Cheonju St. Mary's hospital were recruited from January 2005 to June 2010.

**Results:** In ADHD children with epilepsy, twelve (35.2%) had partial seizures, 11 (32.2%) did generalized seizures and 11 (32.2%) were unclassified. EEG abnormalities were found in the frontal lobe (15 cases), in the central lobe (7 cases), in the temporal lobe (6 cases), and in the occipital lobe (3 cases). In ADHD children with epilepsy, the combined type was major (76.4%) and in ADHD children without epilepsy, the inattentive type was major (50.5%;  $p = 0.004$ ). Learning disability was more common in ADHD with epilepsy than in ADHD without epilepsy ( $p = 0.01$ ).

**Conclusion:** This study showed that ADHD children with epilepsy are more likely to have combined type (76.4%) and learning disability as compared with ADHD without epilepsy.

#### P1051

##### BILATERAL INSULAR EPILEPSY

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We report two patients explored with Stereo-EEG that demonstrated bilateral independent insular epileptic foci.

Both patients had seizures with a facial grin due to a bilateral facial contraction with grunting sounds associated with hypersalivation. They both evolved into a bilateral tonic contraction of the upper limbs and one patient then showed marked bilateral clonic movements whereas the second patient displayed hypermotor activities. The two patients suffered daily seizure frequency with most seizures occurring during sleep. 3T MRI proved normal in both patients while FDG-PET demonstrated right fronto-perisylvian hypometabolism in one patient and bilateral frontal hypometabolism in the other. Based on all available data, an insular seizure onset zone was suspected in both patients, one of whom had had a prior invasive EEG investigation that suggested a right insular epilepsy.

Bilateral opercular and insular implantation was performed in both patients. Very active interictal epileptiform and fast rhythm discharges were recorded in each patient in the right and left insula. More than twenty seizures were recorded in each patient with an EEG pattern characterized by a low voltage fast rapid activity starting in the posterior right or/and left insular cortex, then migrating to different sectors of the insula

and the fronto-parietal operculum on both sides, before more wide spread propagation in one patient. Patients were contra-indicated for surgery.

These cases reveal the existence of truly multifocal epilepsy involving the insular cortex on both sides, which are particularly challenging to detect with non-invasive data.

#### P1052

##### HEMIFACIAL PAROXYSMAL EVENTS RELATED TO A HAMARTOMA OF THE IVTH VENTRICLE: A DRUG-RESISTANT ENTITY THAT CAN BE A CANDIDATE TO SURGERY

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The syndrome of hemifacial seizures in children associated with a lesion of the floor of the fourth ventricle is a rare entity first described in 1996. We report a new case of a 3 years old boy who presented the first paroxysmal episodes at the age of 3 months. The seizures were characterized by right hemifacial spasms limited to the territory of the facial nerve and were drug resistant. Surface EEG was not contributive. As suspected on clinical grounds, the MRI confirmed the presence of an hamartoma of the IVth ventricle, adjacent to the cerebellar peduncle. At the age of 4 years the child benefited from a surgical disconnection of the lesion that resulted into a dramatic reduction in seizure frequency. Episodes are now limited to a very mild contraction of the orbicularis oculi.

This rare entity, with rather unique clinical features, merits to be known because it can often be treated surgically, early in its course. An intralesional recording was performed during surgery. Together with a review of the literature, it gives us the opportunity to discuss the subcortical pathways involved and the pathophysiological mechanisms, compared to similar observations in patients with gelastic seizures and a hypothalamic hamartoma.

#### P1053

##### INTRAVENOUS LEVETIRACETAM IN CHILDREN WITH STATUS EPILEPTICUS: EXPERIENCE FROM A CHILDREN'S HOSPITAL IN TURKEY

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**Purpose:** The aim is to evaluate the effectiveness of levetiracetam at children with status epilepticus (SE), the factors effecting the response to treatment and side effects of the drug.

**Method:** Patients who received levetiracetam as add-on therapy to treat SE between September 2010- August 2012 in our hospital were enrolled in this study. Data including age, sex, seizure type, underlying cause and epilepsy syndrome, the number of drugs used for epilepsy control, medications used during SE before levetiracetam, the initial loading dose of levetiracetam, response to and adverse effects of levetiracetam were collected. Cases were grouped as responsive and nonresponsive to levetiracetam.

**Results:** Study group included 20 females (51.3%), 19 males (48.7%) with median age of 42.4 months (IR:65). Thirty-two of the patients (82%) had generalized epilepsy, and 7 (18%) of them had partial epilepsy. The average initial loading dose of levetiracetam was 17.8 mg/kg (SD±5.3). Response to levetiracetam was taken in 31 (79.5%) patients

whereas 8 (20.5%) of them were nonresponsive. In one case (2.5%) agitation developed which disappeared with reducing maintenance dose. Median age of nonresponsive group was 6.6 months younger than responsive group ( $p = 0.018$ ). Two cases which had syndromic epilepsy (West syndrome) were in the non responsive group, and it was significant when compared with responsive group ( $p = 0.038$ ). Two groups were similar regarding other variables ( $p > 0.05$ ).

**Conclusion:** In this study, levitracetam was found to be an effective drug of choice in status epilepticus in children and well tolerated. Being younger and having syndromic epilepsy are found as negative factors effecting treatment response. For more precise results, further studies including larger number of patients are needed.

#### P1054

### HETEROGENOUS SPECTRUM OF EPILEPTIC SYNDROME WITH ELECTRICAL STATUS EPILEPTICUS DURING SLEEP: EXPERIENCES WITH 20 CASES

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**Purpose:** To describe the clinical spectrum and to evaluate the efficacy of different therapeutic agents in children with electrical status epilepticus in sleep (ESES) and normal brain MRI.

**Method:** Clinical data of all patients with ESES and normal brain MRI (patients with Landau-Kleffner syndrome and Lennox-Gastaut syndrome are excluded) seen in neurophysiology department of teaching military hospital Mohammed V Rabat, were analyzed. Twenty patients had been treated between 1996 and 2012.

**Results:** Ten (50%) children had epileptic encephalopathy with continuous spike and wave during sleep (CSWS), four (20%) had atypical benign epilepsy of childhood with centrotemporal spikes (ABECTS), three (15%) had benign epilepsy of childhood with centrotemporal spikes (BECTS) worsened by carbamazepine, two (10%) had atypical benign occipital epilepsy of childhood (BOEC) and one (5%) had acquired epileptiform opercular syndrome. The duration of follow-up ranged between 8 months and 16 years. The antiepileptic drugs used were: Valproic acid (100%) and clobazam (80%). Steroids were efficacious in all cases of CSWS. Cognitive, behavioral and language deterioration were more frequent and more severe in cases with CSWS whereas the rest presented with more frequent seizures. There was a significant correlation between the duration of ESES and residual intellectual deficit at follow-up.

**Conclusion:** ESES with normal brain MRI reflects an evolution of benign partial epilepsy of childhood in 45% of the patients, whereas CSWS represents 55% of the patients. The duration of ESES correlated significantly with residual intellectual deficit at follow-up.

#### P1055

### WHAT MAKES THE AMYGDALA TALK? EEG IN ACUTE EMOTIONAL DISTRESS

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**Purpose:** EEG in acute emotional distress in seizure free subject led to discovery of epileptogenic brain lesion.

**Method:** Clinical EEG case study.

**History:** Seizure-free for 4 years an adolescent referred for second opinion, managed for seizures unexplained in terms of seizure type (atypical or pseudo absences? focal /generalized?) and aetiology. Discontinuing AEDs is considered. Due to dental appliance MRI had not been done. Sleep deprivation EEG is suggested.

**Acute event:** Entering EEG the whole nightsleep-deprived patient has a phone call notifying her of recent grandparent's death. EEG technician doubts ethically – professionally: to do it or let the patient grieve. Acute mourning follows. Family agrees, videoEEG is done in the cooperative patient.

**Results:** During hyperventilation 6 min continuous focal RTemporal epileptiform discharge is recorded, no clinical phenomena in a normally responsive patient, a feature never seen in previous EEGs reviewed.

**Immediate steps:** Based on EEG, doctor's re-enquiry about seizure history reveals she may not have been seizure free: reports of dysesthesiae, feeling of impending crying, *deja entendu*; seen by parents as adolescent and psychological / psychiatric reaction. No confirmatory evidence is obtained by neuropsychology.

**Other investigations:** Normal MRI is reviewed, interpreted in favour of amygdalar dysplasia. PET-CT: functional abnormality in the same region.

**Conclusion:** Most rare coincidence of unexpected intense grief and known stimuli (sleep deprivation, hyperventilation) seems to have triggered a prolonged clinically silent focal temporal (amygdalar?) epileptiform discharge.

This led to reviewing the history, to substantiate doubt on its accuracy (not seizure free?), to review results of investigations that proved either false (e.g. MRI on first reading) or not paid enough attention to (initial EEGs) in managing a supposedly benign epilepsy.

As of the time of submitting this abstract, it is too early for detailed clinical follow up of this focal (amygdalar?) epilepsy.

#### P1056

### SEVERE HYPOGLYCEMIA IN JUVENILE DIABETIC RATS: PRESENCE AND SEVERITY OF SEIZURES PREDICTIVE FOR MORTALITY

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It is well accepted that insulin-induced severe hypoglycemia is a major limiting factor in the management of diabetes resulting in brain dysfunction and seizures. However, the effects of seizures and treatment strategies have yet to be elucidated, particularly in juveniles. Here we establish a model of severe hypoglycemia and seizures in juvenile diabetic rats.

**Methods:** Diabetes was established in post-weaned 22-day-old rats by streptozotocin (STZ; 80 mg/kg) intraperitoneal (IP) injection. After a week, severe hypoglycemia was induced by insulin IP (15 U/kg) in fasted (14–16 h) diabetic (STZ) and non-diabetic (CON) animals. Experiments were video-monitored and seizures scored to quantify behaviour.

**Results:** Seizures occurred in 86% of STZ and 100% of CON rodents that reached hypoglycemia (defined as  $<3.5$  mm blood glucose). The blood glucose thresholds for seizure onset were not significantly different between these groups; STZ:  $1.8 \pm 0.2$  mm, CON:  $1.6 \pm 0.1$  mm. Mortality in non-seizing animals was 0%, compared to those that seized (STZ: 33%, CON: 42%;  $p < 0.05$ ). Surviving animals exhibited a significantly reduced number of seizures in both CON [survival:  $1.6 \pm 0.3$  seizures ( $n = 11$ ), mortality:  $7.8 \pm 2.7$  ( $n = 5$ ),  $p < 0.01$ ] and STZ [survival:  $1.6 \pm 0.2$  seizures ( $n = 17$ ), mortality:  $4.4 \pm 1.2$  ( $n = 5$ ),  $p < 0.001$ ] groups. Treatment with diazepam, phenytoin and glucose at seizure onset was significantly more successful at ameliorating seizures than glucose alone but did not improve mortality, as subclinical seizures may be present.



**Conclusion:** This model of hypoglycemia and seizures in juvenile diabetic rats provides evidence that severe hypoglycemia (<2.0 mm) is a necessary precondition for seizures, with mortality only occurring in the animals that exhibited seizures.

#### P1057

### IMPAIRED SLEEP QUALITY IN EPILEPTIC CHILDREN AND IMPLICATION OF ANTI-EPILEPTIC DRUGS

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**Purpose:** The comorbidity between epilepsy and sleep disorders is well documented. However the mechanisms underlining this comorbidity are not fully understood. The putative role of anti epileptic drugs in sleep architecture disturbances in epileptic children needs to be explored.

**Method:** We analysed sleep architecture of 75 epileptic children (30 females and 45 males), aged from 4 to 15 years (mean-age: 8.3 years). They were divided in three groups according to their antiepileptic treatments: NT group: no antiepileptic treatment (n = 20), MT group: monotherapy (n = 29) and PT group: polytherapy (n = 26). All underwent video-polysomnographic (VPSG) recordings to assess main sleep parameters: stages of light sleep and slow waves sleep, REM sleep, total sleep time (TST) and awakenings. Percentages of paroxysmic activity duration (PA) on TST were also calculated and classified in three subgroups: (<5%, 5% ≤ PA ≤ 20% and >20%).

**Results:** Significant decreases of REM sleep and of the sleep efficiency as well as significant increased awakenings were observed in PT group comparing to the NT group. A correlation was also observed between awakenings and PA.

**Conclusion:** First of all, our data confirm that sleep disorders remain a hidden companion of childhood epilepsy. Secondly, we demonstrate that anti epileptic drugs may have some causal contribution. Diagnosing sleep disturbances should be part of the management of childhood epilepsy and should be taken into account in the choice of therapeutic strategy.

#### P1058

### EPILEPSY IN CHILDREN WITH MITOCHONDRIAL DISEASES: DIAGNOSTIC AND TREATMENT FEATURES: CLINICAL CASE OF MELAS-SYNDROME

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**Purpose:** To study the clinical features and problems of therapy of epilepsy in children with mitochondrial diseases.

**Method:** The clinical case of MELAS-syndrome in 5 years old girl.

**Results:** A girl aged 5 years old was admitted to hospital urgently. Debut seizures was at age 2 years. The diagnosis was "symptomatic epilepsy". There were focal seizures with secondary generalization, which were accompanied by severe weakness, repeated vomiting 2–3 times a year. Seizures acquired status character. She took valproic acid as monotherapy. Therapy was not effective.

Neurological status at admission: Generalized tonic-clonic seizures. Positive meningeal symptoms. Cranial innervation – external ophthalmoplegia, horizontal nystagmus. Muscle tone: spastic hemiparesis was replaced by hypotonia. The total amount of active and passive movements reducing. Atactic syndrome. Delay psychoverbal and physical development.

Survey results: MRI – ischemic lesions. EEG – generalized spike and wave activity. ECG – carditis. EMG – myopathic syndrome. Ophthalmoscopy – retinal angiopathy. Laboratory data – hyperglycemia, high levels of glucose in the cerebrospinal fluid, expressed lactic acidosis (7.0–13.5–10.0 mm).

The typical clinical picture and laboratory data could diagnose «MELAS-syndrome». The anticonvulsant therapy was corrected: the abolition of valproate and appointment of levetiracetam. L-carnitine was appointed as metabolic therapy. Progressive brain edema and multiple organ pathology led to the death.

**Conclusion:** Epilepsy in children with MELAS-syndrome is characterized by focal seizures with secondary generalization and had status current. Late diagnosis of the syndrome has led to the rise of multiple organ pathology. The multisystem damage increases the severity of epilepsy that generates a poor prognosis. The study of anticonvulsant therapy for mitochondrial diseases is an important issue.

#### P1059

### DEVELOPMENTAL OUTCOME IN CHILDREN WITH INFANTILE SPASMS AFTER TREATMENT WITH ADRENOCORTICOTROPIC HORMONE: EFFECT OF DEMOGRAPHIC AND SEIZURE RELATED VARIABLES – DOES SEIZURE CONTROL IMPLY A BETTER DEVELOPMENTAL OUTCOME?

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**Purpose:** To assess the short term improvement in developmental functioning after 3 months treatment with Adrenocorticotrophic hormone (ACTH) in children with infantile spasms and to examine the impact of demographic and seizure related variables on developmental outcome.

**Method:** Thirty children (M = 10.92 months SD = 5.44) with a diagnosis of infantile spasms were recruited from the Pediatric Neurology clinic from a tertiary care hospital in North India. Children who had previously received either ACTH or another medication were excluded. Developmental functioning of the children was assessed (as Mental and Motor Developmental Quotients) before and after 3 months of treatment with ACTH, using the Indian adaptation of the Bayley's Scales of Infant Development. Seizure control was assessed as percentage reduction in spasms at 3 months. The effect of demographic and seizure related variables was assessed using Independent sample T-test.

**Results:** Majority of the children (83.3%) had flexor spasms and symmetric spasms (90%). Birth asphyxia/ HIE was the commonest etiology (43.3% of total children). Following ACTH treatment, mean improvement in Mental DQ was 5.20 (SD = 2.83, p < 0.001) and that in Motor DQ was 4.88 (SD = 2.83, p < 0.001). However, the overall developmental quotients still remained in the severely retarded range (Mental DQ = 28.73, SD = 5.44; Motor DQ = 28.78, SD = 6.97). Treatment lag of >2 months (change in Mental DQ = 3.90, SD = 2.18, p < 0.001; change in Motor DQ = 3.56, SD = 2.23, p < 0.001) and presence of other seizures (change in Mental DQ = 4.11, SD = 2.26, p = 0.022; change in Motor DQ = 3.87, SD = 1.98, p = 0.034) adversely affected outcome. Seizure control correlated with improvements in mental (r = 0.84, p < 0.001) and motor quotients (r = 0.80, p < 0.001).

**Conclusion:** ACTH therapy improves the developmental functioning in children with infantile spasms; however the outcome still remains poor. Treatment lag and presence of other seizures adversely affect the outcome. Seizure control alone may not imply a better developmental outcome.

## P1060

## JEAVONS SYNDROME – SEIZING THE LIGHT

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**Purpose:** Eyelid myoclonia (EM) with and without absences; eye closure-induced seizures with EEG paroxysms; and photosensitivity are the electroclinical triad characterizing Jeavons Syndrome described in 1977. We performed an electroclinical analysis of the clinical spectrum, and the visual/photoc stimuli relevant for treatment.

**Method:** Four patients fitting the electroclinical features of Jeavons syndrome were found in our EEG database from 2010 to 2012.

**Results:** Seizure onset was age 5–14 years, diagnosis was delayed in all – up to 8 years – facial tics, syncope and OCD were the most frequent misdiagnosis. Comorbidities included learning disability and ADHD in 3/4. Frequent eyelid myoclonias with absences were seen in all and GTCs in 3/4. One patient sustained a severe hot water scald during a GTC seizure prior to correct diagnosis and treatment with VPA. Obsessive reflex self-induction of seizures was seen in all – waving hand in front of one eye (with secondary eyebrow alopecia), seeking out lights, looking into the glare of snow or sunshine on water. EEG showed generalized spikes spontaneous and activated by eye closure and PPR. GTCs responded well to VPA, while EM were medically refractory in all. Light intensity reduction with tinted contact lenses and sunglasses resulted in >90% EM reduction. In two patients the obsessive self-induction responded to CBT.

**Conclusion:** Delayed diagnosis in Jeavons syndrome may not be uncommon due to the brief and subtle nature of the EM. Misdiagnoses such as tics, OCD or syncopes may carry a significant safety risk and put patients at risk for mild cognitive comorbidities due to untreated epileptogenesis. Multimodal treatment with AEDs, light intensity reduction and CBT appears promising.

## P1061

## EFFICIENCY OF ETHOSUXIMIDE IN THE TREATMENT OF BENIGN EPILEPTIFORM DISCHARGES OF CHILDHOOD (BEDC) IN EEG IN CHILDREN WITH FOCAL FORMS OF EPILEPSY

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**Purpose:** Study and evaluation of efficiency of ethosuximide in treatment of benign epileptiform discharges of childhood in EEG during the sleep in children with focal forms of epilepsy.

**Methods:** We observed 23 patients aged from 3 to 12 years old (on the average 8.3 years old) with symptomatic (14 patients) and idiopathic (9 patients) focal forms of epilepsy. All patients were treated by one or two antiepileptic drugs (valproic acid, levetiracetam or topiramate) and were seizures free more than 2 years, but still had a high level of regional epileptiform activity (BEDC) on EEG during the sleep. We added ethosuximide as a second drug for a control of reduction of benign epileptiform discharges of childhood on sleep EEG. Ethosuximide was used in doses from 250 up to 750 mg/day (on an average 467 mg/day), from 13 up to 35 mg/kg/day (on the average 18 mg/kg/day).

**Results:** Duration of using of ethosuximide was from 6 to 30 month (on the average 15 month). As a result, EEG became normal in 12 persons (52%). In five patients (22%) we registered significant reduction of regional epileptiform activity. High positive effect was reached in 17 patients (74%). And six patients (26%) had no a good results and continued to

have a high level of epileptiform discharges. No serious side effects were noted.

**Conclusion:** This study has shown ethosuximide is highly effective for reduction of benign epileptiform discharges of childhood in EEG during the sleep in children with focal forms of epilepsy.

## P1062

## EFFICACY AND SAFETY OF FELBAMATE IN CHILDREN WITH REFRACTORY EPILEPSY

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**Purpose:** To present our experience with felbamate therapy in children with drug-resistant epilepsy.

**Method:** We retrospectively reviewed the medical charts and video-EEG recordings of all patients receiving felbamate until May 2012. Efficacy was determined according to seizure frequency during the week prior to treatment initiation and the week after the maximal dosage of felbamate was attained.

**Results:** Fifty patients (34 boys) aged 4 months to 17 years (mean-5.5 years) were identified. About third of the patients had Lennox-Gastaut syndrome or myoclonic-astatic epilepsy of Doose. Mean epilepsy duration was 3.4 years (range- 1 month to 13 years). The mean number of previous AEDs was 7.5. The mean duration of follow-up was 1.1 years. Seizure frequency decreased in 29 (58%) patients. Felbamate was discontinued in 20 (40%) patients, in 16 of them because of inefficacy. Side effects were reported in 23 (46%) patients, none of them included aplastic anemia or liver failure.

**Conclusion:** Felbamate appears to be effective and safe in children with refractory epilepsy. Early treatment initiation with felbamate can especially benefit children with Lennox-Gastaut syndrome and myoclonic-astatic epilepsy of Doose.

## P1063

## EPILEPSY CHARACTERISTICS IN PATIENTS WITH TYPE 1 DIABETES MELLITUS

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The prevalence of patients suffering from epilepsy and diabetes mellitus type 1 (DM) has been previously reported. However, the electroclinical characteristics of this population need to be studied further.

**Purpose:** To analyze the epilepsy characteristics in children followed at an endocrinology reference center for type 1 DM.

**Methods:** A retrospective study was carried out analyzing the clinical, video-EEG and MRI characteristics of children with epilepsy and DM type 1 diabetic followed at the service of Endocrinology and the Epilepsy Department of the HFME University Hospital in Lyon, France.

**Results:** Thirteen patients are reported with epilepsy and type 1 DM. Six suffered from generalized epilepsy (4 idiopathic, 2 non-idiopathic) while the remaining seven had a form of focal epilepsy (4 non-idiopathic, 3 idi-

opathic). For most of these cases, presence of GAD (glutamic acid decarboxylase) autoantibodies were confirmed and epileptic seizures started after the onset of diabetes.

**Conclusions:** Epilepsy characteristics and the pathophysiological mechanisms involved as well the pattern of evolution as related to the course of the diabetes will be discussed.

#### P1064

##### EPILEPSY AND PCDH19 MUTATION: ELECTROPHYSIOLOGICAL FEATURES

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**Purpose:** To study the electrophysiological characteristics of patients with positive PCDH19 mutation.

**Method:** Thirteen patients aged from 4 to 24 years at the time of the study with PCDH19 mutations were included. Longitudinal EEG videos were retrospectively reviewed (ictal and interictal).

**Results:** Interictal video EEGs recorded during cluster of seizure showed a slowed background activity for age in all patients, with focal slow waves and spike waves, predominantly frontal or temporal in 11 patients. On the EEG recordings of two patients at 4 and 9 months, we registered periodic generalized discharges of slow waves and fast rhythmic activity without any clinical seizure. Interictal EEG recorded during seizure free periods showed normal or slightly slowed background activity in seven patients, and the persistence in six patients of abnormalities which consisted of slowed activity in central regions (2/6), focal spikes (2/6), or generalized spike wave discharges (2/6). Ictal video EEG recorded showed in three patients frontal temporal initiation of seizure. One patient presented with atypical absences associated with myoclonus with generalized abnormalities on the EEG that were persistent during follow up.

**Conclusion:** In patients with PCDH19 mutations, based on the clinical presentation, differential diagnosis includes (i) Dravet syndrome because of fever sensitivity and frequent seizures events and (ii) focal epilepsy due to the type of seizures. The combination of focal abnormalities with global alteration of the background activity on the EEG helps in the early identification of these patients, altogether with the clinical presentation, allowing an earlier molecular diagnosis.

#### P1065

##### PRIMARY HYPOMAGNEAEMIA WITH SEIZURES IN NEONATES

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**Purpose:** Epilepsy is a neurologic disease with many etiologies. Among symptomatic epilepsies due to metabolic abnormalities, primary hypomagnesaemia is a rare condition and the pathogenesis is not well known. Hypomagnesaemia with Secondary Hypocalcaemia (HSH) is an autosomal recessive primary hypomagnesaemia which generates secondary hypophosphocalcemic disorders.

**Method:** We report three cases of HSH in the same family with emphasis on clinical, electrophysiological, biological, imaging and aspects.

**Results:** The cases were three neonates, two males and one female born at term with normal delivery. They presented neonatal generalized seizures (2/3 of cases) at day 15, 21 or focal (1/3 of cases) at day 28. All these neonates also had a psychomotor retardation. Biochemical parameters showed hypomagnesaemia and hypocalcaemia. These disorders were difficult to correct with usual dosages of ions supplementation. Valproic acid, but not phenobarbital, stopped seizures after the correction of the calcaemia even if hypomagnesaemia persisted. EEG recording was abnormal in the three cases with a reduced frequency of background rhythm and some paroxysmal activity. Brain MRI showed cerebellar atrophy and ischemic lesions for the three neonates, and diffuse cerebral atrophy in two cases.

**Conclusion:** Epilepsy due to HSH has a large determinism. These seizures seem to be attributed to hypomagnesaemia and its consequences on calcium distribution. Ischemic lesions, due to central hypomagnesaemic vasospasm, and brain atrophy is also implicated in the development of seizures. The correction of hypomagnesaemia and especially hypocalcaemia seem to be necessary to control seizures. Phenobarbital seems to increase lesions and seizures frequency.

#### P1066

##### THE TEMPORAL LOBE IN WEST SYNDROME (WS) SHOWS ABERRANT STRUCTURAL REMODELLING AND IS FUNCTIONALLY IMPAIRED:

##### ELECTROPHYSIOLOGICAL AND QUANTITATIVE MAGNETIC RESONANCE IMAGING EVIDENCE

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**Purpose:** West syndrome (WS) is a severe epilepsy syndrome whose onset is associated with the development of long-term, acquired impairment of cognitive function. This study uses quantitative magnetic resonance imaging to examine whether the structural architecture of the temporal lobe in WS shows normal developmental plasticity. The extent to which the temporal lobe in WS functions adequately for sensory information processing is formally assessed by electrophysiology.

**Method:** Cross-sectional study of 20 prospectively recruited patients with newly diagnosed WS and 20 healthy age controls. Quantitative magnetic resonance imaging (3D structural MRI and diffusion tensor imaging) data were analysed by voxel based morphometry (VBM) and tract-based spatial statistics (TBSS). Auditory event-related potentials (ERP) and structured neuro-developmental data (Bayley scale) were acquired.

**Results:** WS patients showed intact basic auditory stimulus processing but evidenced a deficit of memory-related processing of auditory stimuli. The temporal lobes in WS had normal total volume but bilateral changes of structural constituents. The grey matter density was increased compared to controls ( $p < 0.005$ ); whilst white matter had normal integrity (DTI metrics: fractional anisotropy and mean diffusivity) but decreased white matter volume of the ( $p < 0.005$ ).

**Conclusion:** The findings objectively demonstrate the pattern of structural remodelling of the temporal lobe in West syndrome for the first time, showing this to differ from normal controls. Functional impairment of the temporal lobe that accompanies this is delineated. The data support the concept that epileptiform activity at a critical age in infancy may promote abnormal changes in the cortical connection architecture.

## P1067

### PRELIMINARY REPORT ON TREATMENT RESPONSE TO ANTI EPILEPTIC DRUGS IN CHILDHOOD EPILEPSIES

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**Purpose:** Patterns of treatment response to anti epileptic drugs (AED) in children are not described. This is the preliminary report of a study performed to describe patterns of response to AEDs in children with epilepsy and to correlate the response patterns to age of presentation and their underlying epilepsy syndromes.

**Method:** A Cohort of 179 children ( $\leq 12$  years) with confirmed epilepsy followed up prospectively by four paediatric neurologists, for minimum of 1 year was recruited. For those epilepsies with onset during infancy, six-month follow up was deemed adequate for inclusion. Epilepsy syndromes were classified according to International League Against Epilepsy 1989 classification. Pattern of response was categorized as early (immediate or within 6 months) response and sustained seizure freedom (A); delayed (after 6 months) response but subsequent sustained seizure freedom (B); fluctuation between periods of seizure freedom and relapse (C); seizure freedom never attained (D).

**Results:** Symptomatic focal epilepsy was commonest (51%) followed by symptomatic generalized (20%), idiopathic generalized (18.4%), and idiopathic focal (10.6%) epilepsy syndromes. Seizure freedom never attained was the commonest response pattern (36.9%), occurring mainly in symptomatic generalised (33%) and symptomatic focal epilepsies (39%). Other patterns seen were delayed response (B) in 21.2%, early response (A) in 21.2% and fluctuating response (C) in 20.1%.

In those with immediate response (pattern A), this was achieved with monotherapy in 79%. Significant proportion of infantile epilepsies never achieved seizure freedom (pattern D) ( $p < 0.05$ ).

**Conclusion:** Absence of seizure freedom was the commonest response pattern seen in children with epilepsy and was significantly higher in those with infantile epilepsies. Poor response to therapy occurred mainly in symptomatic focal and symptomatic generalised epilepsies.

## P1068

### COMPARATIVE ASSESSMENT OF FAMILIES EXPERIENCE OF PATIENTS WITH DRAVET SYNDROME ON THE USE OF RECTAL VALIUM AND ORAL MIDAZOLAM

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Rectal Diazepam (DZ) is the first rescue medication for acute prolonged convulsive seizures in children in many countries. Since February 2012, oral Midazolam (MZ) can be used in France with a nominative temporary use authorization. In this study, we aimed at assessing the experience of the families of patients with Dravet Syndrome (DS) concerning MZ use through a structured questionnaire. This questionnaire was developed for DZ and adapted for MZ with a comparison between the two medications.

We sent an auto-administered on-line questionnaire to french families of patients with DS. Questions addressed different aspects of

oral MZ use: usual administrators, time required, facility, and risk of errors in the preparation and the administration by parents or other care givers. Parents were also questioned about their feelings concerning the efficacy and utility in emergency settings, facility of oral MZ administration, and possible refuse of care givers to use it. These families filled this questionnaire for DZ one year ago (December 2011).

Thirty-five families answered the questionnaire. The majority agreed on the ease of administration by parents (83%) and non-parent care givers (69%) vs. 38% and 8% for DZ. Oral MZ is easier (pre-filled syringes) and quicker to prepare ( $< 1$  min) than rectal DZ. The preparation and administration are not subject to errors as with rectal DZ, especially when given out of the parent's presence. Non-parent care givers accept much more readily to administrate oral MZ.

Parents confirm the ease of preparation and especially the facility of the method of administration of oral MZ: the care givers no longer refuse to administrate it and the dignity of children is finally respected.

## P1069

### RISK FACTORS ASSOCIATED WITH A POOR RESPONSE TO THE FIRST-LINE TREATMENT IN NEONATAL SEIZURES: CASE-CONTROL STUDY

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**Purpose:** Establish risk factors associated with poor response to phenobarbital as first-line anticonvulsant in neonatal seizures.

**Method:** Case-Control Study. We included patients younger than 44 weeks of conceptional age with neonatal seizures treated with phenobarbital. Controls were patients with adequate response to phenobarbital. Cases were those without response, which required a second-line anticonvulsant. Statistical analysis was performed in SPSS17.0®.

**Results:** From 1913 records of hospitalized newborns between January/2008 – June/2012, we selected 35 controls and 20 cases (2:1 ratio). Of 65.7% were male. Most frequent seizure type was clonic (72.7%). Of 65.45% were partial. Seizure-related risk factors were: More than one seizure semiology (OR 11.625 CI95% 2.946–45.877;  $p < 0.001$ ), latency to phenobarbital startup greater than 12 h (OR 9.917 CI95% 2.205–44.607;  $p = 0.001$ ), subtle (OR 5.167 CI95% 1.309–20.39;  $p = 0.014$ ) or tonic seizures (OR 3.271 CI95% 1.042–10.278;  $p = 0.039$ ) and seizures longer than 5 min (OR 2.824 CI95% 1.927–4.137;  $p = 0.026$ ). There was not significant increase in risk of treatment failure with phenobarbital with any etiology. In perinatal history, the antecedents associated with an increase in risk were: low 10th minute Apgar score (OR 7.071 IC95% 1.269–39.415;  $p = 0.014$ ), maternal intrapartum infection (OR 2.944 IC95% 2.023–4.286;  $p = 0.05$ ) and neonatal shock (OR 5.063 CI95% 1.536–16.687;  $p = 0.006$ ). More than six antecedents at birth or adaptation (OR 3.188 IC95% 2.124–4.78;  $p = 0.006$ ) or more than five postnatal antecedents (OR 3.56 IC95% 1.123–11.285;  $p = 0.028$ ) were also a risk factor. Abnormal electrolytes were the only finding in diagnostic tests identified as risk factor (OR 4.255 IC95% 1.159–15.624;  $p = 0.024$ ).

**Conclusion:** There are perinatal antecedents, seizure features and diagnostic tests findings that behave as risk factors for therapeutic failure with phenobarbital as first-line anticonvulsant in neonatal seizures. Early identification of patients at risk of poor response can anticipate the need for additional treatment to prevent complications associated with recurrent seizures.

## P1070

## USE OF NEW ANTIEPILEPTIC DRUGS FOR THE TREATMENT OF NEONATAL SEIZURES

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**Purpose:** To analyze the efficacy and safety of new AEDs in newborns with refractory seizures.

**Method:** Observational prospective study of newborns with seizures admitted between June 2005 and January 2013 at the Hospital Italiano Neonatology Unit.

**Results:** One hundred and thirty-eight consecutive newborns with seizures were included. We analyzed 19 (13.7%) with seizures that received new AEDs, 73.6% term and 26.4% premature. Fifty-eight percent had a symptomatic partial epilepsy and 42% presented a Neonatal Epileptic Encephalopathy. Overall in-hospital mortality was 21%. The new AEDs indicated as a second-line anticonvulsant treatment were: Vigabatrin in 2p., Oxcarbazepine in 4p., Levetiracetam in 2p., and Topiramate in 1p. As a 3<sup>rd</sup> or 4<sup>th</sup> AED: Vigabatrin in 9p., Levetiracetam in 6p., Topiramate in 4p., Oxcarbazepine in 2p. and Valproate in 1 p. We observed a 50% or more seizure reduction in 15p. (78.9%), 5p. (47.4%) with complete cessation of seizures. We noticed a 50% or more seizure reduction with Oxcarbazepine in 5/6p., Levetiracetam 5/8p. and Vigabatrin in 6/11p. No adverse events were reported during treatment with any anticonvulsant.

**Conclusion:** In our study, we observed a favorable seizure control in newborns with seizures with new AEDs. The development of new prospective studies are needed, including more newborns, to assess the efficacy, safety and neuroprotective effect of new AEDs as first-line treatment.

## P1071

## CESSATION OF FARMACORESISTANT EARLY EPILEPTIC ENCEPHALOPATHY WITH THE USE OF KETOGENIC DIET

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**Purpose:** To report a 3 year old boy patient with early epileptic encephalopathy who showed cessation of seizures with ketogenic diet.

**Case Summary:** This patient had a previous history of prematurity, perinatal asphyxia, hypoxic ischemic encephalopathy, developmental delay and sensorial deficit, who developed an early epileptic encephalopathy as a West Syndrome farmacoresistant to Valproic acid, Topiramate, Nitrazepam and Levetiracetam used in polytherapy and with idiosyncratic adverse effects to ACTH, why it had to be suspended. The patient had both, complex partial seizures with and without generalization and myoclonic epileptic spasms with a typical hypsarrhythmia pattern in the EEG. A ketogenic diet was initiated when the patient was 15 month of age in a 3:1 proportion. It has been well tolerated by the patient and after two years with it, he stills seizure free and with progressive improvement of the EEG. Actually the diet is tapering off without seizures recurrence even in some circumstances as febrile syndromes that potentially may precipitate seizures.

**Result:** After the ketogenic diet was started, the patient has been seizure free and the EEG has improved progressively.

**Conclusions:** The ketogenic diet is a good alternative for the treatment of refractory West Syndrome.

## P1072

## NETWORK ANALYSIS OF GENERALIZED SPIKE-AND-WAVE DISCHARGES OCCURRING IN BOTH ANIMAL MODELS AS WELL AS IN CHILDREN

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**Purpose:** The goal of network analysis of generalized discharges is to get a better understanding of the mechanisms related to the cortical-cortico-thalamic interactions responsible for the bilateral synchronously occurring Spike-and-Wave Discharges (SWDs), which are typically for absence seizures, in both animal models as well as in children.

**Method:** For children (age >5 and <16) with absence epilepsy (N = 30) the maximal-association-strength between the MEG signal combinations was calculated for preictal to ictal transition periods following the same procedures as in the WAG/Rij rat study of Meeren et al. (J Neurophys 2002). Furthermore, for the WAG/Rij rat study the dynamics of coupling strength between local field potential recordings in cortical and subcortical layers was assessed in the period as early as 1.25s prior to the onset of the ictal discharge (Lüttjohann & van Luijelaar, Neurobiol Dis 2012).

**Results:** The association analysis results indicate a common pathway for the generalized SWDs. for all the children studied independent of the distinct clinical features of these children. Evidence is discussed that the results are reminiscent to what can be observed for absence seizures of the WAG/Rij rat, namely that the pattern of bilateral synchronous generalized activity (during the waves of the SWDs) is occurring via widespread thalamo-cortical pathways, while there is a cortical source driving these discharges. In addition, the network analysis results of cortico-thalamic and thalamo-thalamic interactions in the WAG/Rij rat presented here modify the current view in showing that the thalamus is heterogeneous with respect to changes in connectivity with the cortex. Some thalamic nuclei get more early involved than others and there is more precursor activity in the cortex than in the thalamus.

**Conclusion:** The methods for network analysis presented to discern the mechanisms generating the SWDs may be therefore of diagnostic help for the clinician.

## P1073

## REFRACTORY NEWLY DIAGNOSED EPILEPSY IN CHILDREN DURING 2011: A CHILEAN MULTICENTRIC STUDY

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**Purpose:** Characterize, clinical and epidemiologically, pediatric patients consulting for the first time for seizures. Determine percentage of patients who evolve with epilepsy and factors correlating with refractory epilepsy (RE).

**Method:** Prospective, observational, multicenter study between January 2011-December 2012 in six Chilean hospitals. Follow up (FU) 15–24 months. Patients between 1 month and 15 years were recruited (symptomatic and simple febrile seizures excluded). Clinical, epidemiological and FU data was collected. RE was defined as seizure persistence after use of two antiepileptic drugs in maximum tolerated dose.

**Results:** Two hundred and sixty-nine patients. Of 50.6% female mean age at first consult 5 years and 5 months and at epilepsy diagnosis 5 years and 11 months. After FU 65 did not have seizure recurrence, 177 (65.8%) fulfilled criteria for epilepsy and 27 had complex febrile seizures. Patients with epilepsy: 47.6% had developmental delay (DD), family history of epilepsy wasn't significant. Thirty-eight percent had abnormal neurological exam. Half of epilepsies were idiopathic. Sixty percent of the first EEG and 30% of neuroimages were abnormal. Seventy-seven percent were with monotherapy, mainly Valproate (56%). About 4.4% had adverse reactions to treatment. Refractory epilepsy: 17/177 (9.7%), 10 male. Mean age at diagnosis was 2 years and 8 months. Was significantly associated ( $p < 0.05$ ) with debut with high seizure frequency, regression or DD, hypotonic syndrome, symptomatic etiology and abnormal neurological examination. Kaplan-Meier analysis shows that RE appears before 13 months of FU, that children with RE come from medium-low income families and have more DD ( $p < 0.01$ ).

**Conclusion:** This is the first epidemiological study in Chilean pediatric patients with epilepsy. The high seizure recurrence may be a local characteristic or recruitment bias. RE are identified early during FU and risk factors include younger age and frequent seizures at debut and presence of DD. Financed: Fonis Chile SA10I20023.

#### P1074

##### USE OF IVIG IN DRAVET SYNDROME: REPORT OF TWO CASES

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**Purpose:** To report the efficacy of IVIG on seizure frequencies and febrile infectious episodes in two patients with Dravet syndrome.

**Methods:** We treated with monthly IVIG two patients with DS aged 9 months and 3 years. Both presented frequent status epilepticus that resulted in many PICU admissions. They presented recurrent viral or bacterial infections. An extended immunological work up showed an isolated deficiency in IgG1 in the first patient and was normal in the second.

**Results:** Both patients presented a significant decrease in seizures frequency and no status epilepticus. First patient was seizure free during 9 months and he is now on Valproate in association with topiramate and clobazam with monthly brief seizures. The second stopped status and long lasting seizures but was not seizure free. He had 9 months of IVIG in association with Valproate, Stiripentol and Clobazam.

**Conclusion:** Status epilepticus in DS at young age is mainly fever induced. The immuno-modulatory therapy might be active in decreasing infectious and viral episodes thus decreasing seizures. We raise also the question of specific immunological profile of patients with DS and the role of inflammatory cascade in the generation and the duration of seizures.

#### P1075

##### FDG-PET/CT WITH EEG RECORDING IN CHILDREN WITH FREQUENT DAILY SEIZURES

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**Purpose:** To determine PET/CT hypo/hypermetabolic regions in three children with daily seizures, normal MRI and generalised epileptiform discharges and one child with ESES.

**Method:** Four children aged 3–6 years, 3 with probably symptomatic epilepsy, daily seizures, normal MRI and generalised epileptiform discharges, and one child with bilateral lesions on MRI and ESES, underwent FDG-PET/CT to determine possible focal epileptogenic region in order to consider surgical treatment. EEG recording started 10 min before and ended 30 min after iv. injection of FDG tracer:

**Results:** EEG recording during injection showed generalised, bifrontal spike-waves, with R frontal predominance in one patient, with myoclonic jerk in his left hand. PET/CT showed asymmetry -hypometabolic region in anterior part of R frontal lobe. Among another two children with generalised discharges, head nodding occurred in one 10 min after injection of FDG tracer; another had generalised myoclonic jerks. PET/CT in first showed hypermetabolic region in right temporo-occipital area, while hypometabolic region in anterior part of R temporal lobe in another. In a child with ESES, no clinical event was observed during 24 h before PET/CT, which demonstrated hypermetabolic region in left frontal and left upper part of temporal lobe

**Conclusion:** Localizing capability of PET/CT demonstrated concordant results with EEG tracings during injection in two children; and revealed possible focal epileptogenic area in the another two with generalised EEG discharges and normal MRI. PET/CT hypermetabolic region in a child with ESES correlates with area of active epileptogenic discharges on awake EEG. PET/CT scan might help in focusing the preoperative imaging workup even in children with daily seizures.

#### P1076

##### QUALITY OF LIFE IN CHILDHOOD EPILEPSY QUESTIONNAIRE: FACTOR STRUCTURE AND PREDICTORS IN NEWLY DIAGNOSED CHILDREN

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**Purpose:** The aim was to examine the factor structure of the Quality of Life in Childhood Epilepsy Questionnaire (QOLCE) in newly-diagnosed children, given that there has been no previous formal assessment. A second aim was to assess the stability of a reduced-form QOLCE compared to the original in identifying risk factors for health-related quality of life (HRQL) 24 months post-diagnosis.

**Method:** Using the Health-Related Quality of Life in Children with Epilepsy Study (HERQULES,  $n = 374$ ), principle axis factor analysis with a promax rotation was conducted to assess factor structure. Exploratory factor analysis was used to reduce the number of items in the QOLCE. Confirmatory factor analysis was used to determine goodness of fit of the original and reduced-form QOLCE. Multiple regression was used to identify risk factors at diagnosis for HRQL at 24 months.

**Results:** A four-factor, 55-item solution was found with 18 items removed for low factor loadings, and 3 for ambiguous loadings. The final model had the following domains of HRQL: Cognitive Functioning, Emotional Well-Being, Social Functioning, and Physical Functioning. The reduced-form QOLCE demonstrated excellent fit to the data:  $\chi^2 = 4.26$   $df = 2$   $RMSEA = 0.056$  (90% CI: 0.001–0.131), CFI = 0.994, GFI = 0.994, SRMSR = 0.019, and had excellent internal consistency ( $\alpha = 0.96$ , subscales  $>0.80$ ). Risk factors for HRQL remained the same when using the reduced-form compared to the original QOLCE.

**Conclusion:** These results indicate that the reduced-form QOLCE is a reliable measure. Given the fewer number of items, it may be a viable option to reduce respondent burden when assessing HRQL in childhood epilepsy.

## P1077

## MYOCLONIC ABSENCE IN PATIENTS WITH DISTINCT PATHOLOGY

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**Purpose:** To clarify the characteristics of myoclonic absence (MA) in patients with distinct pathology.

**Method:** Retrospective analysis from medical records and polygraphic video-EEG documentation of seizures in three patients (all female) with distinct pathology who presented with MA.

**Results:** These patients were diagnosed of having distinct symptomatic syndromes: Sotos syndrome, Angelman syndrome, and infantile spasms due to severe asphyxia. Seizure types other than MA were tonic-clonic seizures, spasms, and startle-induced tonic seizures. The age at onset of MA ranged between 2 and 26 months. The average duration of MA was less than 10 sec in all three patients. No patients had status of MA. Asymmetric features such as asymmetric tonic intensity of upper limbs or eye deviation were commonly observed in all patients and stereotypic intrindividually. MA was controlled in all three patients by combination of sodium valproate (VPA), ethosuximide (ESM) with or without lamotrigine (LTG).

**Conclusion:** MA can occur in some distinct symptomatic syndromes. Compared to the classical MA syndrome, MA in our series have some differences, i.e. shorter duration, earlier onset of age. VPA and ESM with or without LTG are effective for MA even in our series.

## P1078

## CLASSIFICATION OF EPILEPSY BY ETIOLOGY, SEMIOLOGY AND COMPLEXITY LEVEL IN CHILDREN: ANNUAL SERIES STUDY 2011 IN INSTITUTO DE SALUD DEL NIÑO DEL PERÚ (INSN)

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**Purpose:** The new classifications especially those classified the level of complexity help better understand this problem and help design appropriate control programs.

**Method:** We studied 238 patients initially diagnosed pediatric epilepsy treated at one of the outpatient clinics of Neuropediatrics in INSN between January to December 2011. All patients were classified by etiology, semiology and the level of complexity (Classification of Medina Malo)

**Results:** According to the source etiological classification was Cryptogenic 16%, 27% primary and 57% secondary. According to the classification was generalized Semiological 65%, 20% partial, and 15% Syndromic. Depending on the level of complexity were 26.5% level I, level II 4.62%, Level III 25.6% and 43.3% Level IV.

**Conclusion:** This study has allowed us: Have a better understanding of the frequency and distribution of pediatric epilepsy according to the new classifications. Identify the limitations of standard formats to assess the problem in its different dimensions. Knowing the magnitude of epilepsy complex III and IV. This study also allowed us to sustain the equipment to improve diagnosis, propose the most suitable drug procurement and identify types of epilepsy potentially preventable public health actions.

## P1079

## PARRY-ROMBERG SYNDROME ASSOCIATED WITH EPILEPSY: A CASE REPORT

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**Purpose:** Parry-Romberg Syndrome (PRS) is an uncommon condition. It is characterized by a progressive atrophy, affecting one side of the face. The authors reported a case of PRS associated with epilepsy.

**Case report:** A 7 months old girl with no medical past, consulted for partial onset seizure involving right side since the age of 2 months. She had abnormal developmental milestones. Physical examination showed atrophy and hyperpigmentation of right side of face. Neurological examination was normal. Routine hemogram and biochemical tests, cerebrospinal fluid study and autoimmune markers were negative. EEG demonstrated partial epilepsy with theta rhythm. CT brain and MRI scan showed left cerebral hemiatrophy. The girl was started on Carbamazepine 600 mg /day and corticosteroids (1 mg/kg/day) after which her seizures reduced and after six months of follow up she became seizure free.

**Conclusion:** PRS is a rare disorder characterized by progressive hemifacial atrophy. The most common associated complications are: trigeminal neuritis, facial paresthesia, severe headache and epilepsy. Epilepsy is often refractory. Characteristically, the hemifacial atrophy progresses slowly for several years and, soon after, it become stable. This entity needs a multidisciplinary approach and reconstructive surgery with autogenous fat graft can be performed to correct the deformity.

## P1080

## DIAZEPAM USEFUL IN ESES TREATMENT

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**Purpose:** To demonstrate the efficacy of high-dose diazepam in treating electrical status epilepticus of sleep (ESES).

**Method:** Twenty-six patients with ESES were preliminarily included in this retrospective chart review. Patient age, gender, EEG findings including interspike index and location of spikes, as well as MRI findings were noted.

**Results:** The interspike index on EEG/VEEG, which was sometimes over 2000 in these ESES patients, was significantly and often dramatically reduced by high dose diazepam administration. Clinical outcomes improved. MRI abnormalities detected in patients with ESES included cortical dysplasia, schizencephaly, septo-optic dysplasia, hypoxic ischemic injury, but not all patients had MRI abnormalities.

**Conclusion:** High-dose diazepam is effective in the treatment of ESES and leads to significant improvement in spike index, as well as improved preliminary clinical outcomes. Further review will identify any long-term improvements in motor and cognitive function as well as behavior.

## P1081

## INFLUENCE OF CYP1A1, CYP2C9, CYP2C19, CYP2D6, GSTM1, GSTT1, NAT2 GENOTYPES ON SIDE EFFECTS DEVELOPING IN CHILDREN WITH EPILEPSY RECEIVING VALPROIC ACID

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**Background and Objectives:** The inter-individual tolerability of the valproic acid has been observed in patients with epilepsy in different studies. The present study investigated the effect of cytochrome P450 CYP1A1, CYP2C9 (A1075C, C430T), CYP2D6 (G1934A, DelA2637) CYP2C19 (G681A) genetic polymorphisms and *GSTM1(Del)*, *GSTT19(Del)*, *NAT2 S1 (T 341 C)*, *S2 (G 598 A)*, *S3 (G 857 A)* genetic polymorphisms on the side effects in children with epilepsy received the valproic acid.

**Methods:** Fifty patients with different forms of epilepsy, aged from 6 months to 16 years with different illness duration have been studied. Thirty-three patients had side effects such as encephalopathy, epilepsy worsening, hepatotoxicity, muscle fatigue, thrombocytopenia, gastrointestinal problems. DNA samples analysis was performed with method of oligonucleotide biochips hybridization (BIOCHIP Ltd, Russia)

**Results:** In epileptic patients with side effects of valproic acid we obtained the results: heterozygous on CYP1A1 – 5 (15.1%), heterozygous CYP2C9 (C430T) – 9 (27.2%), heterozygous A1075C-3 (9%) - totally on CYP2C9 -12 (36.3%), CYP2C19 (G681A)- 9 hetero and 1 homozygous (30%), CYP2D6 (G1934A)-hetero 11, homo 2 (39.4%), CYP2D6 (DelA2637) -6 (18.2%) – totally on CYP2D6 -19 (57.6%). The second phase of biotransformation shows the homozygous deletion *GSTM1* in 21 patients (63.6%), *GSTT1* in four patients (12.12%), *NAT2* hetero/homo 27 patients (81.8%). Two and more polymorphisms on cytochrome P450 and *GSTM1*, *GSTT1*, *NAT2* had 93.9% of epileptic patients.

**Conclusions:** In our investigation the main role in side effects developing in epileptic patients receiving the valproic acid plays the genetic polymorphisms in CYP2C9, CYP2D6, in genes of the second phase of biotransformation (*GSTM1* and *NAT2*) and two and more of genetic polymorphism in one patient.

#### **P1082 THE CLINICAL COURSE OF SEIZURE CONTROL IN PCDH19 MUTATION RELATED EPILEPSY**

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**Purpose:** Mutations of the PCDH19 gene cause a female-related epilepsy with intractable seizures. Typical feature of this epilepsy is cluster of brief seizures, repeating during follow-up. We present clinical course of seizure-control in two patients with the epilepsy.

**Case 1:** A 6-year-old girl presented with status epilepticus triggered by fever and needed intubation at 7 months of age. Seizure types at onset were myoclonic, focal, tonic, and atonic seizures. Although clinical fea-

tures consistent with Dravet syndrome (DS) spectrum, SCN1A was normal while PCDH19 screening showed point mutations. As seizures were refractory to various anti epileptic drugs, clusters; mainly generalized-tonic-clonic (GTC) following complex partial seizures, occurred several times a year. During the recurrent clusters of brief seizures, the only effective treatment is intravenous or buccal midazolam up to 0.3 mg/kg/h sometimes combined with fos-phenytoine. Mild mental retardation with autistic features was becoming apparent. (IQ; 58 at 6 years and 6 months).

**Case 2:** A 4-year-old girl presented with clusters of GTC at 10 months. We treated her as epileptic encephalopathy at first then clusters of afebrile seizures occurred. She showed clinically DS spectrum, but no SCN1A abnormalities. Mutations in PCDH19 were detected. We dealt with subsequent recurrent clusters including several types of seizures in the same way as case1. Cognitive and behavioral disorder became obvious. (DQ; 56 at 3 years–6 months).

**Conclusion:** In both of our cases, clusters of brief seizures, regardless of phenotypes, recurred and thus weekly hospital treatment were required. We realized what is important is how to manage that clusters in PCDH19-related epilepsy.

#### **P1083 EFFECTIVENESS OF VALPROATE ON ALICE IN WONDERLAND SYNDROME ASSOCIATED WITH PANAYIOTOPOULOS SYNDROME**

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**Purpose:** Alice in wonderland syndrome (AIWS) is a rare condition involving visual perceptions and may associated with viral infections, migraine and epilepsy. Panayiotopoulos syndrome (PS) is an epilepsy with autonomic symptoms and multifocal spikes on EEG. We report a case of AIWS with PS.

**Case presentation:** A 7 years-old girl experienced suddenly and prolonged visual distortions after head banging. She fallen down and banged midline of forehead to the steel bumping post when she was walking to home. She complained visual abnormality everyday from the day of head trauma. Her mother's face were stretched widely, like a view on concave mirror or third mother's eye positioned between eyes or under the left eye. She experienced macropsia and micropsia when she was 6 years old. Her hand expanded threefold. Her mother, 160 cm tall, got smaller to 6 cm length. Her father suffered migraine and had same visual conditions until 12 years old. She vomited at night seven times from 4 years old. Clinical examination, Brain MRI were normal. EEG showed high amplitude spike and waves over bilateral occipital ~left posterior temporal areas. Medication of valproate improved both visual abnormality and vomiting seizures.

**Conclusion:** AIWS associated with epilepsy, especially PS, is a rare condition. Both conditions evolves usually self-limited. We treated as epilepsy because stereotyped vomiting during sleep continued. Valproate may be useful not only for epilepsy but also for migraine.